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CC: Tolbert, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ca0b4a5b9eb4ff5a967e541de9a134c-MTolbert]; Budashewitz, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f38f690da6364b3283d1940fb216e3ee-Philip.Buda]; Goldberg, Brittany [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=669c6aaf23b14e5fbc202960bb10734f-GOLDBERGB]; Roberts, Jeff [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f99ba866ca234f6d826007b9f1429e8e-RobertsJ]
Subject: FW: Mission China COVID-19 Update February 24

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SBU

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Info Office:	EXEC_INFO, IMO_INFO, RSO_INFO, DAO_INFO, CONS_INFO, MGT_INFO, SCIENCE_INFO, ECON_INFO, POL_INFO

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Date/DTG:	Feb 24, 2020 / 241024Z FEB 20
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Action:	WASHDC, SECSTATE *ROUTINE*
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TAGS:	SHLH, CDC, HHS, NIH, PGOV, CN, SENV, PREL, CASC, AMGT, AMED, KPAO, KMDR, ASEC, AID, KHIV, KFLU, KFLO, KFPC, KGHI, KHLS, KSCA, KTBT
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Subject:	Mission China COVID-19 Update February 24

1. (SBU) **Summary and Comment:** U.S. experts on the WHO-led mission reported that they felt the overall mission was a success and remarked that they were impressed by the level of access to information that the

WHO team enjoyed during their visits in China. The Standing Committee of the National People's Congress February 24 approved a draft decision postponing the upcoming session of the country's highest legislative body, one of the PRC's most important annual political and economic events. On February 24, Wuhan's COVID-19 command center announced and then quickly rescinded a notice that healthy non-residents and certain residents would be able to leave the city. Guangdong, Liaoning, Gansu, Guizhou, Shanxi, and Yunnan provinces lowered their public health emergency alert levels, as provinces across much of the country eased road restrictions. President Xi February 23 said the impact of COVID-19 was "temporary and generally manageable" in an address to 170,000 party officials. However, AmCham Suzhou members said manufacturing operations are still experiencing major disruptions due to labor and supply chain challenges, Chinese companies reported they are struggling to pay workers, and ports still face significant backlogs. The PRC denied Xinjiang "vocational education and training centers" were at risk for large-scale COVID-19 infections because "trainees have graduated." The International Air Transport Association (IATA) said the number of countries with China-related travel restrictions increased to 58 on February 23 as several countries upgraded restrictions. No U.S. citizens are reported to be in the prisons where health officials announced COVID-19 outbreaks last week. **End Summary and Comment.**

(U) LATEST UPDATES

2. (SBU) (b)(6) **Impressed by Level of Access to Information:** (b)(6) (b)(6) of the WHO-led expert mission told Embassy Beijing HHS February 23 that they felt the overall mission was a success and remarked that they were impressed by the level of access to information during their visits. The mission traveled to Beijing, Sichuan, Guangdong, and Wuhan [**Note:** the U.S. experts did not participate in the Wuhan visit. **End note.**]. The mission will conclude February 25. It is expected a report will be issued quickly after the experts return to their home countries, and that it will highlight PRC accomplishments in combatting the virus. WHO and the National Health Commission (NHC) will hold a joint press conference late February 24.

3. (U) **NPC Postponed:** Late the afternoon of February 24, the Standing Committee of the National People's Congress (NPC) announced that it had met and approved a draft decision to postpone the NPC's annual session (link). The new date will be announced later.

4. (U) **Wuhan Announces and Immediately Rescinds Easing of Lockdown:** Wuhan's COVID-19 command center issued and then quickly rescinded a notice on February 24 that would have loosened some of the restrictions on persons entering and leaving the city. According to the original notice, non-residents currently trapped in the city would have been permitted to leave in staggered waves. The notice would have also allowed other persons needing to leave Wuhan for epidemic prevention and control purposes, employment, or medical treatment to depart the city. Hours after the first announcement went public, a contact in China's Ministry of Foreign Affairs confirmed to Embassy Beijing's consular section it had been reversed. The recension stated the persons involved in the original notice relaxing the lockdown had acted without the authority of the command center and those responsible had been "severely criticized and dealt with."

5. (SBU) **No U.S. Citizens in Prisons with Reported Cases:** Beijing has been in regular contact with provincial level officials and prison officials in Hubei and Shandong provinces. According to Beijing ACS's contacts, there are no U.S. citizens at any of the prisons in Hubei or Shandong affected by the COVID-19 outbreak. To the knowledge of Shanghai ACS, there are also no U.S. citizens held in the Shilifeng Prison in Zhejiang where COVID-19 cases were reported last week. Furthermore, in Guangzhou's consular district, contacts at the Prison Administration Bureau, Public Security Bureau, and provincial Foreign Affairs Offices confirmed February 21 that there are no cases of coronavirus in any of the 19 prisons and detention centers where 42 AmCits are currently incarcerated.

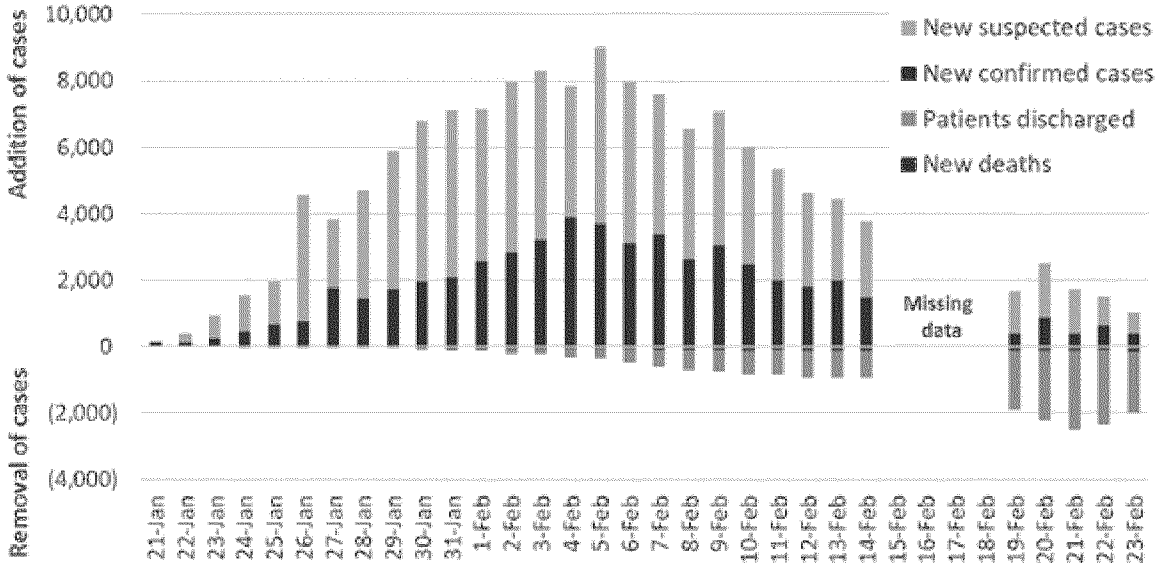
6. (SBU) **Numerous Provinces Downgrade Their Declared Public Emergencies:** Guangdong Health Authorities downgraded the province's public health emergency from Level I to Level II February 24, while emphasizing the outbreak is still at a "critical stage" and residents should maintain social-distancing precautions. The move came as municipal-level restrictions on inter-city transportation and business resumption largely dissipated throughout Guangdong since February 19, while provincial-level restrictions held. Over the weekend, Liaoning Province had lowered its public health emergency declaration from Level I to Level III on the four-level scale. Gansu, Guizhou, Shanxi, and Yunnan also lowered their alert levels. All other provinces have maintained a Level I response.

7. (SBU) **Guangdong Coronavirus Data Center:** Guangdong Province launched an "epidemic prevention core data center" on February 24 that will pull 124 categories of data from 53 separate government departments, including transportation, health, social security, and medical insurance. This data center ties into a parallel rollout of a new province wide "Yuekang Ma" (粤康码) app for biodata, travel history, and health record management. The unified app assigns high risk (red) and low risk/good health (green) for users, based on big data. Users of the app with "green" designation can bypass temperature checks at residential complexes and public places, according to the Health Commission of Guangdong Province. These announcements came amid a proliferation of COVID-19-focused apps that track travel and health history upon access to cities, workplaces, neighborhoods, grocery stories, public transportation, and other public places.

8. (U) **Xinjiang Government Denies Risk of Large-Scale COVID-19 Infection:** During a February 23 press conference in Urumqi, a Xinjiang government spokesperson said there was "no risk of large-scale infections in vocational education and training centers in the Xinjiang Uygur autonomous region," because "trainees have graduated." The spokesperson added any reports to the contrary were "baseless" (China Daily).

9. (U) **Nationwide Cases:** China's National Health Commission (NHC) reported 409 new lab-confirmed cases in Mainland China on February 23 as of 24:00, as the total number of confirmed cases to date rose to 77,150 (link). Another 150 deaths were reported on February 21, including 149 in Hubei, bringing total deaths to date in Mainland China to 2,592. Total COVID-19 patients treated and discharged from the hospital increased to 23,734, leaving 49,824 current lab-confirmed cases presently being treated. The number of current suspected cases dropped to 3,434, as the number of close contacts under medical observation fell to 97,481.

Figure 1: Daily Change in Number of Current Cases in Mainland China



Note: Due to the change in case definitions for "confirmed cases" and the lack of disaggregated data for clinically diagnosed and lab-confirmed cases from February 15 to 18 in Hubei, data are marked as missing for these dates. The NHC reverted the case definitions to remove the distinction between Hubei and the other provinces for data starting on February 19. Source: NHC and provincial health commissions.

Table: Total Officially Reported Cases in Mainland China as of End of February 23

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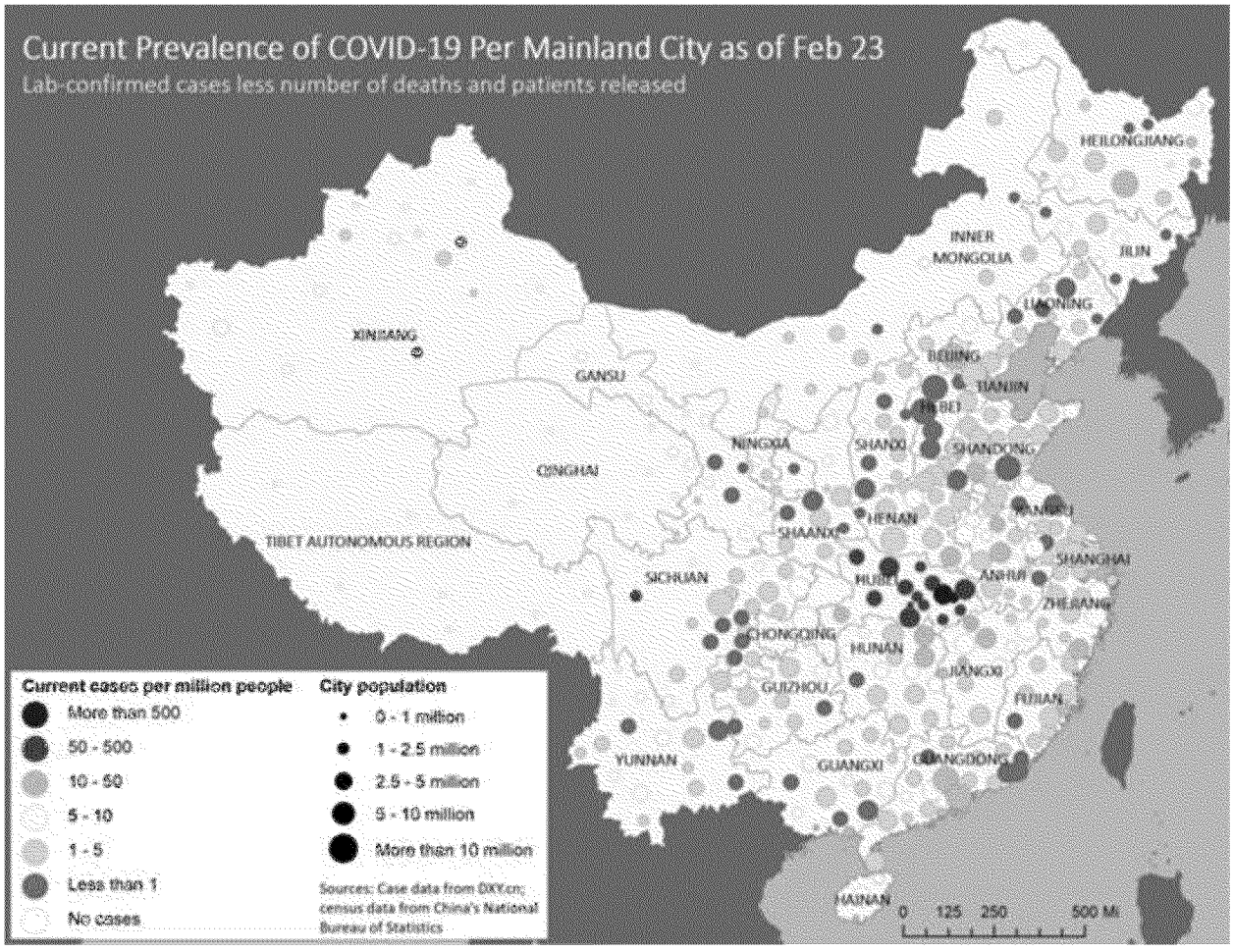
Province/City/Region	Active Cases	Total Cases	New Cases	Total Deaths	New Deaths	Total Discharged	Newly Discharged
Anhui	335	989	--	6	--	648	28
Beijing	197	399	--	4	--	198	9
Chongqing	234	575	2	6	--	335	7
Fujian	118	293	--	1	--	174	9
Gansu	11	91	--	2	--	78	2
Guangdong	567	1,345	3	6	--	772	32
Guangxi	142	251	2	2	--	107	3
Guizhou	42	146	--	2	--	102	11
Hainan	57	168	--	5	1	106	2
Hebei	84	311	--	6	--	221	17
Heilongjiang	244	480	--	12	--	224	9
Henan	322	1,271	--	19	--	930	69
Hubei	45,054	64,287	398	2,495	149	16,738	1,439
Hunan	308	1,016	**	4	--	704	**
Inner Mongolia	45	75	--	--	--	30	4
Jiangsu	204	631	--	--	--	427	16
Jiangxi	288	934	--	1	--	645	34
Jilin	38	93	2	1	--	54	2
Liaoning	47	121	--	1	--	73	5
Ningxia	14	71	--	--	--	57	9
Qinghai	0	18	--	--	--	18	--
Shaanxi	82	245	--	1	--	162	9
Shandong	432	754	2	4	--	318	7
Shanghai	83	335	--	3	--	249	22
Shanxi	44	132	--	--	--	88	7
Sichuan	261	527	1	3	--	263	7
Tianjin	51	135	--	3	--	81	16
Tibet	0	1	--	--	--	1	--
Xinjiang	46	76	--	2	--	28	3
Yunnan	57	174	--	2	--	115	8
Zhejiang	439	1,205	--	1	--	765	36
Total (Provincial Reports)	**49,846**	**77,149**	**410**	**2,592**	**150**	**24,711**	**1,822**
Total (NHC Reported)	**49,824**	**77,150**	**409**	**2,592**	**150**	**24,734**	**1,846**

*Notes: ** no report for February 23 published as of 17:30 on February 24; -- zero cases. Source: NHC and provincial health commissions.*

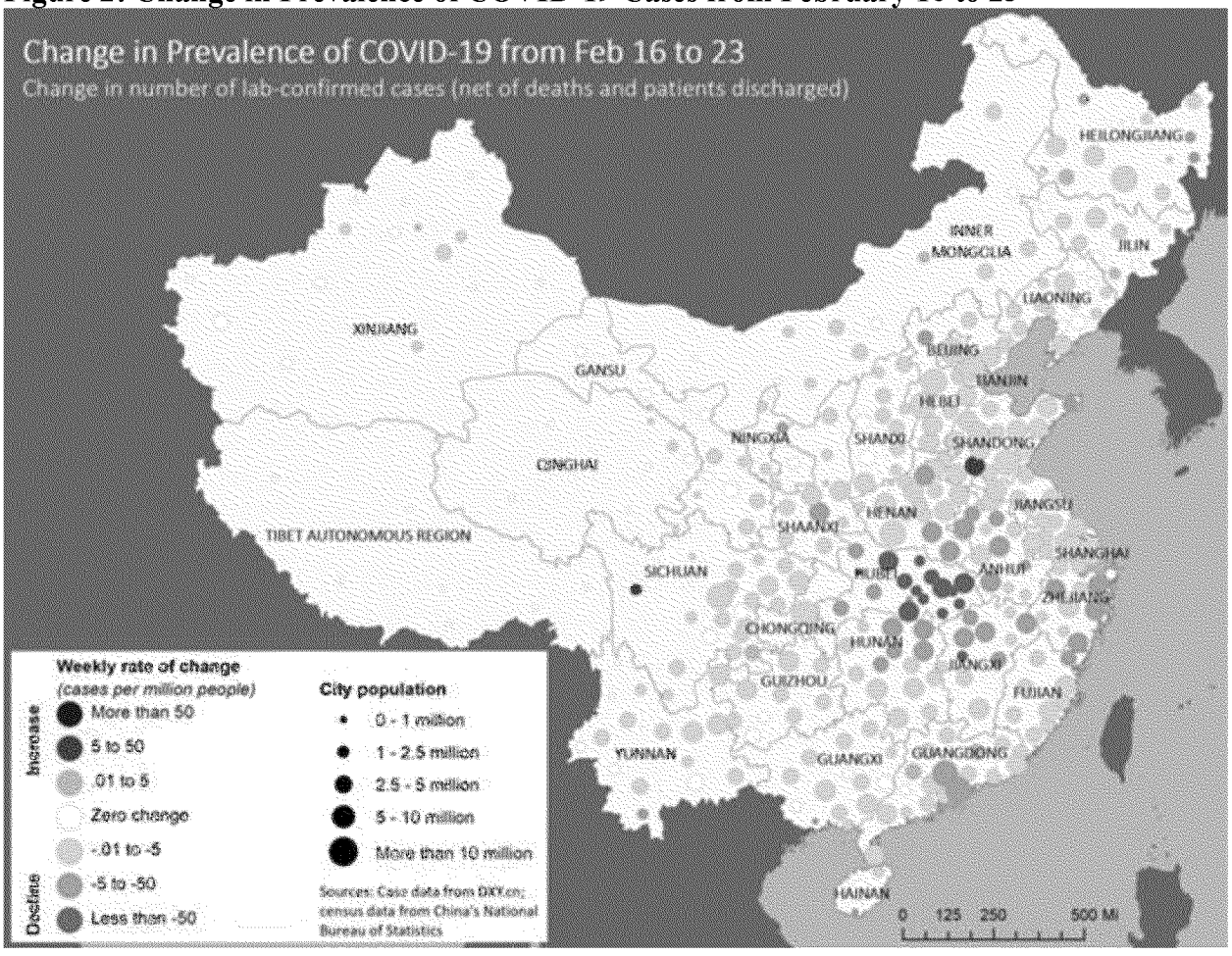
10. (U) **City-level Trends in Prevalence of COVID-19 Cases Show Overall Decline:** Analysis by ESTHOFF of trends over the previous week shows a nearly across-the-board decline in the prevalence of reported COVID-19 cases in China's cities and prefectures. From February 16 to 23, the number of current cases (total lab-confirmed cases net of deaths and the number of patients released) per million residents declined in 244 of the 275 prefectures and cities that had at least one case at the end of the week. Another 21 prefectures saw zero change in the number of current cases. In only 10 prefectures and cities did prevalence increase. [**Note**: China has 333 prefecture-level administrative divisions. The present analysis covered 330 prefecture-level administrative divisions, 4 provincial-level cities, and 10 county-level divisions directly administered by the provinces**. End note**.] All major cities in Hubei saw large decreases in current COVID-19 case prevalence for the first time, as the rate at which patients were discharged from the hospital outstripped the number of new reported infections. Outside Hubei, the only city for which case prevalence showed a sizeable increase over the past week was Jining City in Shandong Province, where the Rencheng Prison is located. [**Note:** The Shandong Health Commission reported confirmed cases among the province's prisoner population for the first time on February 20, with 200 cases in Rencheng Prison (20 BEIJING 360). **End note**.] Case prevalence as of February 23 continued to be the highest in Wuhan, with 3,697 current cases per million residents. By comparison, Wenzhou City in Zhejiang Province had 23 current cases per million residents on February 23. Current cases per million residents in cities with Mission China posts were even lower: 10 in Beijing, four in Chengdu, 12 in Guangzhou, four in Shanghai, and less than one in Shenyang. **[Note:** Prevalence is estimated based on 2010 census population. **End note**.]

Figure 2: Prevalence of Lab-Confirmed COVID-19 in Mainland Cities as of February 23



Source: Map by ESTHOFF using data from Ding Xing Yuan (DXY.cn) and 2010 census data.

Figure 2: Change in Prevalence of COVID-19 Cases from February 16 to 23



Source: Map by ESTHOFF using data from Ding Xing Yuan (DXY.cn) and 2010 census data.

11. (U) **PRC Approves Quick Detection Chip:** China's State Food and Drug Administration (SFDA) approved a quick detection nucleic acid testing chip jointly developed by West China Hospital (Sichuan University), CapitalBio Corporation, and Tsinghua University. The chip can reportedly detect six common respiratory viruses, including the new coronavirus, within 1.5 hours, and can process 16 specimens at a time. The chip will soon be used in China's COVID-19 response, according to a February 23 press announcement.

12. (SBU) **Doctor Believes Wuhan May Begin to Reopen in March**: An expatriate doctor currently working in a Chinese hospital in Wuhan told an evacuated CG Wuhan officer that the city may begin to slowly open as soon as March 10. The doctor emphasized that this news was not official yet, but "is logical." The doctor added that the end of the quarantine would not happen all at once. Wuhan's government would open small sectors of the city, perhaps as discrete as individual housing developments, one at a time, based on how long each housing development had been free of new COVID-19 cases.

13. (SBU) **Wuhan Making Detailed Reports of Disease**: A local contact in Wuhan provided a picture of a detailed analysis of COVID-19 cases for a housing development of Wuhan called Golden Harbor (attached). The document showed detailed record keeping of how many cases are in each part of the housing development as of February 19th. It tracks confirmed cases, cases under observation, and possible cases as well as the number of people who have recovered and died. Several Consulate Wuhan families lived in Golden Harbor before the ordered departure.

(U) THIRD COUNTRY RESPONSE EFFORTS AND INTERNATIONAL TRAVEL

14. (U) **Restrictions on Travelers from China Increase:** IATA announced the number of countries with China-related travel restrictions increased to 58 on February 23. Several countries also upgraded their restrictions (figure 3).

Figure 3: Countries with China-related Travel Restrictions

Source: EconOff with IATA Data.

15. (U) **Relief Supplies through Pudong Airport:** The cargo terminal of the Pudong airport has handled over 1,110 tons of relief materials since the beginning of the COVID-19 outbreak. Qatar Airways freighter delivered 91.9 tons of medical supplies donated by the airline to Shanghai on February 22. The shipment includes 435,000 medical masks and 162,996 bottles of hand sanitizer. This follows a February 2 delivery of 100,000 medical-grade N95 respiratory masks and 2,700 medical-grade disposable latex gloves to Shanghai by the airline.

(U) ECONOMIC AND SUPPLY CHAIN IMPACT

16. (SBU) **AmCham members in Suzhou report manufacturing operations are still experiencing major disruptions due to labor and supply chain challenges.** In a February 21 meeting with Consul General Stein, AmCham members in Suzhou reported their manufacturing operations continue to be severely impacted by COVID-19 prevention and control measures. March is typically the month with the highest volume of production, but company representatives did not anticipate being able to meet targets. Few had more than 40 percent of their workforce in place and said they had been driven to offer bonuses or other financial incentives to lure back workers. In addition, businesses faced three major challenges: the need to extend credit to customers who themselves had cashflow problems stemming from the epidemic; the difficulty in getting supplies from abroad due to the reduction in air transport to China; and in-country road restrictions making it difficult and slow to move goods via truck.

17. (SBU) **Xi Characterizes Economic Impact as "Temporary:"** The economic impact of COVID-19 was "temporary and generally manageable," President Xi reiterated during a February 23 CCP coordination meeting attended by 170,000 party officials, which some analysts characterized as "unusual." Xi vowed to

correct "formalism" and "bureaucratism," during the meeting, and called on "the whole of society" to work together to contain the crisis, according to media reports (*Global Times*, Xinhua, and People's Daily).

18. (U) **MOFCOM Calls on Trade Firms to Resume Business, Manufacturing Back Online**: In a February 24 circular, MOFCOM called upon local commerce departments to encourage trade firms to resume work and production. Efforts should be made to ensure the supply of daily necessities such as vegetables, meat, eggs, dairy products, rice, flour, edible oil, and instant food, the circular said (MOFCOM). Meanwhile, a China Enterprise Association online survey of the top 500 Chinese manufacturing firms found 97.8 percent of manufacturing firms had resumed production (Hexun).

19. (SBU) **Companies Struggle to Pay Workers:** Some Chinese companies were struggling to pay workers, which has resulted in un-/under-paid wages or delayed payments, according to recent *Bloomberg* reporting. The electric car marker Nio recently delayed paychecks a week; returning Foxconn workers in Shenzhen would receive only one-third of their normal salary during a mandatory two-week quarantine period; and "thousands of foreign workers" have had their salaries halted, reported *Bloomberg*. Meanwhile, (b)(6) (b)(6) told EconOff he assessed, based on the number of calls and WeChat messages the organization had received regarding wage arrears, many businesses were likely facing bankruptcy as a result of the COVID-19 outbreak. Additionally, as reported in a *Global Times* article, as of February 21, only 30 percent of China's migrant workers had returned to work and less than 50 percent of companies had resumed operation, according to analysis from CITIC Securities, which based their findings on transportation data and energy consumption.

20. (U) **More Highways Reopened:** Numerous provinces reopened additional stretches of major interprovincial highways over the weekend and reduced checkpoints. Highway closures and vehicle checkpoints have been removed on all roads in Anhui, Jiangsu, and Zhejiang, except for some checkpoints still in place around Wenzhou. In Southwest China, authorities had removed nearly all temporary check points regulating traffic into Chengdu as of February 22, while other areas of Sichuan were in the process of removing highway checkpoints and resuming service at rest areas. In Northeast China, Heilongjiang and Liaoning lifted many of the remaining checkpoints and closures on their highway systems.

21. (U) Easing restrictions on road travel has been spottier in other areas. Local traffic reports from over the weekend showed that authorities in Shaanxi Province, which borders Hubei to the northwest, continued to enforce widespread restrictions on vehicles and passengers traveling from other cities and regions. Transport authorities in many parts of Shaanxi have barred entry by vehicles and persons from Hubei and Henan Provinces, as well as Wenzhou, Guangzhou, Shenzhen, and Hangzhou Cities and the three prefectures in Shaanxi bordering Hubei. [**Comment:** The restrictions in Shaanxi revealed a high level of localized discretion, varying from road to road and city to city, further highlighting the present challenges to the movement of freight and people who must travel long distances across multiple jurisdictions. **End comment**.]

22. (U) **Guangdong Manufacturing Ramps Up Operations**: 42,000 large industrial companies (82 percent of the total) resumed operations in Guangdong by February 21, up from 12,700 (25 percent) on February 10. By February 24 all of the 102 "key" manufacturing companies in Guangdong had resumed operations, including Global Fortune 500 companies Huawei (90 percent normal output), Gree (80 percent normal output), and Midea (70 percent normal output). In Zhuhai, U.S. contract manufacturer Flex re-opened February 11 and now was operating at 50 percent normal output. In Shenzhen, Foxconn was offering RMB 7120 hiring bonuses at its 180,000-person Longhua plant, according to reports. Guangdong would arrange more than 1000 trains and charter buses to return migrant workers to the province, officials said February 22. Guangzhou, Shenzhen, and Dongguan saw the most returned people of all Chinese cities between February 12 and 19, accounting for 10 percent of the country's total, according to reports.

23. (U) **Enterprises Launching New Personal Protective Equipment (PPE) Companies:** Appliance manufacturer Gree opened a new company February 21, Zhuhai Gaoge Medical Technology, to manufacture facemasks, according to press. Eight production lines are expected to reach a daily production capacity of 400,000 at the beginning of March and 800,000 by the end of March. In addition to masks, the company plans to produce multi-purpose goggles, antibacterial gels, and other epidemic prevention products. This is one of six new facemask producers in Zhuhai, where there had previously been zero. Guangzhou Xingshi Equipment Co., Ltd announced it had transitioned production from diapers and sanitary napkins to facemasks and can produce 1.2 million a day. As of February 19, Guangdong has registered 85 mask manufacturers with a combined daily capacity of 7.77 million. Provincial authorities said February 22 they expect shortages "to be greatly reduced" by late February.

24. (U) **Ningbo-Zhoushan Port, the world's fourth largest by container volume, struggles to reduce its backlog of shipments and return to normal operating levels.** The major East China port remained operational during the Lunar New Year, unloading between 30,000 to 60,000 containers each day via automation and remote-control operations, but the outbreak of the coronavirus and a shortage of drivers created a backlog of shipments at the port's storage facility. About 95 percent of the 25,000 truck drivers servicing the port are migrant workers and only now returning to work, according to a February 23 report by the Shanghai International Shipping Research Center Port Development Institute. As of February 22, the inventory of loaded containers for export was only 46 percent of normal levels; however, truck activity at the port's gate reached 75 percent of normal levels and the pick-up rate of empty containers increased rapidly, signaling that manufacturers and logistics companies are preparing goods to export, according to the report.

25. (U) **Costco was ordered to prevent large crowds forming at its Shanghai warehouse.** While Costco took measures including checking customers' temperatures and requiring masks in the store, the Minhang District market regulatory body and public health department found the retailer failed to take all required public health measures, including action to prevent large crowds from forming. Minhang authorities have set a limit of 1,000 shoppers in the store at any time, with designated queuing areas outside. [**Note:** Costco received approval on February 18 to purchase a piece of land in Pudong District, near Shanghai Disney, for a second store. **End note**.]

26. (U) A freight train carrying walnuts for export recently departed Urumqi for the Turkish port of Mersin, the *China Daily* reported in an article about the China-Europe rail trade "getting back on track" (China Daily).

27. (U) **Yunnan Launches Economic Stimulus**: Yunnan Reform and Development Commission February 23 announced two sets of ten infrastructure projects as part of a large economic stimulus package. Provincial authorities said 61 percent of medium to large-scale industrial firms had resumed operations in Yunnan as of February 21.

28. (U) **Chongqing Announces New Cloud Projects, Rolls Out Subsidies to Key Sectors**: Chongqing's Liangjiang New Area announced the signing of nine cloud-related tech projects February 22. Local media depicted the signings as proof of the government's ability to accelerate investment despite the adverse impacts of the coronavirus. Chongqing also announced a series of new policies to assist enterprises, including:

- Technology companies conducting R&D and creating products or technologies related to epidemic control will be eligible to receive a subsidy of up to five million RMB ($710,850).
- SMEs will be eligible for up to three million RMB ($426,000) in interest discounts.
- Farmers and agricultural companies will be eligible for lower interest rates.

29. (U) **Heilongjiang Issues Guidance to Businesses Resuming Operations:** Heilongjiang on February 22 provided detailed guidance to businesses on resuming operations as soon as possible, based on risk level. Businesses in low risk areas must register with local officials, who will periodically inspect their safety

protocols. In medium risk areas, officials will "actively" enforce safety measures such as temperature checks and disinfection. In high risk areas, businesses must obtain government approval and must limit employee work hours.

30. (U) **Heilongjiang Banks Continue to Provide Loans for Key Enterprises:** Harbin Central Branch of People's Bank of China said that as of February 20, 8.65 billion RMB worth of loans were issued to 146 key outbreak prevention enterprises. The loan's average interest rate was 4.5%, the bank noted. Banks throughout the province have also accelerated loan approval process: Provincial China Development Bank completed the approval and issuance of 300 million RMB for emergency procurement loans within 24 hours; Longjiang Bank approved and issued 20 million RMB loans to enterprises in one day; and provincial authorities issued 40 million RMB loans to two companies in less than four hours.

31. (U) **Shenyang Provides Financial Assistance to SMEs:** It was reported that since the outbreak, 137 Shenyang-based enterprises applied for loans worth 2.965 billion RMB, of which 1.822 billion RMB were approved. Since some migrant workers from elsewhere have not yet returned, Shenyang set up online tools to matchmake businesses with workers in the city. Additionally, city officials reduced a total of 73.3 million RMB in rental fees for 5,613 SMEs renting state-owned properties.

32. (SBU) **Shenyang-based SMEs Uncertain of Government Assistance:** Despite government's efforts to provide SMEs with financial assistance, contacts at multiple Shenyang-based SMEs expressed concern that Liaoning may not provide financial aid to all SMEs. A contact at the Huachu Logistics, a logistics company that transports chemical products, told ConGenOff that currently the company is losing approximately $80,000 RMB per day since many chemical companies have not yet resumed operations. Without financial support from the government, the contact was uncertain how much longer SMEs like Huachu can stay afloat.

(SBU) SUPPORT FOR U.S. CITIZENS

Shanghai

33. (SBU) ACS appointments are still just 50 percent of normal volume. ACS resumed routine notary services on February 24.

Shenyang

34. (SBU) U.S. citizens in Northeast China continue to inquire about travel restrictions, flight status and other routine ACS questions. One Citizen Liaison Volunteer in Daqing, Heilongjiang, reported that the city continues to implement strict closed management measures, allowing only one person per household to leave their home once every two days. In one particularly strict district, only those with valid work passes are allowed to leave, and groceries can only be purchased online. As of February 24, Daqing reported 26 confirmed cases and 1 death. Elsewhere in the region, CLVs reported shops and restaurants are gradually reopening.

(SBU) POST OPERATIONS

Beijing

35. (SBU) **Ambassador Town Halls**: Ambassador Branstad held town halls for the Embassy Beijing community on February 24. (b)(6) Chief of Infectious Disease and Tropical Medicine at the Department of State's Bureau of Medical Services, provided an update on Mission China's response to the coronavirus and how it impacts the community.

Shenyang

36. (SBU) Despite ROK raising its emergency alert to the highest level, contacts at China Southern told ConGenOff the airline has no plans to reduce flights from Shenyang to Seoul. Currently, China Southern operates seven flights to Seoul each week. In Yanji, Jilin, where South Korean businesses people and tourists frequently travel, officials announced the airport will set up special corridors to process and check temperatures for passengers arriving from ROK.

X. (U) OTHER COVID-19 DEVELOPMENTS AND GOVERNMENT RESPONSES

Beijing

37. (U) **Quarantine Requirements for Foreign Travelers:** Beijing municipal government announced on February 21 that it would exempt the following categories of incoming travelers from its 14-day quarantine rule:

1. Travelers from overseas who have not been in China for the past 14 days and who enter the country at one of Beijing's two main airports (Beijing Capital Airport and Daxing Airport);
2. Short-term tourists and business travelers coming from parts of China other than Hubei, provided they comply with the health measures put in place by their hotels or employers;
3. Persons returning to jobs in Beijing, provided that their employers have implemented safe "closed-management" systems and the employees conduct regular health checks;
4. Residents from the surrounding cities of Langfang, Sanhe, Xianghe, and Daguang who commute to Beijing for work, provided they only come and go directly from work and submit to temperature and health checks at checkpoints entering Beijing;
5. Flight and train crews, as long as they stay as a group upon arriving Beijing and do not reside with other people in the city;
6. Central government officials returning from major outbreak areas, provided they stay as a group upon arriving in Beijing and do not return to their offices or homes; and
7. People who require medical attention (e.g., pregnant women and sufferers of other illnesses).

Chengdu

38. (U) **Chongqing Government Highlights Low Case Numbers, Sends Cruise Ships to Wuhan**: During a February 23 press conference on the status of Chongqing's COVID-19 response, Health Commission officials stressed the confirmed number of new COVID-19 cases in Chongqing has been in the single digits for nine consecutive days, suggesting the epidemic was being brought under control. However, officials stressed the importance of maintaining area-specific controls in the municipality. Chongqing also announced it has sent its 15th team of medical personnel to Hubei and dispatched four cruise ships along the Yangtze river to Wuhan to provide accommodation (840 beds) for health workers.

39. (U) **Chongqing Priorities Following Xi Speech**: On February 23, Chongqing Party Secretary Chen Min'er chaired a meeting to study Xi Jinping's latest speech on COVID-19 prevention and social-economic development. During the meeting, Chen said that President Xi has guided the nation effectively since the outbreak of COVID-19 and there is "nothing that China can't overcome, so long as everyone follows Xi's instructions and keeps faith in the Party's leadership." Regarding the epidemic itself, Chen said the situation remains serious, and warned officials not to relax their efforts to control the virus and "never declare victory without complete victory." Chen also said Chongqing must support epidemic prevention work in Wuhan and Beijing.

In terms of specific municipal government priorities, Chen underlined the following key issues:

- Providing full support to doctors and their family members.
- Increasing stocks of medical supplies and research.
- Protecting social stability and preventing secondary accidents and extremist incidents.
- Furthering propaganda work and spreading positive news.
- Listening to and responding to the needs of the people.

On social-economic development, Chen said that "pressure must be converted into strength" and "risk into opportunity," outlining the following priorities:

- Helping key enterprises and projects lead the economy.
- Maintaining the industrial and capital supply chains.
- Providing more support to famers and focusing on people's livelihood.
- Promoting high-performing cadres and holding to account those who neglect their duty.

40. (U) **Yunnan Joins "Health Traffic Light" Trend**: Yunnan launched a new health code system on February 22 mandating that every person entering the province declare their personal health status. The system produces a traffic light style red, yellow, and green health status to be used by civil aviation, railway, road transport, and port administrators to ascertain passenger risk.

41. (U) **Guizhou Extends Economic Relief Measures**: Eleven government departments in Guizhou, including the provincial transport department and the reform and development commission, have jointly issued an initiative entitled "Opinion on Promoting Stable and Healthy Development of Road Transport Enterprises amid the COVID-19 Epidemic." The program offers tax relief, fee reductions, financial support, and employment support.

Guangzhou

42. (U) **COVID-19 Isolated From Patient's Urine:** Researchers in Guangzhou successfully isolated the COVID-19 virus from a patient's urine, according to an announcement by the State Key Laboratory of Respiratory Diseases. The Laboratory's Director, Ran Pixin, said the research was reported to the Ministry of Science and Technology of China for further examination.

Shanghai

43. (U) **Grocery stores, businesses, and public spaces continue to re-open in downtown Shanghai.** Nearly all supermarkets in Shanghai are operating, the Shanghai government reported on February 22. Nearly 90 percent of convenience stores and over 95 percent of shopping malls are open. Nearly 70 percent of 51,000 foreign-funded enterprises in Shanghai have resumed operation.

(U) **Zhejiang downgraded Yueqing and four other areas from "higher-risk" (orange) to "medium-risk" (yellow) on their Five-color Risk Map.** Only two areas remained listed as higher-risk as of February 21: Haishu District in Ningbo and Tonglu County in Hangzhou. There are no areas designated as "high-risk" (red). On February 9, when the color-coded map was introduced, there were 13 areas listed as either high- or higher-risk. The number of areas listed as "low-risk" (green) increased from 12 on February 9 to 75 on February 21.

44. (U) **Teams from two Shanghai universities have developed quick, easy-to-use COVID-19 detection kits.** A team from Renji Hospital and Hunan University announced that they have developed a COVID-19 detection product that they claim is so easy to use people can use it at home, providing rapid diagnoses of suspected patients. The team has tested more than 100 samples, with a detection rate of around 90

percent. Another team from East China Normal University developed a kit which they claim can detect the virus in just 10 minutes from a single drop of blood from a patient. The First Hospital of Zhejiang Province is currently doing clinical verification on the kit.

45. (U) **Online medical services in Shanghai to be covered by the public health care insurance system on a trial basis.** Shanghai's Healthcare Security Administration announced on February 23 that medical services provided via internet by designated hospitals to patients with common illnesses and chronic diseases will be partly paid for by medical insurance. The prices and rates of payments will be the same as those provided offline. Other new measures announced on Sunday include one to increase insurance budgets for hospitals to speed up treatment for patients, as well as renewed encouragement for institutions to use new technologies in the service and treatment of patients.

46. (U) **Shanghai needs more blood donations**, according to the Shanghai Health Commission. Officials said there have been fewer blood donations than usual, due to both Spring Festival travel and the current COVID-19 epidemic. The Health Commission recently launched a reservation scheme for blood donation, which will allow donors to come, while avoiding crowds.

47. (U) **Shanghai encouraging science and tech innovation on COVID-19.** The Shanghai Science and Technology Commission is offering financial support for scientists and research projects exploring therapies, new vaccines, and clinical diagnosis for COVID-19. They will also give preference to frontline workers for the 2020 Shanghai Science and Technology Awards. High-tech companies who make "outstanding contributions" will receive the help from the Commission to list on the science and technology innovation board (STIB).

48. (U) **Starting February 21, passengers in Shanghai taxis can scan a QR code in WeChat or Alipay to register their information.** This is a voluntary measure that the city says will only be used for coronavirus prevention and control purposes. Shanghai transportation officials say the registration information can be used to quickly locate travelers in the event of possible coronavirus exposure.

Shenyang

Consul General's Calls with Northeast China FAOs

49. (SBU) **Liaoning:** The Liaoning Foreign Affairs Office Director credited his province's early implementation of broad and strict measures for the low number of cases province-wide. As of February 21, the Dalian FAO reported that while over 70 percent of the city's manufacturing capacity was back on line, city government offices continued to direct only office directors to come to work and all other staff to stay home. The Shenyang FAO noted that the crisis is not over despite looser restrictions, and requested consulates continue providing daily reports of diplomats' fever status. [**Note:** CG Shenyang has not been complying with this request, but all other consulates in Shenyang have reported daily on a WeChat group. **End note**.]

50. (SBU) **Jilin:** While Jilin has yet to downgrade the province-wide response level or remove restrictions on traffic and economic activity, the Jilin FAO Director expressed confidence the outbreak was contained there and Jilin would begin returning to normal soon. He did not express concern about the economic impact of the virus, but asked CG Shenyang to encourage U.S. companies to return to or invest for the first time in Jilin at an appropriate time in the near future. The FAO Director for Changchun, the provincial capital, said throughout the response his office ensured foreign visitors, companies, and schools, including the Changchun American School, had access to food and adequate PPE. The FAO continues working with minimal staff and remains focused on virus-related work, including accepting donations, response to foreigners' health concerns, and resolving passport and visa issues for individuals who need to travel despite restrictions.

51. (SBU) **Heilongjiang:** In the provincial capital Harbin, home to 197 out of Heilongjiang's 479 cases, the FAO described being called upon to perform an unprecedented level of non-foreign affairs work. FAO staff accompanied security officials and Communist Party officials to all districts of the city to help promote and enforce virus-prevention policies and provide propaganda to citizens in closed communities.

52. (U) **Songyuan Relaxes Closed Management:** Songyuan, Jilin, which previously limited each household to one daily grocery trip, significantly relaxed movement restrictions and permitted shopping malls to open, with the exception of restaurants and movie theaters. Officials reopened a fitness center for public while still prohibiting group activities and requiring members to keep at least three-meters distance from each other. As of February 24, Songyuan reported 2 confirmed cases and 0 deaths.

53. (SBU) **Shenyang Businesses and Hospitals Resume Normal Operations:** After Liaoning lowered its emergency alert level from one to three February 22, many Shenyang stores in shopping malls reopened. Some restaurants and ice cream shops now accept sit-in customers. The number of customers at shopping centers, as well as road traffic, also increased significantly in the last two days. Contacts at the Shengjing and Liaoning Provincial People's Hospital, two of four designated hospitals for Consulate staff, said outpatient services fully resumed; the No.6 Hospital—the central facility for COVID-19 treatment in Shenyang— has not resumed outpatient services. Shenyang has reported zero new confirmed cases since February 11.

54. (U) **Over 80 Percent of Cured COVID-19 Patients at Shenyang No. Six Hospital Used TCM:** As of February 20, out of 22 patients cured at the Shenyang No. Six Hospital, more than 80 percent received traditional Chinese medicine. According to statistics, early intervention of traditional Chinese medicine can shorten patients' treatment and hospitalization time, said the hospital's Chinese medicine expert group. At present, more than 90 percent of the patients in the hospital are using Chinese medicine.

(U) SOCIAL MEDIA AND MEDIA ROUNDUP

55. (SBU) South China PAS media contacts discussed an array of topics related to the COVID-19 response including: 1) A Guangzhou-based journalist with a Beijing private media outlet dismissed a rumor reported by Japan's TV-Asahi that that some of the approximately 16,000 flu deaths recently in the U.S. might be the result of COVID-19, which the U.S. CDC suspects is the case. (The TV-Asahi report appears to have relied on allegations by a U.S.-based conspiracy theorist, who claims that CDC employees have been "leaking" information to him about a massive coverup of COVID-19 cases in the U.S.) The contact uses a clarifying article on Toutiao stating, that actually, the CDC only announced that it was unclear what virus resulted in a minority of the deaths 2) A key opinion leader in Guangdong wrote about the respected Wuhan-based writer Fang Fang. Writer Fang noted that the epidemic has not been fully controlled yet, and mentioned that she had enjoyed freedom of expression on Sina Weibo earlier. However, now her Weibo handle has been blocked.

56. (U) Social media users generally reacted positively to the Chengdu government's announcement of a new "QR health code" that individuals can use to gain access to residential compounds, workplaces, shopping malls, and public transportation. The new system is expected to replace the patchwork of ad hoc measures residential areas and enterprises have put in place to comply with municipal "closed management" requirements. Some netizens observed their residential compounds had not yet implemented the new system and instead were requiring health certificates issued by the local health department.

57. (U) On February 22, Liaoning government announced no new cases reported in the province for five consecutive days and downgraded its four-tiered public health emergency response system from its highest level one to level three. The news quickly went viral on social media platforms in Northeast China under the hashtag #Liaoning Downgrades Health Emergency Response to Level Three# and had over 21 million views and 600 comments by February 24. Northeast China netizen had mixed opinions. Many praised the provincial

government for its effective epidemic prevention and control measures while expressing hope that life would return to normal or that students would return to schools soon. Others were skeptical about employees returning to work and raised doubts about the decision to downgrade the response while the epidemic was far from over. Some called for the central government to draft national laws banning bushmeat consumption while others lamented about mask and medical supply shortages. The following additional topics were also trending on social media sites in Northeast China: 1) Dr. Zhong Nanshan's comments on COVID-19 in Heilongjiang, 2) No visitors on Changbai Mountain's on its first day open since the epidemic began 3) Barbeque shops in Northeast China selling out of products after reopening. Local media in northeastern China featured headlines that focused on instructions and guidelines for businesses resuming operations and schools reopening. PAS media contacts discussed guidance from Shenyang government on resuming normal business operations and returning to work.

Signature: Branstad

Action Post: NONE

Dissemination Rule: RSO, CONS_ACTION, POL, ECON, PAS, MGT_ACTION, IMO, POL_INFO, SCIENCE, IMO_INFO, RSO_INFO, DAO_INFO, TSA, MED, CONS_INFO, CLO, CDC, SCIENCE_INFO

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Subject: WHO Nagoya Survey USG Response

Attachments: Nagoya Survey Questions_country_with response boxes.docx

Dear USG sample sharing community,

The WHO recently released the survey on pathogen sharing and access and benefit sharing arrangements, as part of the implementation of decision WHA72(13). Specifically, the purpose of the survey is: “to provide information on current pathogen-sharing practices and arrangements, the implementation of access and benefit-sharing measures, as well as

the potential public health outcomes and other implications." Several contacts receiving this email have probably already received the link for the survey from WHO.

OGA is working to provide a consolidated USG response in collaboration with the interagency by **January 31st.** The survey is extremely broad and touches many different equities across USG. Over the next couple weeks, we will be reaching out to specific sample sharing POCs across HHS Op/Staff Divs and Interagency partners for input to specific questions, and will circulate for feedback draft responses for consolidated USG position.

Please find attached the country specific survey questions and response options in Word format.

Nagoya Survey Questions_count...

Thank you for your help and happy holidays! Feel free to reach out with any questions/comments.

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Nagoya Survey Questions:

AS A COUNTRY

In this section of the questionnaire, you will be asked to provide information on current pathogen sharing practices and/or arrangements that are implemented by your country, in your facility or by your colleagues, based on your experience. This includes practices for all pathogens, including seasonal and pandemic influenza viruses, unless otherwise noted.

1. In your experience, how are pathogens routinely shared (focus is on human pathogens/ pathogens with potential to cause disease in humans):

- Bilaterally (ie country-to-country)
- [HTMLCONTROL Forms.HTML:Checkbox.1]Formal professional network(s)
- [HTMLCONTROL Forms.HTML:Checkbox.1]Formal academic network(s)
- [HTMLCONTROL Forms.HTML:Checkbox.1]Informal network(s)
- [HTMLCONTROL Forms.HTML:Checkbox.1]Lab to lab (academic or industrial)
- [HTMLCONTROL Forms.HTML:Checkbox.1]Other

2. To the best of your knowledge, has your country enacted legislation and/or regulatory measures relevant to pathogen sharing, such as (but not limited to) those pertaining to biosafety, general tracking of genetic resources, or biosecurity?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]I don't know

3. To the best of your knowledge, do your country's existing pathogen-sharing practices or arrangements (including legislation or regulations, if relevant) apply to physical samples of pathogens only, or do they extend to digital sequence information (eg genetic sequence data)?

- Yes, existing pathogen-sharing practices in my country include both physical samples and digital sequence information (e.g. genetic sequence data)
- [HTMLCONTROL Forms.HTML:Option.1]Sometimes (i.e. only physical samples for some pathogens but both physical samples and digital sequence information (e.g. genetic sequence data) for other pathogens)
- [HTMLCONTROL Forms.HTML:Option.1]No, existing pathogen-sharing practices in my country apply only to physical samples
- [HTMLCONTROL Forms.HTML:Option.1]Don't know /it is unclear

4. To the best of your knowledge, do your country's pathogen-sharing practices or arrangements (including legislation or regulations, if relevant) specifically address public health (including the need for rapid sharing of pathogens during public health emergencies)?

- Yes, public health is specifically addressed
- [HTMLCONTROL Forms.HTML:Option.1]No, public health is not specifically addressed
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

5. To the best of your knowledge, do your country's pathogen-sharing practices or arrangements (including legislation or regulations, if relevant) differentiate between pathogens or are all pathogens treated the same – that is, are there special provisions for sharing specific pathogens, such as influenza virus or high threat pathogens such as Ebola virus or the pathogens associated with foodborne illness, or are all pathogens treated the same?

- Different pathogens have different requirements
- [HTMLCONTROL Forms.HTML:Option.1]All pathogens are treated the same
- [HTMLCONTROL Forms.HTML:Option.1]Don't know /it is unclear

6. To the best of your knowledge, do your pathogen-sharing practices or arrangements differentiate between pathogens or are all pathogens treated the same – that is, are there special provisions for sharing specific pathogens, such as influenza virus or high threat pathogens such as Ebola virus or the pathogens associated with foodborne illness, or are all pathogens treated the same?

- Different pathogens have different requirements
- [HTMLCONTROL Forms.HTML:Option.1]All pathogens are treated the same
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

7. In this section of the questionnaire, you will be asked, based on your experience, to provide information on the access and benefit-sharing measures for sharing pathogens that are currently implemented by your country, in your facility or by your colleagues. This includes practices for all pathogens, including seasonal and pandemic influenza viruses, unless otherwise noted.

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

8. Does your country have legislation and/or regulations that address access and benefit sharing (for example, implementing the Nagoya Protocol or Convention on Biological Diversity if your country is a Nagoya Protocol party or other access and benefit sharing measures)?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

9. Do your country's access and benefit-sharing legislation and/or regulations, specifically address public health (including public health emergencies; for example, do pathogens related to public health/public health emergencies receive special consideration given the need for rapid sharing)

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

10. Do your country's access and benefit-sharing legislation and/or regulations apply to pathogens (whether or not they are specifically mentioned in the measures)?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

11. To the best of your knowledge, do your legislation and/or regulations differentiate between pathogens or are all pathogens treated the same (that is, are there distinct/separate provisions for sharing specific pathogens such as influenza virus, high threat pathogens such as Ebola virus or the pathogens associated with foodborne illness)?

- Human pathogens have different requirements from animal pathogens
- [HTMLCONTROL Forms.HTML:Option.1]Different human pathogens have different requirements
- [HTMLCONTROL Forms.HTML:Option.1]All human pathogens are treated the same
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

12. To the best of your knowledge, do your country's access and benefit-sharing legislation or regulatory measures apply to physical samples of pathogens only, or do they extend to digital sequence information (eg. genetic sequence data)?

- Yes, they include both physical samples and digital sequence information (e.g. genetic sequence data)
- [HTMLCONTROL Forms.HTML:Option.1]Sometimes (ie only physical samples for some pathogens but both physical samples and digital sequence information (e.g. genetic sequence data) for other pathogens)
- [HTMLCONTROL Forms.HTML:Option.1]No, they apply only to physical samples
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

13. To the best of your knowledge, has your country ever received benefits resulting from the sharing of pathogens?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]I don't know

14. In you experience, where is the process of negotiating access and benefit sharing arrangements/agreements is conducted?

- Health sector
- [HTMLCONTROL Forms.HTML:Checkbox.1]Environment sector
- [HTMLCONTROL Forms.HTML:Checkbox.1]Agriculture sector
- [HTMLCONTROL Forms.HTML:Checkbox.1]Commerce/trade sector
- [HTMLCONTROL Forms.HTML:Checkbox.1]Other sector
- [HTMLCONTROL Forms.HTML:Checkbox.1]Cross sectoral
- [HTMLCONTROL Forms.HTML:Checkbox.1]Don't know

15. In your experience, does finalization of an access and benefit sharing arrangements for sharing pathogens require approval of a government ministry?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]I don't know

In this section of the questionnaire, you will be asked to provide general information on international and cross-sectoral pathogen sharing. This includes practices for all pathogens, including seasonal and pandemic influenza viruses, unless otherwise noted.

1. On a scale of 1-5, with 1 being "strongly disagree" and 5 being "strongly agree", entities (governments or non-governmental actors) wishing to transfer/share pathogens internationally generally find domestic requirements relating to such transfers easy to understand and to comply with.

2. If you have any, please provide examples of easy transfer/sharing.

3. If you have any, please provide examples of challenging transfer/sharing.

4. Based on your experiences with sharing pathogens internationally and the implementation of related domestic legal/regulatory procedures, what range of challenges have you encountered:

- [HTMLCONTROL Forms.HTML:Checkbox.1]Lack of clarity around requirements
- [HTMLCONTROL Forms.HTML:Checkbox.1]Delays in processing
- [HTMLCONTROL Forms.HTML:Checkbox.1]Different pathogens requiring different procedures /approaches / sharing arrangements
- [HTMLCONTROL Forms.HTML:Checkbox.1]Other: please provide additional information/detail [HTMLCONTROL Forms.HTML:Text.1]

5. Based on your experience with sharing pathogens internationally and the implementation of domestic procedures what improvement have you seen:

- Improved processes
- [HTMLCONTROL Forms.HTML:Checkbox.1]Clarification of responsibilities
- [HTMLCONTROL Forms.HTML:Checkbox.1]Improved benefit sharing
- [HTMLCONTROL Forms.HTML:Checkbox.1]Other: please provide additional information/detail [HTMLCONTROL Forms.HTML:Text.1]

6. On a scale of 1-5, with1 being "strongly disagree" and 5 being "strongly agree", entities (governments or non-governmental actors) wishing to transfer/share pathogens internationally generally find domestic requirements relating to general tracking of genetic resources easy to understand and to comply with.

7. If you have any, please provide examples of easy tracking of genetic resources.

8. If you have any, please provide examples of challenging tracking of genetic resources.

9. On a scale of 1-5, with1 being "strongly disagree" and 5 being "strongly agree", entities (governments or non-governmental actors) wishing to transfer/share pathogens internationally generally find domestic requirements relating to biosafety procedures easy to understand and to comply with.

10. If you have any, please provide examples of easy biosafety procedures.

11. If you have any, please provide examples of challenging biosafety procedures.

12. On a scale of 1-5, with1 being "strongly disagree" and 5 being "strongly agree", entities (governments or non-governmental actors) wishing to transfer/share pathogens internationally generally find domestic requirements relating to procedures related to access and benefit sharing arrangements easy to understand and to comply with.

13. If you have any, please provide examples of easy access and benefit sharing arrangements.

14. If you have any, please provide examples of challenging access and benefit sharing arrangements.

15. Are you aware of any mechanisms that enable or promote collaboration between the human health sector and the agriculture sector regarding access and benefit-sharing measures for pathogens?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

16. Are you aware of any mechanisms that enable or promote collaboration between the human health sector and the **environmental sector** regarding access and benefit-sharing measures for pathogens?

- [HTMLCONTROL Forms.HTML:Option.1]Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

17. Are there any mechanisms that enable or promote collaboration between the human health sector and the **animal health** sector regarding the development and implementation of access and benefit-sharing measures for pathogens?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

18. Are there any mechanisms that enable or promote collaboration between the human health sector and the **commerce/trade** sector regarding the development and implementation of access and benefit-sharing measures for pathogens?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

In this section of the questionnaire, you will be asked to provide your views on the potential public health outcomes and other possible implications of pathogen sharing practices. This includes practices for all pathogens, including seasonal and pandemic influenza viruses, unless otherwise noted.

1. In your view, are there potential public health outcomes and/or implications related to how pathogens are shared (positive, negative or mixed for public health)?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

2. Are the potential public health implications regarding how pathogens are shared different for different pathogens?

- Yes, the implications are different depending on which pathogen is being shared
- [HTMLCONTROL Forms.HTML:Option.1]No, the implications are the same for all pathogens
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

3. In your opinion, are the potential public health outcomes or implications regarding how pathogens are currently shared positive, negative or mixed for public health?

- Positive
- [HTMLCONTROL Forms.HTML:Option.1]Mixed
- [HTMLCONTROL Forms.HTML:Option.1]Negative

4. Please explain your answer. If there are benefits from the current sharing practices/arrangements please give details. If there are challenges for public health please give details. You may give details on both benefits and challenges. Please provide specific details of benefits or challenges for which you have evidence.

5. In your opinion, are the implications different for sharing physical samples than for sharing digital sequence information (e.g. genetic sequence data)?

- Yes
- [HTMLCONTROL Forms.HTML:Option.1]No
- [HTMLCONTROL Forms.HTML:Option.1]Don't know

6. Please explain your answer.

7. In your opinion, how should pathogen sharing be managed in the future to allow scientific and public health applications to proceed in a timely manner while addressing the perspectives of both originator and receiver? Please include any thoughts on what should stay the same and what should, if anything, be changed.

8. Should high priority pathogens (ie those with significant epidemic or pandemic potential where timeliness is particularly critical) be viewed differently than any other pathogens? For example, should some pathogens be considered part of national and global health and economic security and others not?

9. In your opinion, are there public health outcomes or other implications if different pathogens (high threat, others, etc.) are treated differently?

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 1/21/2020 11:08:13 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]; Seedorff, Jennifer E [SeedorffJE@state.gov]; Tobert, Gwen (STATE.GOV) [tobertgm@state.gov]; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) [kayvon.modjarrad.civ@mail.mil]; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) [carmen.t.maher.civ@mail.mil]; Walker, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4d03cc33ba5c4f15bd581b757dc9daa4-HHS-Robert.]; Donis, Ruben (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dea126c25cab404db922973cd7ccb459-HHS-Ruben.D]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Nichol, Stuart T (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b9c163136088456ab15b5378d90948b0-HHS-stn1-cd]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; safarnsworth@usaid.gov; Patel, Anita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8c06ec0295ce4ea4985d72c66e086749-HHS-bop1-cd]; Greene, Carolyn M (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5593b7cf42a472096db48fb69f81c85-HHS-cqg4-cd]; Biggins, Julia E CTR (USA) [julia.e.biggins.ctr@mail.mil]
CC: Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Elvander, Erika (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e95f3e9a68a641e7bfd7ba7dae325e8f-HHS-Erika.E]; Koo, Han J (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=83c125b5f96c4464972f0ff2b60190c3-HHS-Han.Koo]; Kopolow, Aimee (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=568e0645cb7a457a901ba09a7e1c2c4d-HHS-Aimee.K]; Tracy Carson [CarsonTL@state.gov]; Burr, Mara (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e1f90440cd05403a8abf399c1c0f76a6-HHS-Mara.Bu]; Wood, Rachel (OS)

[/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c0dfa4961f1e4c838ea3e23daf00e7a3-HHS-Rachel.]; Kibunja, Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45afa7abc9804a0fae3498d8909905c4-HHS-Julia.K]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]
Subject: RE: Notes from 1/10/2020 WHO R&D Blueprint GCM Call on Wuhan, China Pneumonia Cluster
Attachments: 2019 nCoV GCM call NFR 10_01_2020.docx

Dear Colleagues,

To follow up on my previous email, please find attached WHO's official notes for the record from the January 10, 2020 R&D Blueprint Global Coordination Mechanism call. WHO has not yet announced a second GCM call, but we will circulate the details if/when the next call is scheduled.

Best,
Collin

2019 nCoV GCM call NFR 10_01_...

From: Weinberger, Collin (OS/OGA) (CTR) <Collin.Weinberger@hhs.gov>
Sent: Friday, January 10, 2020 9:39 AM
To: Handley, Gray (NIH/NIAID) [E] <handleygr@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Lane, Cliff (NIH/NIAID) [E] <clane@niaid.nih.gov>; Higgs, Elizabeth (NIH/NIAID) [E] <ehiggs@niaid.nih.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Lane, Cliff (NIH/NIAID) [E] <clane@niaid.nih.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Helfand, Rita (CDC/DDID/NCEZID/OD) <rzh7@cdc.gov>; Vinter, Serena (CDC/DDPHSIS/CGH/OD) <uvv3@cdc.gov>; Kapil, Vikas (CDC/DDPHSIS/CGH/OD) <vck3@cdc.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Krause, Philip (FDA/CBER) <Philip.Krause@fda.hhs.gov>; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) <carl.c.holloway.civ@mail.mil>; Gruber, Marion (FDA/CBER) <Marion.Gruber@fda.hhs.gov>; Kishimori, Jennifer M COL USARMY OSD HA (US) <jennifer.m.kishimori.mil@mail.mil>; LeButt, Kimberly A CIV OSD OUSD ATL (US) <kimberly.a.lebutt.civ@mail.mil>; Seedorff, Jennifer E <SeedorffJE@state.gov>; Tobert, Gwen (STATE.GOV) <tobertgm@state.gov>; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) <kayvon.modjarrad.civ@mail.mil>; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) <carmen.t.maher.civ@mail.mil>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Krause, Philip (FDA/CBER) <Philip.Krause@fda.hhs.gov>; Nichol, Stuart T. (CDC/DDID/NCEZID/DHCPP) <stn1@cdc.gov>; Damon, Inger K. (CDC/DDID/NCEZID/DHCPP) <iad7@cdc.gov>; safarnsworth@usaid.gov; Patel, Anita (CDC/DDID/NCIRD/OD) <bop1@cdc.gov>; Greene, Carolyn M. (CDC/DDID/NCIRD/ID) <cqg4@cdc.gov>
Cc: Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; OGA PET-GHSA Team <OGAPET-GHSATeam@hhs.gov>; Elvander, Erika (OS/OGA) <Erika.Elvander@hhs.gov>; Koo, Han (OS/OGA) (CTR) <Han.Koo@hhs.gov>; Kopolow, Aimee (OS/OGA) <Aimee.Kopolow@hhs.gov>; Tracy Carson <CarsonTL@state.gov>; Burr, Mara (HHS/OS/OGA) <Mara.Burr@hhs.gov>; Wood, Rachel (HHS/OS/OGA) <Rachel.Wood@hhs.gov>
Subject: Notes from 1/10/2020 WHO R&D Blueprint GCM Call on Wuhan, China Pneumonia Cluster

Dear Colleagues,

The WHO R&D Blueprint team held a teleconference this morning to update members of the Global Coordination Mechanism on the cluster of pneumonia cases in Wuhan China. Please find attached my (rough) notes from the call.

WHO also plans to release official notes for the record from both this call, as well as a separate call of the R&D Blueprint Scientific Advisory Group, which I will circulate once they are available.

The R&D Blueprint team said that they plan to hold additional regular update calls for the GCM members and colleagues at a cadence TBD. Once we hear of these, I will circulate that information.

Best Regards,
Collin

Collin Weinberger, MPH
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<< File: WHO R&D Blueprint GCM Wuhan Pneumonia Call Notes 1_10_2020.docx >>

GCM teleconference – Note for the Records

Date : Friday 10 January at 2pm GVA time.

Subject: Pneumonia in Wuhan, China.

Agenda:

1. Overview of emerging data on disease epidemiology
2. Overview of research priorities and a collaborative process to offer support -if requested- to the national authorities in China and elsewhere.
3. Mechanisms for coordination/collaboration in terms of international research
4. Next steps including considerations of potential spread scenarios vis a vis research priorities

1. Overview of emerging data on disease epidemiology

WHO China Country Office was informed of cases of pneumonia of unknown etiology (unknown cause) detected in Wuhan City, Hubei Province of China. As of 5 January 2020, a total of 59 patients with pneumonia of unknown etiology have been reported to WHO by the national authorities in China from 12 to 29 December 2019. Of the 59 cases, 7 are severely ill, no deaths reported.

The causal agent has not yet been identified or confirmed. The genetic sequence is not yet available. WHO DG is discussing with the Chinese Health Authorities to share the genetic sequence of the virus.

National authorities report that all patients are isolated and receiving treatment in Wuhan medical institutions. The clinical signs and symptoms are mainly fever, with a few patients having difficulty in breathing, and chest radiographs showing invasive lesions of both lungs.

Preliminary information from the Chinese investigation team, no evidence of significant human-to-human transmission and no health care worker infections have been reported.

2. Overview of the research priorities.

WHO shared with the GCM members the outcomes of the discussion with the SAG.

Diagnostics

- Diagnostic tools and standardized methodology for data collection are critical to understand the epidemiology of the pneumonia outbreak and the risks
- In the absence of known sequence, pan-coronavirus assays could be developed and used, as a health intervention or under a research protocol, for travel entry screening in neighboring countries and/or at entry point with people likely to have history of travel from the Wuhan province, especially in the context of the upcoming Chinese new year's eve.
- A surveillance strategy should include animal testing component when relevant.

Therapeutic and Vaccine candidates

- 2 clinical characterization protocols exist: SPRINT SARI and ISARIC protocols have been shared with Chinese collaborators for standardized collection of SARI.

- WHO will develop a pipeline of investigational therapeutics and vaccines against the novel coronavirus that could be granted access to under research protocol and will make it available to the scientific community.
- WHO developed guidance on how to reliably evaluate MERS-CoV therapeutics and vaccines that will be adapted to this novel coronavirus.
- WHO will work on a evidence-based framework to transparently select most promising/advanced therapeutics and vaccines candidates to move forward for clinical evaluation.

3. Mechanisms for coordination/collaboration in terms of international research

SAG memebers were invited to suggest research priorities and submit proposal for collaboration.

4. Next Steps

1. WHO R&D Blueprint will set up regulars (weekly) calls to inform GCM partners on the evolution of the outbreak and the research activities
2. WHO R&D Blueprint will produce comprehensive mapping of all therapeutics and vaccine candidates and develop generic protocols for clinical evaluation to be available on WHO website
3. GCM members will provide updated on their R&D activities and proposals to WHO on future collaboration

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 1/10/2020 9:39:08 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]; Seedorff, Jennifer E [SeedorffJE@state.gov]; Tobert, Gwen (STATE.GOV) [tobertgm@state.gov]; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) [kayvon.modjarrad.civ@mail.mil]; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) [carmen.t.maher.civ@mail.mil]; Walker, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4d03cc33ba5c4f15bd581b757dc9daa4-HHS-Robert.]; Donis, Ruben (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dea126c25cab404db922973cd7ccb459-HHS-Ruben.D]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Nichol, Stuart T (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b9c163136088456ab15b5378d90948b0-HHS-stn1-cd]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; safarnsworth@usaid.gov; Patel, Anita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8c06ec0295ce4ea4985d72c66e086749-HHS-bop1-cd]; Greene, Carolyn M (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5593b7cf42a472096db48fb69f81c85-HHS-cqg4-cd]
CC: Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; OGA PET-GHSA Team [OGAPET-GHSATeam@hhs.gov]; Elvander, Erika (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e95f3e9a68a641e7bfd7ba7dae325e8f-HHS-Erika.E]; Koo, Han J (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=83c125b5f96c4464972f0ff2b60190c3-HHS-Han.Koo]; Kopolow, Aimee (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=568e0645cb7a457a901ba09a7e1c2c4d-HHS-Aimee.K]; Tracy Carson [CarsonTL@state.gov]; Burr, Mara (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e1f90440cd05403a8abf399c1c0f76a6-HHS-Mara.Bu]; Wood, Rachel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group

(FYDIBOHF23SPDLT)/cn=Recipients/cn=c0dfa4961f1e4c838ea3e23daf00e7a3-HHS-Rachel.]
Subject: Notes from 1/10/2020 WHO R&D Blueprint GCM Call on Wuhan, China Pneumonia Cluster
Attachments: WHO R&D Blueprint GCM Wuhan Pneumonia Call Notes 1_10_2020.docx

Dear Colleagues,

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Best Regards,
Collin

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WHO R&D
Blueprint GCM ...

(b)(5)

(b)(5)

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From: Locus, Tiffany (OS/OGA) [Tiffany.Locus@hhs.gov]
Sent: 1/23/2020 2:40:23 PM
To: Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Abram, Anna [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fb77660891384232a7cd9086fcbb1a3b-Anna.Abram]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]
CC: Kibunja, Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45afa7abc9804a0fae3498d8909905c4-HHS-Julia.K]; LaHood, Natalie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ef807c1a1b9a4b739bc63954bfb71386-HHS-Natalie]
Subject: [UPDATE] Our US China Vaccine Diplomacy

Good Afternoon:

For your awareness, former Science Envoy Dr. Peter Hotez and team are working with the Chinese to jointly develop a vaccine for the new coronavirus. See email chain below for more details.

Very Respectfully,
Tiffany Locus, MPH

Global Health Officer
U.S. Department of Health and Human Services (HHS)
Office of the Secretary (OS) / Office of Global Affairs (OGA)
Office of Pandemics and Emerging Threats (PET)
Desk Phone: 202-**(b)(6)** ; Mobile Phone: **(b)(6)**
Email: tiffany.locus@hhs.gov

From: Stewart, Jessica L. (HHS/OS/OGA) <Jessica.Stewart@hhs.gov>
Sent: Thursday, January 23, 2020 12:01 PM
To: Kopolow, Aimee (OS/OGA) <Aimee.Kopolow@hhs.gov>; OGA PET-GHSA Team <OGAPET-GHSATeam@hhs.gov>; Koo, Han (OS/OGA) (CTR) <Han.Koo@hhs.gov>
Cc: Elvander, Erika (OS/OGA) <Erika.Elvander@hhs.gov>
Subject: FW: Our US China Vaccine Diplomacy

See below.

Jessica Stewart
Office of Global Affairs
U.S. Dept of Health and Human Services

From: **(b)(6)** @state.gov>
Sent: Thursday, January 23, 2020 11:58 AM
To: Elvander, Erika (OS/OGA) <Erika.Elvander@hhs.gov>; Stewart, Jessica L. (HHS/OS/OGA) <Jessica.Stewart@hhs.gov>; Pandemic-Response-OES <Pandemic-Response-OES@state.gov>; EAP-CM-ECON-DL <EAP-CM-ECON-DL@state.gov>
Cc: **(b)(6)** @state.gov>
Subject: FW: Our US China Vaccine Diplomacy

All,

Flagging in case you didn't see that former Science Envoy Dr. Peter Hotez and team are working with the Chinese to jointly develop a vaccine for the new coronavirus.

OGA: can you please pass on to the appropriate people in NIH?

Thanks,

(b)(6)

From: Hotez, Peter Jay
Sent: Wednesday, January 22, 2020 8:15 PM
To: (b)(6)
Cc: (b)(6) Envoy-Program; H (b)(6)
(b)(6)
Subject: Re: Our US China Vaccine Diplomacy

Thank you (b)(6) me too! Thought this might be something for you to send to China desk at State or embassy, I think it might lead to a vaccine, best Peter

Peter Hotez, MD, PhD, FASTMH, FAAP
Dean, National School of Tropical Medicine
Professor, Departments of Pediatrics, Molecular Virology & Microbiology
Co-Head, Section of Pediatric Tropical Medicine
Health Policy Scholar
Baylor College of Medicine

Texas Children's Hospital Endowed Chair of Tropical Pediatrics
Co-Director, Texas Children's Hospital Center for Vaccine Development

University Professor
Department of Biology, Baylor University

Faculty Fellow, Hagler Institute for Advanced Study
Senior Fellow, Scowcroft Institute of International Affairs
Texas A&M University

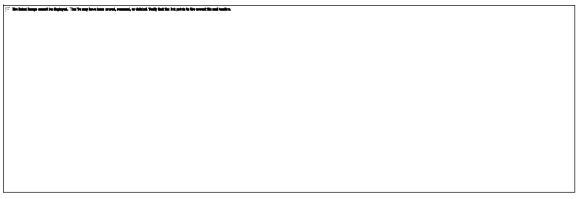
Baker Institute Fellow in Disease & Poverty and Adjunct Professor of Bioengineering, Rice University
Adjunct Professor, University of Texas, School of Public Health

Founding Editor-in-Chief, PLoS Neglected Tropical Diseases

E-mail: hotez@bcm.edu
Twitter: @peterhotez
Skype: (b)(6)
Website: https://protect2.fireeye.com/url?k=b6c66130-ea92481b-b6c6500f-0cc47a6d17cc-60ee497466883536&u=https://peterhotez.org/
Amazon Author Center: https://www.amazon.com/Peter-J.-Hotez/e/B001HPIC48
Like us on Facebook https://protect2.fireeye.com/url?k=50f7acc1-0ca385ea-50f79dfe-0cc47a6d17cc-6249bceae01fae70&u=https://www.facebook.com/BCMNationalSchoolOfTropicalMedicine/

Executive Assistant: Douglas Soriano
(b)(6)

Phone: (b)(6)



Sent from my iPhone

On Jan 22, 2020, at 7:09 PM (b)(6) @state.gov> wrote:

*****CAUTION:*** This email is not from a BCM Source. Only click links or open attachments you know are safe.**

Thanks for flagging Peter! Looking forward to hearing more about this when we're in Israel in a couple weeks.

Talk soon!
(b)(6)

--
(b)(6) Ph.D.
Office of Science and Technology Cooperation (OES/STC)
U.S. Department of State
Email: (b)(6) @state.gov

From: Hotez, Peter Jay
Sent: Wednesday, January 22, 2020 7:28 PM
To: (b)(6) Envoy-Program; (b)(6)
Subject: Our US China Vaccine Diplomacy

Dear all, we're now working with the Chinese jointly to develop the vaccine for this new coronavirus, missing everyone!
Peter

This from XinHua News Agency

http://www.xinhuanet.com/english/2020-01/23/c_138727502.htm

Peter Hotez, MD, PhD, FASTMH, FAAP
Dean, National School of Tropical Medicine
Professor, Departments of Pediatrics, Molecular Virology & Microbiology
Co-Head, Section of Pediatric Tropical Medicine
Health Policy Scholar
Baylor College of Medicine

Texas Children's Hospital Endowed Chair of Tropical Pediatrics
Co-Director, Texas Children's Hospital Center for Vaccine Development

University Professor
Department of Biology, Baylor University

Faculty Fellow, Hagler Institute for Advanced Study
Senior Fellow, Scowcroft Institute of International Affairs
Texas A&M University

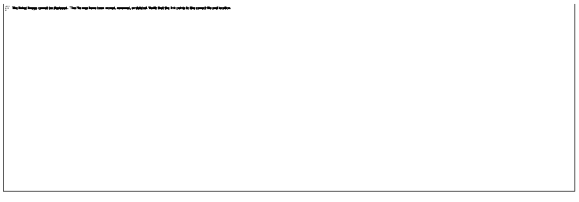
Baker Institute Fellow in Disease & Poverty and Adjunct Professor of Bioengineering, Rice University
Adjunct Professor, University of Texas, School of Public Health

Founding Editor-in-Chief, PLoS Neglected Tropical Diseases

E-mail: hotez@bcm.edu
Twitter: @peterhotez
Skype: (b)(6)
Website: https://protect2.fireeye.com/url?k=1ceda84e-40b98165-1ced9971-0cc47a6d17cc-322b3ef3ca9c5848&u=https://peterhotez.org/
Amazon Author Center: https://www.amazon.com/Peter-J.-Hotez/e/B001HPIC48
Like us on Facebook https://protect2.fireeye.com/url?k=f1b97d54-aded547f-f1b94c6b-0cc47a6d17cc-3ac2f443817b9cb6&u=https://www.facebook.com/BCMNationalSchoolOfTropicalMedicine/

Executive Assistant: Douglas Soriano
(b)(6)

Phone: (b)(6)



Sent from my iPhone

Sent: 6/3/2020 8:25:40 AM
To: McNeill, Lorrie [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=77b0b352c9c24851bf0c7330f53e00d9-McNeill]
Subject: RE: See this instead

SwE

From: McNeill, Lorrie <Lorrie.McNeill@fda.hhs.gov>
Sent: Tuesday, June 2, 2020 12:33 PM
To: Marks, Peter <Peter.Marks@fda.hhs.gov>
Cc: Tierney, Julia <Julia.Tierney@fda.hhs.gov>
Subject: FW: See this instead

Hi Peter –

Karen Riley in OGDP shared the email string below and attachments regarding a letter to the Department of State declining to co-sign a letter to the PRC. The attached draft response notes that HHS has already sent a letter to the Secretary's counterpart and therefore do not want to "confuse issues" by joining this letter.

After Karen sent, she sent a separate note that Mark Abdoo has cleared the draft and at this point it's an FYI only for us (despite the note below that you should review).

Lorrie

From: Riley, Karen <Karen.Riley@fda.hhs.gov>
Sent: Tuesday, June 2, 2020 11:07 AM
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Subject: See this instead

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From: Riley, Karen
Sent: Tuesday, June 2, 2020 10:37 AM
To: Hashemi, Sema <Sema.Hashemi@fda.hhs.gov>; Ross, Bruce <Bruce.Ross@fda.hhs.gov>; Anderson, Erika <Erika.Anderson@fda.hhs.gov>
Subject: Please see

I believe I forwarded this to some of you on Friday. My apologies, I misinterpreted this. I thought it was an FYI, but apparently we are being asked to clear the Agnew letter back to State. Should Janet Woodcock also read and clear?

From: Duarte, Christina <Christina.Duarte@fda.hhs.gov>
Sent: Friday, May 29, 2020 12:49 PM

To: Riley, Karen <Karen.Riley@fda.hhs.gov>
Subject: FW: Referral from FDA/OC/OES/ on Correspondence Control # 2020-2504

Here you go…

From: Duarte, Christina
Sent: Friday, May 29, 2020 12:00 PM
To: Riley, Karen <Karen.Riley@fda.hhs.gov>
Subject: FW: Referral from FDA/OC/OES/ on Correspondence Control # 2020-2504

Hi Karen,

When time permits, can you please review the attached correspondences and information contained in the AIMS email below? Please let me know the POC to send this to.

Thank you,

Christina Duarte
Management and Program Analyst
Communications Team
Office of Global Diplomacy and Partnerships (OGDP)
Office of Global Policy and Strategy
U.S. Food and Drug Administration
(240) 402-5338 (phone)
Christina.Duarte@fda.hhs.gov

From: aimssystem@fda.hhs.gov <aimssystem@fda.hhs.gov>
Sent: Friday, May 29, 2020 11:24 AM
To: Duarte, Christina <Christina.Duarte@fda.hhs.gov>
Subject: Referral from FDA/OC/OES/ on Correspondence Control # 2020-2504

Note: Do NOT reply directly to this E-mail

A referral has been sent to your office by FDA/OC/OES/ on Correspondence Control # 2020-2504 requesting your assistance. A summary of the referral appears below. If you have any questions, please contact VALERIE A. JACKSON WATSON of FDA/OC/OES/.

Action:	**Review and Clear**
Due Date:	**Tuesday, June 2, 2020**
Synopsis:	**Department R/C - Request for Access to Wuhan for International Scientists and Public Health Experts**

Please click the URL below to access the referral:

http://aims.fda.gov/cktoken/ct_token.mainPage?p_token=nrtd6ce3w03d68g9s1z00000vem3vx00001mbksjacetw8324196doqt1z0fnsxs

You can view the original correspondence by clicking the button 'View Orig Corr' (if available). After reviewing all the information provided, please acknowledge receipt of the referral by clicking either the ACCEPT button or the DECLINE button.

If you ACCEPT the referral, a new COMPLETE button is immediately displayed. You can either:

Click the COMPLETE button to complete the referral now
OR
You MUST retain this e-mail with the above URL until you have completed the referral request. Click the above URL again and click the COMPLETE button.

From: McNeill, Lorrie [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=77B0B352C9C24851BF0C7330F53E00D9-MCNEILL]
Sent: 6/2/2020 12:32:36 PM
To: Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]
CC: Tierney, Julia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1160d300bc4248b790ded292a082e9a8-Julia.Tiern]
Subject: FW: See this instead
Attachments: Control Sheet - 00437348-AS-857907.docx; Agnew WIV letter - clean -OGA.docx; Kenna-Agnew memo 202005717.pdf

Hi Peter –

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Thank you,

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U.S. Food and Drug Administration
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Christina.Duarte@fda.hhs.gov

From: aimssystem@fda.hhs.gov <aimssystem@fda.hhs.gov>
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CONTROL SHEET
CORRESPONDENCE

DATE:	05/28/2020

OVERVIEW

SPS#:	00437348
TYPE:	Other Government
SUBJECT:	(SBU) Request for Access to Wuhan for International Scientists and Public Health Experts
AUTHORING AGENCY:	Office of Global Affairs (OGA)
POLICY COORDINATOR:	Ekaterini (Kat) Malliou, (202) (b)(6)
ODRM ANALYST:	Elaine Gross, (202) (b)(6)

ASSIGNMENT

TASK TYPE:	Clearance Request
ACTION REQUIRED:	Clearance
ROUND #:	1
DUE DATE:	06/02/2020 6:00 PM
RECIPIENTS:	ASFR, ASL, ASPA, ASPR, CDC, Danielle Steele, FDA, NIH, OASH, OGC, Paula Stannard
INFO COPY:	

INSTRUCTIONS:

Lisa D. Kenna
Executive Secretary
Department of State

Dear Ms. Kenna:

Thank you for the invitation to U.S. Department of Health and Human Services (HHS) Secretary Alex Azar to co-sign a letter to the People's Republic of China (PRC) Vice Premier Han Zheng and Yang Jiechi, Director of the Office of Foreign Affairs of the Communist Party of China regarding the Wuhan Institute of Virology. After careful consideration, HHS respectfully declines to join the letter. As you may know, we have sent our own letter to Mr. Azar's counterpart at the National Health Commission, Minister Ma Xiaowei, regarding sample sharing. We would like to ensure that line of inquiry remains open, and as such do not wish to confuse issues by joining this letter. Further, we recently ended funding to the institute that this letter is requesting access to. A request for a visit could be construed as opening the possibility for that funding to again be available, something we do not wish to be suggested.

HHS recommends that the State Department reconsider sending the letter as it could be used to curtail access to Chinese vaccine and therapeutic development – something that we also do not wish to do as it could impede other Presidential health initiatives, such as Operation Warp Speed. Finally, the letter is now overtaken by the resolution agreed to at the 73rd World Health Assembly sponsored by more than 130 countries, including the United States, mandating WHO, working with the Food and Agricultural Organization and the World Organization for Animal Health to undertake an investigation into the origins of COVID-19.

Thank you again for the opportunity to join this letter. We wish you the very best.

Sincerely,

Ann C. Agnew
Executive Secretary

United States Department of State

Washington, D.C. 20520

www.state.gov

May 15, 2020

SENSITIVE BUT UNCLASSIFIED

MEMORANDUM FOR MS. ANNE C. AGNEW
EXECUTIVE SECRETARY
DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBJECT: (SBU) Request for Access to Wuhan for International Scientists and Public Health Experts

(SBU) The Secretary of State intends to send a letter to officials of the People's Republic of China (PRC) requesting that the PRC authorize and facilitate a visit of international scientists and public health experts to Wuhan to exchange information with counterparts who have conducted research on coronaviruses (including the origin and characteristics of SARS-CoV-2), examine all relevant data, and visit laboratory facilities where such work has been conducted, including the Wuhan Institute of Virology and the Wuhan Center for Disease Control and Prevention laboratories. The purpose of the visit would be to access critical information needed to fight the COVID-19 pandemic and to prevent future outbreaks.

(SBU) The Department of State hereby respectfully invites the Secretary of Health and Human Services to co-sign a letter to PRC Executive Vice Premier Han Zheng and Yang Jiechi, Director of the Office of Foreign Affairs of the Communist Party of China. A draft of the letter is enclosed with this memorandum. The Department of State is separately requesting OSTP Director Droegemeier co-sign the letter as well.

(b)(6)

Lisa D. Kenna
Executive Secretary

Attachment:
Letter to Executive Vice Premier Han and Director Yang

SENSITIVE BUT UNCLASSIFIED

His Excellency Han Zheng
Vice Premier
of the People's Republic of China
Beijing

His Excellency Yang Jiechi
Director of the Office of Foreign Affairs
of the Communist Party of China
Beijing

Dear Vice Premier Han and Director Yang:

(b)(5)

Sincerely,

Michael R. Pompeo

From: Marks, Peter [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DFBB2B5BD38445CB9C9ADCA3F72DF53A-MARKSP]
Sent: 6/3/2020 8:26:51 AM
To: McNeill, Lorrie [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=77b0b352c9c24851bf0c7330f53e00d9-McNeill]
CC: Tierney, Julia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1160d300bc4248b790ded292a082e9a8-Julia.Tiern]
Subject: RE: See this instead

Dear Lorrie,

Thanks!

Best Regards,
Peter

From: McNeill, Lorrie <Lorrie.McNeill@fda.hhs.gov>
Sent: Tuesday, June 2, 2020 12:33 PM
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<Erika.Anderson@fda.hhs.gov>
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Management and Program Analyst
Communications Team
Office of Global Diplomacy and Partnerships (OGDP)
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Due Date:	**Tuesday, June 2, 2020**
Synopsis:	**Department R/C - Request for Access to Wuhan for International**

Scientists and Public Health Experts

Please click the URL below to access the referral:

http://aims.fda.gov/cktoken/ct_token.mainPage?p_token=nrtd6ce3w03d68g9s1z00000vem3vx00001mbksjacetw8324196doqt1z0fnsxs

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OR
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From: Marks, Peter [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DFBB2B5BD38445CB9C9ADCA3F72DF53A-MARKSP]
Sent: 2/12/2021 1:02:05 PM
To: Blair, Joan W. (CBER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8cc3d088be164491a76b9ce048d71a02-BLAIR]
Subject: RE: additional reporting cable from WHO/Geneva - All COVID-19 origin hypotheses open

Dear Joan,

Thanks so much for forwarding. Wow.

Best Regards,
Peter

From: Blair, Joan W. (CBER) <Joan.Blair@fda.hhs.gov>
Sent: Friday, February 12, 2021 10:05 AM
To: Marks, Peter <Peter.Marks@fda.hhs.gov>
Subject: FW: additional reporting cable from WHO/Geneva - All COVID-19 origin hypotheses open

See final paragraph/comments

From: Ross, Bruce <Bruce.Ross@fda.hhs.gov>
Sent: Friday, February 12, 2021 10:00 AM
To: Abdoo, Mark <Mark.Abdoo@fda.hhs.gov>; 2019-nCoV FDA IMG Leadership (b)(6) (b)(6) @fda.hhs.gov>; OGPS OGO Managers/Supervisors (b)(6) (b)(6) @fda.hhs.gov>; Anderson, Erika <Erika.Anderson@fda.hhs.gov>
Cc: Torres, Melissa A <Melissa.Torres@fda.hhs.gov>; Mullin, Theresa <Theresa.Mullin@fda.hhs.gov>; Blair, Joan W. (CBER) <Joan.Blair@fda.hhs.gov>; Oehlsen, Michael <Michael.Oehlsen@fda.hhs.gov>; Moss, Julie <Julie.Moss@fda.hhs.gov>; ORA ACRA EAC <oraacraeac@fda.hhs.gov>; Yiannas, Frank <Frank.Yiannas@fda.hhs.gov>; Mayne, Susan <Susan.Mayne@fda.hhs.gov>; Prater, Donald <Donald.Prater@fda.hhs.gov>; Moss, Julie <Julie.Moss@fda.hhs.gov>
Subject: additional reporting cable from WHO/Geneva - All COVID-19 origin hypotheses open

The attached cable is a follow-on to the original reporting cable on WHO's Team's recent in-country visit (shared previously and remaining below).

Bruce

Bruce Ross, MA, MPH
Director

Office of Global Operations
Office of Global Policy and Strategy

COVID-19 Outbreak Response, FDA IMG Logistics – Repatriation

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From: Ross, Bruce
Sent: Tuesday, February 9, 2021 4:41 PM
To: Abdoo, Mark <Mark.Abdoo@fda.hhs.gov>; 2019-nCoV FDA IMG Leadership (b)(6) (b)(6) @fda.hhs.gov>; OGPS OGO Managers/Supervisors (b)(6) (b)(6) @fda.hhs.gov>
Cc: Torres, Melissa A <Melissa.Torres@fda.hhs.gov>; Mullin, Theresa <Theresa.Mullin@fda.hhs.gov>; Blair, Joan W. (CBER) <Joan.Blair@fda.hhs.gov>; Oehlsen, Michael <Michael.Oehlsen@fda.hhs.gov>; Moss, Julie <Julie.Moss@fda.hhs.gov>; ORA ACRA EAC <oraacraeac@fda.hhs.gov>
Subject: FW: Geneva/WHO: COVID-19 Did Not Come from a Lab According to International Investigators, Origins Investigation Continues

Attached in text below is the reporting cable on the WHO Team's initial findings...that likely have a broader audience and interest.

Bruce

MRN: 21 GENEVA 130
Date/DTG: Feb 09, 2021 / 091823Z FEB 21
From: USMISSION GENEVA
Action: WASHDC, SECSTATE IMMEDIATE
E.O.: 13526
TAGS: PREL, ECON, SHLH, KNCV, WHO, CDC, HHS, FDA, UN, CN
Captions: SENSITIVE
Subject: Geneva/WHO: COVID-19 Did Not Come from a Lab According to International Investigators, Origins Investigation Continues

1. (SBU) Key Points:

* The World Health Organization (WHO) and the Chinese Government presented initial findings from the January 14 - February 10 joint international investigation into the origins of SARS-CoV-2 at a February 9 press conference held in Wuhan, China (Full press conference here http://who.canto.global/b/V1MF4).

* The joint team stated it is highly unlikely SARS-CoV-2 originated from a lab, including the Wuhan Institute of Virology and will not pursue that hypothesis further.

* The team identified the earliest case of COVID-19 with onset of disease on December 8. That case had no link to the Wuhan seafood market. The team concluded some additional early cases had no link to the Wuhan seafood market. Based on clinical records and epidemiologic surveillance, the team found no evidence of COVID-19 in Wuhan or elsewhere in China prior to early December 2019.

* The presence of multiple early clusters in Wuhan of SARS-CoV-2 transmission in mid-December 2019, including at the Wuhan seafood market, suggests, the team leads continued, that SARS-CoV-2 may have originated from outside Wuhan.

* The investigators will gather and analyze more evidence in line with three SARS-CoV-2 origin hypotheses: 1) Direct animal to human transmission from a zoonotic source; 2) Intermediate host transmission

from an animal reservoir to an animal closer to human populations; or 3) Cold-chain transmission of SARS-CoV-2 either through a frozen, infected zoonotic source or on a frozen surface.

* The team will produce a formal report in the coming weeks providing evidence to support its recommendations.

2. (U) Dr. Liang Wannian, the Chinese team lead and Executive Vice Dean of the School of Public Health at Tsinghua University, summarized the Chinese team's initial findings during Phase One of the investigation, prior to the arrival of the international team. The Chinese team investigated three areas to identify a possible source of SARS-CoV-2: 1) Viral zoonotic transmission; 2) Viral sequences; and 3) evolution of the SARS-CoV-2 in the human population. Dr. Peter Ben Embarek, WHO International Team Lead, summarized the results of the international team's investigations which included site visits to the Wuhan Huanan Market and the Wuhan Institute of Virology. The team leads stated they will provide a full report with detailed analysis, evidence and recommendations for future studies.

3. (U) On a possible animal origin, Wannian stated SARS-CoV-2 sequences most similarly matched viruses found in bats and pangolins, but the samples were not exact matches to sequences found in humans suggesting there could be a different original zoonotic source. He noted feline susceptibility to SARS-CoV-2, particularly in mink populations, may suggest a link, but urged more sampling in broader animal populations and in populations outside the Wuhan region in order to draw any conclusions.

4. (U) Wannian stated there was no evidence of SARS-CoV-2 in the Wuhan region in animal or human populations prior to the first case with onset of symptoms on December 8. Similarly, mortality data in the region did not provide evidence of undetected and misidentified cases of COVID-19. Wannian stated in mid-December there were multiple, early clusters and chains of transmission around Wuhan province. While one of the clusters centered around the Wuhan seafood market, Wannian stated the team was unable to determine how SARS-CoV-2 first arrived at the market. Wannian stated one working theory was that frozen foods brought the virus to the market, transmitted either on the cold surface or via a frozen animal already infected with SARS-CoV-2. He indicated further research would be needed to draw any conclusions.

5. (U) Embarek's statement tracked closely the analysis of Wannian noting the international team "followed the science" using a rational approach to evaluate the likelihood of four origin hypotheses. These included:

1. Direct animal to human transmission from a zoonotic source;

2. Intermediate host transmission from an animal reservoir to an animal with closer contact with human populations;

3. Cold-chain transmission of SARS-CoV-2 either through a frozen, infected zoonotic source or on a frozen surface;

4. Leakage from an infectious disease research laboratory.

(U) On the first three, Embarek indicated the team has not yet found any evidence to identify the original source of SARS-CoV-2, and research and analysis would continue as more data was necessary to draw any conclusions. Regarding a possible zoonotic source, Embarek stated the team would focus on zoonotic data outside of Wuhan and internationally given the lack of evidence linking SARS-CoV-2 directly to animal populations around Wuhan. He noted Wuhan does not have bat species that are a possible reservoir for the

virus. Wannian further reported sampling from farm and wild animals from over 30 provinces in China found no evidence of SARS-CoV-2 or related antibodies and suggested the team should widen the investigation to look internationally, including countries or regions with similar bat populations. He also recommended additional studies on frozen wild animal and other animal products sold in the Wuhan market.

6. (U) On the possibility that SARS-CoV-2 leaked from a lab, Embarek stated "the laboratory incident hypothesis is extremely unlikely" and doesn't warrant further study. Embarek said based on interviews with lab management, staff, and following review of the Wuhan Institute of Virology research initiatives, they found no evidence of SARS-CoV-2 related work. Furthermore, Embarek stated the procedures and regular audits of safety measures made a leak highly unlikely. When pressed by members of the press on this conclusion, Wannian said the scientific community had already dismissed any possibility that SARS-CoV-2 was the result of genetic modification in a lab. He continued by stating that leaves the possibility of SARS-CoV-2 entering a lab from a zoonotic source and through an accident it leaving the lab, which was also highly unlikely as there was no evidence of SARS-CoV-2 in any lab samples. Due to the lack of evidence, the team agreed not to pursue the "lab leakage" hypothesis in further research.

7. (SBU) Comment: This structured press conference in China did not get into the details necessary to evaluate the team's conclusions and recommendations. And, even when pressed, the team would not provide an assessment of which area for follow-up studies they consider most probable to determine the origins of SARS-CoV-2. In broad strokes, the team seemed to indicate there was little evidence SARS-CoV-2 originated in Wuhan, and it likely was introduced into Wuhan from an external source, either domestic or international. Additional investigation will help the team better assess if the external source was from a surrounding animal population or introduced through an infected traveler or through the food chain via cold-storage. That the lab-theory was dismissed so quickly, but the cold-chain theory was accepted for further study is curious, (b)(5) (b)(5) This general message also mirrors what the Communist Party of China has been saying during 2020 regarding the origins of COVID-19. Press questioned the initial conclusions of the group, but it is difficult to assess their claims without seeing the evidence. Member States will have an opportunity to ask questions once the initial report is presented to WHO in the coming weeks. It is unclear if the forthcoming report will provide raw data to back up any conclusions, but such data will be critical to the credibility of the investigation and the international community's ability to assess the Chinese data evaluated by the team. End Comment.

SENSITIVE BUT UNCLASSIFIED

Signature: CASSAYRE

Dissemination Rule: Released Copy

UNCLASSIFIED
SBU

From: Garcia, Mayra [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DB05677732D4023BCDF772EE0474055-GARCIAM]
Sent: 10/3/2018 4:44:32 PM
To: Harrington, Conor B. EOP/USTR (b)(6)@ustr.eop.gov]; Weinberger, Collin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd4fd713e0de4d899676030918973af8-HHS-Collin.]; andreas.vonbubnoff@fas.usda.gov; Arcuri, Guy M (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=129594fa21ef4d25b0579ff17675a127-HHS-GArcuri]; Babcock, Sarah [sarah.babcock@HQ.DHS.GOV]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Bell, Tammie Jo (CDER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bb3d1b8803c245689b15a0c5cd9cd625-Tammie.Bell]; Berkley, Dale D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d2ec3b9be3cc4903a272d25d47ebfb6a-HHS-Berkley]; Beth.N.Harris@aphis.usda.gov; Ellen.Bohon@trade.gov; Borio, Luciana L. EOP/NSC (b)(6)@nsc.eop.gov]; Brand, Kevin (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=980d7ad635e74ede97d34dffb3761cf3-HHS-yfb0-cd]; Bresee, Joseph S (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a97e60bafd2145e19d9b7e3a465e8cf0-HHS-jsb6-cd]; Peter.Bretting@ARS.USDA.GOV; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Bryan.Norrington@ars.usda.gov; ButlerCR@si.edu; Caird.RexroadIII@ARS.USDA.GOV; Mayra.Caldera@fas.usda.gov; Carter, Hillary H. EOP/NSC (b)(6)@nsc.eop.gov]; Cassetti, Cristina G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f5a44e839c5642abb30e10feb69800b4-HHS-CCasset]; CBC [CBC@bis.doc.gov]; Chacko, Betsie [betsie.chacko@HQ.DHS.GOV]; Chandrasekera, Ruvani (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=266badb99a8b4d2b90e5b4e019bb0636-HHS-Ruvani.]; Santerre, Charlie R. EOP/OSTP (b)(6)@ostp.eop.gov]; Cho, David S (CBER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d47af9d991af4c1fbf7cb4c1d287f83e-ChoD]; Fan-Li.Chou@fas.usda.gov; Chretien, JP EOP/OSTP (b)(6)@ostp.eop.gov]; Christian.Hannon@USPTO.GOV; kimberly.coleman@fema.dhs.gov; Cox, Nancy J (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4572d0057a7b40c291cfec4486737d29-HHS-njc1-cd]; Crank, Michelle C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0e1ebedad5964d69bbd64c7851fc40a7-HHS-crankm1]; Davey, Richard T (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6fef626fc4644203810758bb62c7c784-HHS-RDAVEY-]; diane.dieuliis.civ@ndu.edu; kdittmar@nsf.gov; Dominique, Joyelle K (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c948ff2734604738b1e1f739a594902c-HHS-joyelle]; Donis, Ruben (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dea126c25cab404db922973cd7ccb459-HHS-Ruben.D]; Eisenberg Lobelo, Emily (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=729fffed5a474613a4e00af6cad651ad-HHS-idq5-cd]; Epstein, Jay [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00aeafbff9fd4af9ac9e533c8689c202-epsteinj]; david.w.evans1.ctr@mail.mil; Fan-Li.Chou@fas.usda.gov; Ferriter, Karin [Karin.Ferriter@USPTO.GOV]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Foster, Joseph A (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b88c70a10f1843c49dafb981ae48f09c-HHS-jbf7-cd]; Mark.Freeman@fas.usda.gov; cindy.k.fuchs.civ@mail.mil; Galloway, Summer (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=287a8ac7a6164ea9ac21d2802d45c0d9-HHS-nmd3-cd]; Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Harvey.Blackburn@ars.usda.gov; Burke.L.Healey@aphis.usda.gov; dhegwood@usaid.gov; Ivan.Zapata@HQ.DHS.GOV; Chretien, JP EOP/OSTP (b)(6)@ostp.eop.gov]; jennifer.boger@trade.gov; Jennifer.Woodward@ARS.USDA.GOV; Jernigan, Daniel B (CDC) [/o=ExchangeLabs/ou=Exchange Administrative

Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=83b3dd3de35d489aa4012b73d93f133f-HHS-dbj0-cd]; Jodi.Kouts@bis.doc.gov; Johnson, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9c7eb3a419464ea2917f9d1e3f6e57a4-HHS-Robert.]; franca.r.jones.mil@mail.mil; Katz, Jacqueline M (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e7e8bf32a5224c5faa0b2a8c208b31e0-HHS-jmk9-cd]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Kevin.Hackett@ARS.USDA.GOV; jennifer.m.kishimori.mil@mail.mil; michael.p.kozar.mil@mail.mil; Kuhnert-Tallman, Wendi L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=01f8ee10758c4677b417de6b7c8ec5b5-HHS-wdk1-cd]; lmatukumalli@nifa.usda.gov; jlong@usaid.gov; Lopez, Arnela (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae7690968fb24808b12e266810327569-HHS-Arnela.]; Lueptow, Rebekka (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=944f0156dbf64ffaa95cc785bb56ca0f-HHS-Rebekka]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Marano, Nina (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=77923a0ee56945c28bc1ae23862bed97-HHS-nbm8-cd]; Marina.Lamm@USPTO.GOV; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Mark.Freeman@fas.usda.gov; Mayra.Caldera@fas.usda.gov; Mcclee, Vondguraus (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=78f9c27b17c04d0da8568604abf26a12-HHS-clo2-cd]; melinda.belisle@fas.usda.gov; SMiers@niaid.nih.gov; MillerS@si.edu; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Muir-Paulik, Sarah (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9d3b461222ef4629b8d313a50c2fa404-HHS-Sarah.M]; MullinsP@si.edu; Music, Francesca (MIL) [francesca.c.music2.civ@mail.mil]; Eileen.N.Ostlund@aphis.usda.gov; lianne.parr.ctr@darpa.mil; Paul.Zankowski@ams.usda.gov; nathan.j.pawlicki.ctr@mail.mil; Pearson, Katherine L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=922bae28136f43fa82553c5bb2a7b61f-HHS-gvm4-cd]; Peter.Bretting@ARS.USDA.GOV; Mamacos, Peter D. EOP/NSC (b)(6)@nsc.eop.gov]; PJOHNSON@nifa.usda.gov; kevin.r.porter3.civ@mail.mil; Post, Diane J (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=744c07cceebc45018bf9ee97dbc20bbd-HHS-postd-n]; randijohnson@nifa.usda.gov; Ranjan, Mukul (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=40fa81127c2042fa913539af005560d6-HHS-MRanjan]; sremold@nsf.gov; Beverly.J.Schmitt@aphis.usda.gov; Shaw, Michael W (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ddc530330f74747b3b7f47e36c4c778-HHS-mws2-cd]; Sherman, Susan (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cac01b38636f4165b03a0fbb18bba1c9-HHS-Susan.S]; smalcomb@nsf.gov; Snyder, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=23d431d47ba14ca4958b452186c2a690-HHS-Anne.Sn]; Spiro, David (NIH/NIAID) [E] [david.spiro@nih.gov]; Stevens, James (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=351b3d3575c14defbfe22d316ae3e4f6-HHS-fwb4-cd]; Stewart, Jessica L (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ddbad5915de4419eacb96dfdd49e4687-HHS-Jessica]; Touchette, Nancy A (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ba9d039f359423380697670fcdf1241-HHS-ntouche]; renee.wegrzyn@darpa.mil; Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; aclements@usaid.gov; (b)(6)@state.gov]; dcarroll@usaid.gov; Eisenberg Lobelo, Emily (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=729fffed5a474613a4e00af6cad651ad-HHS-idq5-cd]; Greene, Carolyn M (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5593b7cf42a472096db48fb69f81c85-HHS-cqg4-cd]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]; Giovanni, Maria Y (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a2067889b17e4250ab8a87687d8da227-HHS-

MGiovan]; pace.lubinsky@fas.usda.gov; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Bleimund, Emily (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=51b4d2c10a014d879a71e78d878542f2-HHS-Emily.B]; Schmeissner, Peter (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41ee9becd7ff492585aa8b06088f4b0a-HHS-Peter.S]; Danelski, Ann (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d53bc4b5ae2a4270a3ae912aa76f42b8-HHS-Ann.Dan]; Koonin, Lisa M (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=077ca3b1b0c940e2a83488c8a87c54e1-HHS-lmk1-cd]; (b)(6) (b)(6) @state.gov]; (b)(6) @state.gov]; Aziz, Anjam EOP/USTR (b)(6) @ustr.eop.gov]; Wang, Katherine E. EOP/USTR (b)(6) @ustr.eop.gov]

CC: (b)(6) @state.gov]

Subject: RE: WHO Pandemic Influenza Preparedness Framework Analysis on GSD, Seasonal viruses, GISRS, Nagoya --FOR COMMENT BY COB THURS OCT 4

Dear all,

DMD/CDRH/FDA does not have any comments.

Best regards,

Mayra Garcia, Ph.D., M.B.A.
Scientific Reviewer

Center for Devices and Radiological Health
Office of In Vitro Diagnostics and Radiological Health
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Sent: Friday, September 28, 2018 12:48 PM
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Subject: RE: WHO Pandemic Influenza Preparedness Framework Analysis on GSD, Seasonal viruses, GISRS, Nagoya--FOR COMMENT BY COB THURS OCT 4

+Anjam and Kat who now cover these issues for USTR.

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Subject: WHO Pandemic Influenza Preparedness Framework Analysis on GSD, Seasonal viruses, GISRS, Nagoya--FOR COMMENT BY COB THURS OCT 4

Good afternoon, influenza, pathogen sample sharing, and pathogen genetic sequence data colleagues,

WHO Pandemic Influenza Preparedness (PIP) Framework Secretariat recently released a draft analysis that considers how the PIP framework should address a number of key issues and emerging technologies including pathogen genetic sequence data, whether seasonal influenza virus sharing should be included under PIP, the Global Influenza Surveillance and Response System (GISRS), and the implications of the Nagoya Protocol on these issues. The PIP Secretariat conducted these analyses at the behest of the World Health Assembly's 2017 resolution, WHA70(10)8(b).

This is an optional request for feedback. Please send any policy recommendations, redlines, and comments back to (b)(6)@state.gov) and I (Collin.Weinberger@hhs.gov) no later than COB pm on Thursday, October 4,

2018. Sending your feedback earlier would also be warmly welcomed. Please feel free to only review the relevant sections. **We respectfully request ask that each agency coordinate among relevant SMEs and send a single, consolidated version of comments so we do not need to deconflict comments from different groups within the same agency.**

BACKGROUND:
Purpose: These WHO analyses presented in the draft paper will be discussed at a WHO member state consultation in Geneva from October 15-16. After the consultation, the draft paper will be revised based on member state feedback, sent to the January WHO Executive Board meeting for consideration, and then will likely be considered at the 2019 World Health Assembly next May.

Interagency Stakeholders: This distro includes a wide range of interagency stakeholders who have previously been engaged in or been included on a distro related to influenza, genetic sequence data, the Nagoya Protocol as it relates to pathogen and pathogen genetic sequence data sharing, and associated policy issues. (b)(6) replacement at State, and we are still working to rebuild the appropriate networks for our policy work on influenza, pathogen genetic sequence data, pathogen sample sharing, and bioinformatics. If you only cover a narrow set of these issues, please let us know what topics you would like to be copied on, and we will update the distros for sub-topics accordingly. **If you are on this email, but would prefer not to be – please let (b)(6) and I know. Alternatively, if there are key stakeholders we missed – please feel free to forward them the information and send us their contact info.**

Documents for review: We have converted the PIP Secretariat's Analysis pdf document to Word in order to facilitate consolidating interagency edits, so there may be minor typos (typically near quotes or in web addresses) or formatting discrepancies (font sizes aren't identical, but content was kept on the same page it was in the original pdf). We have not converted the Annexes. If you have already started making comments on top of the pdf document, feel free to use that version.

- **(Priority): 8bAnalysis_Draft1_17Sep2018_EN_word.docx**
- (optional): Interagency Feedback on WHA70108b – Template for submitting topline comments intended to help inform the U.S. position paper
- (optional) Supporting Documents:
- Guide to Fact Sheets
- Fact Sheets
- Purpose of the Analysis
- Process for Amending the PIP-FW
- Biosecurity and Biosafety
- Nagoya Protocol and Public Health
- GISRS
- GSD
- New Tech
- References
- WHO's Draft 8bAnalysis-Draft1_17Sep2018_EN.pdf
- WHA70(10) decision point

Thank you in advance for your comments. We look forward to working with you on one or more of these issues!
Best,

Collin & (b)(6)

Collin Weinberger, MPH

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'PJOHNSON@nifa.usda.gov' [PJOHNSON@nifa.usda.gov]; 'Dominic.Keating@USPTO.GOV' [Dominic.Keating@USPTO.GOV] (b)(6) @state.gov]; (b)(6) @state.gov]; (b)(6) @state.gov]; Eisenberg Lobelo, Emily (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=729fffed5a474613a4e00af6cad651ad-HHS-idq5-cd]; Steiger, William R. (AID/A) [wsteiger@usaid.gov]; Raychaudhuri, Gopa [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b739675f501e460a987b765d0bd77d94-Raychaudhur]; Bell, Tammie Jo (CDER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bb3d1b8803c245689b15a0c5cd9cd625-Tammie.Bell]; Donis, Ruben (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dea126c25cab404db922973cd7ccb459-HHS-Ruben.D]; Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; (b)(6) (b)(6) @state.gov]; 'Urban, JoEllen' [JoEllen_Urban@omb.eop.gov]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M] (b)(6) (b)(6) @state.gov]; Pearson, Katherine L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=922bae28136f43fa82553c5bb2a7b61f-HHS-gvm4-cd]; Cho, David S (CBER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d47af9d991af4c1fbf7cb4c1d287f83e-ChoD]; Arcuri, Guy M (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=129594fa21ef4d25b0579ff17675a127-HHS-GArcuri]; 'Colby, Michelle - NIFA' [Michelle.Colby@nifa.usda.gov]; 'Epting, Mallory (OS/OGA)' [Mallory.Epting@hhs.gov]; Galloway, Summer (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=287a8ac7a6164ea9ac21d2802d45c0d9-HHS-nmd3-cd]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; (b)(6) (b)(6) @state.gov]; 'Chretien, JP EOP/OSTP' [Jean-Paul_Chretien@ostp.eop.gov]; Olsen, Sonja J (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dbfbc65cfb6440b1aca73e3fcf70c919-HHS-sco2-cd]; (b)(6) J (b)(6) @state.gov]; Karem, Kevin L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1b573d4ee0ee450db6f866a50f1e9ce7-HHS-kdk6-cd]; 'Azar, Ramzy G CTR DHA HEALTH OPS DIR (US)' (b)(6) @mail.mil]; 'West, William Lionel (Lionel) II CIV DHA READINESS (US)' (b)(6) @mail.mil]; 'Kishimori, Jennifer M COL USARMY OSD HA (US)' (b)(6) @mail.mil]; 'Pawlicki, Nathan J CTR DHA MED COUNTERMEASURES (US)' (b)(6) @mail.mil]; 'Petersen, Juliette R CTR OSD OUSD P-R (US)' (b)(6) @mail.mil]; West, Matthew B [WestMB@state.gov]; 'Borio, Luciana L. EOP/NSC' [Luciana.L.Borio@nsc.eop.gov]; Carter, Hillary H. EOP/NSC [Hillary_H_Carter@nsc.eop.gov]; Carroll, Dennis (GH/ID) [dcarroll@usaid.gov]

CC: Maccannell, Duncan R (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=129d489e06514ed3b0511a3c9dbed2c3-HHS-fms2-cd]; Giovanni, Maria Y (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a2067889b17e4250ab8a87687d8da227-HHS-MGiovan]; Armstrong, Gregory L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=67c30c93e434442a9c6786330560e995-HHS-gca3-cd]; Cheever, Anne (contr-bto) (b)(6) @darpa.mil]; 'Patterson, Jenica (contr-i2o)' (b)(6) tr@darpa.mil]; Jafari, Hamid S (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7cb198bda13b4e26826d746fe22175e6-HHS-hsj0-cd]; Frame, Alicia - NIFA [Alicia.Frame@nifa.usda.gov]; Beach, Thomas [Thomas.Beach@USPTO.GOV]; Peerbolte, Stacy (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=99f029a37dd741609d28480c379bb26b-HHS-Stacy.P]; Fonda, Kathleen [Kathleen.Fonda@USPTO.GOV]; McGuigan, Stacy M CTR OSD OUSD ATL (US) (b)(6) @mail.mil]; (b)(6) @state.gov]; Fuchs, Cindy K CIV USARMY MEDCOM USAMRIID (US) (b)(6) @mail.mil]

Subject: March 8th Bioinformatics Meeting summary, conclusions and next steps.

Attachments: dos_bioinformatics_capacity_questions CDC Armstrong.pdf; JWARG_Benefits of Global Bioinformatics Capacity Building Questionnaire.pdf; NSF responses Questionnaire for Global Bioinformatics Capacity Mapping Consultation

on 8 March 2018.pdf; Questionnaire for Global Bioinformatics Capacity Mapping Consultation_AFHSB-GEIS_PreDec_FOUO.pdf; Questionnaire on USG International Bioinformatics Capacity Building Activities NIH Spiro.pdf; NIH-NIAIDFINAL.pdf; Draft Summary of State-HHS 8 March Bioinformatics meeting as of 3-20-20....docx

Dear All,

1. Attached is the draft summary of the 8 March meeting with the Gates Foundation.

-Please provide feedback on the summary, conclusion and next steps in the document by next Wed (4 March). No feedback = concurrence as written.

-I would like to thank (b)(6) Juliette Petersen and Collin Weinberger for sharing their excellent note for this summary.

2. Also attached are the USG agencies completed survey forms on international bioinformatics activities/initiatives.

- Thank you for taking the time to do the research and complete the surveys. There is much here to be proud in the work the USG is doing to advance bioinformatics for global public health and US National Security.

- These surveys will be used to construct the high level paper for use in gaining stakeholder support, developing partnerships and shaping the international policy objectives.

3. (b)(6) in the Office of International Health and Biodefense will be taking over this effort as I depart the State Department for my next challenge. I know (b)(6) s in good hands.

4. It has been a pleasure and privilege to work with each one of you. I am looking forward to working with you in the future.

-Bioinformatics and associated biotechnology (is) will drastically change both clinical medicine and global public health - much faster than most realize. It is vital that there is an ongoing international effort to deliberatively and strategically work through the policy implications.

V/r

(b)(6)

USG Survey Forms Attached:

1. CDC
2. DoD (Joint West Africa Working Group)
3. NSF
4. DoD (Armed Forces Health Surveillance Branch)
5. NIH (Fogarty International Center)
6. NIH (inclusive)

-----Original Appointment-----
From (b)(6)
Sent: Tuesday, September 26, 2017 10:07 AM
To: (b)(6) 'wve1@cdc.gov'; 'uvv3@cdc.gov'; (b)(6) 'sremold@nsf.gov'; 'Katz, Jackie M. (CDC/OID/NCIRD)'; (b)(6) @state.gov); (b)(6) 'Stevens, James

(CDC/OID/NCIRD)'; Ye, Tun (CDC/CGH/OD); 'cstmary@nsf.gov'; 'kdittmar@nsf.gov'; 'Bohon, Ellen'; 'Urban, JoEllen'; 'Epstein, Gerald L. EOP/OSTP'; Morton, Lindsay C CTR DHA HEALTH SURV (US); 'Jones, Franca R CDR USN DHA HEALTH SURV (US)'; Jones, David M; 'Weinberger, Collin (OS/OGA) (CTR)'; 'Barna, Lauren (OS/ASPR/OPP)'; 'Marinissen, Maria (OS/ASPR/OPP)'; 'Bright, Rick (OS/ASPR/BARDA)'; 'Wong, Holly (HHS/OS/OGA)'; (b)(6) (Geneva); 'deborah_e_lashley-johnson@ustr.eop.gov'; 'Touchette, Nancy (NIH/NIAID) [E]'; (b)(6) 'conor_b_harrington@ustr.eop.gov'; 'York, George E.'; 'Moezie, Minna F.'; 'Ranjan, Mukul (NIH/NIAID) [E]'; (b)(6) 'Parr, Lianne (contr-bto)'; 'Post, Diane (NIH/NIAID) [E]'; 'Spiro, David (NIH/NIAID) [E]'; 'Mowatt, Michael (NIH/NIAID) [E]'; 'Miers, Sarah (NIH/NIAID) [E]'; 'Shaw, Michael (CDC/OID/OD)'; 'Snyder, Anne (HHS/OS/OGA)'; (b)(6) 'Chandrasekera, Ruvani (HHS/ASPR/OPP)'; (b)(6) 'Sherman, Susan (HHS/OGC)'; 'Foster, Joseph (CDC/OCOO/OGC)'; Music, Francesca; 'DuLaney, Megan M CTR OSD OSD (US)'; (b)(6) 'Jernigan, Daniel B. (CDC/OID/NCIRD)'; 'Marano, Nina (CDC/OID/NCEZID)'; 'Berkley, Dale (NIH/OD) [E]'; (b)(6) 'Peter.Bretting@ARS.USDA.GOV'; 'Jiang, Chengyong G CTR (US)'; 'lmatukumalli@nifa.usda.gov'; 'PJOHNSON@nifa.usda.gov'; 'Dominic.Keating@USPTO.GOV'; Kim, Elizabeth AB (OES); Reed, Allison D; Margolis, Jonathan A; 'Eisenberg, Emily (CDC/OID/NCIRD)'; Steiger, William R. (AID/A); 'Raychaudhuri, Gopa (FDA/CBER)'; 'Bell, Tammie Jo (CDER) (FDA/CDER)'; 'Donis, Ruben (OS/ASPR/BARDA)'; 'Yu, Anne (HHS/OS/OGA)'; (b)(6) 'Moudy, Robin (OS/ASPR/OPP)'; (b)(6) (Geneva); 'Pearson, Kate L. (CDC/OID/NCIRD)'; 'Cho, David S (CBER) (FDA/CBER)'; 'Arcuri, Guy (NIH/NIAID) [E]'; Colby, Michelle - NIFA; 'Epting, Mallory (OS/OGA)'; 'Galloway, Summer (CDC/OID/NCIRD) (CTR)'; 'Kerr, Lawrence (HHS/OS/OGA)'; 'Handley, Gray (NIH/NIAID) [E]'; (b)(6) L; 'Chretien, JP EOP/OSTP'; 'Olsen, Sonja (CDC/OID/NCIRD)'; (b)(6) 'Karem, Kevin (CDC/CGH/OD)'; 'Azar, Ramzy G CTR DHA HEALTH OPS DIR (US)'; 'West, William Lionel (Lionel) II CIV DHA READINESS (US)'; 'Kishimori, Jennifer M COL USARMY OSD HA (US)'; 'Pawlicki, Nathan J CTR DHA MED COUNTERMEASURES (US)'; 'Petersen, Juliette R CTR OSD OUSD P-R (US)'; (b)(6) ; Borio, Luciana L. EOP/NSC; Carter, Hillary H. EOP/NSC; Dennis Carroll
Cc: MacCannell, Duncan (CDC/OID/NCEZID); Giovanni, Maria (NIH/NIAID) [E]; Armstrong, Gregory (CDC/OID/NCEZID); Cheever, Anne (contr-bto); Patterson, Jenica (contr-i2o); Jafari, Hamid (CDC/CGH/OD); Frame, Alicia - NIFA; (b)(6) Peerbolte, Stacy (OS/ASPR/OEM); (b)(6) McGuigan, Stacy M CTR OSD OUSD ATL (US); (b)(6) M; Fuchs, Cindy K CIV USARMY MEDCOM USAMRIID (US)
Subject: Confirmation and Concept Note for Global Bioinformatics Capacity Mapping Consultation with representatives from the Bill and Melinda Gates foundation
When: Thursday, March 08, 2018 1:00 PM-4:00 PM Customized Time Zone.
Where: U.S. Department of State, 2201 C ST NW, Washington, DC 20520, Room 6833

Dear All,

- This email is to confirm the *Global Bioinformatics Capacity Mapping Consultation* with representatives from the Bill and Melinda Gates foundation for Thursday, March 8, 2018; 1:00– 4:00 pm at U.S. Department of State, 2201 C ST NW, Washington, DC 20520, Room 6833.
- (b)(6) State) and Dr. Maria Giovanni (NIH) will be co-chairing the consultation.
- Representatives from the BMGF will be sharing their perspectives and initiatives on Global Bioinformatics Capacity.
- A detailed meeting agenda will be forward shortly that includes a USG information sharing session with the BMGS followed by a USG only discussion session.
- Attached is the Concept Note for the meeting.

o We ask that you read the concept note and take time to complete the questions at the end so that we can have a valuable information exchange with the BMGF and a separate USG only international policy discussion.

o We would like to have your responses in writing in order to accurately capture all of the input for the meeting summary.

- Please responds to the meeting invite, if you have not already.

o This will allow us to pre-clear you with State Security and to make your name tent for the table.

- As background for this meeting, recall that at the 5 Dec 2017 Consultation on Pathogen Genetic Sequence Data, participants identified a follow-up U.S. government discussion with the BMGF on global bioinformatics capacity as a next step. (See attached)

- Finally, I have updated the meeting invite list to best reflect the current information I have on interested participant in this policy discussion. Please forward to anyone I may have inadvertently missed.

- We are looking forward to seeing you on the 8th and please let me know if you have any questions.

<< File: Executive Summary of 5 Dec 2017 PGSD meeting.pdf >>

<< File: Concept note for Global Bioinformatics Capacity Mapping Consultation on 8 March 2018.docx >>

v/r

(b)(6)

Official

UNCLASSIFIED

Questionnaire on USG International Bioinformatics Capacity Building Activities/Initiatives
Responses from CDC

- *Using 2-5 examples, briefly describe the bioinformatics international capacity building your agency supports/conducts, and in what region(s)/country(ies) this work is currently being accomplished.*

Since 2014, CDC, through its "AMD Program", has been working to integrate NGS and bioinformatics in the US public health system to improve surveillance for and outbreak response to a broad range of infectious diseases. Overseas, CDC has a presence in a number of countries, usually partnering with the ministry of health. At the sites with more technical capacity, such as Kenya, Nigeria, Thailand, India, and Chile, the programs have been working to implement sequencing (both Sanger and next-generation [NGS]) and bioinformatics in targeted areas. For example, in Kenya, the program has been working with KEMRI to better understand the epidemiology of typhoid fever and cholera. In Thailand, CDC's malaria program has worked with local partners to implement an NGS-based system for assessing antimalarial resistance. The program has included basic bioinformatics training. In Georgia, CDC's viral hepatitis program has worked with the laboratory to implement an NGS-based system that has proven useful for surveillance and outbreak response in the US. In Chile, the influenza program has worked Chile's influenza monitoring system to switch to a [NGS] "sequence-first" approach based on a system now in place in the US. Bioinformatic analysis is Cloud-based and automated.

In short, CDC has a substantial presence abroad and is now starting to make greater use of NGS in its (usually MOH-based) collaborating laboratories.

- *Which internal and external U.S. government partners are involved in these efforts?*

CDC partners with various USG organizations overseas: USAID (as with PMI and PEPFAR), DTRA, USAMRID, AFRIMS, the national labs (specifically, Los Alamos) and others. CDC's programs work with several international efforts and institutions, such as WHO (several programs), Critical Path (TB) and GISAID (influenza data sharing). CDC also collaborates with a number of academic institutions around the globe.

- *What are the major opportunities in these countries/regions in assuring successful bioinformatics capacities?*
- *What are the major challenges/gaps in these countries/regions in assuring successful bioinformatics capacities?*

One of the challenges of building microbial genomics capacity is that bioinformatics is so different from the rest of microbiology—very mathematical, and often dependent on access to high-performance computing capacity. In addition, the entire field of bioinformatics very new and very dynamic. A challenge in supporting bioinformatics in the field is providing the right environment. In middle-income countries such as Thailand or Brazil, those conditions already exist. In lower-income countries, this is much more challenging. The Cloud provides some opportunities to make this more practical, but uploading NGS data (typically, 15 GB or more) to

the cloud can be a challenge even in many US public health settings, and will be difficult where internet access is more limited. The Los Alamos laboratory, with DTRA funding, has developed an interesting platform (EDGE) based on commodity hardware that can facilitate implementation of bioinformatics in areas with limited connectivity.

- *What are the actual or perceived benefits of bioinformatics capacity that have been communicated from the recipient countries/agencies in the regions where you work?*

Overseas partners are echoing similar comments to those we're hearing from state and local public-health agencies in the US:

- The opportunity to be bring in novel, state-of-the-art technologies like NGS and bioinformatics is a boost to the morale of the labs and potentially very valuable in attracting the next generation of public health laboratory scientists
- NGS technology is very convergent—once implemented for one purpose (or one pathogen), it's easy to extend it for other purposes. For example, in India, they're sequencing TB bacilli to infer drug resistance. But they can also use the technology in investigating potential outbreaks of TB. In addition, once one protocol for bacterial whole-genome sequencing is established for one species (such as *Mycobacterium tuberculosis)*, it's easy to apply it to another species, for example to understand the emergence of antimicrobial resistance or infer phenotype (such as the serotype of *Streptococcus pneumonia).*

- *What are some of the challenges and opportunities in benefit/risk communication with decision makers and the general public you have experienced?*

The main challenges are around the capacity building, including physical infrastructure such as IT infrastructure and sequencing equipment. Workforce issues are also big. In the public health settings where CDC works, recruitment and retention are major challenges even for *relatively common* fields such as microbiology, and are likely to be even great for fields like bioinformatics. On the positive side, the field of bioinformatics is relatively young, and as a result so are bioinformaticians. CDC has been able to attract talented staff despite relatively low salaries (we're competing with Silicon Valley for bioinformaticians) because of the nature of the work—the opportunity to be part of something new and the opportunity have an impact.

Benefits of Bioinformatics Capacity
Global Bioinformatics Capacity Mapping Consultation
Thursday, March 8, 2018; 1:00– 4:00 pm
U.S. Department of State
2201 C ST NW, Washington, DC 20520

Questionnaire on USG International Bioinformatics Capacity Building Activities/Initiatives

Disclaimer: From Captain Suzanne Mate, PhD of the Medical Service Corps and U.S. Army Assistant Deputy Director for Research Operations in West Africa, who drafted these responses:
"I should add a disclaimer that these comments reflect my frank, personal opinions about the capacity. When I refer to funding gaps, it points to the country inability to self-fund these efforts. USG fills many funding gaps but it is still a challenge to maintain research capabilities overseas as a platform that ebbs and flows with research protocol turnover and funding strategies. Worth the challenge? Absolutely."

Using 2-5 examples, briefly describe the bioinformatics international capacity building your agency supports/conducts, and in what region(s)/country(ies) this work is currently being accomplished.

With the Joint West Africa Working Group (JWARG), The US Military HIV Research Program at Walter Reed Army Institute of Research is leading the research protocol RV466, "Severe Infectious Disease: Surveillance, Detection, Risks and Consequences in West Africa." This protocol transfers molecular strategies for pathogen detection and characterization, to include next-generation sequencing and the bioinformatics to process the data for pathogen characterization. The JWARG is leveraging existing host nation sequencing laboratories in Liberia, Ghana, and Nigeria and increasing capacity as needed.

In **Liberia**, the sequencing lab and informatics capacity remains from the US Army Medical Research Institute for Infectious Diseases (USAMRIID) capacity building during the 2013-2015 West Africa Ebola outbreak response, led by Dr. Gustavo Palacios in the Center for Genome Sciences (CGS). Since the outbreak, personnel working under STRATCOM's University Affiliate Research Center (UARC) with the National Strategic Research Institute (NSRI) who are located in USAMRIID CGS, have maintained the sequencing capacity in partnership with the Liberian Institute for Biomedical Research (LIBR). In addition to Ebola virus, they have also sequenced the Lassa virus genome for cases in Liberia that explained why existing PCR-based diagnostics failed; the diagnostics were designed on strains in Nigeria that genetically were not identical to that in Liberia. It is through this single partnership between NSRI-USAMRIID-LIBR that the sequencing capacity exists today to support the RV466 protocol for pathogen surveillance. The current bioinformatics capability is a single linux server located at LIBR that includes the informatics pipelines delivered by CGS. It is a local implementation and there is currently one Liberian national trained to complete the sequencing workflow from sample to data analysis. Reach-back support to the CGS is essential for on-site production of sequence data.

In **Ghana**, the sequencing lab and informatics capacity existed at the Noguchi Memorial Research Institute and use is through its partnership with the Navy Medical Research Unit in Ghana (NAMRU-3-GD), which is primarily funded by GEIS. NAMRU-3-GD is leading RV466 protocol implementation in Ghana at the 37th Military Hospital in Accra and again calls upon the expertise of NSRI-USAMRIID to

deliver sequencing training, instrument service, protocols, and informatics solutions. The current bioinformatics capability is a single linux server located at Noguchi that includes the informatics pipelines delivered by CGS. It is a local implementation and there is currently < 5 Ghanaian nationals trained to complete the sequencing workflow from sample to data analysis. Reach-back support to the CGS is essential for on-site production of sequence data.

In **Nigeria**, African Centre of Excellence for the Genomics of Infectious Diseases (ACEGID), Redeemer's University has advanced sequencing laboratories and staff to support the JWARG research studies. In addition, they have had a long-standing partnership with the Broad Institute and Dr. Pardis Sabeti's team to collaborate on sequencing methods and strategies, particularly for viral hemorrhagic fevers. They currently use a commercial web-hosted service, DNAnexus, as a shared place to centralize data collection and analysis through a single serviced sequencing pipeline.

Which internal and external U.S. government partners are involved in these efforts?

MRMC: WRAIR, USAMRIID
NMRC: NAMRU-3-GD
STRATCOM-NSRI
GEIS for funding and for the developing Bioinformatics Consortium.
DHP- For funding through JPC-2 (Joint Program Committee)
DTRA- R&D funds for reagent and protocol development

What are the major opportunities in these countries/regions in assuring successful bioinformatics capacities?

Sustained training and learning environments with expertise (US or African Partners) available for reach-back and on-site support. This includes Academic communities within University and Research Institutes that have funding to sustain sequencing strategies for biomedical research applications. The young medical professionals are interested in learning these techniques for professional advancement and careers within their country health systems.

Ministry of Health recognition and support for use of genomic evidence toward epidemiologic investigations demonstrating source and transmission events.

What are the major challenges/gaps in these countries/regions in assuring successful bioinformatics capacities?

Funding to provide the informatics solutions that include hardware and local staff with expertise to lead the capacity. This includes a sustainable accounting line for staff salaries.

Funding for web-hosted services to support licensing and subscriptions.

A solid number of local experts who can drive an informatics department or service.
Internet access, speed/bandwidth. They lack this due to funding or due to local infrastructure with minimal cell and communications coverage near their work locations.

Funding for reagents. It costs our African Partners 3x's the amount we can purchase reagents in the US. It is cheaper to purchase reagents in the US and ship them to our collaborators than to have them purchase through a vendor, which there is only one for Africa.

Service contracts to maintain the sequencer that delivers the data to perform informatics. With a single vendor, the locals have minimal options to obtain service in reasonable time at appropriate costs.

What are the actual or perceived benefits of bioinformatics capacity that have been communicated from the recipient countries/agencies in the regions where you work?

1. Identification for the pathogen causing fevers of unknown origins.
2. Identification of diagnostic escape at assay target sites due to pathogen genetic variation across a small geographic region. (examples: the Lassa primers of the Nikison's Assay used in Liberia with no/minimal efficacy; seen during the West African Ebola virus outbreak.)
3. Ability to make decisions in near real-time while working with their health system to understand source of transmission. Example- April 2016 Ebola flare-up in Liberia were linked to the cases across the border in Guinea through genetic sequencing.

What are some of the challenges and opportunities in benefit/risk communication with decision makers and the general public you have experienced?

The ability for decision-makers to understand the large lift it takes to develop a sequencing and informatics capacity and platform in West Africa and then an even larger lift to sustain it for use when a health crisis or emerging infectious disease is noticed in the health system.

Benefit- deeper visibility in the nature and character of pathogens to add certainty to health definitions of infection etiology.

Risk- it's a science that doesn't always produce complete data sets. There are several times a complete genome cannot be obtained from a sample, which diminishes the interpretative value and application for public health investigations.

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Questionnaire on USG International Bioinformatics Capacity Building Activities/Initiatives

- **Using 2-5 examples, briefly describe the bioinformatics international capacity building your agency supports/conducts, and in what region(s)/country(ies) this work is currently being accomplished**.

  The National Science Foundation supports scientific and engineering research and education that positions the Nation as a global leader in discovery and innovation. Within that framework, we support investigator-driven proposals from US institutions, primarily universities. Two mandatory components are related to the development of bioinformatics capacity. The first, broader impact activities (i.e., contributions to public wellbeing or infrastructure) routinely include student and postdoctoral training. While this training occurs at US institutions, some of the postdoctoral employees and students include foreign nationals who may return to their home country. The second, a data management plan details how the data, programs, software, and pipelines generated will be made publicly available, and assures that best current standards of data and analytical infrastructure sharing are adhered to. Most of the bioinformatics resources (along with other data and analysis materials) are deposited in globally accessible repositories (e.g. GitHuB), and are thus available to an international community of researchers.

  Some examples of NSF programs funding US research and capacity building in the area of bioinformatics include: STEM Capacity building programs in the Directorate for Education and Human Resources, programs in the Directorate of Biological Sciences (BIO) such as the Advances in Biological Informatics program (Division of Biological Infrastructure), or the Evolutionary Processes and Systematics and Biodiversity Sciences Clusters (Division of Environmental Biology), as well as NEON (National Ecological Observation Network). Finally, one of the NSF 10 Big Ideas is Harnessing the Data Revolution. Links to these program descriptions are below.

- **Which internal and external U.S. government partners are involved in these efforts?**

  NSF directly funds US Universities and other US institutions that conduct research. However, the US investigators we support conduct their research all over the world and thus represent a distributed network for bioinformatic capacity building.

The NSF also partners with funding agencies in other nations to support joint projects. These efforts are unevenly distributed across the NSF but are coordinated via the NSF Office of International Science and Engineering. The BIO directorate currently collaborates with the UK, Brazil, Israel, China, and South Africa in this manner. Specifically, the Ecology and Evolution of Infectious Disease (EEID) program has recently co-funded projects with the UK and with Israel. The Dimensions of Biodiversity program, has cofunding arrangements with the UK, Brazil, and South Africa. The Plant Genome Research Program likewise has a partnership with the UK. All of these programs involve substantial bioinformatic components. There are also cases of partnerships with other USG agencies, for example, the EEID program which involves partners at USDA and NIH, the Plant Biotic Interactions program (within the Division of Integrative and Organismal systems) which partners with USDA-NIFA, and the Plant Genome Research Program which also partners with USDA-NIFA.

- **What are the major opportunities in these countries/regions in assuring successful bioinformatics capacities?**

  In the case of cofunding partnerships, the NSF aims for policies that have the same expectations for training and data management as solely NSF funded projects, for example several programs employ a lead agency model in which review is conducted under the auspices of the NSF. Overall, our requirement of public access is making US developed resources widely available to the community of US scientists. But, because cutting-edge science operates at a global level, this includes global accessibility of bioinformatics resources.

- **What are the major challenges/gaps in these countries/regions in assuring successful bioinformatics capacities?**

  This is outside our purview.

- **What are the actual or perceived benefits of bioinformatics capacity that have been communicated from the recipient countries/agencies in the regions where you work?**

  This is also outside our purview, but collaborations both at the level of individual investigators and in program cofunding are based on continued mutual benefit.

- **What are some of the challenges and opportunities in benefit/risk communication with decision makers and the general public you have experienced?**

  This is also primarily out of our hands and falls to the investigators who are responsible for publications of products, training and outreach as part of their broader impact activities.

Links:

Dimensions of Biodiversity
https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=503446

Directorate for Education and Human Resources
https://www.nsf.gov/funding/programs.jsp?org=EHR)

Division of Biological Infrastructure's Advances in Biological Informatics program
https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5444&org=DBI&from=home

Ecology and Evolution of Infectious Disease program
https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5269&org=BIO&from=home

NEON
https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=13440&org=BIO&from=home

NSF's 10 Big Ideas and Harnessing the Data Revolution
https://www.nsf.gov/news/special_reports/big_ideas/harnessing.jsp

Office of International Science and Engineering
https://www.nsf.gov/dir/index.jsp?org=OISE

Plant Biotic Interactions
https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505267

Plant Genome Research Program
https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5338

Division of Environmental Biology's Systematics and Biodiversity Cluster
https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=503666&org=DEB&from=home

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Questionnaire on USG International Bioinformatics Capacity Building Activities/Initiatives

Using 2-5 examples, briefly describe the bioinformatics international capacity building your agency supports/conducts, and in what region(s)/country(ies) this work is currently being accomplished.

The Armed Forces Health Surveillance Branch (AFHSB) Global Emerging Infections Surveillance (GEIS) Section has been engaged in providing critical information for force health protection since its inception in 1997. While other DoD entities work directly with host country partners to build capacity, the GEIS program is currently focused on expanding the DoD laboratory network's capability. Internationally, DoD medical research and public health laboratories provide regional expertise in infectious disease surveillance and can serve as a resource for host country partners.

GEIS has recently established a next-generation sequencing (NGS) and bioinformatics (BI) Consortium in order to rapidly detect and characterize known, emerging, and novel infectious disease agents through establishment of a harmonized DoD laboratory network capability that uses pathogen identification and pathogen sequence data to inform force health protection decision making. The Consortium brings GEIS partner DoD laboratories together to share information on capabilities, standard operating procedures, and expertise, so that a harmonized approach to NGS and BI is achieved and the goal of improving force health protection decision making through NGS and BI is realized in the next five years.

The Consortium leverages and supports existing DoD NGS and bioinformatics capabilities for pathogen sequencing and surveillance at partner DoD medical research and public health laboratories. Currently, basic to advanced-level bioinformatics capabilities are present at several overseas laboratories: Armed Forces Research Institute of Medical Services (AFRIMS) in Thailand, Naval Medical Research Unit (NAMRU) No. 2 in Cambodia, NAMRU-3 detachment in Ghana, NAMRU-6 in Peru, US Army Medical Research Directorate (USAMRD)-Kenya, and Public Health Command Regional Pacific (PHCR-P) in Japan. Additional capabilities are being explored at USAMRD-Georgia and Landstuhl Regional Medical Center (LRMC) in Germany. Most overseas facilities face limitations in IT infrastructure and support, or trained personnel to conduct bioinformatics, thus relying on external reach back support, semi-automated workflows and servers such as EDGE (bioedge.lanl.gov), or commercially available bioinformatics programs (e.g. CLC workbench and Geneious). Additional overseas DoD laboratories have NGS wet lab instruments (i.e. Illumina MiSeq) but no existing bioinformatics infrastructure.

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Which internal and external U.S. government partners are involved in these efforts?

GEIS sequencing and bioinformatics efforts are focused on medical and public health laboratories in all military services (e.g. Army, Navy, and Air Force) and Uniformed Services University. We also collaborate with other DoD partners such as the Defense Threat Reduction Agency (DTRA) Cooperative Biological Engagement Program, DTRA J9, Walter Reed Army Institute of Research Military HIV Research Program, and the US Army Medical Research Institute of Infectious Diseases (USAMRIID) who are involved more directly with next generation sequencing and bioinformatics capacity building with host nation partners.

What are the major opportunities in these countries/regions in assuring successful bioinformatics capacities?

GEIS funds surveillance activities at fixed DoD facilities overseas (e.g. AFRIMS, USAMRD-K, NAMRU-2, NAMRU-3, and NAMRU-6). These institutions have a multi-year, and sometimes multi-decade, history of DoD funded infectious disease research and surveillance activities. GEIS overseas partners are also frequently located in close proximity to other existing USG partner programs (e.g. CDC, USAID, and DTRA), host-nation universities, or economic hubs in the region. Thus, when buy-in from key stakeholders is achieved, strategic investments made at these institutions can have a greater likelihood of sustainability. These laboratories could also provide regional expertise and reach back support to host country partners as they establish their own sequencing capabilities. Additionally, sustainability requires ongoing projects to maintain skillsets, which could be a target of USG funding that mutually benefits the US and the host partner.

What are the major challenges/gaps in these countries/regions in assuring successful bioinformatics capacities?

- IT Infrastructure and support:
  - Limited or variable access to secure and reliable networks
  - Security or IT restrictions and firewalls block access to open source data, databases, and bioinformatics tools
  - Cloud-based solutions versus local servers and high-performance computing resources
  - "Plug and play" workflows versus coding/command line
  - Labs may not have existing LIMS
  - Limited support for non-Windows based environments

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- Data transfer issues:
  - Sending or downloading large files over the internet is problematic or slow
  - Concerns over internet security when sharing data
  - Network regulations/restrictions may prohibit large data collaboration via remote access
  - Limited access to VPNs, sFTP servers, etc. or long approval processes
- Lack of appropriately trained personnel:
  - What constitutes a sufficient bioinformatics skillset?
    - PhD computational biologists versus MS or BS level education
  - Limited in country workforce trained in bioinformatics (or related disciplines)
  - Funding/salary, or career advancement, may not be attractive for highly trained personnel
  - Once personnel are trained and fully independent they are often recruited by academia, industry, other agencies, or other projects
  - Limited or variable access to training and continuing education resources, courses, or programs
  - Skill erosion after training
- Lack of sustainable funding streams for equipment maintenance, consumables, salaries, overhead, etc.

What are the actual or perceived benefits of bioinformatics capacity that have been communicated from the recipient countries/agencies in the regions where you work?

- Building and standardizing the DoD laboratory in-country capabilities facilitates cooperation on NGS and bioinformatics with host nation partners and development of their local workforce
- Results from sequencing and bioinformatics efforts are beneficial to US force health protection and global health security goals but also to host country public health organizations
- Reliance on sending samples or raw data out of country is reduced when bioinformatics capabilities exist – potentially circumventing complicated material transfer agreements and in an effort to comply with increasing host country restrictions in sample sharing
- Desire to keep data and resources "in house" at overseas locations
- Greater force health protection decision making

What are some of the challenges and opportunities in benefit/risk communication with decision makers and the general public you have experienced?

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Opportunities:

- Enhanced communications with DoD stakeholders, including the Geographic Combatant Commands, regarding infectious disease risks in their Areas of Responsibility
- Sequencing and bioinformatics training and projects to enhance USG and host country partnerships
- GEIS partners are aware of political ramifications of data sharing from infectious disease surveillance projects
- Resultant sequence data can benefit the host country and the US

Challenges:

- Stakeholders may not be aware of benefits of molecular sequence data for supplementing standard epidemiological data
- Data sharing may run into political sensitivities with host country partners, particularly when it highlights circulating diseases that may reflect poorly on the country (and affect trade or travel)
- Host country ownership of the data, and perceived lack of benefit to the country, may limit data sharing or willingness to open the data to the public
- Dual use research may be of concern, particularly for especially dangerous pathogens

Questionnaire on USG International Bioinformatics Capacity Building Activities/Initiatives

Fogarty International Center at NIH (FIC)

- Division of International Training and Research (DITR)
- Division of International Epidemiology and Population Studies (DIEPS)

- Using 2-5 examples, briefly describe the bioinformatics international capacity building your agency supports/conducts, and in what region(s)/country(ies) this work is currently being accomplished.
    1. FIC supports bioinformatics capacity building through the H3Africa Global Health Bioinformatics Research Training Program. Four grants were funded in September 2018 to support the development of bioinformatics curricula and pay for professors to train Masters, PhD and Postdoctoral students in bioinformatics skill sets. The grants were awarded to:
        Covenant University, Nigeria
        University of Sciences, Techniques and Technologies of Bamako, Mali
        International Centre of Insect Physiology and Ecology, Kenya
        Makarere University, Uganda
    2. DIEPS supports international bioinformatics through a series of training workshops. These five-day workshops teach sequence comparison and evolutionary analysis, computational modeling of epidemiological outbreaks and disease transmission and R programming for analysis of large epidemiological datasets and data visualization. 2018 workshops were held in Nepal, South Africa, UAE and Madagascar for over 100 participants from Nepal, India, Pakistan, South Africa, Tanzania and Madagascar. Previous workshops were held in Taiwan, China, Peru and Senegal. DIEPS is in the process of developing curricula and partners to add a Genomic Epidemiology component to the training workshops that will teach sequencing methods, bioinformatic and evolutionary analysis for the MinION sequencing platform.

- Which internal and external U.S. government partners are involved in these efforts?
    - H3Africa funding comes through the NIH Common Fund and is administered by Fogarty. Other partners include NIAID, NHGRI, Wellcome Trust and AESA
- What are the major opportunities in these countries/regions in assuring successful bioinformatics capacities?
    - Tremendous amount of interest and need in Africa
    - Talented pool of students
    - Excellent research opportunities to address genetic elements of chronic disease and infectious disease outbreaks.
- What are the major challenges/gaps in these countries/regions in assuring successful bioinformatics capacities?
    - Lack of programming experience in applicant pool
    - Sustainability concerns with development of new programs- will in-country institutions be able take over in the absence of external funding.
    - Career sustainability in Africa. What does that career trajectory look like?
    - Development of African leadership of genomics projects requiresin-country bioinformatics capacity

- What are the actual or perceived benefits of bioinformatics capacity that have been communicated from the recipient countries/agencies in the regions where you work?
  - Great deal of enthusiasm from PIs in developing degree-based programs
  - Energy from the Fellows
  - Scientifically the PIs understand the need for capacity at an expert level to lead the field in those countries

- What are some of the challenges and opportunities in benefit/risk communication with decision makers and the general public you have experienced?
  - Communicating the benefits and risks of understanding patients' own genetic information. FIC is offering H3Africa funding for the establishment of Collaborative Centers to study ethical, legal and societal issues of human genomics across the Africa.

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- **Using 2-5 examples, briefly describe the bioinformatics intentional capacity building your agency supports/conducts, and in what region(s)/country(ies) is working currently being accomplished**.

Bioinformatics capacity building supported by NIH includes range of activities as data management, data analysis, training and infrastructure.

Examples:

NIAID Genomic Sequencing Centers, Emerging Diseases/Outbreaks, and Nigeria

Long standing collaboration/partnership on emerging infectious diseases as Ebola, Dengue, and Lassa Fever with NIAID, Broad Institute and Redeemer University /Irrua Specialist Teaching Hospital in Nigeria through NIAID Genomic Sequencing Center at Broad Institute and includes Drs. Pardis Sabeti (Broad Institute) and Christian Happi (Redeemer University.) Over the last 5 years, the collaboration has focused on emerging diseases and outbreaks using next generation sequencing and bioinformatics capacity funded by NIAID in place at Broad Institute and transferring that capacity to Nigerian sites. For example, Broad Institute staff have traveled to Nigeria to assist with helping to continue to build sequencing and bioinformatics capacity and pipelines to perform sequencing and analysis in country and Nigerian staff have traveled to Broad Institute for hands-on-genomics and bioinformatics training.

NIAID International Centers of Excellence in Research (ICER) and NIAID West, Southern/Central Africa and East Africa International Centers of Excellence in Malaria Research

Centers focused on collaborative research projects with African and US scientists in country studying diseases as HIV, Malaria, TB in disease endemic countries and perform basic and clinical research in collaboration with NIAID Intramural scientists and extramurally funded scientists.

For example, of one ICER Center in Uganda, NIAID supports the Uganda Rakai Health Sciences Program that focuses on incidence and prevalence of HIV/AIDS in community settings. NIAID has built extensive data management and analysis platforms for easy access to data and are used beyond NIAID funded projects to build bioinformatic capacity and infrastructure and available beyond this project. In collaboration with Makerere University in Uganda, NIAID is hoping to increase bioinformatics training of Africa scientists and assist

in the development of degree-based programs. NIAID is also launching African Centers of Excellence in Bioinformatics and Data Intense Science (private-public partnerships) to continue to work with African scientists to build bioinformatics capacity and special emphasis in training based on 20 years of experience in capacity building in Africa.

NIAID Bioinformatics Resource Centers-publicly accessible data resources that provide infectious diseases community with data access, sharing, analysis, workspaces and training over the last 10 years and have been successful in helping scientists have easy access to diverse data sets and computational tools. 4 Centers have provided state of the art hands-on-training in country as Kenya, South Africa, and other Africa countries in genomics/ bioinformatics with emphasis on trainees' own data sets in a collaborative setting.

NIH H3Africa Consortium/H3AfricaBionet-Consortium in partnership with Wellcome Trust is funded for the last 5 years to enhance leading-edge research in Africa for understanding the complex interplay between environmental and genetic factors which determine communicable and non-communicable disease susceptibility and drug responses in African populations. The goals of the consortium include increasing the number of African scientists in country who are trained in genomics and bioinformatics and create and expand resources for genomics research as bioinformatics training and infrastructure. Over the last 5 years, H3AfricaBionet has developed bioinformatics infrastructure and human capacity/training programs that are directed to enable H3Africa consortium members to share, access, analyse genomic and clinical data in country generated by the H3Africa Consortium African based projects. H3AfricaBionet is based in South Africa headed up by Dr. Nicky Mulder with 32 nodes in 15 other African countries. This also including with NIH and Wellcome Trust building policies and SOPs for data sharing and analysis and is very much web based and publicly accessible.

NIH Fogarty International Center has several international fellowship programs and for example, in collaboration with NIH H3Africa Consortium are funding 4 Global Health Bioinformatics Training Programs in Africa and extend to almost 10 countries in Africa. 4 training programs are focused on masters, Ph. D and postdoctoral training opportunities and one in University of Bamako is partnering with NIAID first funded African Center of Excellence in Bioinformatics hosted at University of Bamako.

NIH Fogarty International Center-Multinational Influenza Seasonal Mortality Study (MISMS) Builds analytical capacity in influenza research with global partners and includes hands-on-bioinformatics workshops and partners for example with the African Network for Influenza Surveillance and Epidemiology.

- **Which internal and external U.S. government partners are involved in these efforts?**

Information in examples above.

- **What are the major opportunities in these countries/regions in assuring successful bioinformatics capacities?**

Bioinformatics capacity was built in partnership with projects generating data in country and critical need to allow full use of the data being generated and provide scientists in country with access to infrastructure, tools, and training. There is some commitment from NIH and African institutions to build capacity together on high priority infectious disease projects that can be extended for use beyond that. Opportunity to work with African scientists who have strong dedication, expertise, training, and understanding of diseases in country is the major opportunity and to allow them to be have the necessary tools and infrastructure to generate and analyse their data sets at their home institutions with international collaborators on diseases that are high burden in Africa is a critical goal.

Major opportunity is also the availability of equipment and the broad availability of computers and mobile phones that are increasing in computational power and capabilities.

- **What are the major challenges/gaps in these countries/regions in assuring successful bioinformatics capacities?**

Challenges are many and include poor internet connectivity and bandwidth in some areas, limited bioinformatics resources and funding and infrastructure, wide range of access to state-of-the-art computational tools and platforms for data management and data analysis, diverse range of bioinformatics skills and training opportunities, high disease burden and variety of health care infrastructure. Africa is not one country but many countries, many regions, many cultures and range of commitments from established universities and governments. Collaborations across Africa and with international collaborators are challenging for sharing data among collaborators at different institutions, especially if large and complex data sets and there are some services currently available.

A related issue is that there is limited funding for African clinicians and scientists to be supported financially to perform basic and clinical studies on African populations and communicable and non-communicable diseases in Africa as well as lack of infrastructure and data analysis capacity in Africa for large scale diverse data sets. In many cases, samples for analysis are sent to collaborators in other countries and data generation and analysis were not primarily performed in Africa.

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- **What are the actual or perceived benefits of bioinformatics capacity that have been communicated from the recipient countries/agencies in the regions where you work?**

Empowering African scientists with bioinformatics skills and infrastructure creates an environment that allows those generating data to analyse the data and have the data close in hand, even if it eventually will be shared in more public databases. International collaborations with African scientists to enhance research projects can continue but African scientists will have the knowledge they need in data analysis and will change how research is done in Africa and decrease continued dependency on international scientists for bioinformatics. Building bioinformatics infrastructure and capacity and increasing skills in Africa is a necessary as research has become data intensive enterprise. Hands-on-bioinformatics training on actual data sets generated in country is considered extremely valuable and serve to move the data toward publishable data and provide bioinformatics training for those who generated the data and extends bioinformatics expertise starting within a laboratory and adds expertise to a department or Center.

- **What are some of the challenges and opportunities in benefit/risk communication with decision makers and the public you have experienced?**

Challenges also include sustainability of computational infrastructure and equipment across Africa and increases in basic and clinical research support for African scientists to study diseases that affect African populations.

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Global Bioinformatics Capacity Mapping Consultation

Held March 8, 2018, at Department of State2201 C Street NW, Washington, DC

Meeting Summary

The Departments of State and Health and Human Services convened a consultation with U.S. federal agencies and senior representatives from the Bill and Melinda Gates Foundation (BMGF) on March 8, 2018. This meeting on bioinformatics capacity was a result of recommendations by agency representatives at the Dec. 5, 2018 U.S. Government Consultation on Pathogen Genetic Sequence Data (PGSD) to gain a better understanding of the challenges and opportunities surrounding role of global bioinformatics capacity in the surveillance, detection, treatment, and prevention of infectious diseases in low- and middle-income countries.

BMGF representatives shared the organization's strategic objective for bioinformatics capacity development, which is to move public health from a reactive posture to a strategic approach. The foundation's bioinformatics effort is aligned with the framing of the Global Health Security Agenda of prevent, detect, and respond. The BMGF is working to "democratize" sequencing by making catalytic investments in Africa (and South Asia) to build bioinformatics capacity. The "democratization of sequencing" focuses on open access/data access /open science.

The BMGF identified challenges to increasing data sharing and rapid data access, including academics not wanting to share their data immediately for fear of being "scooped" as well as commercial and university enterprises' concerns regarding privacy and patents and other intellectual property, among other issue. There are also concerns from governments that rapid sharing of surveillance data could adversely affect trade and commerce, especially in countries experiencing disease outbreaks. Countries also have concerns related to access and benefits sharing, seeking to realize monetary benefits for sharing biological samples from the country and, in some cases, data originating from those samples. The BMGF views bioinformatics capacity development as having multiple complex technical domains of sample collection, laboratory processing, digital sequencing, sequence analysis, database integration and information extraction. The BMGF is interested in pursuing a consortium of global stakeholders

and views this as the best approach to develop and implement a comprehensive solution for building needed bioinformatics capacity in different regions of the world.

Following the BMGF's presentation, each USG agency provided examples of its international efforts in bioinformatics development using a survey that was distributed prior to the meeting. (See attachments for agency survey responses.) Multiple common themes were identified during the discussion. Overall, there was consensus that the technical domains of sequence analysis, database integration and information extraction are the most challenging for the development of bioinformatics capacity building in middle- and lower-income countries. Current USG and external stakeholder efforts do not attempt to create a systematic approach to building global capacity with data sharing, but certain options for such an approach were discussed with a view toward addressing all technical domains. Any systematic approach would also have to address the shortage of bioinformaticians and other technical personnel in the host nations and the lack of IT infrastructure to support such a data-intensive endeavor.

The group discussed options for advancing international bioinformatics capacity. A viable effort would need to include a sustainable, multi-stakeholder "platform". This could be a consortium of donor countries, non-governmental organizations (e.g., Wellcome Trust, CEPI, Chan Zuckerberg, among others), research entities, industry and other private sector entities. Regional centers of excellence could also play an important role –this could be a place where the nascent Africa CDC could play an important role. Participants agreed that recipient/host countries should be involved (or work with donor countries) when identifying any tangible benefits from bioinformatics capacity development. This partnership would include host nation investment and an understanding that all parties are contributing something and all parties will benefit. It should not just be a matter of donor countries building capacity for host nations.

U.S. Government Only Discussion

U.S. government participants had a closed policy discussion following the meeting with the BMGF. Dr. Giovanni initiated the session's discussion by highlighting that the issues, challenges and opportunities discussed with the BMGF were not new. The U.S. government

agencies have been involved in data sharing issues internationally for at least the last 10 years. Dr. Giovanni shared that while significant challenges remain, measurable progress is being made in certain countries with data sharing and capacity building. However, there is a level of urgency to addressing bioinformatics and data sharing given discussions at the World Health Organization related to the sharing of pathogen genetic sequence data and under the Conventional on Biological Diversity related to "digital sequence information." In addition, all participants believed that the collection, storage and application of sequencing data are likely to explode in the near future into *predictive analytics*. (Predictive analytics makes predictions about unknown future using data mining and predictive modeling)

(b)(6) reminded the group that the conversation today stemmed from discussions regarding the Pandemic Influenza Preparedness Framework and questions of what data access and benefit sharing should look like for pathogen genetic sequence data. He proposed that the U.S. government has opportunities to refine international diplomacy efforts, determine U.S. government policy agendas and develop external narratives for future conversations. Further U.S. government discussions should help refine our thinking and good practices with external stakeholders. As we move forward, the U.S. government needs to hone and streamline its message and diplomatic strategy for future engagement with other potential external stakeholders and donor countries.

Agency representatives affirmed the critical need to continue internal USG dialogue and to expand the conversation with a broader group of intentional stakeholders. A summary of the main challenges facing bioinformatics capacity internationally, and next steps in moving forward to address these challenges, are summarized below.

Summary of main challenges

1) Building bioinformatics infrastructure on the ground, including IT infrastructure to handle the large volume of data, scientists, and bioinformaticians/computer programmers to handle analyses.
2) Building an international framework, platform, or consortium for genetic sequencing, data sharing, and information analysis". Most likely this will end up being a multilateral partnership with

government and nongovernmental partners. The BMGF suggested that building a software platform for this framework could be the type of catalytic investment opportunity they could make.

3) Articulating overall objectives and the USG efforts in a concise way.
4) Encouraging donor nations to join bioinformatics capacity building efforts/process.
5) Determine opportunities and challenges in improving global public health and US national security synergistically with the efforts GHSA and WHO PIP Framework, and other efforts.
6) Clearly communicate desired end-point in terms of GHSA's "prevent, detect, and respond" framing and the geopolitical goal of protecting the US role in harnessing and advancing the possibilities of a critical new technology.

Nest Steps:

1) Informed by the discussion with the Bill and Melinda Gates Foundation, the US government only discussion identified specific next steps to advance U.S. objectives regarding the international collection, use, and application of PGSD. Expand external stakeholder dialogue via a Federal Registry Notice soliciting public input on development and use of bioinformatics capacity to enhance global health security;
2) Develop a single concise paper that captures the scope, breadth and depth of the whole of the U.S. government efforts in supporting/advancing bioinformatics capacity internationally
3) Develop draft diplomatic strategy to engage other donor countries that may have a willingness to partner/collaborate on bioinformatics capacity building

Attachments:

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 11/15/2019 11:22:43 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; 'Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US)' [carl.c.holloway.civ@mail.mil]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; Cox, Edward M (FDA/CDER) [Edward.Cox@fda.hhs.gov]; 'Kishimori, Jennifer M COL USARMY OSD HA (US)' [jennifer.m.kishimori.mil@mail.mil]; 'Bavari, Sina CIV USARMY MEDCOM USAMRIID (US)' [sina.bavari.civ@mail.mil]; 'LeButt, Kimberly A CIV OSD OUSD ATL (US)' [kimberly.a.lebutt.civ@mail.mil]; 'Seedorff, Jennifer E' [SeedorffJE@state.gov]; Tobert, Gwen (STATE.GOV) [tobertgm@state.gov]; 'Pandemic-Response-OES@state.gov' [Pandemic-Response-OES@state.gov]; 'Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US)' [kayvon.modjarrad.civ@mail.mil]; 'Maher, Carmen T CIV USARMY DOD JPEO CBRND (US)' [carmen.t.maher.civ@mail.mil]; Walker, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4d03cc33ba5c4f15bd581b757dc9daa4-HHS-Robert.]; Boucher, David (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a5c89aa5b44a4042803c3d8ebd414d20-HHS-David.B]; Diaz-Diaz, Carol J (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=54ff795276224eab9847ff70e2693fd4-HHS-Carol.D]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Nichol, Stuart T (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b9c163136088456ab15b5378d90948b0-HHS-stn1-cd]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; 'safarnsworth@usaid.gov' [safarnsworth@usaid.gov]
CC: Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Tracy Carson [CarsonTL@state.gov]; Lamourelle, Gabrielle (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12371f75797c4de6aef3d8e072dc9373-HHS-Gabriel]; Burr, Mara (OS)

[/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e1f90440cd05403a8abf399c1c0f76a6-HHS-Mara.Bu]; Tracy Carson [CarsonTL@state.gov]

Subject: WHO R&D Blueprint TPPs for Nipah and Lassa Diagnostics Out for Comments

Attachments: who-cchf-tpp-dx-draft-v1-0.pdf; cchf-diagnostics-tpp-comment-form.doc; who-nipah-dx-tpps-d.pdf; nipah-diagnostics-tpp-comment-form.doc; ATT12262; ATT21072

Dear Colleagues,

The WHO R&D Blueprint team has published for comment draft target product profiles for Nipah and Lassa diagnostics (see below two emails). The emphasis of these TPPs is toward acute and early detection of disease during outbreaks. I have attached both TPPs here and they are also available via the below links. WHO asks that you please provide comments by Friday, December 13, using the comment forms provided for each TPP (also attached) and send them to the emails indicated below.

Best Regards,
Collin

Collin Weinberger, MPH
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U.S. Department of Health and Human Services
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collin.weinberger@hhs.gov

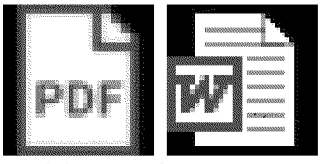
Dear Colleagues,

We are pleased to announce that a **WHO NIPAH diagnostics target product profile (TPP)** has been posted on the WHO website (https://www.who.int/news-room/articles-detail/nipah-diagnostics-target-product-profile) for a first round of call for comments.

All comments received by the published deadline (**Friday, 13 December 2019**) will be considered in the preparation of the next version of the TPP and will guide the development of effective diagnostics against this R&D Blueprint priority disease. Should you be interested in providing your feedback, please send your comments to NIPAHDxTPP@who.int with the subject line "Comments on draft NIPAH Diagnostics TPP" no later than COB Friday, 13 December 2019.

Thank you for further sharing this call for comments with others who may be interested in reviewing the TPP.

With many advanced thanks and kindest regards,
Virginia



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R&DBlueprint
Powering research
to prevent epidemics

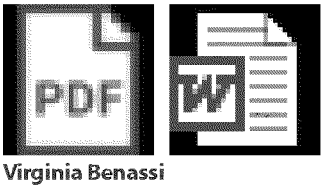
Dear Colleagues,

We are pleased to announce that a **WHO CCHF diagnostics target product profile (TPP)** has been posted on the WHO website (https://www.who.int/news-room/articles-detail/crimean-congo-hemorrhagic-fever-(cchf)-diagnostics-target-product-profile) for a first round of call for comments.

All comments received by the published deadline (**Friday, 13 December 2019**) will be considered in the preparation of the next version of the TPP and will guide the development of effective diagnostics against this R&D Blueprint priority disease. Should you be interested in providing your feedback, please send your comments to CCHFDxTPP@who.int with the subject line "Comments on draft CCHF Diagnostics TPP" no later than COB Friday, 13 December 2019.

Thank you for further sharing this call for comments with others who may be interested in reviewing the TPP.

With many advanced thanks and kindest regards,
Virginia



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Powering research
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3

WHO R&D Blueprint: Priority Diagnostics for CCHF

Use Scenarios and Target Product Profiles

4

Abstract

Documentation and coordination for diagnostic Target Product Profiles for CCHF as part of selected WHO R&D Blueprint and Roadmaps priority diseases in compliance with the WHO harmonized methodology

World Health Organization

This WHO TPP document should inform product developers, regulatory agencies, procurement agencies and funders on R&D and public health priorities, and is intended to facilitate the most expeditious development of products that address the greatest and most urgent public health need.

Table of Contents

Abbreviations

Ag	Antigen
BSL	Biosafety level
CCHF	Crimean-Congo haemorrhagic fever
CCHFV	Crimean-Congo haemorrhagic fever virus
CE	CE marking, Conformité Européene
CLIA	Chemiluminescence assay
CO, S/CO	Cutoff, Sample vs. cutoff signal
ECL	Electrochemiluminescence immunoassay
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
FDA	US FDA, Food and Drug Administration
IFA	Immunofluorescence assay
IgG	Immunoglobulin G (late immune response)
IgM	Immunoglobulin M (early immune response)
IU	International units
LAT	Latex agglutination test
LFA	Lateral flow assay (see RDT)
LMIC	Lower to middle income country
LOD	Limit of detection
LOQ	Limit of quantitation
mL	Milliliter
NAT	Nucleic acid test, also Nucleic acid amplification test
NPT	Near-patient (test used in a peripheral laboratory setting)
POC	Point of care (test used outside of a laboratory setting)
RDT	Rapid diagnostic test (lateral flow assay POC test)
RNA	Ribonucleic acid (viral nucleic acid)
RUO	Research use only
RT-PCR	Reverse transcriptase polymerase chain reaction
SRA	Stringent regulatory authority
TPP	Target product profile
uL	Microliter
USD	US dollar
WB	Western blot
WHO PQ	World Health Organization Pre-Qualification

WHO R&D Blueprint: Priority Diagnostics for CCHF

Introduction

The WHO R&D Blueprint for Action to Prevent Epidemics establishes a platform for R&D preparedness that is intended to accelerate research and product development in advance of and during epidemics caused by the world's most significant infectious disease threats.[1–4] The R&D Roadmaps are intended to focus and catalyze international R&D effort to ensure the coordinated development of medical countermeasures (diagnostics, therapeutics and vaccines) thus reducing the time for new medical technologies and products to reach affected countries in a public health crisis. For diagnostics in particular, the emphasis of the R&D Roadmaps is toward acute and early detection of disease during outbreaks.

The R&D Roadmap for Crimean-Congo Haemorrhagic Fever (CCHF) is the product of broad consultation with leading experts from CCHF-affected countries, international product R&D experts and other stakeholders.[5] In 2018 and 2019, Roadmap goals and strategic priorities were defined and updated for developing improved diagnostics, therapeutics, and vaccines for CCHF.[6,7] Part of the overarching vision for the CCHF Roadmap is 'to be able to reduce death and morbidity from CCHF through safe and affordable effective treatments informed by rapid, reliable, simple-to-use and easily accessible diagnostics by 2023'. The development and validation of *in vitro* diagnostic assays for CCHF is therefore a priority for the WHO R&D Roadmap to enable effective medical intervention and infection control in both centralized and decentralized settings.

This CCHF TPP document is intended to be a framework for facilitating the diagnostic development goals of the WHO R&D Roadmap for CCHF, following prioritization of the diagnostic needs identified in the R&D Roadmap for acute and early case detection of CCHF. Use scenarios have been developed to define the critical functionality for testing in centralized reference laboratories as well as decentralized/peripheral health center or district hospital settings.[a] These scenarios serve as a bridge to the target product profile (TPP), a detailed technical document for product development that describes the desired characteristics, features, and performance of diagnostics for a specific setting. Following expert consultation, the highest priority CCHF TPPs will be published to engage the diagnostic community for refinement and validation.

R&D Roadmap: Strategic Goals and Milestones for CCHF Diagnostics

Updated in 2019,[7] the CCHF R&D Roadmap outlines the strategic goal of 'affordable, qualified nucleic acid and serology tests accessible for use in CCHF-affected countries by 2020 followed by the development and introduction of near-patient and/or point-of-care tests by 2023. Specifically the R&D Roadmap prioritized the need for development and validation of 1) molecular diagnostics for pan-CCHFV detection

[a] Decentralized diagnostics are often described as point-of-care (POC) tests if they can be used at the bedside or community setting, or as near-patient (NPT) tests if they are intended to be used in an adjacent hospital or clinic laboratory.

for use in reference labs and near-patient settings, and 2) serology tests including ELISA and rapid diagnostic tests (RDTs). Specific diagnostic gaps were identified for quantitative viral RNA detection, lineage/clade coverage, sample type, antigen capture sensitivity, and sample collection/inactivation.

The Landmark milestones in the 2019 update include (*in chronological order*):

- By **March 2019**, define TPPs for molecular (RT-PCR) and serologic/antigen (IgM, Ag) CCHF diagnostic tests suitable for use (i) in reference laboratories and (ii) decentralised near-patient settings.
- By **2020**, through international collaboration, validation of commercial real-time RT-PCR tests (qualitative and quantitative) and serological tests using panels of well-characterised clinical samples that cover the main circulating CCHFV strains.
- By **2022**, develop and qualify one or more commercial tests suitable for near-patient diagnosis of CCHF, including evaluation in relevant healthcare settings in CCHF-affected regions to a standardised protocol.
- By **2022**, define TPPs for rapid point-of-care tests (with minimal requirements for biosafety precautions and staff training).
- By **2023**, develop and qualify commercial tests suitable for point-of-care use, including evaluation in relevant healthcare settings in CCHF-affected regions to a standardised protocol.

In summary, the CCHF R&D Roadmap Landmark milestones describe the identification, development, and validation of nucleic acid (RNA) and serologic/antigen tests (IgM, Ag) for use across reference laboratory, near-patient, and point-of-care settings. The timelines described above define the relative development priority for CCHF diagnostic TPP development:

1. CCHF RT-PCR – reference laboratory & near patient laboratory settings
2. CCHF IgM, Ag ELISA – reference laboratory & near patient laboratory settings
3. CCHF IgM, Ag RDT – lateral flow assay (LFA), point-of-care (POC) design

CCHF Diagnostic Overview

Diagnostic tests used to diagnose CCHF[8,9] include nucleic acid tests (NAT)[b] for RNA detection, serological (IgG, IgM) and antigen (Ag) capture, and virus isolation.[c] Active CCHFV infection can be detected by amplification of CCHFV RNA, or by the capture of CCHFV-specific IgM or viral antigen, or by a significant increase in CCHF-specific IgG titer following the acute phase of infection. For survivors, IgG antibodies can be detected long after acute viral infection.

NAT assays can detect active infection (CCHFV RNA) with the greatest sensitivity at the earliest time point. NAT tests can produce a qualitative or a quantitative result; a quantitative viral load test may provide

[b] For CCHF, RT-PCR is the most common type of NAT, however other nucleic acid test methods can be used.
[c] Virus isolation is rarely used because of the stringent biosafety containment (BSL-4) recommended for CCHF virus.

additional information on disease severity, effect of therapeutic interventions, and prognosis. Depending on the probe design, NAT assays can be sensitive (or insensitive) to genetic sequence.[d] A positive PCR test result indicates active CCHFV infection, however negative PCR may not rule out CCHFV infection due to variations in test sensitivity and genetic diversity of the virus.

Protein assays (ELISA, IFA, LFA) selectively capture CCHFV-specific antibodies or antigens, and are less impacted by genetic diversity, however it has been observed that severe cases of CCHFV infection may not mount a detectable antibody response. Given the observed range of CCHFV sequence diversity and immune response, it has been recommended that nucleic acid tests be used in combination with serological assays for highest clinical sensitivity,[10–12] though many low-resource settings may not have the capacity, especially at the early stages of an outbreak.[13]

Standardization. There is currently no "gold standard" or reference test for CCHF that is universally accepted. Further, there is a lack of standardization within the existing NAT and serology assays available for CCHF. Though several commercial tests are available, the majority of reference laboratories use in-house assays that were developed from regional circulating strains, providing limited diagnostic application across all clades and variants. Only a few of these tests have published data for external quality assurance (EQA) or proficiency testing. Moreover, there are no reference reagents (including International Standards) for calibrating and harmonizing assays.

Infrastructure and containment. Nucleic acid amplification is highly susceptible to contamination and typically requires laboratory infrastructure for containment (e.g. biosafety hood, clean room); several automated "self-contained" solutions have been successfully implemented for decentralized NAT testing.[14,15] ELISA tests can be run on the benchtop in a more modest laboratory environment, however a POC counterpart for ELISA-based antibody and antigen detection would be valuable. Antibody and antigen RDTs are designed for field use and are useful for rapid screening, but can fall short of the sensitivity needed for confirmation.

CCHF patient samples present an extreme biohazard risk and should only be handled under maximum biological containment conditions (BSL-3/4 where available) or unless inactivated[16,17] for processing in a more modest biosafety environment. Most peripheral laboratories have limited containment and would be better served by a minimal sample preparation protocol – preferably only specimen transfer into an enclosed cartridge or cassette, with diagnostic testing under enhanced BSL-2 conditions.[18]

Use Scenarios for High Priority CCHF Diagnostics

The CCHF R&D Roadmap recommended the development and validation of diagnostics for both reference laboratory and decentralized near-patient settings. Use scenarios help inform test design, specifically here in describing the setting for CCHF testing as it exists today: available infrastructure, skill level for test

[d] There are six (possibly seven) CCHF viral lineages/clades identified across Africa, Asia, Europe, and the Middle East. Clade I (Africa 3), Clade II (Africa 2), Clade III (Africa 1), Clade IV (Asia 1/Asia 2), Clade V (Europe 1), Clade VI (Greece), Clade VII (Iran-Kerman/22).

operation, anticipated test demand (at peak of outbreak), and timing for results. In this way, the use scenario serves as a bridge to the more detailed target product profile (TPP) characteristics for the diagnostic test features and performance.

The use scenarios below are intended for acute and early case detection during an outbreak of CCHF. Use Scenario 1 describes a typical LMIC reference laboratory; Use Scenario 2 describes a typical peripheral near-patient laboratory.[19] These scenarios are intended to highlight general features and challenges. For example, most central reference laboratories have the infrastructure for any test, however results may have a longer turnaround time due to specimen transport and batch processing. Decentralized testing can enable a more rapid intervention, however peripheral laboratories often lack the infrastructure for more complex tests. Other use scenarios can be designed for routine screening or surveillance for endemic disease (not included here).

Use Scenario 1: Reference laboratory

Use Scenario 1 describes the capacity for CCHF case detection in a reference laboratory setting, using specimens transported to the laboratory and processed in batch. Most central reference laboratories have the infrastructure for any test. Test results are generally available within 1-2 days, though sample transport and return of test results from reference laboratory to clinic often requires days to weeks.

Use Scenario 1: CCHF case detection in a reference laboratory	
Clinical Impact	Detection and confirmation of active CCHFV infection, preferably acute/early stages Quantitative result may indicate severity of infection
Use Setting	Reference laboratory (requires specimen transport) Resources typically include: biosafety hood, centrifuge, calibrated pipets, refrigerator, -20°C and -80°C freezers, network for specimen transport and storage
Target Population	Patient meeting the clinical definition of suspect CCHF, specimen transported from health care facility to reference lab
Test Demand (max)	Up to 100 specimens per day at peak outbreak (200-300 tests during convalescence[e])
Test Operator	Laboratory technician (2+ year certificate)
Test Complexity	Operators can reliably process high (≤ 5 steps) to moderate (≤ 3 steps) test complexity Capacity for manual sample preparation and processing in biosafety hood Capacity for daily/weekly external controls and calibration
Turnaround Time	Next-day test results (batch processing), may have 2 week turnaround to clinic

Use Scenario 2: Peripheral health center or district hospital

Use Scenario 2 describes the capacity for CCHF case detection at a peripheral laboratory setting, using specimens obtained within 1 hour from patients presenting to an adjacent health care facility. Peripheral

[e] If no access to RT-PCR testing (ELISA only)

laboratories typically have fewer resources and limited capacity for manual processing. Test results are can obtained within a day for rapid case management, preferably while the patient is still at the clinic.

Use Scenario 2: CCHF case detection in a near-patient laboratory	
Clinical Impact	Detection of active CCHFV infection for case management Detection of active CCHFV infection, preferably acute/early stages
Use Setting	Health care facility or near-patient hospital laboratory Resources may be limited: benchtop, microcentrifuge, transfer pipets, refrigerator
Target Population	Patient meeting the clinical definition of suspect CCHF, presenting to adjacent health care facility
Test Demand (max)	Up to 20 specimens per day at peak outbreak (up to 50 tests if multiple tests per patient)
Test Operator	Laboratory technician (1-2 year certificate); doctor, nurse, healthcare worker
Test Complexity	Operators can reliably process moderate (≤ 3 steps) to minimal (sample addition only) test complexity Little to no capacity for manual sample preparation and processing Capacity for weekly external controls
Turnaround Time	Same-day or next-day test results (can be while-you-wait test)

Target Product Profiles for CCHF Diagnostics

From the diagnostic use scenarios, target product profiles (TPPs) have been developed to provide detailed performance specifications for the tests needed for CCHF. TPP characteristics are typically described with a range for minimal to optimal performance specifications. Any diagnostic test is acceptable as long as performance falls within the range of parameters outlined in the TPP, however the preferred test is expected to meet most of the optimal performance specifications.

The TPPs presented below are designed for CCHFV test performance inclusive for near-patient laboratory and reference laboratory settings, as NPT platforms have demonstrated high performance even in low infrastructure settings.[14,15] TPP 1 is designed for a CCHFV NAT assay, TPP 2 is designed for a CCHFV ELISA assay, and TPP 3 is included for a CCHFV RDT. (Specifications for near-patient instrumentation are included as a separate TPP in Annex A.)

TPP 1: CCHF RT-PCR Assay

RT-PCR is the most common type of NAT test used for CCHF, and is used as a general descriptor for NAT testing. CCHF tests are needed that more broadly detect the circulating CCHFV clades (African clades I-III, Eurasian clades IV-VII), with appropriate clinical validation and quality assurance.

Specification	Minimal Performance	Optimal Performance
Intended Use	**Qualitative** RT-PCR test for detection of CCHFV RNA in human specimens for evidence of active CCHFV infection	**Quantitative** RT-PCR test for detection of CCHFV RNA in human specimens for evidence of active CCHFV infection

Kit Overview	Kit includes most assay components and reagents; user may supply third-party reagents (e.g. water or buffer) and consumables for sample collection and preparation	Kit includes all assay components and reagents; all materials required to test one patient are included in individually packaged, self-contained cartridge for cartridge-based platforms
Analytes	CCHFV RNA, validated for Eurasian clades IV-VII	CCHFV RNA, validated for Eurasian and African clades I-VII
Time to Result	<6 hours	<2 hours
Specimen Type	Plasma, serum, urine	Plasma, serum, urine, whole blood
Sample Input	≤ 1 mL	≤ 100 uL
Sample Preparation	Manual (conventional) sample prep for CCHFV RNA extraction and purification.	Automated or semi-automated sample prep: ≤3 manual steps.
Test Output	Qualitative: CCHFV detected/not detected above threshold	Quantitative: CCHFV IU/mL or Ct
Limit of Detection (LOD)	1000 IU/mL	100 IU/mL or Ct??
Linear Range (LOQ)	10^4 to 10^7 IU/mL	10^3 to 10^8 IU/mL or Ct15-Ct38
Clinical Sensitivity	≥95%	≥98%
Clinical Specificity	≥95%	≥98%
Cross Reactivity	No cross-reactivity with other endemic or syndromic pathogens	
Interfering Substances	No interference for individual or mixtures of analytes, endogenous/exogenous substances	
Assay Process Controls and Calibration[f]	Process may require external positive control Daily calibration for quantitative result	Internal full process control integrated into assay Weekly calibration for quantitative result
Third-Party Instrumentation	Centrifuge, calibrated pipettors, pipet tips, timer, miscellaneous lab consumables; -20C freezer, IPC sets, laboratory boxes, ventilation/negative pressure	Requires transfer pipettes only
Opened Kit Stability	2-8 °C for up to 3 hours prior to use	≤30 °C for up to 1 hour prior to use
Unopened Kit Storage and Shelf Life	-20°C (or dry ice) for transport, up to 6 months storage	No cold chain requirements for transport or storage: 12 months, 70% humidity from date of manufacture (based on stability studies) at up to 30°C
Biosafety/Disposal Requirements	Biohazard disposal as appropriate for potentially infectious material	Specimens deactivated and enclosed within cartridge; biohazard disposal (as appropriate)
Kit Certification	ISO 13485:2016 certified	ISO 13485:2016 certified; approved by stringent regulatory authority (SRA)
Price of Single Test	≤$30 USD at volume production	≤$10 USD at volume production

[f] Calibrated to international standard when available

TPP 2: CCHF ELISA Assay

ELISA tests for CCHF are typically limited to reference laboratories, as they require high biosafety containment to process CCHFV. In the case of CCHF, commercial ELISA tests are indicated for research-use only (RUO); clinically validated and quality-assured commercial tests for detection of active CCHFV infection are needed.

Specification	Minimal Performance	Optimal Performance
Intended Use	ELISA test for detection of CCHFV-specific human IgM or CCHFV Ag in human specimens for evidence of active CCHFV infection	ELISA test for detection of CCHFV-specific human IgM and CCHFV Ag in human specimens for evidence of active CCHFV infection
Kit Overview	Kit includes most assay components and reagents for 96-well plate or 12x8 strip format. User may supply some reagents (e.g. water or buffer) and some consumables for sample collection and preparation; 96-well plates or 12x8 strips are pre-coated with capture Ag/Ab	Kit includes all assay components and reagents. All materials required to test one patient are included in individually packaged, self-contained cartridge; 96-well plates or 12x8 strips are pre-coated with capture Ag/Ab
Analytes	IgM or Ag detection, validated for Eurasian clades IV-VII	IgM and Ag detection, validated for Eurasian and African clades I-VII
Time to Result	≤6 hours for 1x 96-well plate: 12 batched samples (including dilution series)	≤6 hours for 3x 96-well plates: 36 batched samples (including dilution series)
Specimen Type	Plasma, serum	Plasma, serum, whole blood, saliva (breastmilk)
Sample Input	≤5 mL venepuncture	≤200 uL
Sample Preparation	Manual (conventional) centrifugation and dilution of specimen for use in BSL-3/4	Inactivation protocol for use in BSL-2 sample preparation
Test Output	Qualitative (positive, negative) result as defined by signal (S) relative to an empirical cutoff (CO) established for each assay run	Semi-Quantitative (sample to cut-off value, S/CO) for calibrator dilution series
Limit of Detection (LOD)	Empirical cutoff (CO) for each assay run using positive and negative controls	Reference (statistical) methods to define an assay cut-off
Linear Range (LOQ)	Defined by "normal range" of positive specimen control dilution series	
Clinical Sensitivity	>85%	>90%
Clinical Specificity	>85%	>95%
Cross Reactivity	Minimal but characterized cross-reactivity with other endemic or syndromic pathogens	
Interfering Substances	No interference for individual or mixtures of analytes, endogenous/exogenous substances	
Assay Process Controls and Calibration[g]	Each run includes positive and negative controls – not supplied with kit	Each run includes positive and negative controls - lyophilized controls included in kit
Third-Party Instrumentation	Manual ELISA plate washer and reader, calibrated pipettors; IPC sets, laboratory boxes, ventilation/negative pressure	Automated ELISA plate washer, reader

[g] Calibrated to international standard when available

Opened Kit Stability	Diluents stable at 2-8°C until expired; reagent dilutions stable at RT for 1 working day	
Unopened Kit Storage and Shelf Life	-20°C (or dry ice) for transport and up to 6 months storage	Kit reagent stability 2-8°C for transport and up to 12 months storage
Biosafety/Disposal Requirements	Biohazard disposal as appropriate for potentially infectious material	Specimens deactivated and sealed within cartridge/microplate; biohazard disposal (as appropriate)
Kit Certification	ISO 13485:2016 certified	ISO 13485:2016 certified; WHO PQ or CE or FDA approved
Price of Single Test	≤$15 USD at volume production	≤$10 USD at volume production

TPP 3: CCHF RDT

RDTs are ideal screening tests, suitable for field testing and triage in low infrastructure settings. RDTs have been used to effectively screen and triage suspected high-risk cases of diseases such as Ebola and dengue [20,21], a RDT for screening of active CCHFV infection would be valuable.

Specification	Minimal Performance	Optimal Performance
Intended Use	Rapid lateral flow immunoassay (RDT) for detection of CCHFV-specific human IgM or CCHFV Ag in human specimens for evidence of active CCHFV infection	Rapid lateral flow immunoassay (RDT) for detection of CCHFV-specific human IgM and CCHFV Ag in human specimens for evidence of active CCHFV infection
Kit Overview	Kit includes rapid test cassette, buffer/developer solution, disposable transfer pipette	
Analytes	IgM or Ag detection, validated for Eurasian clades IV-VII	IgM and Ag detection, validated for Eurasian and African clades I-VII
Time to Result	≤30 minutes	≤10 minutes
Specimen Type	Plasma, serum (venepuncture)	Plasma, serum, whole blood (venepuncture and fingerstick)
Sample Input	≤100 uL of specimen	≤30 uL of specimen
Sample Preparation	Serum or plasma separation	None
Test Output	Qualitative: detected/not detected visual readout compared to full process control line	
Limit of Detection	Empirical cutoff (CO) established for each assay run using positive control	Signal detected over background at clinically relevant minimum
Linear Range	Defined by "normal range" of positive specimen control dilution series	
Clinical Sensitivity	>80% IgM, Ag	>90% IgM, Ag
Clinical Specificity	>90% IgM, Ag	>95% IgM, Ag
Cross Reactivity	Minimal but characterized cross-reactivity with other endemic or syndromic pathogens	
Interfering Substances	No interference for individual analytes, endogenous/exogenous substances	
Assay Controls and Calibration	Full process internal control, external positive/negative controls (not supplied with kit)	Full process internal control, external positive/negative controls (lyophilized, included in kit)

Third-Party Consumables	Timer, materials required for venepuncture or fingerstick	
Opened Kit Stability	Stable at 18-30°C for 1 working day	Stable at 15-40°C for 1 working day
Unopened Kit Storage / Shelf Life	Kit reagent stability 2-30°C for transport and up to 6 months storage	Kit reagent stability 2-30°C for transport and up to 12 months storage
Biosafety/Disposal Requirements	Biohazard disposal as appropriate for potentially infectious material	
Kit Certification	ISO 13485:2016 certified	ISO 13485:2016 certified; WHO PQ or CE or FDA approved
Price of Single Test	≤$15 USD at volume production	≤$10 USD at volume production

Conclusions

The WHO R&D Blueprint for Action to Prevent Epidemics and the R&D Roadmaps are intended to focus international R&D effort for medical countermeasures, and reduce the time for new medical technologies to reach affected countries in a public health crisis. Following the identification and prioritization of the diagnostics outlined in the 2019 CCHF R&D Roadmap, the development priorities for CCHF testing have been further described here as target product profiles (TPP).

The TPPs in this document are intended to catalyze the development of diagnostic tests to detect active CCHFV infection, specifically for early detection of regional and globally circulating clades in the event of an outbreak. TPPs were developed for RT-PCR and ELISA tests that could be implemented in both centralized and decentralized settings (including a RDT TPP), and clinically validated across the broad geographic distribution of CCHF.

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Annex A

TPP for NPT Automated Platform

The TPP presented below is intended to provide platform specifications for decentralized, instrument-based testing for CCHF.

Specification	Minimal Performance	Optimal Performance
Platform Overview	Semi-automated platform with external sample preparation	Fully automated platform with integrated sample preparation
Throughput	Up to 20 samples per 8-hour day, capacity for random access (spot testing)	Up to 100 samples per 8-hour day, capacity for random access (spot testing)
Dimensions	Benchtop approx. 60 cm x 60 cm, <60 kg	Benchtop approx. 30 cm x 30 cm, <20 kg
Power Requirements	110-220 V AC, external/internal UPS	110-220 V AC
Data Readout	Visual readout via on-board or attached computer display	Same as minimal, including on-board algorithms for data interpretation with simple 'final result' readout and connectivity to data network for direct data transfer
Training Required	<5 days training for skilled laboratory technicians	<3 days for minimally skilled medical personnel (minimal laboratory training)
System Maintenance	Daily preventative maintenance <30 min; Mean time between failures: 12 months or 10,000 tests	Weekly preventative maintenance <30 min; Automated alert for errors or warnings; Mean time between failures: 24 months or 20,000 tests
System Calibration	Annual service call for calibration	Remote calibration service
Connectivity	USB interface, Integrated Local Network (LAN) port, local printer port.	Same as minimal, also supports connectivity to data network with end-to-end encryption.
Sample ID and Tracking	None – manual sample identification and tracking	Software-enabled unique identifiers for assay and sample, with accessory barcode, RFID, or other reader
Environmental Stability	Operation within 15°C-30°C	Operation within 10°C-40°C
Platform Certification	ISO 13485:2016 certified	ISO 13485:2016 certified; WHO PQ or CE or FDA approved
List Price of Platform	<$50,000 USD	<$25,000 USD

Comment Form: Crimean-Congo hemorrhagic fever (CCHF) diagnostics Target Product Profile

Please send your comments to [HYPERLINK "mailto:CCHFDxTPP@who.int"] no later than COB Friday, 13 December 2019

Reviewer's Name in Full, Title, Institution, City, Country, Tel., Email address:

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WHO R&D Blueprint: Priority Diagnostics for Nipah

Use Cases and Target Product Profiles

Abstract

Documentation and coordination for diagnostic Target Product Profiles for Nipah as part of selected WHO R&D Blueprint and Roadmaps priority diseases in compliance with the WHO harmonized methodology

World Health Organization

This WHO TPP document should inform product developers, regulatory agencies, procurement agencies and funders on R&D and public health priorities, and is intended to facilitate the most expeditious development of products that address the greatest and most urgent public health need.

Table of Contents

Abbreviations

Ag	Antigen
BSL	Biosafety level
CE	CE marking, Conformité Européene
CedV	Cedar virus
CO, S/CO	Cutoff, Sample vs. cutoff signal
EIA	Enzyme immunoassay (also, ELISA)
ELISA	Enzyme-linked immunosorbent assay
HeV	Hendra virus
IFA	Immunofluorescence assay
IgG	Immunoglobulin G (late immune response)
IgM	Immunoglobulin M (early immune response)
LAMP	Loop-mediated isothermal amplification
LAT	Latex agglutination test
LFA	Lateral flow assay
LMIC	Lower to middle income country
MCM	Medical countermeasure
mL	Milliliter
NAT	Nucleic acid test (also, nucleic acid amplification test)
NiV	Nipah virus
NPT	Near-patient (appropriate for hospital-adjacent laboratory)
NRA	National regulatory authority
POC	Point-of-care (appropriate for bedside and field testing)
RDT	Rapid diagnostic test (also, lateral flow assay)
RNA	Ribonucleic acid (viral nucleic acid)
RT-PCR	Reverse transcriptase polymerase chain reaction
TPP	Target product profile
uL	Microliter
USD	US dollar
WHO PQ	World Health Organization Pre-Qualification

WHO R&D Blueprint: Priority Diagnostics for Nipah

Introduction

The WHO R&D Blueprint for Action to Prevent Epidemics establishes a platform for R&D preparedness that is intended to accelerate research and product development in advance of and during epidemics caused by the world's most significant infectious disease threats.[1–4] The R&D Roadmaps are intended to focus and catalyze international R&D effort to ensure the coordinated development of medical countermeasures (diagnostics, therapeutics, vaccines) thus reducing the time for new medical technologies and products to reach affected countries in a public health crisis. For diagnostics in particular, the emphasis of the R&D Roadmaps is toward acute and early detection of disease during outbreaks.

The Nipah Research and Development (R&D) Roadmap is the product of broad consultation with leading experts from Nipah-affected countries, international R&D diagnostic experts and other stakeholders for collaborative development of high priority medical countermeasures (MCMs) to prevent and control NiV outbreaks and disease in humans.[5] In 2018 and 2019, the Nipah R&D Roadmap was updated as a 5-year framework for identifying the vision, underpinning strategic goals, and prioritizing areas and activities for developing improved MCMs in diagnostics, therapeutics, and vaccines for NiV.[6] For diagnostics, the strategic goals were defined to reduce death and morbidity from NiV through interventions informed by rapid, reliable, and well-characterized tests, reagents and standards by 2020. The development and validation of *in vitro* diagnostic assays for NiV is a part of the collaborative development of high priority WHO R&D Roadmap MCMs to enable effective NiV infection prevention and control.

This NiV target product profile (TPP) document is intended to be a framework for facilitating the diagnostic development goals of the WHO R&D Roadmap for NiV, following the identification and prioritization of the diagnostic needs outlined in the R&D Roadmap. Use cases have been developed to define the critical functionality of diagnostic testing in the setting where it is most needed. The use case serves as a bridge to the TPP, a more detailed technical document for product development that describes the product's desired characteristics, features, and performance. High priority TPPs have been developed for the top priority NiV diagnostic test(s) and published to engage the diagnostic community for refinement and validation.

R&D Roadmap: Strategic Goals and Milestones for NiV Diagnostics

The 2019 Nipah R&D Roadmap identified the primary challenges for NiV that can lead to delays in diagnosis, outbreak investigation, and response. For NiV, there is a need for diagnostic tests with high sensitivity and specificity for early detection of NiV infection in humans, particularly given its nonspecific (febrile) symptoms.[7] The Nipah R&D Roadmap identified the key priority actions needed to drive new NiV diagnostic test development, further developed below as use cases for how and where diagnostics should

be implemented, and target product profiles (TPPs) to define the specific performance characteristics for high priority NiV diagnostics:

- **Screening for active NiV infection.** Rapid screening is needed for suspected cases of active NiV infection, to support early outbreak detection and case management, and to ensure early implementation of infection control measures. There is a particular need for rapid first-line screening options, particularly in peripheral settings.
- **Confirmation of active NiV infection.** Rapid confirmatory testing is needed for active NiV infection, preferably with high sensitivity to all relevant NiV strains and specificity to differentiate from other febrile diseases, including henipaviruses, with rapid turnaround to initiate the appropriate medical countermeasures.

The R&D Roadmap set strategic goals thorough 2022 for the development of at least two point-of-care (POC) or near-patient (NPT) NiV diagnostics that are affordable, appropriately sensitive for first-line screening and for confirmation, and sufficiently robust for a range of peripheral settings.[a]

The Landmark milestones in the 2019 R&D Roadmap include (*in chronological order*):

- By **2019**, generate NiV diagnostic TPPs that identify the primary use cases and optimal and desirable characteristics to guide the development of promising NiV diagnostic assays.
- By **2019**, engage appropriate international and national regulatory authorities (NRAs) to inform commercialization pathways for NiV diagnostic assays.
- By **2021**, complete preclinical evaluation for at least two of the most promising NiV POC or NPT diagnostic assays that align with the TPP.
- By **2022**, complete field studies for at least two of the most promising NiV POC or NPT diagnostic assays that align with the TPP.

The NiV Roadmap also identified parallel efforts needed to support diagnostic test development and implementation, including 1) a specimen repository (held and maintained in the countries of origin) to assess and validate diagnostic tests, 2) international reference standards to calibrate diagnostic test performance, 3) validation of new diagnostics in endemic and at-risk geographic regions using defined performance and use criteria, 4) committed laboratory support for diagnostic test implementation, proficiency testing, and field monitoring (post-market surveillance), and 5) improved diagnostic preparedness in at-risk areas with appropriate deployment strategies for different geographic areas.

[a] Decentralized diagnostics are often described as point-of-care (POC) tests if they can be used at the bedside or community setting, or as near-patient (NPT) tests if they are intended to be used in an adjacent hospital or clinic laboratory.

NiV Diagnostics Overview

Nipah virus (NiV) is a highly pathogenic virus with potential for zoonotic and human transmission, with few options for treatment and prevention.[8,9] Early diagnosis of NiV infection is critical for containment of an outbreak and to facilitate appropriate patient care. NiV symptoms are similar to other febrile diseases including encephalitis with features of acute brain dysfucntion.[10,11] NiV infection often occurs in rural locations with minimal laboratory facilities, however there are currently no tests appropriate for remote settings. Moreover, diagnostic laboratories in district level and tertiary hospitals lack the biosafety infrastructure required to handle highly fatal pathogens like NiV.

Diagnostic tests used to detect NiV include nucleic acid tests (NAT), enzyme-linked immunosorbent assay (ELISA), immunofluorescence assay (IFA), and virus isolation.[12–14] ELISA IgM or Ag have been used for first-line testing for active infection, followed by serum neutralization or PCR as a confirmatory test.[5,17] ELISA IgG is more useful in epidemiological and surveillance studies for retrospective diagnosis. Newer ELISAs enable pan-henipavirus (NiV and HeV) detection, as well as some differentiation between NiV and HeV.[18,19] Increasingly, PCR is used for first-line NiV testing where available. Virus isolation is not a first-line test in due to the challenges with containment and processing time.[15,16]

In general, ELISA tests can be run on the benchtop in a modest laboratory environment, while rapid diagnostic tests (RDTs) are simple enough to be used for rapid screening in field or community settings. Newer automated NAT platforms have been developed for decentralized testing, and have been successfully implemented in the field under outbreak conditions.[20–23]

Standardization. Currently there are few standardized or regulated tests for NiV. The majority of international labs use "in-house" assays rather than commercial kits, with significant variation in reagents, methods, and instrumentation.[10,11] Clinical validation of NiV assays and kits has also been a challenge due to a lack of NiV-positive specimens and reference reagents (including International Standards) for calibrating and harmonizing assays. Strain variation of NiV between and within countries is still an open question for diagnostic sensitivity.

Containment. Pathogen containment in the field is a major concern during a NiV outbreak. Henipaviruses (NiV and Hendra virus, HeV) are classified as a Biosafety Level-4 (BSL-4) pathogens which require the highest containment infrastructure of a reference laboratory.[24,25] Most NiV patients are identified in peripheral settings, which typically have modest-to-minimal support infrastructure. Peripheral testing would be better served by a minimal protocol for sample preparation under enhanced BSL-2 conditions. For field testing, a "best practices" approach could be served by providing infrastructure for viral inactivation prior to testing, e.g. patient samples aliquoted directly into lysis buffer or trizol, or heat inactivated prior to testing.[12,14,24]

Use Cases for High Priority Nipah Diagnostics

Diagnostic use cases are helpful to identify the infrastructure and resources of the setting where tests are needed. Use cases typically identify the intended use, target patient population, personnel and skill level, and any limitations that may be imposed by the setting – characteristics which help identify the setting-appropriate diagnostic options. In this way, the use case serves as a bridge to the target product profile for the preferred diagnostic test's features and performance.

The Nipah R&D Roadmap recommended the development of diagnostics for rapid screening and confirmation of active NiV infection.[b] Use Case 1 describes the need for rapid detection of active NiV infection at a peripheral health center (highest priority setting), and Use Case 2 describes the need for standardized confirmatory testing performed at a central reference laboratory. These use cases are intended to highlight capacity and challenges for NiV testing during an outbreak. For example, decentralized or community-based testing can enable more rapid outbreak detection and intervention, however peripheral facilities often lack the infrastructure for higher complexity tests.

Use Case 1: Rapid detection of active NiV at a peripheral health center or hospital

Use Case 1 describes the need for detection of active NiV infection at a peripheral setting during an outbreak, ideally for rapid screening of patients who meet the clinical definition of suspected NiV infection.[25] Diagnostic test results should be available within the same day for rapid case management, preferably while the patient is still present for triage.

Active NiV infection is generally screened by detection of NiV-specific IgM, NiV antigen (Ag), or NiV RNA. For peripheral settings, diagnostic options for screening can include ELISAs, lateral flow assays (LFAs), latex agglutination assays (LATs), and NPT/POC NAT platforms.

Use Case 1: Rapid detection of active NiV infection in a peripheral setting	
Clinical Impact	Rapid detection of active NiV infection to support early outbreak detection and case management, and to ensure early implementation of infection control measures Confirmation should identify NiV from other diseases including henipaviruses.
Use Setting	Primary care facility, near-patient hospital laboratory, community clinic Resources may be limited: benchtop, microcentrifuge, transfer pipets, refrigerator
Target Population	Patient meeting the clinical definition of suspect NiV, presenting to health care facility
Test Demand (max)	Up to 50 specimens per day at peak outbreak for screening Up to 20 specimens/day for confirmation

[b] Diagnostics for peripheral settings are often described as point-of-care (POC) tests if they can be used at the bedside or community setting, or as near-patient (NPT) tests if they are intended to be used in an adjacent hospital or clinic laboratory.

Test Operator	Laboratory technician (1-2 year certificate); doctor, nurse, healthcare worker
Test Complexity	Lab tech can reliably process moderate test complexity (≤ 3 steps) but preferably minimal (sample addition only) processing Minimal to no capacity for manual sample preparation; preferably BSL-1 containment
Turnaround Time	Same-day or next-day test results (can be while-you-wait test)
Appropriate Diagnostic Options	Screening tests: RDT, ELISA, NPT/POC NAT Confirmatory tests: NPT/POC NAT

Use Case 2: Confirmation of active NiV infection at a centralized reference laboratory

Use Case 2 below describes the confirmation of active NiV infection in a centralized laboratory setting, using specimens transported to the laboratory and processed in batch. Test results are generally available within 1-2 days, though sample transport and return of test results from reference laboratory to clinic often requires several days to weeks.

Active NiV infection can be confirmed by detection of NiV RNA or viral culture. For a reference laboratory setting, diagnostic options for confirmation can include laboratory NAT, NPT/POC NAT assays, virus isolation (if BSL-3/4 available), and serum neutralization assays. Typically virus isolation and neutralization take days to weeks for processing.

Use Case 2: Confirmation of active NiV infection at a centralized reference laboratory	
Clinical Impact	Detection of NiV infection to support early outbreak detection and case management, and to ensure early implementation of infection control measures; may also be used for vaccine and therapeutic trials Quantitative result may indicate severity of infection
Use Setting	Reference laboratory (typically requires specimen transport) Resources typically include: biosafety hood, centrifuge, calibrated pipets, refrigerator, -20°C and -80°C freezers, network for specimen transport and storage BSL-3/4 containment not typical
Target Population	Patient meeting the clinical definition of suspect NiV, or screening-positive specimen transported from health care facility to reference lab Patient inclusion criteria for vaccine (NiV negative) or therapeutic (NiV positive) trials
Test Demand (max)	Up to 100 specimens per day at peak outbreak
Test Operator	Laboratory technician (2+ year certificate)
Test Complexity	Operators can reliably process high complexity (≤ 5 steps) to moderate (≤ 3 steps) process Capacity for manual sample preparation and processing in biosafety hood Capacity for daily/weekly external controls and calibration
Turnaround Time	Next-day test results (batch processing), may have 1-2 week turnaround to clinic

Appropriate Diagnostic Options	NPT/POC NAT, laboratory NAT, virus isolation, serum neutralization

Target Product Profiles for NiV Diagnostics

The target product profiles (TPPs) below present the highest priority diagnostic needs as identified in the R&D Roadmap: NPT/POC rapid screening for active NiV infection in a peripheral setting (**TPP 1**) and NPT/POC rapid confirmation of active NiV infection in a peripheral setting (**TPP 2**). TPPs provide highly detailed specifications for new diagnostic test development, within a range from minimal to optimal performance characteristics. A diagnostic test is acceptable as long as performance meets the minimal requirements, however the preferred diagnostic test is expected to meet most of the optimal performance specifications.

TPP 1: NPT/POC test for rapid screening of active NiV infection

For peripheral settings, tests for first-line screening should require minimal infrastructure and training, and provide adequate precautions for safe specimen handling. ELISA tests can be implemented in some near-patient laboratories, though LFAs (specifically the cassette-based RDT format) better match the limitations for clinic or community-based screening. RDTs are commonly used for POC testing and are easy to use, but can be less sensitive than laboratory tests due to tradeoffs in simplicity. Presently there are no RDTs for NiV.

Henipaviruses have high homology across the G, N, and P proteins, making it difficult to differentiate between NiV, HeV, and Cedar (CedV) virus by antibody or antigen detection. A general henipavirus RDT could be useful, provided that confirmatory testing can provide greater test specificity.

Specification	Minimal Performance	Optimal Performance
Intended Use	Detection of NiV-specific IgM **or** NiV Ag in patients meeting clinical criteria for NiV infection	Detection of NiV-specific IgM **and** NiV Ag in patients meeting clinical criteria for NiV infection
Kit Overview	**ELISA kit** includes most assay components and consumables. User may supply some reagents (e.g. water or buffer) and some consumables for sample collection and preparation	**RDT kit** (single-use lateral flow immunoassay) includes all assay components and consumables required to test one patient in individually packaged, self-contained cartridge
Analytes	NiV-specific IgM **or** Ag capture using recombinant NiV proteins and antibodies, validated for NiV-B and NiV-M strains	NiV-specific IgM **and** Ag capture using recombinant NiV proteins and antibodies, validated for NiV-B, NiV-M strainsalong with Cambodian, Thai, and Philippine variants
Time to Result	≤ 4 hours	≤ 30 minutes
Specimen Type	Serum	Serum, plasma, whole bloodoral fluid

Sample Input	≤ 500 uL of specimen(serum)	≤ 50 uL of specimen (serum, plasma, blood, oral fluid)
Sample Preparation	Biosafe collection; Inactivation protocol for BSL-2 sample preparation (heat inactivation or lysis)	Biosafe collection; field Field-appropriate inactivation protocol (aliquot into lysis buffer or similar)
Test Output	Instrument readout: detected/not detected above threshold	Visual readout: detected/not detected visual readout compared to internal full process control line
Limit of Detection	Empirical cutoff (CO) threshold established for each assay run using positive control	NiV analyte signal detectable by human eye (empiric faint positive threshold)
Linear Range	Defined by "normal range" of positive specimen control dilution series	
Clinical Sensitivity	>90%	> 95%
Clinical Specificity	> 80% for NiV/henipavirus genus	> 90% for NiV/henipavirus genus
Cross Reactivity	Minimal but characterized cross-reactivity with other endemic or syndromic pathogens Anticipated cross-reactivity with other henipaviruses, henipah paramyxoviruses	
Interfering Substances	No interference for individual or mixtures of analytes, endogenous/exogenous substances	
Assay Controls and Calibration	External positive and negative controls	Full process internal control, external positive/negative controls (lyophilized, included in kit)
Third-Party Consumables	ELISA microwell plates, calibrated pipettors/tips	Timer, materials required for venepuncture or fingerstick
Third-Party Instrumentation	ELISA plate washer and reader	None
Opened Kit Stability	Test components stable at 18-30°C for 1 working day, reagents stable at 2-8°C until expired	Test components stable at 15-40°C for 1 working day
Unopened Kit Storage, Shelf Life	Kit reagent stability 2-8°C (or dry ice) for transport and up to 6 months storage	Test kit stability 2-30°C for transport and up to 12 months storage
Biosafety/Disposal Requirements	Biohazard disposal as appropriate for potentially infectious material	Specimens sealed within single-use disposable; biohazard disposal (as appropriate)
Kit Certification	ISO 13485:2016 certified	ISO 13485:2016 certified; approved by stringent regulatory authority (SRA)
Price of Single Test	≤$10 USD at volume production	≤$3 USD at volume production

TPP 2: NPT/POC test for rapid confirmation of active NiV infection

Diagnostic tests are needed that can rapidly confirm active NiV infection in peripheral settings, with appropriate clinical validation and quality assurance of reproducibility. NPT/POC nucleic testing platforms have been implemented for confirmatory testing in decentralized settings, and employed for a more rapid turnaround in higher infrastructure settings. Presently there are no validated NPT/POC NAT tests for NiV.

NAT assays can be used for tandem screening and confirmation, provided the assay targets two or more distinct genomic regions; distinct targets also reduce the risk of false negatives that can arise from genomic mutations. RT-PCR is the most common type of NAT test used for NiV detection,[c] and is used below (without limitation) as the NiV assay.

Specification	Minimal Performance	Optimal Performance
Intended Use	RT-PCR test for detection of NiV (main circulating strains) and differentiation from HeV	RT-qPCR test for detection and confirmation of NiV (main circulating strains) and differentiation from other henipaviruses, henipah paramyxovirus
Platform Overview	Semi-automated platform with manual sample preparation	Fully automated platform with integrated sample preparation
Kit Overview	Kit includes most assay components and reagents in an individually packaged, self-contained cartridge; user may supply some reagents and consumables for sample collection and preparation	Kit includes all components required to test one patient, and all assay reagents in an individually packaged, self-contained cartridge
Throughput	Up to 20 samples per 8-hour day	Up to 100 samples per 8-hour day, capacity for random access (spot testing)
Analytes	NiV RNA, validated for at least one genomic target for detection of NiV-B and NiV-M strains	NiV RNA, validated for at least 2 distinct genomic targets for detection of NiV-B, NiV-M strains along with the Cambodian, Thai,Philippine variants
Time to Result	<6 hours	<2 hours
Specimen Type	Plasma, serum	Blood, plasma, serum, /oral fluid, saliva, CSF, brain tissue
Sample Input	≤ 1 mL	≤ 100 uL
Sample Preparation	Manual or semi-automated (≤3 steps) sample prep for RNA extraction and purification; inactivation protocol for BSL-2 sample preparation (heat inactivation or lysis)	Automated sample prep (sample addition only); field-appropriate inactivation protocol (aliquot into lysis buffer or similar)

[c] Loop-mediated isothermal amplification (LAMP) has also been recently developed for NiV[26]

Test Output	Qualitative: NiV detected/not detected above threshold	Quantitative: NiV copies/mL
Limit of Detection	1000 copies/mL	100 copies/mL
Linear Range	Qualitative only	10^2 to 10^9 copies/mL
Clinical Sensitivity	≥95%	≥98%%
Clinical Specificity	≥95%	≥98%
Cross Reactivity	No cross-reactivity with other endemic or syndromic pathogens (henipaviruses or henipah paramyxoviruses)	
Interfering Substances	No interference for individual or mixtures of analytes, endogenous/exogenous substances	
Assay Process Controls	Process may require external negative and positive control	Internal full process control integrated into assay to ensure sample integrity
Assay Calibration	Daily external positive/negative calibration for quantitative result	Weekly external positive/negative calibration for quantitative result
Third-Party Instrumentation	Centrifuge, calibrated pipettors, pipet tips, timer, miscellaneous lab consumables	Requires transfer pipettes only
Opened Kit Stability	2-8 °C for up to 3 hours prior to use	≤30 °C for up to 3 hours prior to use
Unopened Kit Storage, Shelf Life	-20°C (or dry ice) for transport, up to 6 months storage	No cold chain requirements for transport or storage: 12 months, 70% humidity from date of manufacture (based on stability studies) at up to 30°C
Biosafety/Disposal Requirements	Biohazard disposal as appropriate for potentially infectious material	Specimens deactivated and enclosed within cartridge; biohazard disposal (as appropriate)
Dimensions	Benchtop approx. 60 cm x 60 cm, <60 kg	Benchtop approx. 30 cm x 30 cm, <20 kg
Power Requirements	110-220 V AC, external/internal UPS	110-220 V AC
Data Readout	Visual readout via on-board or attached computer display	Same as minimal, including connectivity to data network for direct data transfer
Training Required	<2 days training for skilled laboratory technicians	<2 days for minimally skilled medical personnel (minimal laboratory training)
Test Process Controls	Process may require external negative and positive control	Internal full process control integrated into assay
Calibration	Daily external positive/negative calibration for quantitative result	Weekly external positive/negative calibration for quantitative result
System Maintenance	Daily preventative maintenance <30 min; Mean time between failures: 12 months or 10,000 tests	Weekly preventative maintenance <30 min; Automated alert for errors or warnings; Mean time between failures: 24 months or 20,000 tests

System Calibration	Annual service call for calibration	Remote calibration service
Connectivity	USB interface, Integrated Local Network (LAN) port, local printer port.	Same as minimal, also supports connectivity to data network with end-to-end encryption.
Sample ID and Tracking	None – manual sample identification and tracking	Software-enabled unique identifiers for assay and sample, with accessory barcode, RFID, or other reader
Environmental Stability	Operation within 15°C-30°C	Operation within 10°C-40°C
Kit and Platform Certification	ISO 13485:2016 certified	ISO 13485:2016 certified; WHO PQ or CE or FDA approved
List Price of Platform	<$50,000 USD	<$25,000 USD
Price of Single Test	≤$30 USD at volume production	≤$10 USD at volume production

Conclusions

The WHO R&D Blueprint for Action to Prevent Epidemics and the R&D Roadmaps are intended to focus and catalyze international R&D effort for medical countermeasures, and reduce the time for new medical technologies and products to reach affected countries in a public health crisis. Following the initial work of identification and prioritization of the diagnostic needs outlined in the Nipah R&D Roadmap, the diagnostic development priorities for NiV have been further described in this document as Use Cases and Target Product Profiles.

The TPPs in this document are intended to catalyze the development and validation of diagnostic tests to detect active NiV infection, specifically for early detection of regional strains in the event of an outbreak. TPPs were developed for rapid screening and confirmation testing that could be implemented in decentralized settings, specifically for high quality and validated diagnostics appropriate for remote patient settings. Following internal WHO consultation and consensus, these top priority NiV diagnostic TPP(s) will be published to engage the diagnostic community for refinement and validation.

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Comment Form: Nipah Virus diagnostics Target Product Profile

Please send your comments to [HYPERLINK "mailto:NIPAHDxTPP@who.int"] no later than COB Friday, 13 December 2019

Reviewer's Name in Full, Title, Institution, City, Country, Tel., Email address:

Name:
Title:
Institution:
City:
Country:
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Locator (Page & Line No)	**Comment**	**Suggested Amendment**	**Internal Use Only [blank]**

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Subject: RE: OGA Adjusted Dosing Paper

Attachments: Adjusted Vx Dosing HHS Position Options 06_05_2019 clean.docx; Ebola Vaccine Reduced Dosing Options Assessment Matrix 06_05_2019.docx

Dear All,

I've attached an updated version of the options paper, with some edits to reflect the discussions yesterday during our call and today at the DLG, as well as typo fixes. One significant change is (b)(5)

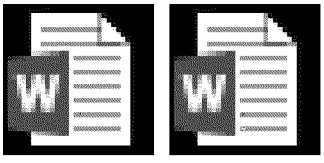
(b)(5)

(b)(5). This is an option that WHO discussed in their presentation of the modeling data on May 24th and which we initially included in the paper, but pulled out of an earlier version for simplicity when we were focused on the question of the use of the 1/5 DRC dose. However, given recent discussions about potential operational challenges and other considerations beyond the science, I thought would be better to add it back into the document. CDC Modelers—please note that I included a request to add in the latest estimates for how long the vaccine supply would last with this strategy.

I have also attached a decision matrix that Michael Mair from FDA developed, which presents the data and considerations outlined in the memo in a different way and makes it a little easier to compare across the different potential strategies based on different criteria. This could be a really excellent complement to the memo and particularly useful for discussions at the DLG.

We would welcome your feedback and edits on both documents. The options paper is still quite long, so would also welcome any suggestions for how to condense/streamline it for leadership.

Best,
Collin



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Subject: OGA Adjusted Dosing Paper

Hello, everyone. I just wanted to start a new message thread here so that Collin can jump on later this afternoon with an update on the OGA Adjusted Dosing paper that we discussed yesterday.

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From: Armand Sprecher [Armand.Sprecher@brussels.msf.org]
Sent: 9/27/2018 3:38:00 AM
To: Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; 'BENASSI, Virginia' [benassiv@who.int]; aug@alima.ngo; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; michael.jacobs@ucl.ac.uk; Rebecca GRAIS [Rebecca.GRAIS@epicentre.msf.org]; Mulangu Sabue [(b)(6)]@yahoo.fr]; timo.wolf@kgu.de; mvitek@samaritan.org; Cavaleri Marco [marco.cavaleri@ema.europa.eu]; richard.kojan@alima.ngo; Browne, Sarah [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=43044a5f1d3c4548b627436ddd2d7fcd-Sarah.Brown]
CC: PREZIOSI, Marie-pierre [preziosim@who.int]; RIVEROS BALTA, Alina Ximena [lauriex@who.int]; DIAZ, Janet Victoria [diazj@who.int]; DIXIT, Devika [dixitd@who.int]; GSELL, Pierre [gsellp@who.int]
Subject: Re: [Non-DoD Source] RE: Follow up - EVD Therapeutics and Vaccines for compassionate PEP use Working Group

Thanks Sina. Good to have this.

Armand Sprecher MD MPH
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From: Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil>
Sent: Saturday, September 22, 2018 1:03:37 AM
To: Cox, Edward M; 'BENASSI, Virginia'; aug@alima.ngo; Gruber, Marion; michael.jacobs@ucl.ac.uk; Rebecca GRAIS; Mulangu Sabue; timo.wolf@kgu.de; mvitek@samaritan.org; Cavaleri Marco; richard.kojan@alima.ngo; Armand Sprecher; Browne, Sarah
Cc: PREZIOSI, Marie-pierre; RIVEROS BALTA, Alina Ximena; DIAZ, Janet Victoria; DIXIT, Devika; GSELL, Pierre
Subject: RE: [Non-DoD Source] RE: Follow up - EVD Therapeutics and Vaccines for compassionate PEP use Working Group

All,
Based on our discussions we examined Favi and Remdesivir activities against VSV. Below is the initial data from our screening group. I will plot the data and send it to the group next week.

"- T705 (Favi) inhibited VSV in Hela cells with EC50~150uM (similar to for EBOV in Hela cells), but I need to calculate exact value.
- GS-5734 (Remdesivir)did not inhibit VSV even in Hela cells at 10uM dose (EC50 for EBOV is about 0.2uM)."

From: Cox, Edward M [mailto:Edward.Cox@fda.hhs.gov]
Sent: Tuesday, September 11, 2018 7:35 PM
To: 'BENASSI, Virginia' <benassiv@who.int>; aug@alima.ngo; Gruber, Marion <Marion.Gruber@fda.hhs.gov>; michael.jacobs@ucl.ac.uk; Rebecca GRAIS <rebecca.grais@epicentre.msf.org>; Mulangu Sabue <[(b)(6)]@yahoo.fr>; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil>; timo.wolf@kgu.de; mvitek@samaritan.org; Cavaleri Marco <Marco.Cavaleri@ema.europa.eu>; richard.kojan@alima.ngo; Armand Sprecher <Armand.Sprecher@brussels.msf.org>; Browne, Sarah <Sarah.Browne@fda.hhs.gov>; Cox, Edward M

<Edward.Cox@fda.hhs.gov>
Cc: PREZIOSI, Marie-pierre <preziosim@who.int>; RIVEROS BALTA, Alina Ximena <lauriex@who.int>; DIAZ, Janet Victoria <diazj@who.int>; DIXIT, Devika <dixitd@who.int>; GSELL, Pierre <gsellp@who.int>
Subject: [Non-DoD Source] RE: Follow up - EVD Therapeutics and Vaccines for compassionate PEP use Working Group

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Hello All,

Attached I've tried to summarize some key points from our discussions regarding PEP for potential Ebola virus exposures. I used material from the paper by Mike Jacobs and colleagues and have tried to cite the material so as to recognize the source of the work.

Please feel free to edit, correct, improve, etc.

Thank you for the discussion earlier today. It was very helpful!

-Ed

From: BENASSI, Virginia <benassiv@who.int>
Sent: Tuesday, September 11, 2018 9:33 AM
To: Cox, Edward M <Edward.Cox@fda.hhs.gov>; aug@alima.ngo; Gruber, Marion <Marion.Gruber@fda.hhs.gov>; michael.jacobs@ucl.ac.uk; Rebecca GRAIS <rebecca.grais@epicentre.msf.org>; Mulangu Sabue <(b)(6)@yahoo.fr>; sina.bavari.civ@mail.mil; timo.wolf@kgu.de; mvitek@samaritan.org; Cavaleri Marco <Marco.Cavaleri@ema.europa.eu>; richard.kojan@alima.ngo; Armand Sprecher <Armand.Sprecher@brussels.msf.org>; Browne, Sarah <Sarah.Browne@fda.hhs.gov>
Cc: PREZIOSI, Marie-pierre <preziosim@who.int>; RIVEROS BALTA, Alina Ximena <lauriex@who.int>; DIAZ, Janet Victoria <diazj@who.int>; DIXIT, Devika <dixitd@who.int>; GSELL, Pierre <gsellp@who.int>
Subject: RE: Follow up - EVD Therapeutics and Vaccines for compassionate PEP use Working Group

Dear All,

Please find here attached a Summary of inclusion/exclusion criteria, dose and route of administration for the investigational agents that could inform our discussion in a few minutes,

Many thanks,
Virginia

From: BENASSI, Virginia
Sent: 11 September 2018 09:40
To: 'Cox, Edward M'; 'aug@alima.ngo'; 'Marion.Gruber@fda.hhs.gov'; 'michael.jacobs@ucl.ac.uk'; 'Rebecca GRAIS'; 'Mulangu Sabue';sina.bavari.civ@mail.mil < Caution-mailto:sina.bavari.civ@mail.mil > ; 'timo.wolf@kgu.de'; 'mvitek@samaritan.org'; 'Cavaleri Marco'; richard.kojan@alima.ngo < Caution-mailto:richard.kojan@alima.ngo > ; Armand Sprecher; Browne, Sarah
Cc: PREZIOSI, Marie-pierre; RIVEROS BALTA, Alina Ximena; DIAZ, Janet Victoria; DIXIT, Devika; GSELL, Pierre
Subject: RE: Follow up - EVD Therapeutics and Vaccines for compassionate PEP use Working Group

Dear Colleagues,

Hoping this finds you all well.

Please find here attached a summary of key points from our last week teleconference (5 Sept) for your consideration and edits (thanks again to our chair, Dr Cox, for putting this together). Please feel free to send any feedback you may have on the notes directly to me.

Below the dial in details:
(b)(6) / Participant code: (b)(6)

Looking forward to continuing our discussion today.

Best wishes,
Virginia

-----Original Appointment-----
From: BENASSI, Virginia
Sent: 05 September 2018 16:40
To: BENASSI, Virginia; Cox, Edward M; aug@alima.ngo < Caution-mailto:aug@alima.ngo > ;Marion.Gruber@fda.hhs.gov < Caution-mailto:Marion.Gruber@fda.hhs.gov > ;michael.jacobs@ucl.ac.uk < Caution-mailto:michael.jacobs@ucl.ac.uk > ; Rebecca GRAIS; Mulangu Sabue; sina.bavari.civ@mail.mil < Caution-mailto:sina.bavari.civ@mail.mil > ;timo.wolf@kgu.de < Caution-mailto:timo.wolf@kgu.de > ;mvitek@samaritan.org < Caution-mailto:mvitek@samaritan.org > ; Cavaleri Marco; PREZIOSI, Marie-pierre; RIVEROS BALTA, Alina Ximena; GSELL, Pierre; DIXIT, Devika;richard.kojan@alima.ngo < Caution-mailto:richard.kojan@alima.ngo > ; Armand Sprecher; DIAZ, Janet Victoria
Cc: Browne, Sarah
Subject: Follow up - EVD Therapeutics and Vaccines for compassionate PEP use Working Group
When: 11 September 2018 15:30-16:30 (UTC+01:00) Amsterdam, Berlin, Bern, Rome, Stockholm, Vienna.
Where: Teleconference

Dear All,

Thank you very much for your time on the call today and for the excellent discussion. A warm thank-you to our chair, Dr Ed Cox.

As anticipated, we are inviting you for a second teleconference **Tuesday 11 September 2018**, at **15:30 Geneva time**.

Dial in details will be provided in the coming days by my colleagues. Hopefully this time the line will work better on our side. Apologies again for delay once again.

A warm thank-you in advance to you all,
Virginia *on behalf of the* WHO Secretariat

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Technical Officer, Flagship Projects
Initiative for Vaccine Research, WHO/IVB
World Health Organization
Avenue Appia 20
CH-1211 Geneva 27, Switzerland
+41 22 79 14274

<< OLE Object: Picture (Device Independent Bitmap) >>

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 8/17/2018 10:01:57 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]; Seedorff, Jennifer E [SeedorffJE@state.gov]; Tobert, Gwen (STATE.GOV) [tobertgm@state.gov]; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) [kayvon.modjarrad.civ@mail.mil]; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) [carmen.t.maher.civ@mail.mil]; Walker, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4d03cc33ba5c4f15bd581b757dc9daa4-HHS-Robert.]; Boucher, David (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a5c89aa5b44a4042803c3d8ebd414d20-HHS-David.B]; Diaz-Diaz, Carol J (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=54ff795276224eab9847ff70e2693fd4-HHS-Carol.D]
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group

(FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Tracy Carson [CarsonTL@state.gov]; Burgess, Jacqueline (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=15aa5a09afe64a538ab5557a3cd1050b-HHS-Jacquel]; Klein, Mackenzie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12a00d5cedc045d48ebaff6bdde49c33-HHS-Mackenz]; Mbagwu-Mahlik, Adaugo (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2b9bf0d416aa495e84fdb917217c222a-HHS-Adaugo.]; Lamourelle, Gabrielle (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12371f75797c4de6aef3d8e072dc9373-HHS-Gabriel]; Schmeissner, Peter (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41ee9becd7ff492585aa8b06088f4b0a-HHS-Peter.S]; Danelski, Ann (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d53bc4b5ae2a4270a3ae912aa76f42b8-HHS-Ann.Dan]

Subject: RE: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Attachments: Notes_GCM and SAG TC 1_20180817.docx

Dear Colleagues,

I apologize, the previous document was just the agenda. The notes are attached here.

Best Regards,
Collin

From: Weinberger, Collin (OS/OGA) (CTR)
Sent: Friday, August 17, 2018 9:57 AM
To: Handley, Gray (NIH/NIAID) [E] <handleygr@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Higgs, Elizabeth (NIH/NIAID) [E] <ehiggs@niaid.nih.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Schafer, Julie (OS/ASPR/BARDA) <Julie.Schafer@hhs.gov>; Helfand, Rita (CDC/OID/NCEZID) <rzh7@cdc.gov>; Craig, Allen (CDC/OID/NCIRD) <afc0@cdc.gov>; Vinter, Serena (CDC/CGH/OD) <uvv3@cdc.gov>; Kapil, Vikas (CDC/CGH/OD) <vck3@cdc.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Krause, Philip (FDA/CBER) <Philip.Krause@fda.hhs.gov>; Marinissen, Maria (OS/ASPR/SPPR) <Maria.Marinissen@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Barna, Lauren (OS/ASPR/SPPR) <Lauren.Barna@hhs.gov>; 'Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US)' <carl.c.holloway.civ@mail.mil>; Gruber, Marion (FDA/CBER) <Marion.Gruber@fda.hhs.gov>; 'Cox, Edward M' <Edward.Cox@fda.hhs.gov>; 'Kishimori, Jennifer M COL USARMY OSD HA (US)' <jennifer.m.kishimori.mil@mail.mil>; 'Bavari, Sina CIV USARMY MEDCOM USAMRIID (US)' <sina.bavari.civ@mail.mil>; Korch, George (OS/ASPR/IO) <George.Korch@hhs.gov>; Balliram, Richard (OS/ASPR/SPPR) <Richard.Balliram@hhs.gov>; 'LeButt, Kimberly A CIV OSD OUSD ATL (US)' <kimberly.a.lebutt.civ@mail.mil>; 'Seedorff, Jennifer E' <SeedorffJE@state.gov>; Tobert, Gwen (STATE.GOV) <tobertgm@state.gov>; 'Pandemic-Response-OES@state.gov' <Pandemic-Response-OES@state.gov>; 'Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US)' <kayvon.modjarrad.civ@mail.mil>; 'Maher, Carmen T CIV USARMY DOD JPEO CBRND (US)' <carmen.t.maher.civ@mail.mil>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>; Diaz-Diaz, Carol (OS/ASPR/BARDA) <Carol.Diaz-diaz@hhs.gov>
Cc: Yu, Anne (HHS/OS/OGA) <Anne.Yu@hhs.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Locus, Tiffany (OS/OGA) <Tiffany.Locus@hhs.gov>; Adeniyi-Jones, Samuel (HHS/OS/OGA) <Samuel.Adeniyi-Jones@hhs.gov>; Ekpenyong, Elana (HHS/OS/OGA) <Elana.Ekpenyong@hhs.gov>; Tracy Carson <CarsonTL@state.gov>; Burgess, Jacqueline (HHS/OS/OGA) <Jacqueline.Burgess@hhs.gov>; Klein, Mackenzie (HHS/OS/OGA)

<Mackenzie.Klein@hhs.gov>; Mbagwu-Mahlik, Adaugo (HHS/OS/OGA) <Adaugo.Mbagwu-Mahlik@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; Schmeissner, Peter (HHS/OGA) <Peter.Schmeissner@hhs.gov>; Danelski, Ann (HHS/OGA) <Ann.Danelski@hhs.gov>
Subject: RE: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Dear Colleagues,

Please find attached my notes capturing the discussion on the WHO R&D Blueprint GCM and SAG teleconference this morning. Please understand that these notes are rough since the call ended less than an hour ago, but I share them in the interest of providing a readout from the call as soon as possible for those unable to join. When WHO's official notes for the record are available, I will circulate those as well.

On the call WHO and Dr. Muyembe (head of the DRC Institute for Biomedical Research or INRB) provided a summary of the current epidemiological and operational response status, progress on ring vaccination and vaccination of healthcare workers with rVSV-ZEBOV vaccine (under a compassionate use protocol), use of therapeutics to date (also under a compassionate use protocol), efforts to develop a randomized clinical trial protocol to evaluate the most promising therapeutics candidates, and discussions around evaluating vaccine candidates beyond the rVSV-ZEBOV vaccine.

Best Regards,

Collin

Collin Weinberger, MPH
Senior Global Health Officer, Office of Pandemics and Emerging Threats
Futrend Technology, Inc (contractor)
Office of Global Affairs
U.S. Department of Health and Human Services
(O): (202) (b)(6) (M): (202 (b)(6)
collin.weinberger@hhs.gov

From: Weinberger, Collin (OS/OGA) (CTR)
Sent: Thursday, August 16, 2018 12:03 PM
To: Handley, Gray (NIH/NIAID) [E] <handleygr@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Higgs, Elizabeth (NIH/NIAID) [E] <ehiggs@niaid.nih.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Schafer, Julie (OS/ASPR/BARDA) <Julie.Schafer@hhs.gov>; Helfand, Rita (CDC/OID/NCEZID) <rzh7@cdc.gov>; Craig, Allen (CDC/OID/NCIRD) <afc0@cdc.gov>; Vinter, Serena (CDC/CGH/OD) <uvv3@cdc.gov>; Kapil, Vikas (CDC/CGH/OD) <vck3@cdc.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Krause, Philip (FDA/CBER) <Philip.Krause@fda.hhs.gov>; Marinissen, Maria (OS/ASPR/SPPR) <Maria.Marinissen@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Barna, Lauren (OS/ASPR/SPPR) <Lauren.Barna@hhs.gov>; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) <carl.c.holloway.civ@mail.mil>; Gruber, Marion (FDA/CBER) <Marion.Gruber@fda.hhs.gov>; 'Cox, Edward M' <Edward.Cox@fda.hhs.gov>; Kishimori, Jennifer M COL USARMY OSD HA (US) <jennifer.m.kishimori.mil@mail.mil>; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil>; Korch, George (OS/ASPR/IO) <George.Korch@hhs.gov>; Balliram, Richard (OS/ASPR/SPPR) <Richard.Balliram@hhs.gov>; LeButt, Kimberly A CIV OSD OUSD ATL (US) <kimberly.a.lebutt.civ@mail.mil>; Seedorff, Jennifer E <SeedorffJE@state.gov>; Tobert, Gwen (STATE.GOV) <tobertgm@state.gov>; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) <kayvon.modjarrad.civ@mail.mil>; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) <carmen.t.maher.civ@mail.mil>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>; Diaz-Diaz, Carol (OS/ASPR/BARDA) <Carol.Diaz-diaz@hhs.gov>
Cc: Yu, Anne (HHS/OS/OGA) <Anne.Yu@hhs.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Locus, Tiffany (OS/OGA) <Tiffany.Locus@hhs.gov>; Adeniyi-Jones, Samuel (HHS/OS/OGA) <Samuel.Adeniyi-Jones@hhs.gov>;

Ekpenyong, Elana (HHS/OS/OGA) <Elana.Ekpenyong@hhs.gov>; Tracy Carson <CarsonTL@state.gov>; Burgess, Jacqueline (HHS/OS/OGA) <Jacqueline.Burgess@hhs.gov>; Klein, Mackenzie (HHS/OS/OGA) <Mackenzie.Klein@hhs.gov>; Mbagwu-Mahlik, Adaugo (HHS/OS/OGA) <Adaugo.Mbagwu-Mahlik@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; Schmeissner, Peter (HHS/OGA) <Peter.Schmeissner@hhs.gov>; Danelski, Ann (HHS/OGA) <Ann.Danelski@hhs.gov>
Subject: FW: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Dear Colleagues,

Please find attached and below the dial in information for tomorrow morning's teleconference for the WHO R&D Blueprint Global Coordination Mechanism and Scientific Advisory Group call on the research response to the current Eastern DRC Ebola outbreak.

As a reminder, the call will be **Tomorrow, August 17, at 8a Eastern (2p in Geneva)**.
Dial in details as per below:
(b)(6) / Participant code: (b)(6)

I have pasted below the agenda. Attached, please also find:
1. Draft Agenda
2. Latest external situation report (14 August 2018)
3. Latest Disease Outbreak News (DON)
4. Interim SAGE recommendations
5. INRB Statement - Genome Sequences
6. Timelines
7. Draft NFR 1st Ebola Therapeutics Clinical Trial Protocol Working Group – please note that these are not yet validated by the Working Group
8. National Plan for the response to the EVD epidemic in North Kivu Province

Best Regards,
Collin

Collin Weinberger, MPH
Senior Global Health Officer, Office of Pandemics and Emerging Threats
Futrend Technology, Inc (contractor)
Office of Global Affairs
U.S. Department of Health and Human Services
(O): (202) (b)(6) (M): (202) (b)(6)
collin.weinberger@hhs.gov

EVD outbreak in the DRC - Update to GCM and SAG members Teleconference

Friday, August 17 2018, 14:00 Geneva time

Dial in details

→ (b)(6)

→ Participant code: (b)(6)

Agenda

- Overview of the epidemiological situation
- Update on the status of the operational response
- Update on the implementation of the MEURI
- Update on the implementation of the Expanded Access/Compassionate Use protocols
- AOB

From: BENASSI, Virginia <benassiv@who.int>
Sent: Thursday, August 16, 2018 9:57 AM
To: BENASSI, Virginia <benassiv@who.int>
Cc: HENAO RESTREPO, Ana Maria <henaorestrepoa@who.int>; GSELL, Pierre <gsellp@who.int>; COSTA, Alejandro Javier <costaa@who.int>; RIVEROS BALTA, Alina Ximena <lauriex@who.int>; PREZIOSI, Marie-pierre <preziosim@who.int>
Subject: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

In preparation of our call tomorrow, **Friday, 17 August 2018,** at **14:00 GVA** time, please find here attached the following documents:

1. Draft Agenda
2. Latest external situation report (14 August 2018)
3. Latest Disease Outbreak News (DON)
4. Interim SAGE recommendations
5. INRB Statement - Genome Sequences
6. Timelines
7. Draft NFR 1st Ebola Therapeutics Clinical Trial Protocol Working Group – please note that these are not yet validated by the Working Group
8. National Plan for the response to the EVD epidemic in North Kivu Province

Dial in details as per below:
+ (b)(6) / Participant code: (b)(6)

We look forward to your participation. Many thanks in advance.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

Virginia Benassi, LLM, MA
Technical Officer, Flagship Projects
Initiative for Vaccine Research, WHO/IVB
World Health Organization
Avenue Appia 20
CH-1211 Geneva 27, Switzerland
+41 22 79 14274

R&DBlueprint
Powering research to prevent epidemics

From: BENASSI, Virginia
Sent: 09 August 2018 17:02
To: BENASSI, Virginia
Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena
Subject: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

We hope this message finds you all well.

On 1 August 2018, the Ministry of Health of the Democratic Republic of the Congo declared a new outbreak of Ebola virus disease in North Kivu Province. The province of North Kivu is among the most populated provinces, with eight million inhabitants. It shares borders with four other provinces (Ituri, South Kivu, Maniema and Tshopo) as well as with Uganda and Rwanda. The subregion has been experiencing intense insecurity and worsening humanitarian crisis, with over one million internally displaced people and a continuous efflux of refugees to the neighbouring countries, including Uganda, Burundi and Tanzania. The Ministry of Health, WHO and partners are responding to this event, and working to establish the full extent of this outbreak. Attached for more information, please find the latest external situation report, and the links to the Interim recommendation Ebola vaccines and the WHO Ebola webpage.

The R&D Blueprint is pleased to invite you to a **60 min teleconference** next **Friday, 17 August 2018,** at **14:00 GVA** time. The purpose of the call is to provide an update on the current epidemiological situation and the R&D activities ongoing and planned in response to the outbreak.

A detailed agenda and dial in details will follow in the coming days.

We look forward to your participation. Many thanks in advance.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

Virginia Benassi, LLM, MA
Technical Officer, Flagship Projects
Initiative for Vaccine Research, WHO/IVB
World Health Organization
Avenue Appia 20
CH-1211 Geneva 27, Switzerland
+41 22 79 14274

R&DBlueprint
Powering research to prevent epidemics

(b)(5), (b)(6)

(b)(5), (b)(6)

(b)(5), (b)(6)

(b)(5), (b)(6)

(b)(5), (b)(6)

(b)(5), (b)(6)

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 5/9/2018 8:43:18 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Michael, Nelson L COL USARMY MEDCOM WRAIR (US) [nelson.l.michael2.mil@mail.mil]; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) [kayvon.modjarrad.civ@mail.mil]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]
CC: Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]
Subject: Fwd: [2018 Ebola DRC outbreak] - R&D Blueprint Global Coordination Mechanism TC invitation

Importance: High

Dear Colleagues,

WHO will be holding a call for members of the R&D Blueprint Global Coordination Mechanism and Scientific Advisory Group to discuss priority research activities for the current Ebola Outbreak in DRC. The call will be held TODAY at 11a

eastern time (5p in Geneva, 4p in Kinshasa). Please feel free to join because of your work on the blueprint and heavy involvement in the 2014 West Africa Ebola research response. Details are below.

Best,
Collin

Begin Forwarded Message:

From: "GSELL, Pierre" <gsellp@who.int>
Subject: [2018 Ebola DRC outbreak] - R&D Blueprint Global Coordination Mechanism TC invitation
Date: 09 May 2018 06:05
To:

Dear GCM and R&D Blueprint SAG members,

WHO is pleased to invite you to a teleconference **TODAY Wednesday 9 May, 4pm Kinshasa time (5 pm Geneva time)** to provide a briefing of the current Ebola Virus Disease outbreak in DRC and to identify and discuss key research activities to be conducted.

Please dial-in
+ (b)(6) / Participant code: (b)(6)

Kind regards

Pierre on behalf of the Secretariat

Pierre-Stéphane Gsell
Technical Officer
FWC/IVB/IVR | M 125
World Health Organization | Avenue Appia 20 | 1211 Geneva 27 | Switzerland
Desk: +41.22.791.50.74 | Mob: (b)(6) | gsellp@who.int

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 8/30/2018 11:52:38 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]; Seedorff, Jennifer E [SeedorffJE@state.gov]; Tobert, Gwen (STATE.GOV) [tobertgm@state.gov]; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) [kayvon.modjarrad.civ@mail.mil]; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) [carmen.t.maher.civ@mail.mil]; Walker, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4d03cc33ba5c4f15bd581b757dc9daa4-HHS-Robert.]; Boucher, David (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a5c89aa5b44a4042803c3d8ebd414d20-HHS-David.B]; Diaz-Diaz, Carol J (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=54ff795276224eab9847ff70e2693fd4-HHS-Carol.D]
CC: Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group

(FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Tracy Carson [CarsonTL@state.gov]; Burgess, Jacqueline (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=15aa5a09afe64a538ab5557a3cd1050b-HHS-Jacquel]; Klein, Mackenzie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12a00d5cedc045d48ebaff6bdde49c33-HHS-Mackenz]; Mbagwu-Mahlik, Adaugo (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2b9bf0d416aa495e84fdb917217c222a-HHS-Adaugo.]; Lamourelle, Gabrielle (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12371f75797c4de6aef3d8e072dc9373-HHS-Gabriel]; Schmeissner, Peter (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41ee9becd7ff492585aa8b06088f4b0a-HHS-Peter.S]; Danelski, Ann (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d53bc4b5ae2a4270a3ae912aa76f42b8-HHS-Ann.Dan]

Subject: FW: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Attachments: WHO R&D BP_GCM&SAG_EVD Outbreak in DRC_NfR_DRAFT_20Aug2018.docx; Ebola in the DRC_29082018.pptx

Dear Colleagues,

Please see below for information on the next WHO R&D Blueprint GCM/SAG call, scheduled for **Tomorrow, August 31, at 9a Eastern (3p in Geneva).** Attached are the notes for the record from the previous call as well as an updated timeline of WHO's/DRC's key research response actions in the Eastern DRC outbreak to date.

Also, FYSA, I will be on leave starting tomorrow August 31 through Tuesday September 25 (I'm getting married!) and so my colleague Tiffany Locus (cc'd) will be sharing the announcements, readouts, and WHO's notes for the record of any GCM/SAG calls while I am out.

Best Regards,
Collin

Collin Weinberger, MPH
Senior Global Health Officer, Office of Pandemics and Emerging Threats
Futrend Technology, Inc (contractor)
Office of Global Affairs
U.S. Department of Health and Human Services
(O): (202) (b)(6) (M): (202) (b)(6)
collin.weinberger@hhs.gov

From: GSELL, Pierre <gsellp@who.int>
Sent: Thursday, August 30, 2018 9:54 AM
Cc: HENAO RESTREPO, Ana Maria <henaorestrepoa@who.int>; COSTA, Alejandro Javier <costaa@who.int>; RIVEROS BALTA, Alina Ximena <lauriex@who.int>; PREZIOSI, Marie-pierre <preziosim@who.int>; BENASSI, Virginia <benassiv@who.int>
Subject: RE: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

The R&D Blueprint is pleased to invite you to a **60 min teleconference** tomorrow **Friday, 31 August 2018,** at **15:00 Kivu/Geneva** time. The purpose of the call is to provide an update on the current epidemiological situation and the R&D activities ongoing and planned in response to the outbreak.

Dial in details as per below:
+ (b)(6) / Participant code: (b)(6)

In preparation of our call tomorrow, please find here attached the following documents:

1.Draft Agenda
- Overview of the epidemiological situation
- Update on the implementation of the MEURI / Clinical trials for therapeutics
- Update on the implementation of the Compassionate Use of vaccines
- Update on partners research activities

2. Latest external situation report (28 August 2018)
3. Latest MoH report (29 August 2018)
4. Interim SAGE recommendations
5. Research response timelines - attached
6. NFR from last GCM call - attached

We look forward to your participation. Many thanks in advance.

Kind regards,
Pierre *on behalf of the* WHO R&D Blueprint

From: BENASSI, Virginia
Sent: 23 August 2018 11:20
To: BENASSI, Virginia
Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena; PREZIOSI, Marie-pierre
Subject: RE: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

Hoping this finds you all well.

Attached for your information and consideration, please find the draft Notes for the Record from our last call, 20 August 2018. Many thanks to those colleagues who were able to participate to the call.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

Virginia Benassi, LLM, MA
Technical Officer, Flagship Projects
Initiative for Vaccine Research, WHO/IVB
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R&DBlueprint
Powering research to prevent epidemics

From: BENASSI, Virginia
Sent: 16 August 2018 15:57
To: BENASSI, Virginia
Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena; PREZIOSI, Marie-pierre
Subject: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

In preparation of our call tomorrow, **Friday, 17 August 2018,** at **14:00 GVA** time, please find here attached the following documents:

1. Draft Agenda
2. Latest external situation report (14 August 2018)
3. Latest Disease Outbreak News (DON)
4. Interim SAGE recommendations
5. INRB Statement - Genome Sequences
6. Timelines
7. Draft NFR 1st Ebola Therapeutics Clinical Trial Protocol Working Group – please note that these are not yet validated by the Working Group
8. National Plan for the response to the EVD epidemic in North Kivu Province

Dial in details as per below:
+(b)(6) / Participant code: (b)(6)

We look forward to your participation. Many thanks in advance.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

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R&DBlueprint
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From: BENASSI, Virginia
Sent: 09 August 2018 17:02
To: BENASSI, Virginia
Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena

Subject: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

We hope this message finds you all well.

On 1 August 2018, the Ministry of Health of the Democratic Republic of the Congo declared a new outbreak of Ebola virus disease in North Kivu Province. The province of North Kivu is among the most populated provinces, with eight million inhabitants. It shares borders with four other provinces (Ituri, South Kivu, Maniema and Tshopo) as well as with Uganda and Rwanda. The subregion has been experiencing intense insecurity and worsening humanitarian crisis, with over one million internally displaced people and a continuous efflux of refugees to the neighbouring countries, including Uganda, Burundi and Tanzania. The Ministry of Health, WHO and partners are responding to this event, and working to establish the full extent of this outbreak. Attached for more information, please find the latest external situation report, and the links to the Interim recommendation Ebola vaccines and the WHO Ebola webpage.

The R&D Blueprint is pleased to invite you to a **60 min teleconference** next **Friday, 17 August 2018,** at **14:00 GVA** time. The purpose of the call is to provide an update on the current epidemiological situation and the R&D activities ongoing and planned in response to the outbreak.

A detailed agenda and dial in details will follow in the coming days.

We look forward to your participation. Many thanks in advance.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

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V.20August2018_DRAFT

WHO R&D Blueprint update on the Ebola Virus Disease (EVD) Outbreak in DRC

17 August 2018

Draft Notes for the record

1. Overview of the epidemiological situation & Update on the status of the operational response

- On 1 August 2018, the Ministry of Health of the Democratic Republic of the Congo notified WHO of a new outbreak of Ebola virus disease (EVD) in North Kivu Province, in the eastern part of the country. The event was initially reported by the North Kivu Provincial Health authority on 28 July 2018 when a cluster of 26 cases of acute haemorrhagic fever, including 20 deaths (mostly in the community), occurred in Mabalako Health Zone during mid-late July 2018. Local health officials additionally identified sporadic, antecedent deaths in the community since May 2018 (tentatively classified as probable cases), which are subject to ongoing investigations to determine if they are related to the current outbreak. Blood specimens collected from six hospitalized case-patients on 31 July 2018 were shipped to the Institut National de Recherche Biomédicale (INRB) in Kinshasa. On 1 August 2018, four of the six blood specimens tested positive for Ebolavirus by GeneXpert automated-polymerase chain reaction (PCR) and conventional PCR. The Ministry of Health Officially declared the outbreak on 1 August 2018.
- On 6 August 2018, the INRB confirmed that the current outbreak is caused by a distinct *Ebolavirus* (EBOV) strain, different from the one that caused the outbreak in Equateur Province in May-July 2018. This means that, although both events are caused by *Zaire Ebolavirus* species, the two outbreaks are not connected.
- The province of North Kivu is among the most populated provinces, with eight million inhabitants. It shares borders with four other provinces (Ituri, South Kivu, Maniema and Tshopo) as well as with Uganda and Rwanda. The subregion has been experiencing intense insecurity and worsening humanitarian crisis, with over one million internally displaced people and a continuous efflux of refugees to the neighboring countries, including Uganda, Burundi and Tanzania.
- As of 16 August[1], 78 cases, 51 confirmed and 27 probable; among the 78, 44 deaths. These numbers included a total of 10 HCWs, 9 confirmed and 1 probable. All these HCWs were recorded from Mangina. The bulk of the 78 cases have occurred end of July, beginning of August; all the newly confirmed cases in that period have been knowns contacts of previous Ebola cases.
- 24 suspected under investigation in and around the epicenter and neighboring *zones de santé* (health zones); geography: cases are localized in 2 provinces: North Kivu and Ituri; in North Kivu we have 3 health zones with confirmed cases (Mabalako, Beni City and Mandima). The epicenter is capital of North Kivu; 27 probable cases in areas surrounded the epicenter (in this context it means deaths that have not been investigated further for the moment or are in the process of being investigated), may or may not be related to the outbreak.

[1] As of 18 August 2018: Total cases: 91 - Confirmed cases: 64 - Probable cases: 27; Deaths: 50 - 23 confirmed - 27 probable.

- Risk assessment conducted by WHO: national and regional risks are both high, while the global risk is low.
- Contact tracing: as of 16 August, 1578 contacts under surveillance, on average 83% on that particular day were followed up; some of the contacts are starting dropping off after the 21 days surveillance period.
- Complete different operational response to that in Equateur: North Kivu is one of the most densely populated in the DRC; it has a very high mobile population (that includes IDPs) of 8 million people; border crossing is the second most frequented in Africa between Goma and Rwanda (80,000 people cross the border on a daily basis).
- The region is a conflict zone and this has an impact on the scale of the response and access to the affected populations, in terms of deployment of the MoH, UN agencies and partners but also in term of supplies and staff; the surveillance active cases finding and contact tracing are also affected and potentially vaccination, when we talk about a ring definition approach.
- Lastly, Kivu is an ongoing humanitarian crisis with a broad range of public health issues, that include food insecurity, and many other vaccine preventable diseases. Currently CTBP2 polio outbreak ongoing, for the last 8 to 12 months and large scale SIAs are being planned for the end of August in all of Eastern DRC, including the areas surrounding the actual outbreak.
- Security: UN level 4, which means as substantial risk and constrains; curfews in places, all WHO personnel requires a 3-day special training before being allowed on site; people need to wear their security PPE and an escort is required for travelling outside Mangina and Beni.
- WHO is working closing with UNDSS and MONUSCO and all the partners on the ground to ensure the safety of all deployed staff.
- Operational activities follow the standard pillars, and include vaccination, emphasis is placed on contact tracing and infection, prevention and control. It appears ca 7-10 days ago there was an amplifying event in Mangina health center (thus explaining the upsurge of cases we are witnessing now) and most of the cases are related to the health center (very little ongoing in the community itself). Vaccination: colleagues from Guinea who helped in the Equateur outbreak are back in the DRC and have started with the operations. Currently, we have 13 most recent cases covered in 5 rings (in Mandima and Ituri). Lab testing: takes place in Beni and Mangina, with GeneXpert and additional capacity has been established in Goma. 2 ITUs established by MSF in Mandima (35 confirmed bed capacity) and one by ALIMA (10) on site in Beni.
- Strengthening contact tracing in the epicenter Magina, Beni and Mandima is top priority, as well as scaling up and accelerating vaccination of the contacts and the contacts of the contracts in each of these locations; providing access to the investigational therapeutics for confirmed patients; looking at operational preparedness for both the neighboring provinces, as well as neighboring countries such as Uganda and Rwanda; and ensuring security and safety of all staff.
- *Given the significant health center amplification event and very highly mobile population: where do people go to seek high level health care and what's being done to protect against amplification events in hospitals? Vaccination ahead of their anticipated movements? Do people go to Goma?*
  Thought they would go to Goma, but this does not seem to be the case. Currently in the process of strength preparedness capacity and treatment in the hospitals in Goma, vis-a-vis IPC and knowledge about EVD. Surprisingly, HCWs in this regions have very, very little understanding of VHF, given that this is the 10th EVD outbreak in the country. Beni, the closest major population centers (ca 350,000 pp) is very connected to Uganda and people in this areas are highly mobile across the border (porous

and not controlled) and WHO has been told that many patients would go to Uganda. Uganda is on alert with rapid response teams and control at the major points of entry, with strengthened capacities of regional hospitals and provinces in the area. Hence, this event seems to be focused on a perimeter of 10-15 km around Magina and Beni.

- *Diagnostics capacity in the affected areas, borders and Uganda is sufficient?*
  GeneXpert capacity in Beni and Mangina. INRB is in the process and/or has established a mobile lab in Beni and it is in the process to move to Mangina. Uganda has good capacity to start with and is being further strengthened by CDC which has a presence in the country right now – it seems that there is no shortages on the Ugandan side. INRB has been requesting additional tech lab capacity to have the possibility of rotating staff - this has been addresses through the GOARN request; for the time being current capacity seems to be established to satisfaction – but it is important to note that this is an evolving situation and every day there are new developments;

2. Update on the implementation of the MEURI

- The five molecules imported for the last outbreak are in the DRC (ZMapp, Redemesvir, Favipiravir, Regeneron, and MAb114. The authorizations form the regulation authorities are still valid.
- Ethics committee approval for one molecule (MAb114) was received – approval for the remaining ones was submitted. On August 16 a letter from ERC recommended to use all the molecules in an RCT protocol – however they authorized only MaB114 under the MEURI. INRB discussed with the President of the ERC regarding this decision – the president was not aware of the number of cases and in the letter the argumentation was that the number were still low. Based on the current number of cases, INRB is therefore in the process of appealing the ERC decision and have all 5 molecules authorized to be used under the MEURI.
- INRB arrived in Beni on 7 August. On 10 August they started treating patients under the MEURI with MAb114, for a total of 10 patients. Friday 17 is day 7 after the first treatment. All patients are still live and doing fine; only one patients has some medical issues. INRB is now in the process of analyzing the virology and other biological parameters. It is too early now to draw any conclusions on the status of the disease course of the patients when they were receiving the MAb114 (baseline clinical and virology information)- however patients are doing well – very few adverse events and most of them related to the disease; information are being collected and need to be summarized and will be shared when available.
- As for the intention of continuing to give to MAb114 in the meantime (i.e. after the 10 patients and while waiting for the approval for the other molecules from the ERC), a clinical committee has been established together with colleagues from INRB, WHO, MSF and ALIMA and decisions will be taken on a case-by-case basis. It will be an " on the ground" decision with treating clinicians – INRM is open to use all the available molecules.
- For the moment WHO has not heard that any infected patients have crossed and/or identified at the border; next to impossible to have a tight controlled situation given the characteristics of the border itself. Contacts of confirmed cases that have crossed the border were immediately followed up when WHO got knowledge of that: they all returned to the DRC with no damage having being done; movement across borders in both directions is a massive challenge and there is not easy solution re: control.

- INRB is open to use all the therapeutics that are in town – they requested a change in location for the use of therapeutics; the ERC approved only one molecule for MEURI and suggested move forward with a RCT for all the molecules. INRB is now appealing this situation and asking to use all the molecules due to the increasing number of cases;

3. Expanded access/compassionate use for vaccination

- Situation is challenging; trained Guinean teams returned to the DRC, following a letter of the DRC MoH to the MoH of Uganda. The teams started to arrive in batches – now the Guinea team is complete. Additional 50 Congolese colleagues has been trained on the SOPs of the protocol.
- Regulatory and Ethics approvals have been obtained for amending the protocol – the amendment follows the ad-interim recommendation from the SAGE WG on Ebola vaccines and vaccination and the SAGE members.
- The recommendations state that *"[..] While ring vaccination remains the preferred strategy [...], geographic targeted approach was proposed as an exceptional alternative if the ring vaccination around a laboratory confirmed case of Ebola proves unfeasible. [...]"*. In this context, targeted geographic vaccination does NOT refer to entire provinces or districts or entire municipality; it refers to a village if the cases are in the village and to and contacts and contacts of contacts and people most at risk are assumed to live in that village; it refers to a neighborhood in a big city.
- For the time being WHO is organizing ring vaccination for the more recent cases, progress made in Mangina, Ituri and Beni – rings conducted around 13 cases, in five rings, with over 500 hundred people being vaccinated (this does not included HCWs are only contacts and contacts of contacts, however 250 HCWs have been vaccinated since 8 August); this is a close operation in high coordination with the MoH. The ultimate goal is to build capacity in the DRC so in the future vaccine can be administered with no issues – unfortunately there was not the opportunity for training between outbreaks and conduct the planned training workshop.
- Challenges with logistics, with security – however, so far success in reaching the contacts and the contacts of the contacts of these 13 cases, but anticipated that for a handful of them targeted geo vaccination will need to be conducted.
- Further adjustment to the vaccination strategy may be needed, based on the development of the situation, and SAGE is alerted to this;
- Close discussion with Merck about the supply of vaccine. Import permit form the national regulatory authorities in the DRC obtained for up to 20,000 doses, that have been shipped in batches for security reasons and will be available in country by the end of the week (week of August 20).
- The intention was first that the Guinean colleagues will train or help train teams in Uganda for preparedness reasons – 250 Guinean colleagues trained on GCP for ring vaccination – only 46/47 in the DRC, remaining 210 ca available to participate in training workshop in both Uganda and Rwanda -- discussion with WR and colleagues responsible for country preparedness are ongoing as it is buying supplies for cold chain.
- The SAGE recommendations and the protocol indicate that all the HCWs and FLW in the affected areas (with a loose description, i.e. ambulance drivers, motorcycle drivers, hygienist etc.) are eligible for vaccination. WHO is moving with implementing this as per protocol and SAGE recs.
- J&J vaccine: WHO as an organization is open and very clearly understands the need or another or more vaccines (and this will be probably reflected in the discussions before SAGE in October) – in line

with this commitment, WHO has been in interactions with Chinese producers and J&J (second most advanced vaccine) and has encouraged J&J to move forward with the development of a protocol and a proposition that can be tested NOT at the center of the outbreak and for people that are already eligible for the rVSV, but in areas where the outbreak can spread too without causing any potential interference with the response.

- The current epicenter of this epidemic is fraught with enormous problems and the focus there is on the epidemiological, public health and clinical response. Strong sense that in other parts of the country that are not suffering from the current epidemic, the Merck, J&J and potentially other vaccines should be moved on, with the ultimate aim that every single HCWs and other individual in affected areas/countries would be offered vaccination in a preventative way. Areas still under discussion – additional info will be shared when further clarity is reached.
- 2 teams of global carriers, EBOVAC and PREVAC that involve numerous institutions around the world. They are both discussing with J&J and WHO has also approached the government for its inputs and interest in the matter – everybody is very interested in doing such testing not in an area affected by the outbreak now, but in neighboring areas. The protocol and the final design is still under development – details will be provided once had emerged.
- *Intent is to generate a platform of immunity in these geographies in case this outbreak goes to these in order to generate efficacy or is more a discussion around immunogenicity and safety in a geography of relevance?* The protocol is still under discussion – however the objectives agreed upon so far are twofold: (1) primary objective of immunogenicity and safety and (2) a secondary objective of efficacy. Of course, the hope is that the outbreak will not spread therefore the primary objective will be continue gathering date on at least the two most advanced vaccines for immunogenicity and safety, and durability of immunogenicity.
- Intention of continuing to strengthen the capacity for clinical research in the DRC by collaboration in those trials.
- Diagnostics and sequencing data: intense work to ensure lab capacity is strong in country.
- Small protocol writing group, including NIH and FDA colleagues, agreed that the RCT is the way to proceed; discussion is ongoing to decide how to select based on the available evidence the thx that would be included initially; discussions on developing a protocol that spans several outbreaks, end point and design for the randomization and inclusion/exclusion criteria, moving into discussions of detailed protocol. WHO decided to try to work with a smaller group to move forward rapidly and efficiently, however when ready the protocol will be shared with the larger group.

WHO is preparing for the most dire circumstances and
thanks everyone for their unfaltering support for all the challenges ahead.

World Health Organization

V_August2018

Ebola in the DRC (North Kivu)*

The research response timeline

Coordination ☐
SAGE WG on Ebola ☐
Vaccination ☐
Therapeutics ☐

1 August
MoH of the DRC declares a new outbreak of Ebola virus disease in North Kivu Province

2 August
1st TC of the co-Chairs of the SAGE Working Group on Ebola Vaccines and Vaccination

3 August
TC with the Chair of the SAGE Working Group on Ebola Vaccines and Vaccination

4 August
ADG (WHE) and Director NIAID discuss outbreak situation and critical actions for research

4 August
Supplies leftover from Equateur mobilized to North Kivu

6 August
1st TC with J&J to potentially assess a second vaccine

7 August
ERC approves amended protocol

8 August
Ebola vaccination begins in North Kivu (HCWs and FLWs) – work begins to prepare ring vax in the Mangina health area

9 August
SAGE Working Group on Ebola Vaccines and Vaccination - Interim recommendation published

9 August
NRA grants import permit for extra doses of vaccine

10 August
2nd TC with J&J to potentially assess a second vaccine

10 August
Guinean vaccination teams start arriving in the DRC

1 August
1st bilateral TC MSF-WHO

2 August
TC with focal point US OGA

2 August
Discussions start with the Chair of the R&D Blueprint SAG

6 August
ERC approves of use of mAB114

7 August
INRB team travels to North Kivu

8 August
All therapeutics in country – and transferred to North Kivu by INBR, except ZMapp (in Kinshasa) due to cold-chain issues

8 August
2nd bilateral TC MSF-WHO

10 August
TC of GloPID-R Chairs

10 August
1st TC of the Ebola Therapeutics Clinical Trial Protocol WG

13 August
Amended protocol for 4 therapeutics submitted to ERC for approval

13 August
Discussion on post-exposure prophylaxis starts with MappBio, Gilead and Merck

14 August
3rd bilateral TC MSF-WHO, ALIMA invited to join

15 August
Discussion on post-exposure prophylaxis starts with Regeneron

15 August
TC with MSF and ALIMA on therapeutics

15 August
TC with INRB and NIH on protocol for MEURI

16 August

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 8/23/2018 10:06:04 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]; Seedorff, Jennifer E [SeedorffJE@state.gov]; Tobert, Gwen (STATE.GOV) [tobertgm@state.gov]; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) [kayvon.modjarrad.civ@mail.mil]; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) [carmen.t.maher.civ@mail.mil]; Walker, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4d03cc33ba5c4f15bd581b757dc9daa4-HHS-Robert.]; Boucher, David (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a5c89aa5b44a4042803c3d8ebd414d20-HHS-David.B]; Diaz-Diaz, Carol J (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=54ff795276224eab9847ff70e2693fd4-HHS-Carol.D]
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group

(FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Tracy Carson [CarsonTL@state.gov]; Burgess, Jacqueline (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=15aa5a09afe64a538ab5557a3cd1050b-HHS-Jacquel]; Klein, Mackenzie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12a00d5cedc045d48ebaff6bdde49c33-HHS-Mackenz]; Mbagwu-Mahlik, Adaugo (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2b9bf0d416aa495e84fdb917217c222a-HHS-Adaugo.]; Lamourelle, Gabrielle (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12371f75797c4de6aef3d8e072dc9373-HHS-Gabriel]; Schmeissner, Peter (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41ee9becd7ff492585aa8b06088f4b0a-HHS-Peter.S]; Danelski, Ann (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d53bc4b5ae2a4270a3ae912aa76f42b8-HHS-Ann.Dan]

Subject: RE: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Attachments: WHO R&D BP_GCM&SAG_EVD Outbreak in DRC_NfR_DRAFT_20Aug2018.docx

Dear Colleagues,

WHO has distributed their draft notes for the record from last Friday's (August 17) Global Coordination Mechanism and Scientific Advisory Group research call. Please find them attached.

Best Regards,
Collin

Collin Weinberger, MPH
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Sent: Friday, August 17, 2018 9:57 AM
To: Handley, Gray (NIH/NIAID) [E] <handleygr@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Higgs, Elizabeth (NIH/NIAID) [E] <ehiggs@niaid.nih.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Schafer, Julie (OS/ASPR/BARDA) <Julie.Schafer@hhs.gov>; Helfand, Rita (CDC/OID/NCEZID) <rzh7@cdc.gov>; Craig, Allen (CDC/OID/NCIRD) <afc0@cdc.gov>; Vinter, Serena (CDC/CGH/OD) <uvv3@cdc.gov>; Kapil, Vikas (CDC/CGH/OD) <vck3@cdc.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Krause, Philip (FDA/CBER) <Philip.Krause@fda.hhs.gov>; Marinissen, Maria (OS/ASPR/SPPR) <Maria.Marinissen@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Barna, Lauren (OS/ASPR/SPPR) <Lauren.Barna@hhs.gov>; 'Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US)' <carl.c.holloway.civ@mail.mil>; Gruber, Marion (FDA/CBER) <Marion.Gruber@fda.hhs.gov>; 'Cox, Edward M' <Edward.Cox@fda.hhs.gov>; 'Kishimori, Jennifer M COL USARMY OSD HA (US)' <jennifer.m.kishimori.mil@mail.mil>; 'Bavari, Sina CIV USARMY MEDCOM USAMRIID (US)' <sina.bavari.civ@mail.mil>; Korch, George (OS/ASPR/IO)

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Cc: Yu, Anne (HHS/OS/OGA) <Anne.Yu@hhs.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Locus, Tiffany (OS/OGA) <Tiffany.Locus@hhs.gov>; Adeniyi-Jones, Samuel (HHS/OS/OGA) <Samuel.Adeniyi-Jones@hhs.gov>; Ekpenyong, Elana (HHS/OS/OGA) <Elana.Ekpenyong@hhs.gov>; Tracy Carson <CarsonTL@state.gov>; Burgess, Jacqueline (HHS/OS/OGA) <Jacqueline.Burgess@hhs.gov>; Klein, Mackenzie (HHS/OS/OGA) <Mackenzie.Klein@hhs.gov>; Mbagwu-Mahlik, Adaugo (HHS/OS/OGA) <Adaugo.Mbagwu-Mahlik@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; Schmeissner, Peter (HHS/OGA) <Peter.Schmeissner@hhs.gov>; Danelski, Ann (HHS/OGA) <Ann.Danelski@hhs.gov>
Subject: RE: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Dear Colleagues,

Please find attached my notes capturing the discussion on the WHO R&D Blueprint GCM and SAG teleconference this morning. Please understand that these notes are rough since the call ended less than an hour ago, but I share them in the interest of providing a readout from the call as soon as possible for those unable to join. When WHO's official notes for the record are available, I will circulate those as well.

On the call WHO and Dr. Muyembe (head of the DRC Institute for Biomedical Research or INRB) provided a summary of the current epidemiological and operational response status, progress on ring vaccination and vaccination of healthcare workers with rVSV-ZEBOV vaccine (under a compassionate use protocol), use of therapeutics to date (also under a compassionate use protocol), efforts to develop a randomized clinical trial protocol to evaluate the most promising therapeutics candidates, and discussions around evaluating vaccine candidates beyond the rVSV-ZEBOV vaccine.

Best Regards,

Collin

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From: Weinberger, Collin (OS/OGA) (CTR)
Sent: Thursday, August 16, 2018 12:03 PM
To: Handley, Gray (NIH/NIAID) [E] <handleygr@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Higgs, Elizabeth (NIH/NIAID) [E] <ehiggs@niaid.nih.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Schafer, Julie (OS/ASPR/BARDA) <Julie.Schafer@hhs.gov>; Helfand, Rita (CDC/OID/NCEZID) <rzh7@cdc.gov>; Craig, Allen (CDC/OID/NCIRD) <afc0@cdc.gov>; Vinter, Serena (CDC/CGH/OD) <uvv3@cdc.gov>; Kapil, Vikas (CDC/CGH/OD) <vck3@cdc.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Krause, Philip (FDA/CBER) <Philip.Krause@fda.hhs.gov>; Marinissen, Maria (OS/ASPR/SPPR) <Maria.Marinissen@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Barna, Lauren (OS/ASPR/SPPR) <Lauren.Barna@hhs.gov>; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US)

<carl.c.holloway.civ@mail.mil>; Gruber, Marion (FDA/CBER) <Marion.Gruber@fda.hhs.gov>; 'Cox, Edward M' <Edward.Cox@fda.hhs.gov>; Kishimori, Jennifer MCOL USARMY OSD HA (US) <jennifer.m.kishimori.mil@mail.mil>; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil>; Korch, George (OS/ASPR/IO) <George.Korch@hhs.gov>; Balliram, Richard (OS/ASPR/SPPR) <Richard.Balliram@hhs.gov>; LeButt, Kimberly A CIV OSD OUSD ATL (US) <kimberly.a.lebutt.civ@mail.mil>; Seedorff, Jennifer E <SeedorffJE@state.gov>; Tobert, Gwen (STATE.GOV) <tobertgm@state.gov>; Pandemic-Response-OES@state.gov; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) <kayvon.modjarrad.civ@mail.mil>; Maher, Carmen T CIV USARMY DOD JPEO CBRND (US) <carmen.t.maher.civ@mail.mil>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>; Diaz-Diaz, Carol (OS/ASPR/BARDA) <Carol.Diaz-diaz@hhs.gov>
Cc: Yu, Anne (HHS/OS/OGA) <Anne.Yu@hhs.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Locus, Tiffany (OS/OGA) <Tiffany.Locus@hhs.gov>; Adeniyi-Jones, Samuel (HHS/OS/OGA) <Samuel.Adeniyi-Jones@hhs.gov>; Ekpenyong, Elana (HHS/OS/OGA) <Elana.Ekpenyong@hhs.gov>; Tracy Carson <CarsonTL@state.gov>; Burgess, Jacqueline (HHS/OS/OGA) <Jacqueline.Burgess@hhs.gov>; Klein, Mackenzie (HHS/OS/OGA) <Mackenzie.Klein@hhs.gov>; Mbagwu-Mahlik, Adaugo (HHS/OS/OGA) <Adaugo.Mbagwu-Mahlik@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; Schmeissner, Peter (HHS/OGA) <Peter.Schmeissner@hhs.gov>; Danelski, Ann (HHS/OGA) <Ann.Danelski@hhs.gov>
Subject: FW: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Dear Colleagues,

Please find attached and below the dial in information for tomorrow morning's teleconference for the WHO R&D Blueprint Global Coordination Mechanism and Scientific Advisory Group call on the research response to the current Eastern DRC Ebola outbreak.

As a reminder, the call will be **Tomorrow, August 17, at 8a Eastern (2p in Geneva)**.
Dial in details as per below:
(b)(6) / Participant code (b)(6)

I have pasted below the agenda. Attached, please also find:
1. Draft Agenda
2. Latest external situation report (14 August 2018)
3. Latest Disease Outbreak News (DON)
4. Interim SAGE recommendations
5. INRB Statement - Genome Sequences
6. Timelines
7. Draft NFR 1st Ebola Therapeutics Clinical Trial Protocol Working Group – please note that these are not yet validated by the Working Group
8. National Plan for the response to the EVD epidemic in North Kivu Province

Best Regards,
Collin

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EVD outbreak in the DRC - Update to GCM and SAG members Teleconference

Friday, August 17 2018, 14:00 Geneva time

Dial in details

→ (b)(6)

→ Participant code: (b)(6)

Agenda

- Overview of the epidemiological situation
- Update on the status of the operational response
- Update on the implementation of the MEURI
- Update on the implementation of the Expanded Access/Compassionate Use protocols
- AOB

From: BENASSI, Virginia <benassiv@who.int>
Sent: Thursday, August 16, 2018 9:57 AM
To: BENASSI, Virginia <benassiv@who.int>
Cc: HENAO RESTREPO, Ana Maria <henaorestrepoa@who.int>; GSELL, Pierre <gsellp@who.int>; COSTA, Alejandro Javier <costaa@who.int>; RIVEROS BALTA, Alina Ximena <lauriex@who.int>; PREZIOSI, Marie-pierre <preziosim@who.int>
Subject: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

In preparation of our call tomorrow, **Friday, 17 August 2018,** at **14:00 GVA** time, please find here attached the following documents:

1. Draft Agenda
2. Latest external situation report (14 August 2018)
3. Latest Disease Outbreak News (DON)
4. Interim SAGE recommendations
5. INRB Statement - Genome Sequences
6. Timelines
7. Draft NFR 1st Ebola Therapeutics Clinical Trial Protocol Working Group – please note that these are not yet validated by the Working Group
8. National Plan for the response to the EVD epidemic in North Kivu Province

Dial in details as per below:
(b)(6) **Participant code** (b)(6)

We look forward to your participation. Many thanks in advance.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

Virginia Benassi, LLM, MA
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R&DBlueprint
Powering research to prevent epidemics

From: BENASSI, Virginia
Sent: 09 August 2018 17:02
To: BENASSI, Virginia
Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena
Subject: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

We hope this message finds you all well.

On 1 August 2018, the Ministry of Health of the Democratic Republic of the Congo declared a new outbreak of Ebola virus disease in North Kivu Province. The province of North Kivu is among the most populated provinces, with eight million inhabitants. It shares borders with four other provinces (Ituri, South Kivu, Maniema and Tshopo) as well as with Uganda and Rwanda. The subregion has been experiencing intense insecurity and worsening humanitarian crisis, with over one million internally displaced people and a continuous efflux of refugees to the neighbouring countries, including Uganda, Burundi and Tanzania. The Ministry of Health, WHO and partners are responding to this event, and working to establish the full extent of this outbreak. Attached for more information, please find the latest external situation report, and the links to the Interim recommendation Ebola vaccines and the WHO Ebola webpage.

The R&D Blueprint is pleased to invite you to a **60 min teleconference** next **Friday, 17 August 2018,** at **14:00 GVA** time. The purpose of the call is to provide an update on the current epidemiological situation and the R&D activities ongoing and planned in response to the outbreak.

A detailed agenda and dial in details will follow in the coming days.

We look forward to your participation. Many thanks in advance.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

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R&DBlueprint
Powering research to prevent epidemics

World Health Organization

V.20August2018_DRAFT

WHO R&D Blueprint update on the Ebola Virus Disease (EVD) Outbreak in DRC

17 August 2018

Draft Notes for the record

1. Overview of the epidemiological situation & Update on the status of the operational response

- On 1 August 2018, the Ministry of Health of the Democratic Republic of the Congo notified WHO of a new outbreak of Ebola virus disease (EVD) in North Kivu Province, in the eastern part of the country. The event was initially reported by the North Kivu Provincial Health authority on 28 July 2018 when a cluster of 26 cases of acute haemorrhagic fever, including 20 deaths (mostly in the community), occurred in Mabalako Health Zone during mid-late July 2018. Local health officials additionally identified sporadic, antecedent deaths in the community since May 2018 (tentatively classified as probable cases), which are subject to ongoing investigations to determine if they are related to the current outbreak. Blood specimens collected from six hospitalized case-patients on 31 July 2018 were shipped to the Institut National de Recherche Biomédicale (INRB) in Kinshasa. On 1 August 2018, four of the six blood specimens tested positive for Ebolavirus by GeneXpert automated-polymerase chain reaction (PCR) and conventional PCR. The Ministry of Health Officially declared the outbreak on 1 August 2018.
- On 6 August 2018, the INRB confirmed that the current outbreak is caused by a distinct *Ebolavirus* (EBOV) strain, different from the one that caused the outbreak in Equateur Province in May-July 2018. This means that, although both events are caused by *Zaire Ebolavirus* species, the two outbreaks are not connected.
- The province of North Kivu is among the most populated provinces, with eight million inhabitants. It shares borders with four other provinces (Ituri, South Kivu, Maniema and Tshopo) as well as with Uganda and Rwanda. The subregion has been experiencing intense insecurity and worsening humanitarian crisis, with over one million internally displaced people and a continuous efflux of refugees to the neighboring countries, including Uganda, Burundi and Tanzania.
- As of 16 August[1], 78 cases, 51 confirmed and 27 probable; among the 78, 44 deaths. These numbers included a total of 10 HCWs, 9 confirmed and 1 probable. All these HCWs were recorded from Mangina. The bulk of the 78 cases have occurred end of July, beginning of August; all the newly confirmed cases in that period have been knowns contacts of previous Ebola cases.
- 24 suspected under investigation in and around the epicenter and neighboring *zones de santé* (health zones); geography: cases are localized in 2 provinces: North Kivu and Ituri; in North Kivu we have 3 health zones with confirmed cases (Mabalako, Beni City and Mandima). The epicenter is capital of North Kivu; 27 probable cases in areas surrounded the epicenter (in this context it means deaths that have not been investigated further for the moment or are in the process of being investigated), may or may not be related to the outbreak.

[1] As of 18 August 2018: Total cases: 91 - Confirmed cases: 64 - Probable cases: 27; Deaths: 50 - 23 confirmed - 27 probable.

- Risk assessment conducted by WHO: national and regional risks are both high, while the global risk is low.
- Contact tracing: as of 16 August, 1578 contacts under surveillance, on average 83% on that particular day were followed up; some of the contacts are starting dropping off after the 21 days surveillance period.
- Complete different operational response to that in Equateur: North Kivu is one of the most densely populated in the DRC; it has a very high mobile population (that includes IDPs) of 8 million people; border crossing is the second most frequented in Africa between Goma and Rwanda (80,000 people cross the border on a daily basis).
- The region is a conflict zone and this has an impact on the scale of the response and access to the affected populations, in terms of deployment of the MoH, UN agencies and partners but also in term of supplies and staff; the surveillance active cases finding and contact tracing are also affected and potentially vaccination, when we talk about a ring definition approach.
- Lastly, Kivu is an ongoing humanitarian crisis with a broad range of public health issues, that include food insecurity, and many other vaccine preventable diseases. Currently CTBP2 polio outbreak ongoing, for the last 8 to 12 months and large scale SIAs are being planned for the end of August in all of Eastern DRC, including the areas surrounding the actual outbreak.
- Security: UN level 4, which means as substantial risk and constrains; curfews in places, all WHO personnel requires a 3-day special training before being allowed on site; people need to wear their security PPE and an escort is required for travelling outside Mangina and Beni.
- WHO is working closing with UNDSS and MONUSCO and all the partners on the ground to ensure the safety of all deployed staff.
- Operational activities follow the standard pillars, and include vaccination, emphasis is placed on contact tracing and infection, prevention and control. It appears ca 7-10 days ago there was an amplifying event in Mangina health center (thus explaining the upsurge of cases we are witnessing now) and most of the cases are related to the health center (very little ongoing in the community itself). Vaccination: colleagues from Guinea who helped in the Equateur outbreak are back in the DRC and have started with the operations. Currently, we have 13 most recent cases covered in 5 rings (in Mandima and Ituri). Lab testing: takes place in Beni and Mangina, with GeneXpert and additional capacity has been established in Goma. 2 ITUs established by MSF in Mandima (35 confirmed bed capacity) and one by ALIMA (10) on site in Beni.
- Strengthening contact tracing in the epicenter Magina, Beni and Mandima is top priority, as well as scaling up and accelerating vaccination of the contacts and the contacts of the contracts in each of these locations; providing access to the investigational therapeutics for confirmed patients; looking at operational preparedness for both the neighboring provinces, as well as neighboring countries such as Uganda and Rwanda; and ensuring security and safety of all staff.
- *Given the significant health center amplification event and very highly mobile population: where do people go to seek high level health care and what's being done to protect against amplification events in hospitals? Vaccination ahead of their anticipated movements? Do people go to Goma?*
  Thought they would go to Goma, but this does not seem to be the case. Currently in the process of strength preparedness capacity and treatment in the hospitals in Goma, vis-a-vis IPC and knowledge about EVD. Surprisingly, HCWs in this regions have very, very little understanding of VHF, given that this is the 10th EVD outbreak in the country. Beni, the closest major population centers (ca 350,000 pp) is very connected to Uganda and people in this areas are highly mobile across the border (porous

and not controlled) and WHO has been told that many patients would go to Uganda. Uganda is on alert with rapid response teams and control at the major points of entry, with strengthened capacities of regional hospitals and provinces in the area. Hence, this event seems to be focused on a perimeter of 10-15 km around Magina and Beni.

- *Diagnostics capacity in the affected areas, borders and Uganda is sufficient?*
  GeneXpert capacity in Beni and Mangina. INRB is in the process and/or has established a mobile lab in Beni and it is in the process to move to Mangina. Uganda has good capacity to start with and is being further strengthened by CDC which has a presence in the country right now – it seems that there is no shortages on the Ugandan side. INRB has been requesting additional tech lab capacity to have the possibility of rotating staff - this has been addresses through the GOARN request; for the time being current capacity seems to be established to satisfaction – but it is important to note that this is an evolving situation and every day there are new developments;

2. Update on the implementation of the MEURI

- The five molecules imported for the last outbreak are in the DRC (ZMapp, Redemesvir, Favipiravir, Regeneron, and MAb114. The authorizations form the regulation authorities are still valid.
- Ethics committee approval for one molecule (MAb114) was received – approval for the remaining ones was submitted. On August 16 a letter from ERC recommended to use all the molecules in an RCT protocol – however they authorized only MaB114 under the MEURI. INRB discussed with the President of the ERC regarding this decision – the president was not aware of the number of cases and in the letter the argumentation was that the number were still low. Based on the current number of cases, INRB is therefore in the process of appealing the ERC decision and have all 5 molecules authorized to be used under the MEURI.
- INRB arrived in Beni on 7 August. On 10 August they started treating patients under the MEURI with MAb114, for a total of 10 patients. Friday 17 is day 7 after the first treatment. All patients are still live and doing fine; only one patients has some medical issues. INRB is now in the process of analyzing the virology and other biological parameters. It is too early now to draw any conclusions on the status of the disease course of the patients when they were receiving the MAb114 (baseline clinical and virology information)- however patients are doing well – very few adverse events and most of them related to the disease; information are being collected and need to be summarized and will be shared when available.
- As for the intention of continuing to give to MAb114 in the meantime (i.e. after the 10 patients and while waiting for the approval for the other molecules from the ERC), a clinical committee has been established together with colleagues from INRB, WHO, MSF and ALIMA and decisions will be taken on a case-by-case basis. It will be an " on the ground" decision with treating clinicians – INRM is open to use all the available molecules.
- For the moment WHO has not heard that any infected patients have crossed and/or identified at the border; next to impossible to have a tight controlled situation given the characteristics of the border itself. Contacts of confirmed cases that have crossed the border were immediately followed up when WHO got knowledge of that: they all returned to the DRC with no damage having being done; movement across borders in both directions is a massive challenge and there is not easy solution re: control.

- INRB is open to use all the therapeutics that are in town – they requested a change in location for the use of therapeutics; the ERC approved only one molecule for MEURI and suggested move forward with a RCT for all the molecules. INRB is now appealing this situation and asking to use all the molecules due to the increasing number of cases;

3. Expanded access/compassionate use for vaccination

- Situation is challenging; trained Guinean teams returned to the DRC, following a letter of the DRC MoH to the MoH of Uganda. The teams started to arrive in batches – now the Guinea team is complete. Additional 50 Congolese colleagues has been trained on the SOPs of the protocol.
- Regulatory and Ethics approvals have been obtained for amending the protocol – the amendment follows the ad-interim recommendation from the SAGE WG on Ebola vaccines and vaccination and the SAGE members.
- The recommendations state that *"[..] While ring vaccination remains the preferred strategy [...], geographic targeted approach was proposed as an exceptional alternative if the ring vaccination around a laboratory confirmed case of Ebola proves unfeasible. [...]"*. In this context, targeted geographic vaccination does NOT refer to entire provinces or districts or entire municipality; it refers to a village if the cases are in the village and to and contacts and contacts of contacts and people most at risk are assumed to live in that village; it refers to a neighborhood in a big city.
- For the time being WHO is organizing ring vaccination for the more recent cases, progress made in Mangina, Ituri and Beni – rings conducted around 13 cases, in five rings, with over 500 hundred people being vaccinated (this does not included HCWs are only contacts and contacts of contacts, however 250 HCWs have been vaccinated since 8 August); this is a close operation in high coordination with the MoH. The ultimate goal is to build capacity in the DRC so in the future vaccine can be administered with no issues – unfortunately there was not the opportunity for training between outbreaks and conduct the planned training workshop.
- Challenges with logistics, with security – however, so far success in reaching the contacts and the contacts of the contacts of these 13 cases, but anticipated that for a handful of them targeted geo vaccination will need to be conducted.
- Further adjustment to the vaccination strategy may be needed, based on the development of the situation, and SAGE is alerted to this;
- Close discussion with Merck about the supply of vaccine. Import permit form the national regulatory authorities in the DRC obtained for up to 20,000 doses, that have been shipped in batches for security reasons and will be available in country by the end of the week (week of August 20).
- The intention was first that the Guinean colleagues will train or help train teams in Uganda for preparedness reasons – 250 Guinean colleagues trained on GCP for ring vaccination – only 46/47 in the DRC, remaining 210 ca available to participate in training workshop in both Uganda and Rwanda -- discussion with WR and colleagues responsible for country preparedness are ongoing as it is buying supplies for cold chain.
- The SAGE recommendations and the protocol indicate that all the HCWs and FLW in the affected areas (with a loose description, i.e. ambulance drivers, motorcycle drivers, hygienist etc.) are eligible for vaccination. WHO is moving with implementing this as per protocol and SAGE recs.
- J&J vaccine: WHO as an organization is open and very clearly understands the need or another or more vaccines (and this will be probably reflected in the discussions before SAGE in October) – in line

with this commitment, WHO has been in interactions with Chinese producers and J&J (second most advanced vaccine) and has encouraged J&J to move forward with the development of a protocol and a proposition that can be tested NOT at the center of the outbreak and for people that are already eligible for the rVSV, but in areas where the outbreak can spread too without causing any potential interference with the response.

- The current epicenter of this epidemic is fraught with enormous problems and the focus there is on the epidemiological, public health and clinical response. Strong sense that in other parts of the country that are not suffering from the current epidemic, the Merck, J&J and potentially other vaccines should be moved on, with the ultimate aim that every single HCWs and other individual in affected areas/countries would be offered vaccination in a preventative way. Areas still under discussion – additional info will be shared when further clarity is reached.
- 2 teams of global carriers, EBOVAC and PREVAC that involve numerous institutions around the world. They are both discussing with J&J and WHO has also approached the government for its inputs and interest in the matter – everybody is very interested in doing such testing not in an area affected by the outbreak now, but in neighboring areas. The protocol and the final design is still under development – details will be provided once had emerged.
- *Intent is to generate a platform of immunity in these geographies in case this outbreak goes to these in order to generate efficacy or is more a discussion around immunogenicity and safety in a geography of relevance?* The protocol is still under discussion – however the objectives agreed upon so far are twofold: (1) primary objective of immunogenicity and safety and (2) a secondary objective of efficacy. Of course, the hope is that the outbreak will not spread therefore the primary objective will be continue gathering date on at least the two most advanced vaccines for immunogenicity and safety, and durability of immunogenicity.
- Intention of continuing to strengthen the capacity for clinical research in the DRC by collaboration in those trials.
- Diagnostics and sequencing data: intense work to ensure lab capacity is strong in country.
- Small protocol writing group, including NIH and FDA colleagues, agreed that the RCT is the way to proceed; discussion is ongoing to decide how to select based on the available evidence the thx that would be included initially; discussions on developing a protocol that spans several outbreaks, end point and design for the randomization and inclusion/exclusion criteria, moving into discussions of detailed protocol. WHO decided to try to work with a smaller group to move forward rapidly and efficiently, however when ready the protocol will be shared with the larger group.

WHO is preparing for the most dire circumstances and
thanks everyone for their unfaltering support for all the challenges ahead.

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 5/21/2018 8:58:06 AM
To: Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Rollin, Pierre (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5eac15e024294bf7b4f6b6273669ce64-HHS-pyr3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kilmarx, Peter H (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=89c2bfe8538b487b93d461752b7c2315-HHS-peter.k]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Sadove, Elizabeth [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd45c627000d4f34b9db362ff2b6af4b-SADOVEE]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Gruber, Marion [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=019cd2669c7048f7a116d72b7682de44-gruber]; Scherf, Uwe [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b184b713fc4d4edc84d1aed078aafec7-UXS]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; kimberly.a.lebutt.civ@mail.mil; Pitt, Margaret L CIV USARMY MEDCOM USAMRIID (US) [margaret.l.pitt.civ@mail.mil]; george.w.christopher.civ@mail.mil; Michael, Nelson L COL USARMY (US) [nelson.l.michael2.mil@mail.mil]; Modjarrad, Kayvon CIV USARMY MEDCOM WRAIR (US) [kayvon.modjarrad.civ@mail.mil]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]
CC: Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Schmeissner, Peter (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41ee9becd7ff492585aa8b06088f4b0a-HHS-Peter.S]
Subject: Fwd: [2018 Ebola DRC outbreak] - R&D Blueprint Global Coordination Mechanism TC NFR

Attachments: SitRep 5_EVD DRC_final_v2.pdf; [Ebola in DRC] NFR GCM tc 18 May.docx; DRC Ebola 21 May.pdf; Ebola in the DRC_research response.pdf

Dear All,

Please see below and Attached for the official notes from Friday's WHO R&D Blueprint GCM and SAG call on the DRC Ebola outbreak, the latest sit rep, a timeline of research activities, and a presentation with the most recent information.

Best,
Collin

Begin Forwarded Message:

From: "AL-SHORBAJI, Farah" <alshorbajif@who.int>
Subject: [2018 Ebola DRC outbreak] - R&D Blueprint Global Coordination Mechanism TC NFR
Date: 21 May 2018 06:03
To: "AL-SHORBAJI, Farah" <alshorbajif@who.int>

Dear all,

Thank you very much for your participation in the call on Friday 18 May, notes for the record are attached.

I also attach a brief timeline of research support activities, a presentation of the most recent information, and the latest SitRep.

The Notes for the Record for the consultation on Monitored Emergency Use of Unregistered and Investigational Interventions for EVD can be found here.

Best wishes,
Farah on behalf of the WHO Secretariat

Dr Farah Al-Shorbaji
Technical Officer
WHO R&D Blueprint

Phone: +41 2279 12786

R&D BLUEPRINT

For information on the WHO R&D Blueprint:
http://www.who.int/csr/research-and-development/en

From: AL-SHORBAJI, Farah
Sent: 18 May 2018 11:31
To: AL-SHORBAJI, Farah
Subject: [2018 Ebola DRC outbreak] - R&D Blueprint Global Coordination Mechanism TC invitation

Dear GCM and R&D Blueprint SAG members,

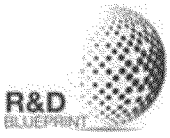
WHO is pleased to invite you to a high-level teleconference **TODAY Friday 18 May, 3 pm Kinshasa time (4 pm Geneva time)** to provide an update on the current Ebola Virus Disease outbreak in DRC and key research activities being planned.

Please dial-in:
(b)(6) / Participant code (b)(6)

Best wishes,
Farah on behalf of the WHO Secretariat

Dr Farah Al-Shorbaji
Technical Officer
WHO R&D Blueprint

Phone: +41 2279 12786



For information on the WHO R&D Blueprint:
http://www.who.int/csr/research-and-development/en

World Health Organization
Africa

EPIDEMIE DE LA MALADIE A VIRUS EBOLA

PROVINCE DE L'EQUATEUR, REPUBLIQUE DEMOCRATIQUE DU CONGO

Réunion de coordination pour la riposte à l'épidémie de l'Ebola à Bikoro.

RAPPORT DE SITUATION N°5– 18 MAI 2018

1. POINTS SAILLANTS

- Cinq (5) nouveaux cas suspects de la maladie à virus Ebola (MVE) ont été enregistrés dans les zones de santé Iboko (4 cas) et Wangata (1 cas) en date du 17/05/2018.
- Six (6) cas confirmés positifs par RT-PCR ; trois (3) cas dans la zone de santé de Iboko et trois (3) cas dans celle de Wangata.
- C'est la première fois depuis le début de l'épidémie que des cas sont confirmés dans la zone de santé d'Iboko.
- Aucun décès notifié en date du 17/05/2018 dans les trois zones de santé
- Depuis le début de l'épidémie, un total de 43 cas de MVE dont 23 décès (létalité de 58%) ont été rapportés. La répartition se présente comme suit : 17 cas confirmés, 21 cas probables et 5 cas suspects.
- Arrivée de deux cents cartouches de Genexpert à Kinshasa, dont 150 seront expédiées à Mbandaka demain 19/05/2018.

2. CONTEXTE

Le 08 Mai 2018, conformément aux dispositions du règlement sanitaire international, le Ministère de la santé de la République Démocratique du Congo (RDC) a notifié à l'OMS deux cas confirmés de la maladie à virus Ebola (MVE) dans la zone de santé de Bikoro dans la province de l'Equateur. Depuis cette déclaration, deux autres zones de santé ont rapporté des cas (Iboko et Wangata dans la ville de Mbandaka). Les zones affectées sont frontalières à la République du Congo. Il s'agit de la neuvième épidémie d'Ebola en RDC, mais la première dans la province démembrée de l'Equateur. Ayant débuté dans une zone rurale, l'épidémie a atteint une zone urbaine avec la notification des premiers cas à Mbandaka en date du 11/05/2018, puis la confirmation d'un cas en

date du 15/05/2018. Mbandaka est reliée quotidiennement à la ville de Kinshasa par les voies aériennes et fluviales.

3. MISE A JOUR DE LA SITUATION EPIDEMOLOGIQUE

- Cinq (5) nouveaux cas suspects de la maladie à virus Ebola (MVE) ont été enregistrés dans les zones de santé d'Iboko (4 cas) et de Wangata (1 cas) en date du 17/05/2018.
- Le cas suspect de Wangata est une jeune fille de 13 ans, contact d'un cas confirmé présentement hospitalisé au CTE de Wangata. Elle est cachée par sa famille et ne bénéficie par conséquent pas de soins médicaux.
- Six (6) cas ont été confirmé positifs par RT-PCR ; trois (3) cas dans la zone de santé de Iboko et trois (3) autres dans celle de Wangata.
- Depuis le début de l'épidémie, la zone de santé de Wangata a rapporté 5 cas dont 1 décédé (létalité : 20%).
- C'est la première fois depuis le début de l'épidémie que des cas sont confirmés dans la zone de santé d'Iboko.
- Parmi les 28 tests effectués, 11 échantillons se sont révélé négatifs. Ils ont été ainsi re-classifiés comme « non cas ».
- Aucun décès n'a été notifié en date du 17/05/2018 dans les trois zones de santé
- Depuis le début de l'épidémie, 43 cas de MVE dont 23 décès (létalité de 58%) ont été rapportés: 17 cas confirmés, 21 cas probables et 5 cas suspects.

- La **figure 1** présente la courbe épidémique des cas par date de notification.

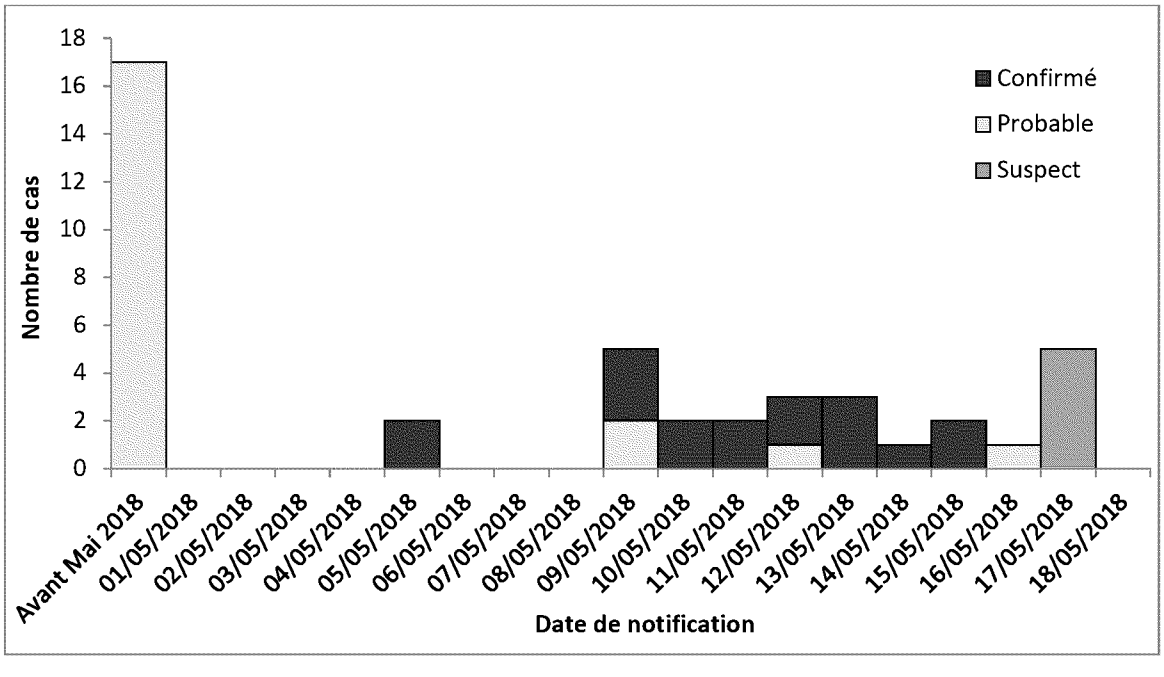


Figure 1: Courbe épidémique des cas par date de notification, du 29 janvier au 17 mai 2018.

- L'épidémie demeure active dans les trois (3) zones de santé affectées, à savoir: Bikoro (29 cas dont 10 confirmés), Iboko (9 cas dont 3 confirmés) et Wangata (5 cas dont 4 confirmé). La ZS de Bikoro reste le principal foyer de l'épidémie avec 67% des cas rapportés. La majorité des cas de Bikoro (72%) proviennent de l'aire de santé d'Ikoko-Impenge.

- La **figure 2** présente la distribution spatiale des cas par zones de santé

-

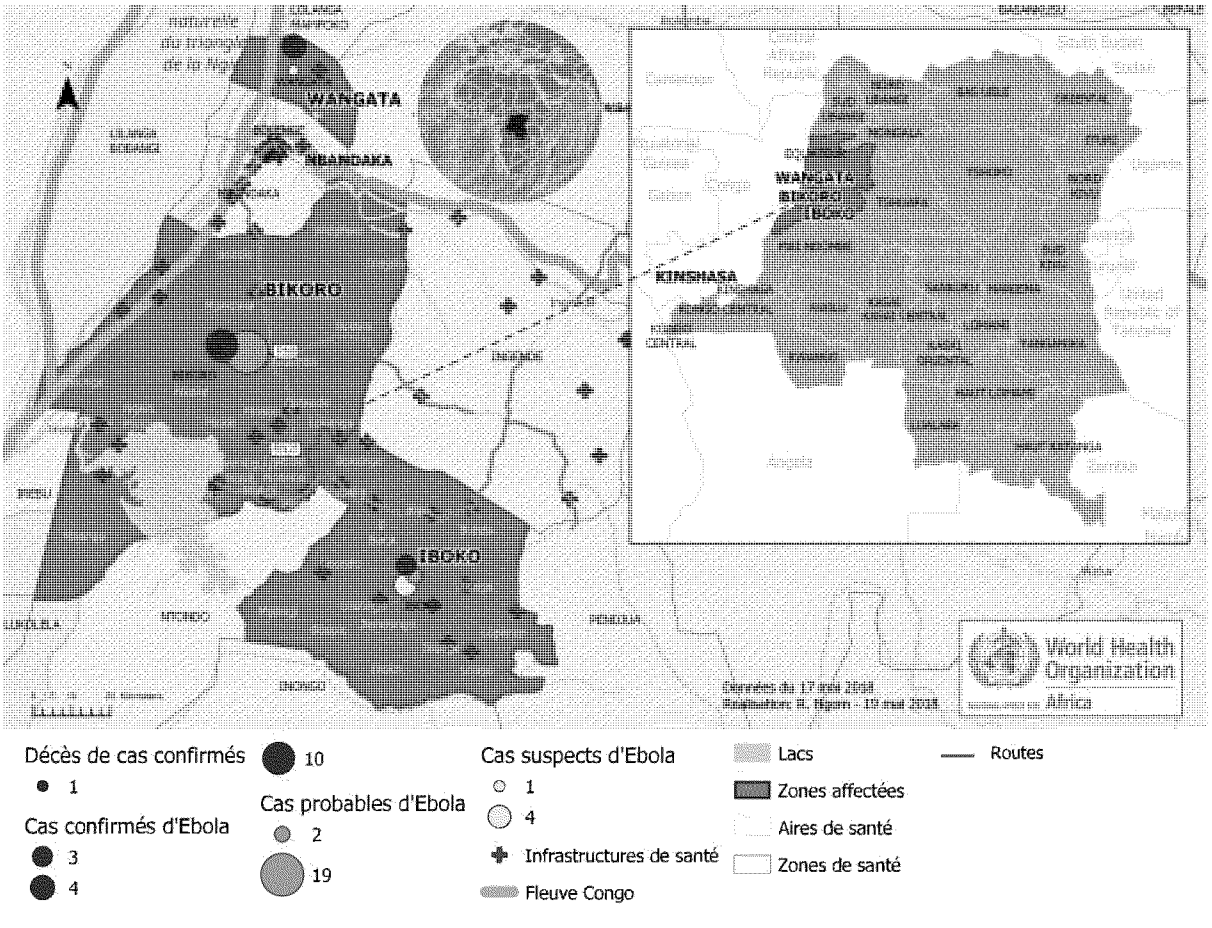


Figure 2: Distribution des cas cumulés de la maladie à virus Ebola par zones de santé, au 17/05/2018

- Le tableau I présente la synthèse des données épidémiologiques au 17 mai 2018.

Tableau I: Synthèse des données épidémiologiques de la maladie à virus Ebola dans la province de l'Equateur, RD Congo, au 17/05/2018

Description	Bikoro	Iboko	Wangata	Total
Nouveaux cas enregistrés du jour				
Nouveaux cas suspects	0	4	1	5
Nouveaux cas probables	0	0	0	0
Nouveaux cas confirmés	0	0	0	0
Total nouveaux cas	***0***	***4***	***1***	***5***
Cumul des cas				
Total des cas suspects	0	4	1	5
Total ces cas probables	19	2	0	21
Total des cas confirmés	10	3	4	17
Total des cas	***29***	***9***	***5***	***43***
Décès				
Nouveaux décès du jour	0	0	0	0
Total des décès	20	4	1	25
Dont total des décès parmi les cas confirmés	1	0	1	2
Agents de santé				
Nouveaux cas parmi les agents de santé	0	0	0	0
Cumul des cas parmi les agents de santé	2	1	0	3
Dont cumul de cas confirmés par les agents de santé	0	0	0	0
Total des décès parmi les agents de santé	0	1	0	1
Admissions et sorties CTE				
Total des cas hospitalisés dans le CTE ce jour	9	8	4	21
Dont nouvelles admissions au CTE	0	4	1	5
Total des sorties du jour - guéri	0	0	0	0
Total des sorties du jour - décédé	0	0	0	0
Contacts				
Nouveaux cumulés de contacts enregistrés	330	120	169	619
Laboratoire				
Nombre de cas prélevés ce jour	0	0	0	0
Nombre d'échantillons en cours de test	1	0	2	3

Cumul des échantillons testés avec résultats disponibles	18	6	4	28
Nombre d'échantillons négatifs	8	3	0	11
Nombre d'échantillons positifs	10	3	4	17
Date de confirmation du dernier cas	16/05/2018	17/05/2018	15/05/2018	

5. ACTIONS DE SANTE PUBLIQUE

Coordination

- Le Comité National de Coordination de la lutte contre la maladie (CNC), présidée par le Ministre de la santé, s'est réuni ce 18/05/2018 pour faire le point sur l'évolution de la situation de l'épidémie et de la réponse.

- Deux réunions importantes sur l'évolution des activités de surveillances et le suivi des contacts, ainsi que la mobilisation des fonds ont eu lieu ce 18/05/2018. La première avec la représentante spéciale du secrétaire des nations unies, la coordinatrice humanitaire et les responsables de la MONUSCO; et la deuxième avec le ministre de la santé.

- Visite du centre des opérations d'urgences du bureau pays de l'OMS par le représentant spécial du secrétaire General des nations Unies (RSSG) en date du 17/05/2018.

- Le comité d'expert du RSI pour l'épidémie de la MVE en RDC s'est réuni ce 18/05/2018. A l'issue de cette réunion il a été conclu que la MVE sévissant en RDC ne constitue pas pour l'instant un évènement de santé publique d'intérêt international. Une série de recommandations visant à limiter la propagation de l'épidémie et son contrôle rapide ont été formulées par le Comité.

Surveillance épidémiologique

- Imperial College London continue la modélisation de l'évolution de l'épidémie, sous financement DFID.

- Les kits EWARS seront déployés le 20/05/2018, pour renforcer les activités de surveillance et de suivi des contacts dans les trois zones de santés affectées.

Prise en charge des cas

- MSF Belgique continue d'appuyer la prise en charge des cas au niveau du centre de traitement de la MVE (CTE) au sein de l'HGR de Bikoro.
- Un expert dans la prise en charge des cas a été déployé à Mbandaka ce 19/05/2018.

Laboratoire

- Le laboratoire mobile de l'INRB installé au niveau de l'hôpital de référence de Bikoro a réalisé les analyses PCR de tous les échantillons en instance provenant de cas suspects.
- Arrivés de deux cents cartouches de Genexpert à Kinshasa, dont 150 envoyées à Mbandaka en date du 19/05/2018.

Eau, Hygiène et Assainissement

- Identification des écoles qui vont bénéficier de 400 lave-mains au niveau des zones de santé de Bikoro et Iboko;
- Poursuite de l'appui de MSF-Belgique, la Croix Rouge Congolaise de la Fédération internationale de la Croix Rouge et du Croissant Rouge (IFRC) à l'organisation des enterrements dignes et sécurisés au niveau de Bikoro et Iboko.

Communication de risque et engagement communautaire

- Poursuite de la sensibilisation des populations dans les villages affectés et les environs à travers les différents canaux de communication (médias, communication interpersonnelle).

Vaccination

- Poursuite de la formation de 18 agents de santé et logisticiens sur la collecte des données de vaccination avec les tablettes. Ces agents ont été déployés à Mbandaka le 19/05/2018 pour appuyer les activités de vaccination.

Logistique

- Poursuite des préparatifs pour la campagne de vaccination.
- La chaine de froid est fonctionnelle à Kinshasa. L'installation de la chaine de froid de Mbandaka est en cours.
- Appui de la FAO aux préparatifs de la vaccination par la mise à disposition de trois. voitures et un chauffeur.

6. DÉFIS

- La capacité de prise en charge des cas reste limitée. En dehors du seul CTE actuellement fonctionnel à l'hôpital général de Bikoro, les équipements de protection individuelle pour le personnel de santé et de sécurisation des enterrements ne sont pas pré-positionnés dans les structures de santé des zones affectées.
- Le processus actuel de suivi des contacts est inadéquat
- Amélioration des conditions IPC dans les centres de santé de Mbandaka afin de permettre notamment l'isolement transitoire avant le transfert vers le CTE ;
- Mise en place des mesures de surveillance de la MVE dans les points d'entrée ;
- Amélioration de l'efficacité et la couverture du système d'alerte précoce;
- Développement d'un model prédictif de la dynamique évolutive de l'épidémie ;

- Promotion de la collaboration transfrontalière avec la République du Congo et la République Centrafricaine dans la réponse à l'épidémie.

7. RECOMMANDATIONS ET ACTIONS PRIORITAIRES A SUIVRE

- Déployer les Experts du PNHF en charge de la surveillance épidémiologique et contrôle aux Points d'Entrée de Mbandaka, Bikoro, Lukolela, Irebu, Ntondo pour le screening des voyageurs ;
- Poursuivre les efforts de renforcement du suivi des contacts dans les trois zones de santé affectées et en particulier à Iboko (pourcentage de suivi des contacts : 26%)
- Renforcer les mesures de communication des risques à Mbandaka
- Mettre en place des équipes de réponse rapide au niveau des provinces
- Renforcer la surveillance et les mesures de prévention au niveau des points d'entrée
- Mettre en place un plan de préparation contre l'épidémie d'Ebola au niveau des provinces.
- Finalisation de déploiement de l'EWARS a Bikoro et Mbandaka.
- Acheminer une partie des vaccins reçus à Mbandaka dans la perspective de l'organisation de la campagne de vaccination en ceinture.

Pour plus d'informations, prière, contactez :

- Pour le ministère de la Santé Publique:
- ✓ Dr Bathe Ndjokolo (Directeur Général de la Lutte contre la maladie) :
- ✓ Dr Leopold Lubula (Directeur a.i. de la surveillance épidémiologique):
- Pour l'OMS :
- ✓ Dr Franck Mboussou (Information Management Officer Lead) :
- ✓ Dr Patricia Ndumbi (Information Management Officer Deputy) :

GCM/SAG Update on Ebola Virus Disease in DRC, 18 May 2018: Note for the Record

Invited: H. Marston (NIH), J. Golding (WT), Y. Yazdanpanah (APHP), C. Weinberger (US/OGA), Nadia Khelef (IP), L. Matthiessen (EC), B. Halloran (FH), C. Roth (DFID), C. Holloway (DoD MCM), B. Kerstiens (EC), A. Epelboin (CNRS), H. Rees (UW), Y. Teerawattananon (HITAP), L. Kerr (USG), E. Torreele (MSF Access), S. Günther (BNITM), R. Hatchett (CEPI), M. Kieny (Inserm), J. Mulligan (DFID), P. Krause (FDA), N. Lurie (USG), Dan Bausch (PHE), M. Agama-Anyeti (AU), F. Fernando (ASEAN), M. Fireman (MoH Brazil), T. Tam (Health Canada), D. Xie (MoH China), M. Ospina Martinez (NIH Colombia), A. Asseffa (ARI), M. Makango (EDCTP), C. Karp (BMGF), J. Lazdins (COHRED), M. Datla (DCVMN), A. Sall (GOARN), C. Brechot (GVN), T. Cueni (IFPMA), J. Liu (MSF), T. Evans (World Bank), S. Kinyanjui (KEMRI), L. Fromm Cea (Proyecto Mesoamericano), I. Korobko (MoH Russia), D. Heymann (CH), J. Savill (UK MRC), K. Littler (WT), R. Bright (BARDA), M. Osterholm (CIDRAP), D. Kaslow (PATH), V. Dzau (NAM), J. Farrar (WT), S. Bavari (USAMRIID), L. Higgs (NIH), A. Kinsey (UK MRC), R. Helfand (CDC), R. Donis (HHS), J. Pearce (UK MRC), B. McCloskey (PHE), A. Antierens (MSF), M. Serafini (MSF), M. Tatay (MSF), N. Gupta (Indian CMR), K. Hamilton (OIE), L. Bigger (IFPMA), G. Carson (GOARN), P. Beattie (EDCTP), M. Klimathianaki (EC), T. Balcha (ARI), C. Lane (NIH), G. Poliquin (Health Canada), K. de Melo Chalegre (MoH Brazil), R&D Blueprint SAG members, WHO, INRB.

Current situation

- Rick Brennan, Director of EMO provided an update of the outbreak and the WHO response to date. As of 17 May there are a total of 43 cases (17 confirmed, 21 probable, 5 suspected).
- The DRC government is well experienced with Ebola, with fully committed and engaged leadership. A multisectoral response has been rapidly mobilized with MSF, UNICEF, ICRF, and WFP as critical partners.
- WHO is increasing its presence on the ground, and is deploying additional case investigation teams as new information on cases becomes available. The location of the outbreak adds complexity to the response.
- WHO has developed a strategic response plan to prevent transmission within Equateur province and beyond, which includes research. The plan estimates resource needs of 25.9M USD.
- While this has not been declared a PHEIC based on the recommendations of the IHR Emergency Committee, WHO has gone to Grade 3 emergency. The committee issued public health advice in a [HYPERLINK "http://www.who.int/news-room/detail/18-05-2018-statement-on-the-1st-meeting-of-the-ihr-emergency-committee-regarding-the-ebola-outbreak-in-2018" \l ".Wv7t2uSMHD8.twitter"].
- WHO is advancing operational preparedness in 11 priority countries with an elevated risk, including assessing capacities to identify/isolate/care for cases, safe burials, surveillance and contact tracing. The IHR focal points in each of these countries have been informed of the risks and advice issued. Outreach activities are taking place in regional offices, and there are extensive efforts at communication with key stakeholders: Member States, IASC, GOARN, other networks.
- There is a network of anthropologists involved in this response. A systematic review of the evidence learned has been commissioned; activities for community engagement are happening daily, with UNICEF and many partners.
- WHO is also supporting readiness of health facilities to ensure continuity of regular healthcare.

Research response

- The technical leadership team of the Blueprint provided an overview of planned research activities, focusing on therapeutics, diagnostics and vaccines.
- In terms of country capacity and support for research, the Institut National de Recherche Biomedicale (INRB) has extensive experience with Ebola, well supported at the moment and working closely with WHO.

- WHO convened a group of independent scientific experts for the purpose of evaluating the currently available information and data on investigational therapeutics intended to treat EVD.
    - In an outbreak characterized by high mortality, it can be ethically appropriate to offer individual patients investigational interventions on an emergency basis outside clinical trials (Monitored Emergency Use of Unregistered Interventions (MEURI)).
- 5 investigational therapies were reviewed: ZMapp; Remdesivir (GS-5734); REGN3470-3471-3479; Favipiravir; and mAb 114. This group may assess other agents if needed.
- The group noted:
    - the available evidence for these investigational therapies is below the usual level of evidence for formulating recommendations;
    - the importance of moving to appropriate clinical trials as soon as possible to evaluate which products are beneficial to patients with EVD. MEURI is designed for the period before clinical studies can take place, and not as a replacement. WHO is currently collaborating with partners and networks of trial methodologists on trial design to evaluate candidate investigational therapeutics and assess which are beneficial to patients with EVD as early as feasible.
- A Note for the Record on MEURI expert consultation for this outbreak will be published shortly. WHO will re-visit this assessment as more information becomes available or the circumstances of the outbreak change.
- Patients will only receive investigational treatment after approval by country authorities, including national regulatory authorities and an appropriately qualified ethics committee, and after informed consent.
- WHO has reached out to manufacturers for information about availability; for some drugs there is a limited supply but it is sufficient to move forward. WHO reiterated that this was a framework to assess the evidence, not based on the resources available or needed for the different molecules.
- The R&D Blueprint clinical trials experts group is being alerted and a potential design will be drawn up next week. Inputs from clinicians will also be incorporated.

Laboratory and Dx

- WHO has held meetings with DRC MOH to create a network of laboratory analysis through the combined use of RDTs and GeneXpert.

Vaccination

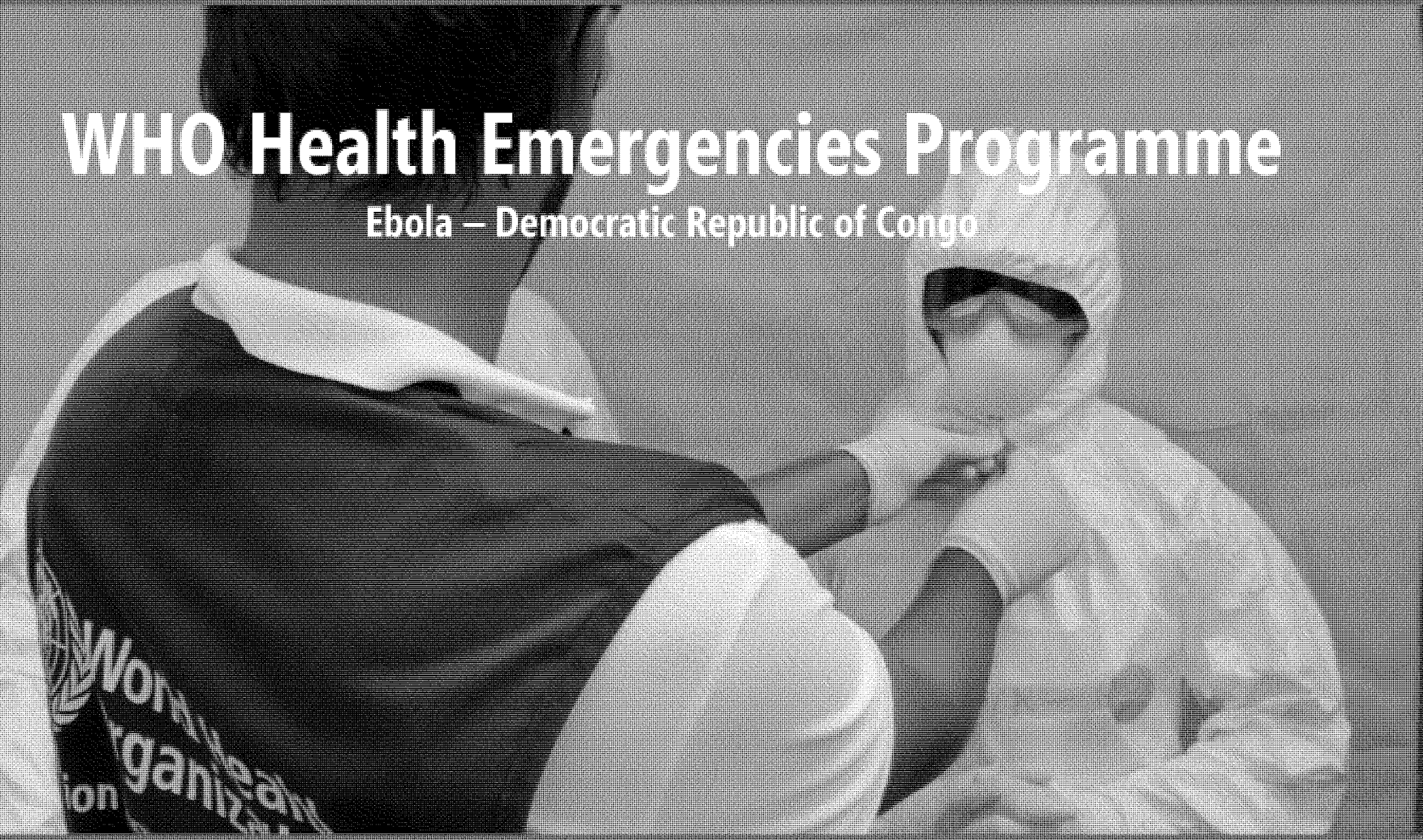
- Current plan is for ring vaccination using the rVSVΔG-ZEBOV- GP vaccine, as recommended by SAGE and in partnership with MOH, MSF, UNICEF and other partners under an expanded access protocol (not EUAL). Frontline workers and international HCWs will also be vaccinated as per [HYPERLINK "http://www.who.int/immunization/sage/meetings/2017/april/SAGE_April_2017_Meeting_Web_summary.pdf"]. Eligible individuals in the rings (contacts and contacts of contacts and HCWs and FLWs will need to sign an informed consent form before being vaccinated, and vaccination it is not compulsory.
- The Blueprint recognizes the importance of considering other vaccine candidates, such as the J&J vaccine, and will assess the possibility of evaluating candidates beyond the rVSV ZEBOV vaccine. A preliminary call already took place with the SAGE WG on Ebola vaccines and the Chair of SAGE and preliminary needs regarding policy guidance were drawn up. The R&D Blueprint clinical trials experts group is being alerted and a potential design will be drawn up next week.
- The WHO regulatory team is working to ensure we have most updated data including clinical quality and programmatic aspects for vaccine applications for EUAL (Merck, J&J) and IVDs.

    - The Emergency Use and Assessment Listing (EUAL) process established after Ebola is being revised to integrate preparedness procedures and add flexibility around use outside of PHEICs. A regulatory preparedness roadmap will be published soon.
- Approximately 7500 doses have been sent to DRC, with further doses available in Geneva in the event that cases are reported in other countries. Merck has up to 300,000 doses and has offered access to WHO. Nearly 50 staff from MOH have been trained on GCP and SOPs for protocol, the PI is Prof Jean-Jacques Muyembé, Director General INRB. Nearly 40 staff from Guinea who have already done ring vaccination will work together and train others in DRC.
- All the logistics are in place, and vaccination will start as soon as possible.
- The leadership of the blueprint will be in DRC from May 21 agreeing local research priorities with DRC authorities and scientists and assisting in progression of next steps.
- WHO reiterated its data sharing position that any study results relevant to this outbreak that have not been published must be made available now.
- Other research topics under consideration include: potential to obtain additional information on adding an immune subset to the ring and HCW/FLW Ebola vaccination campaign going into the field in the DRC early next week. The goal would be to learn something about immune correlates of risk from vaccinated and unvaccinated exposed people. There are suggestions on immune markers of infection. Use of various rehydration approaches and their impact on survival, etc.

Another call will be arranged in the next weeks to update the group.

WHO Health Emergencies Programme

Ebola – Democratic Republic of Congo



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Background

3 May 2018: 21 cases of fever with haemorrhagic signs reported in the Provincial Health Division of Equateur. This includes 17 community deaths in the Ikoko-Impenge Health Area.

5 May 2018: Deployment of a Ministry of Health (MoH) team to Bikoro and Ikoko-Impenge Health Areas. Support provided by the World Health Organization (WHO) and Médicines Sans Frontièrs (MSF).

6 May 2018: Five cases detected (2 at Ikoro General Hospital, 3 at Ikoko health center). Samples sent for analysis at the Institute National de Recherche Biomédicale, Kinshasa.

8 May 2018: Two tests reverse transcription polymerase chain reaction (RT-PCR) positive for Ebola virus disease (EVD).

8 May 2018: MoH declares an outbreak of EVD in Bikoro Health Zone, Equateur Province.

Situation Update

As of the 18 May, 2018

- **46 cases (26 deaths)**
  - **21 confirmed**
  - **21 probable**
  - **4 suspected**

- **Bikoro, Mbandaka (Wangata Health Zone)** and **Iboko in Equateur province**
  - Mbandaka (important port with 1.2 million people).
  - Near the Congo river and neighboring countries (Republic of Congo and Central African Republic)

- **3 affected healthcare workers (1 death)**

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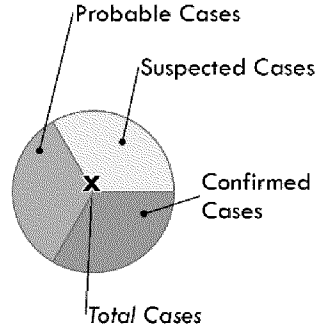
HEALTH EMERGENCIES programme

Democratic Republic of the Congo
Ebola cases per Health Zone in Equateur province as of May 19, 2018

World Health Organization

Map date: 21 May 2018



Health Center

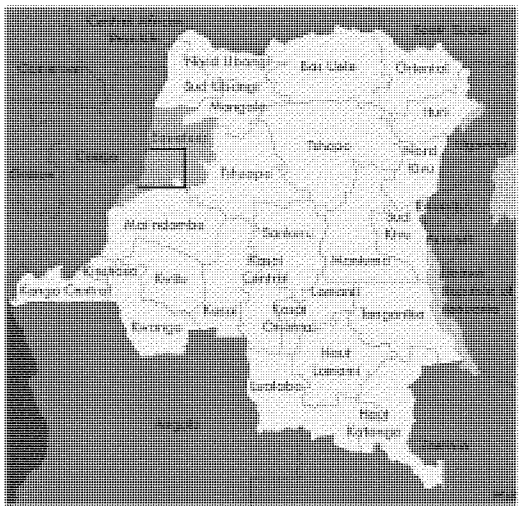
National boundary

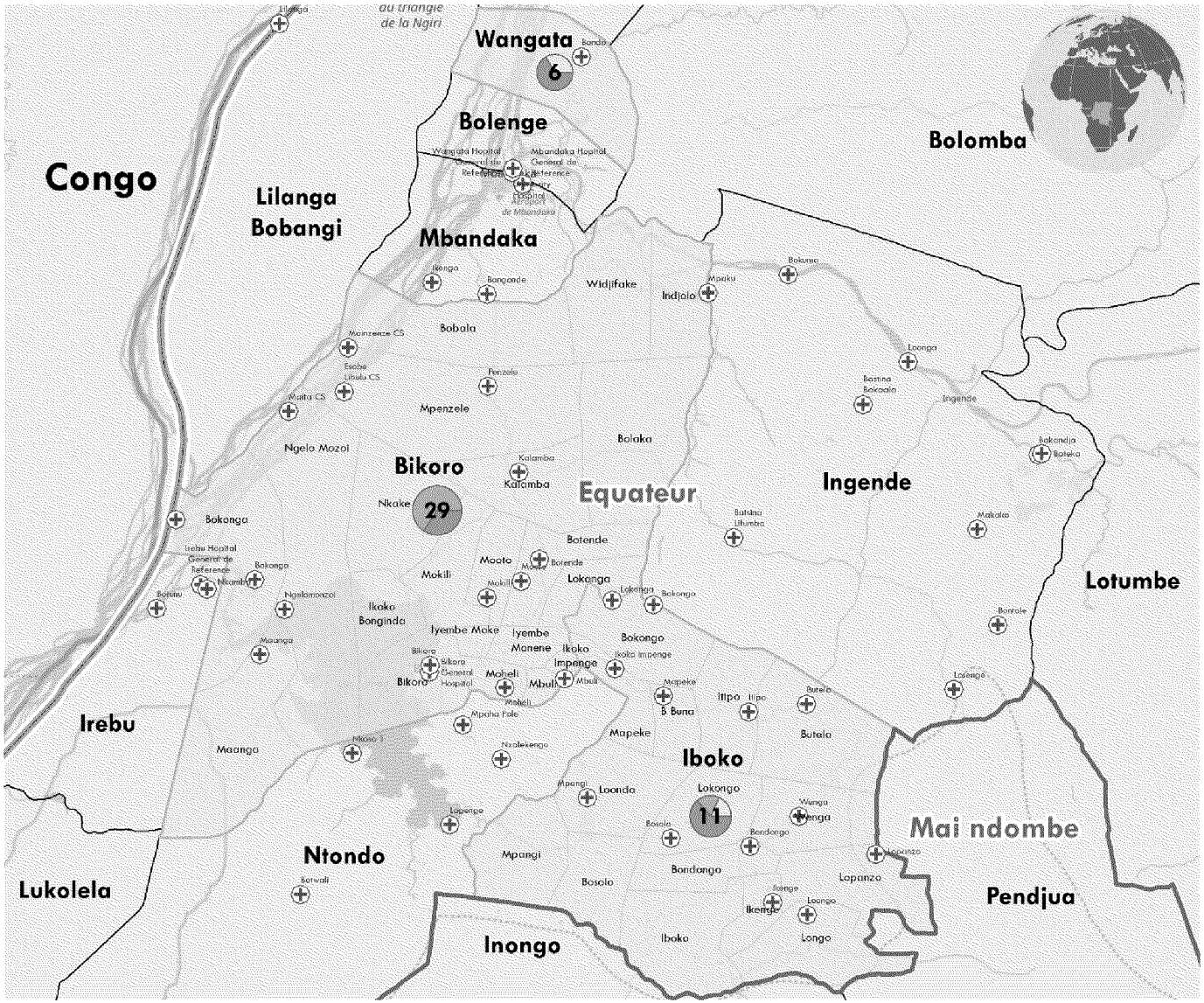
Province Boundary

Affected Health Zones

Health Zones

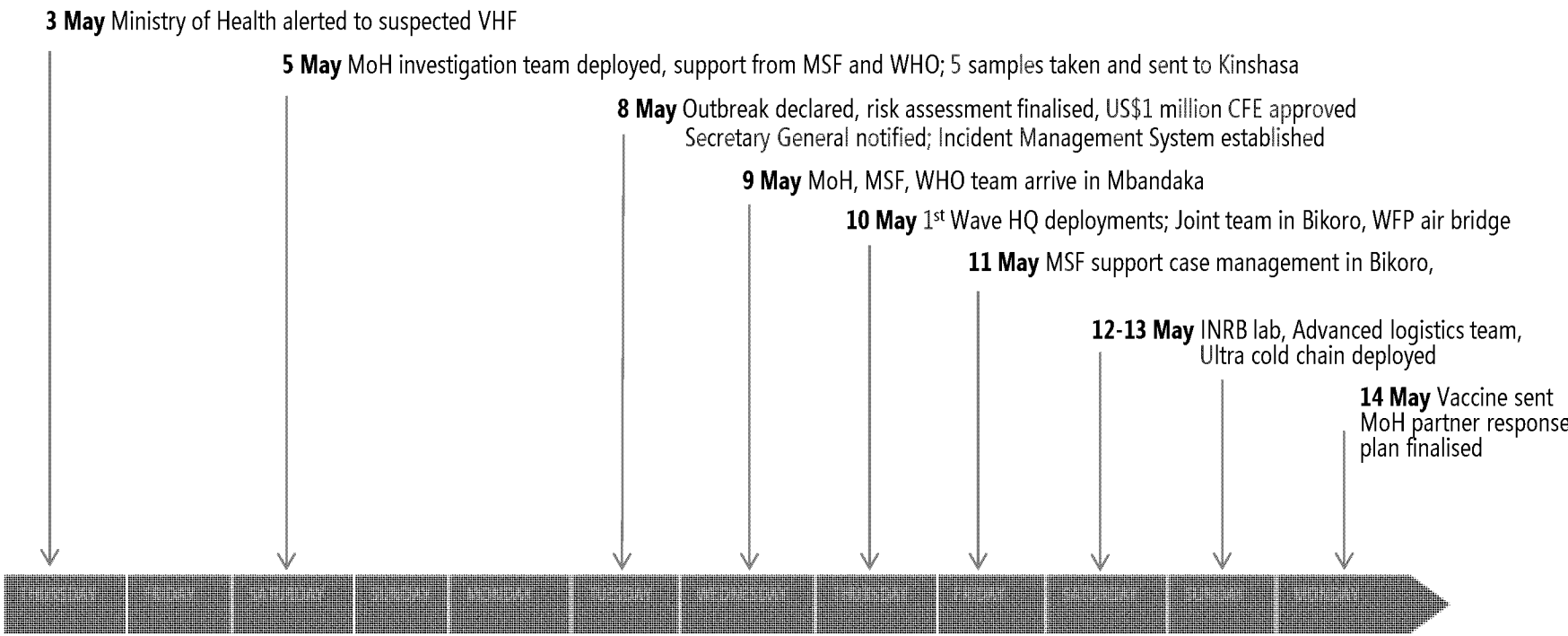
Health Areas





Timeline of implemented key actions

3 – 14 May 2018



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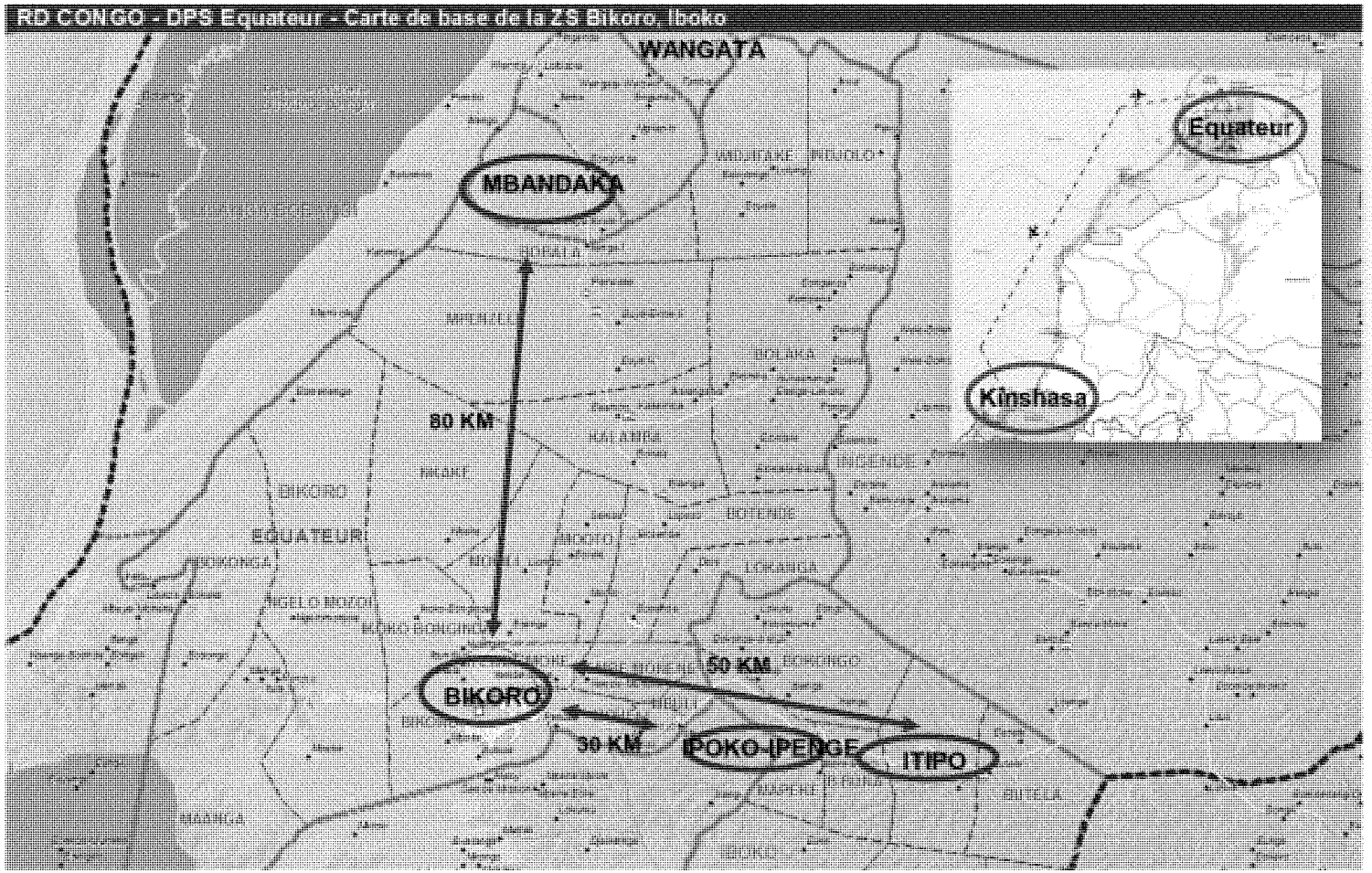
Operational zones



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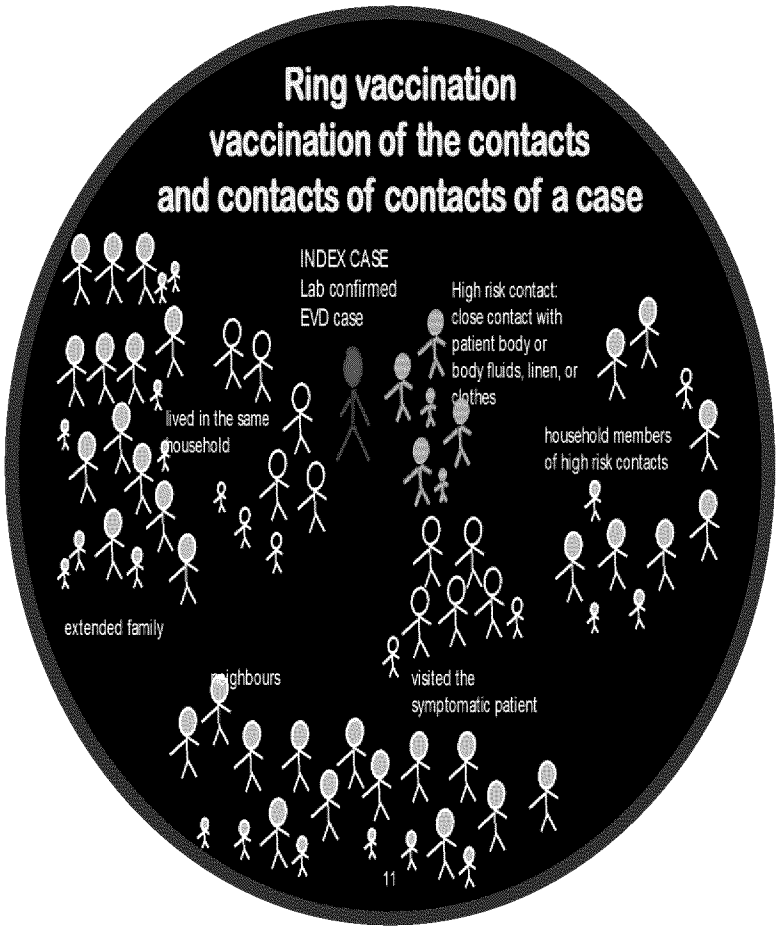
Immediate Operational Priorities

- Strong multi-agency operations and logistics platform to sustain field operations
- Scaling up infection prevention control, clinical care and safe/dignified burials
- Intensified social mobilisation and community engagement
- Systematic tracing and follow-up of all contacts
- **Ring vaccination to begin ASAP** (more than 7,000 vaccines in DRC)

Ring Vaccination

In close collaboration with the DRC authorities:

- **Protocol** approved by DRC NRA and Ethics committee plus **Insurance** contracted
- **More than 7,000 doses of Vaccine** (rVSV-ZEBOV) have arrived to DRC
- **Experienced teams** from Guinea were deployed thanks to MOH Guinea collaboration to support the response in DRC
- **Cold chain and logistics** deployed including to store vaccines at – 60 degrees
- **Partnerships** forged with UNICEF, MSF and other actors



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Key Operational Updates

Following confirmation of a case in Mbandaka, the DRC Ebola outbreaks was re-graded as an internal Grade 3 Public Health Emergency. The new grade reflects the following:

- Revised risk assessment – National: Very High, Regional: High, Global: Low
- Resources required across the three-levels of the organization to scale the response

IHR Emergency Committee, 18 May:

- Considers the event to be very serious, but advised that it does not constitute a public health emergency of international concern
- The committee will reconvene and reevaluate as the situation evolves.

Achievements to date

- MOH, WHO & MSF investigation team deployed within **2 days**
- First CFE released within **4 hours** of confirmation
- Three level Incident Management System set-up on the **day of confirmation**
- Airbridge established within **2 days**
- Lab deployed within **5 days**
- Ultra-cold chain deployed within **6 days**
- **87** people deployed within **10 days**

Goal

Reduce mortality and morbidity related to the EVD outbreak in the province of Equateur, and to prevent the spread of the outbreak to other provinces and countries.

Response Strategy: DRC Ebola Outbreak 2018

- Coordination of multisectoral response
- Surveillance, active case finding and follow-up of contacts
- Infection prevention and control
- Medical management of patients and suspected cases
- Laboratory / diagnostic capabilities
- Risk communication and social mobilization
- Immunization of risk groups and research response
- Operations support and logistics
- Operational readiness in at risk provinces and countries

Planning assumptions

- 80-100 cases
- EOC setup in Mbandaka
- National multisector coordination cell
- 3-month operation (May-July 2018)
- 4 separate geographic response zones
- Ring vaccination and access to experimental antivirals

Estimated cost:
$25.9 million

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Funding Update : WHO & Partners $26M

WHO Funding Requirement: $15.6 million

The current funding received toward the Strategic Response Plan for the Ebola Response, is from **Italy (€ 300,000), CERF ($800,000), GAVI $1 million), USAID ($1 million) and Wellcome Trust & UK DFID ($4,1 million), totalling around $7,3 million.**

Firm pledges have been received from Canada, ECHO, UN CERF and the African Development Bank.

WHO has a funding gap of **$8.3 million** of the total required to support the Ebola outbreak response.

Funding Needs:

- **Funding for Air bridge**
- **Logistics and supplies**
- **Laboratory**
- **Infection Prevention control and case management**
- **Human Resources**

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Ebola in the DRC

The research response timeline

Coordination
R&D Blueprint product
Vaccination
Case management and Therapeutics

08 May
WHO notified by the DRC MoH of confirmed cases of EVD

09 May
First deployments of teams to Bikoro

10 May
Distribution of Notes for the Record and circulation of draft research response plan

WHO, MoH DRC, MSF and Merck prepare for implementation of ring vaccination, pending support of DRC authorities

13 May
DRC formally asks to use experimental Merck vaccine

13 May
WHO forms expert working group to prioritize candidate investigational Ebola therapeutics for MEURI

15 May
NIH support to vaccinate deployed frontline workers from NIH

16-17 May
TCs on use of investigational therapeutic agents (NFR)

18 May
TC with GCM & SAG

Partner contributions
Wellcome Trust pledged 2M GBP and is engaging with other funding partners through GloPID-R. DFID has pledged 1M GBP, Gavi has pledged 1M USD.

EDCTP has 2 networks (ALERRT/PANDORA) ready to provide support

GOARN research will support definition of the non-product R&D, including research to assess acceptability of experimental interventions.

09 May
R&D Blueprint Ebola Roadmap online for public consultation

09 May
TC between WHO, R&D Blueprint GCM and SAG, and the DRC MoH

10 May
Merck offers support to facilitate access of experimental vaccine under the framework of an FDA Expanded Use.

10-14 May
WHO approaches Sponsors of investigational therapeutics to access data for scientific assessment under WHO ethical framework.

WHO is working with MSF and DRC MoH to prepare to use those investigational therapeutics.

16 May
First shipment of vaccine arrives in DRC

18 -19 May
Cold chain set up

Guinean team arrives, begins vaccination training with MOH

Planned activities
Ring vaccination

TC to discuss interpretation of lab results, EVD diagnostic tools, and laboratory capacity

TC on clinical management to discuss the standard of care, clinical core variables, and clinical evaluation

Recommendations on MEURI for therapeutic agents

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 8/2/2018 12:02:38 PM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Tracy Carson [CarsonTL@state.gov]; Burgess, Jacqueline (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=15aa5a09afe64a538ab5557a3cd1050b-HHS-Jacquel]; Klein, Mackenzie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12a00d5cedc045d48ebaff6bdde49c33-HHS-Mackenz]
Subject: [DRC Ebola]: Conversation with Ana Maria Restrepo from WHO on Research Response to New Ebola Cluster

Dear Colleagues,

As you may be aware, the DRC Ministry of Health and WHO announced yesterday that there is a new cluster of suspected Ebola cases that have been in North Kivu province with 4 of six samples testing positive for Ebola in preliminary lab tests (see WHO Press Release: http://www.who.int/news-room/detail/01-08-2018-cluster-of-presumptive-ebola-cases-in-north-kivu-in-the-democratic-republic-of-the-congo, and MoH Press Release: https://mailchi.mp/49b37201b847/declaration_ebola_kivu?e=f656adbaff). The cluster is in an active conflict zone in the northeast corner of DRC, near the city of Beni and the border with Uganda. DRC MOH officials do not believe this cluster is connected to the outbreak that was just last week declared over in Equator Province, although they are still waiting for typing results to determine the strain of Ebola in these new suspected cases.

I spoke briefly this morning with Ana Maria Henao Restrepo, one of the technical leads of the WHO R&D Blueprint, to inquire about WHO's coordination of the potential research response and the status of the Ebola vaccines and therapeutics clinical trial protocols that have been under discussion by WHO-convened expert working groups during the outbreak that just ended. (b)(5)

(b)(5)

(b)(5) The blueprint team have not scheduled a call of the Global Coordination Mechanism yet, but they will reassess next week. She also said that she would be open to scheduling another call with USG later next week to discuss research response.

Best Regards,
Collin

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From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 8/9/2018 12:07:29 PM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]; Seedorff, Jennifer E [SeedorffJE@state.gov]; Tobert, Gwen (STATE.GOV) [tobertgm@state.gov]; Pandemic-Response-OES@state.gov
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Tracy Carson [CarsonTL@state.gov]; Burgess, Jacqueline (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=15aa5a09afe64a538ab5557a3cd1050b-HHS-Jacquel]; Klein, Mackenzie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12a00d5cedc045d48ebaff6bdde49c33-HHS-Mackenz]

Subject: Re: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members

Dear All,

Correction: the GCM/SAG call will be **next Friday, August 17 at 8a eastern** and NOT tomorrow.

Apologies for the error,

Collin

On: 09 August 2018 11:52, "Weinberger, Collin (OS/OGA) (CTR)" <Collin.Weinberger@hhs.gov> wrote:

Dear Colleagues,

Please see below for information on a WHO R&D Blueprint Global Coordination Mechanism and Scientific Advisory Group call to discuss the research response to the Ebola outbreak in North Kivu province, which will be **held tomorrow, Friday, August 10, at 8a Eastern time (1400 in Geneva)**.

Attached, please find a WHO Emergencies Program External Situation report, dated August 7, which provides an overview of the WHO and DRC response actions to date, including in the areas of response coordination, surveillance, laboratory, case management, vaccination, and pysychosocial care, risk communications and social mobilization, resource mobilization, preparedness, operations partnership, and IHR travel measures and cross border health. On resource mobilization, it notes: A **joint strategic response plan and budget totaling US$ 43 million** has been developed and approved by the Minister of Health of the Democratic Republic of the Congo. **WHO has released US$ 2 million from its Contingency Fund** for Emergencies to initiate response interventions.

Also attached and excerpted below is an updated recommendations from the WHO Advisory Group of Experts (SAGE) Working Group on Ebola
Vaccines, which recommends that a targeted geographic vaccination approach with the rVSVΔG-ZEBOV-GP vaccine used in Guinea and May-July's Ebola outbreak in DRC's Equateur province can be considered in the event that ring vaccination is not feasible:

"Ring vaccination [with rVSVΔG-ZEBOV-GP vaccine], as used in the Phase 3 study in Guinea, is the recommended delivery strategy. This should be adapted to the social and geographic conditions of the outbreak areas and include people at risk including but not limited to: (i) contacts and contacts of contacts; (ii) local and international health-care and front-line workers in the affected areas and (iii) health-care and front-line workers in areas at risk of expansion of the outbreak."

A geographically targeted vaccination strategy can be considered in settings where it is not possible to identify the individuals making up the ring vaccination cohorts because of serious security, social or epidemiological issues. In this case, the geographic area immediately around an Ebola case, such as a village or a neighborhood, is most likely to include those individuals who were the contacts or contacts-of-contacts of the index case. An expanded strategy to vaccinate all individuals in this defined geographic area will require a larger number of vaccinations than would be used in a ring vaccination intervention in the same area. Even in this setting, informed consent and compliance with Good Clinical Practice will be required, but the intensity of follow up of vaccinated individuals will be determined by the context of the intervention."

Best,
Collin

Collin Weinberger, MPH
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From: BENASSI, Virginia <benassiv@who.int>
Sent: Thursday, August 09, 2018 11:04 AM
To: BENASSI, Virginia <benassiv@who.int>
Cc: HENAO RESTREPO, Ana Maria <henaorestrepoa@who.int>; GSELL, Pierre <gsellp@who.int>; COSTA, Alejandro Javier <costaa@who.int>; RIVEROS BALTA, Alina Ximena <lauriex@who.int>
Subject: [EVD outbreak in the DRC] Teleconference -- update to GCM and SAG members
Importance: High

Please note that all GCM and SAG members are receiving this message

Dear GCM and SAG Colleagues,

We hope this message finds you all well.

On 1 August 2018, the Ministry of Health of the Democratic Republic of the Congo declared a new outbreak of Ebola virus disease in North Kivu Province. The province of North Kivu is among the most populated provinces, with eight million inhabitants. It shares borders with four other provinces (Ituri, South Kivu, Maniema and Tshopo) as well as with Uganda and Rwanda. The subregion has been experiencing intense insecurity and worsening humanitarian crisis, with over one million internally displaced people and a continuous efflux of refugees to the neighbouring countries, including Uganda, Burundi and Tanzania. The Ministry of Health, WHO and partners are responding to this event, and working to establish the full extent of this outbreak. Attached for more information, please find the latest external situation report, and the links to the Interim recommendation Ebola vaccines and the WHO Ebola webpage.

The R&D Blueprint is pleased to invite you to a **60 min teleconference** next **Friday, 17 August 2018,** at **14:00 GVA** time. The purpose of the call is to provide an update on the current epidemiological situation and the R&D activities ongoing and planned in response to the outbreak.

A detailed agenda and dial in details will follow in the coming days.

We look forward to your participation. Many thanks in advance.

Kind regards,
Virginia *on behalf of the* WHO R&D Blueprint

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Initiative for Vaccine Research, WHO/IVB
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+41 22 79 14274

The linked image cannot be displayed. The file

From: Marinissen, Maria (OS/ASPR/OPP) [Maria.Marinissen@hhs.gov]
Sent: 6/7/2018 1:49:41 PM
To: Weinberger, Collin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd4fd713e0de4d899676030918973af8-HHS-Collin.]; Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Lim, Matt (STATE.GOV) [limml@state.gov]; Tracy Carson [CarsonTL@state.gov]
Subject: RE: [2018 Ebola DRC outbreak] - Readout from 6/6 WHO R&DB GCM DRC Research Priorities Meeting

Thanks much Collin. Appreciate the info.

Maria Julia Marinissen, Ph.D.

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From: Weinberger, Collin (OS/OGA) (CTR)
Sent: Thursday, June 07, 2018 1:47 PM
To: Handley, Gray (NIH/NIAID) [E]; Marston, Hilary (NIH/NIAID) [E]; Lane, Cliff (NIH/NIAID) [E]; Higgs, Elizabeth (NIH/NIAID) [E]; Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Helfand, Rita (CDC/OID/NCEZID); Craig, Allen (CDC/OID/NCIRD); Vinter, Serena (CDC/CGH/OD); Kapil, Vikas (CDC/CGH/OD); Mair, Michael (FDA/OC); Krause, Philip (FDA/CBER); Marinissen, Maria (OS/ASPR/OPP); Moudy, Robin (OS/ASPR/OPP); Balliram, Richard (OS/ASPR/OPP); Barna, Lauren (OS/ASPR/OPP); Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US); Kishimori, Jennifer M COL USARMY OSD HA (US); Bavari, Sina CIV USARMY MEDCOM USAMRIID (US); Korch, George (OS/ASPR/IO)
Cc: Yu, Anne (HHS/OS/OGA); Kerr, Lawrence (HHS/OS/OGA); Locus, Tiffany (OS/OGA); Adeniyi-Jones, Samuel (HHS/OS/OGA); Ekpenyong, Elana (HHS/OS/OGA); Lim, Matt (STATE.GOV); Tracy Carson
Subject: [2018 Ebola DRC outbreak] - Readout from 6/6 WHO R&DB GCM DRC Research Priorities Meeting

Dear All,

Yesterday, WHO held a meeting in Geneva for the members of the R&D Blueprint GCM members to discuss the DRC's prioritized Ebola research response plan developed by the National Institute for Biological Research (INRB; designated domestic lead for research response by DRC MoH). This was a quickly convened meeting (announced late last week) and WHO was quite strict about the number of people they invited to attend or call in. Because of the limited invitee list, I wanted to circulate my notes for all of your situational awareness. WHO will also be releasing their official notes for the record in the coming days and I will circulate those once they are available.

In addition the below notes, please find attached: 1) the INRB Ebola Research Plan, 2) INRB Director Prof. Muyembe's presentation on the plan, 3) WHO presentation on DRC ring vaccination progress to date, 4) WHO presentation on Ebola therapeutics-related activities for DRC outbreak to date, 5) WHO's timeline for the research response.

Best,
Collin

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Readout from the WHO meeting in Geneva June 6, 2018 with Prof. Muyembe, the Director of the DRC National Institute for Biological Research (INRB) on Ebola research priorities. I've attached the DRC Research Plan, which includes their research priorities for prevention, detection, and response as well as a research response timeline to date. I've also attached three of the presentations which WHO circulated:

- Prof. Muyembe's presentation of the key objectives and asks in their research plan
- A summary of ring vaccination completed to date (this one is particularly interesting and worth a look)
- A summary of expert working group recommendations and status of therapeutics in DRC to date

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From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 6/7/2018 1:46:58 PM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]
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Subject: [2018 Ebola DRC outbreak] - Readout from 6/6 WHO R&DB GCM DRC Research Priorities Meeting
Attachments: INRB research plan.pdf; Muyembe_Research Plan DRC Ebola INRB.PDF; Ring vaccination progress DRC for SAGE WG_sm.pdf; therapeutics slides.pdf; Ebola in the DRC timeline_05062018.pdf

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Best,
Collin

Collin Weinberger, MPH
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(O): (202) (b)(6) (M): (202) (b)(6)
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Readout from the WHO meeting in Geneva June 6, 2018 with Prof. Muyembe, the Director of the DRC National Institute for Biological Research (INRB) on Ebola research priorities. I've attached the DRC Research Plan, which includes their research priorities for prevention, detection, and response as well as a research response timeline to date. I've also attached three of the presentations which WHO circulated:

- Prof. Muyembe's presentation of the key objectives and asks in their research plan
- A summary of ring vaccination completed to date (this one is particularly interesting and worth a look)
- A summary of expert working group recommendations and status of therapeutics in DRC to date

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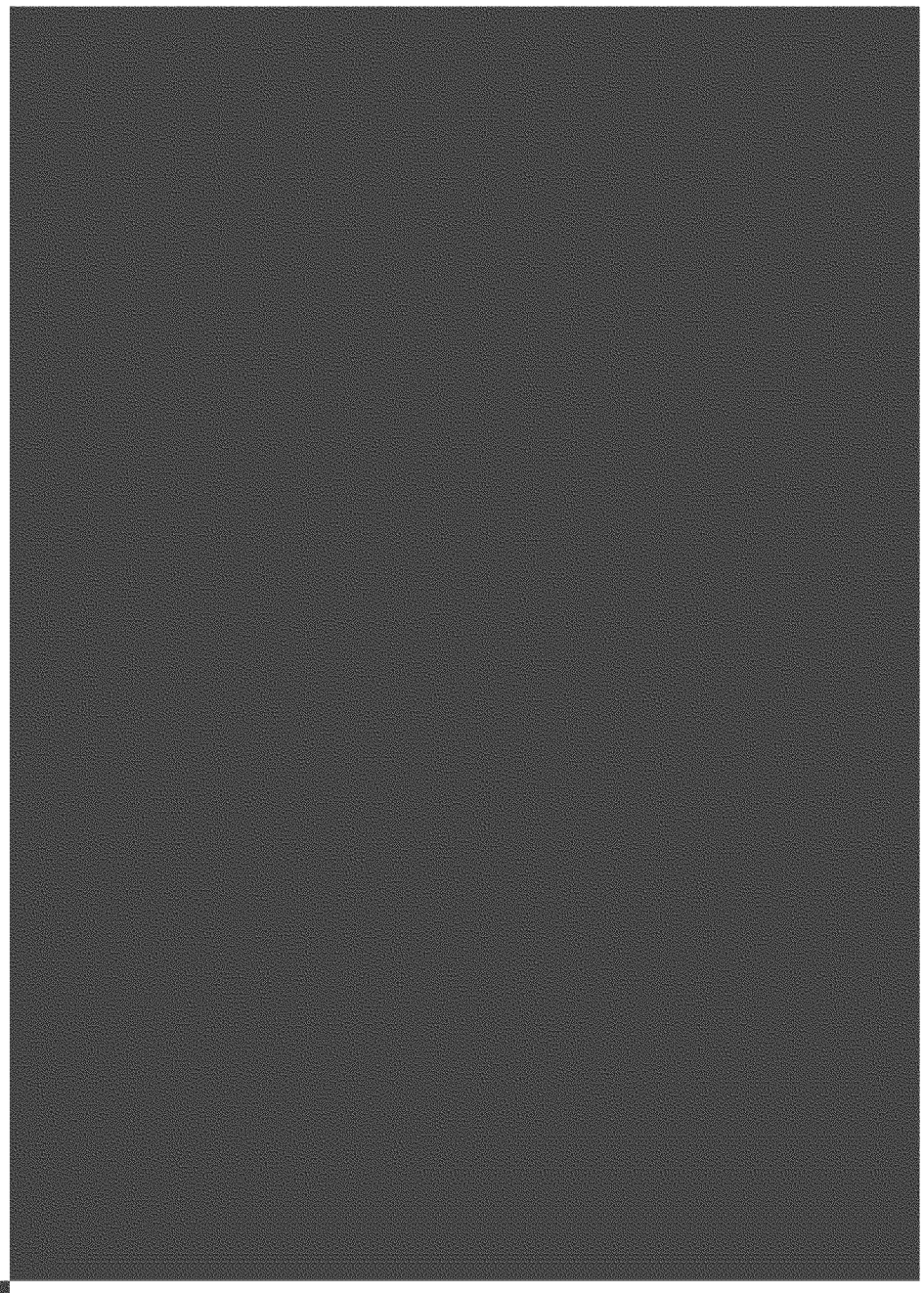
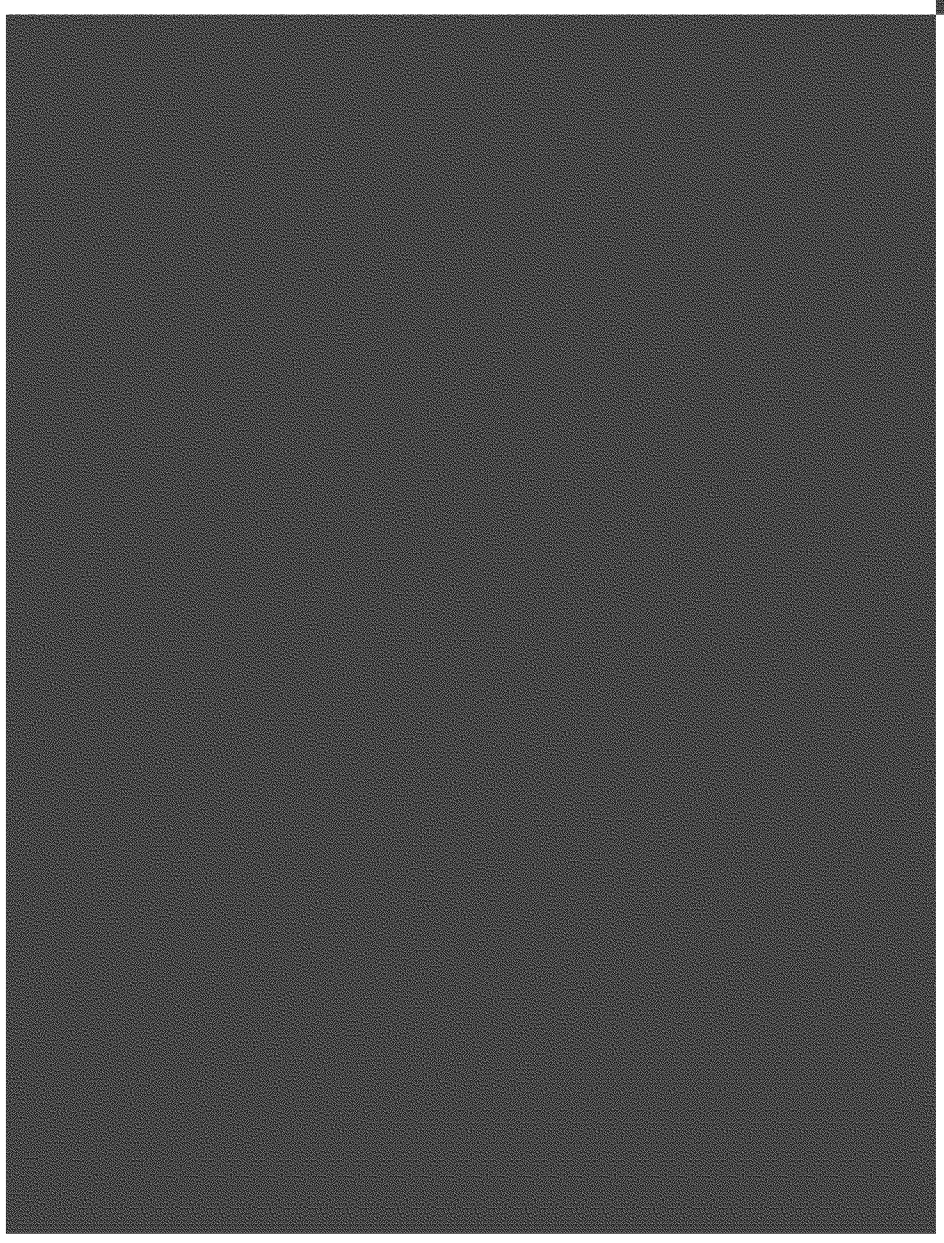
Ebola Virus Disease

RESEARCH PLAN





Democratic Republic of Congo
(DRC)

5 June 2018
Version 1.0

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OBJECTIVES OF THE PLAN

1. To expand the knowledge about Ebola during the present outbreak and beyond.

2. To expand existing research capacity in DRC.

3. To incorporate numerous research suggestions by international partners in view of The country priorities, feasibility and other considerations.

IMMEDIATE RESEARCH PRIORITIES

1. Urgently conduct a retrospective investigation on origins of the current outbreak.

2. Develop local centre of excellence for molecular biology, diagnostics and VHF immunology.

3. To create and train a local cadre of Congolese physicians that can deploy rapidly with associated equipment and set up an ETC.

A cohort protocol to provide access (expanded access/compassionate use) to rVSV-ZEBOV Ebola vaccine is being implemented since May 21, 2018. In addition, concrete actions to provide access to candidate therapeutics have taken place.

SHORT, MEDIUM AND LONG-TERM PRIORITIES

3 areas of work, with twelve sets of activities are presented in this research plan.
This breakdown into short, medium and long-term priorities for DRC to better detect, prevent, control and treat Ebola infection and disease

RESEARCH OUTCOMES

PREVENTION

1. To improve and strengthen the surveillance system for the early detection of and response to VHF outbreaks in three pilot EVD affected Health Zones in DRC

2. To better understand the epidemiology, the risk factors and the ecology of VHF in DRC

DETECTION

3. To strengthen the DRC capacities for safe handling, diagnosis and reporting of major VHF diseases in DRC.

RESPONSE/PREPAREDNESS

4. To increase the capacity of DRC nationals to respond to EVD outbreak including the case management

5. To support the isolation and the GMP development of mAbs against other filovirus from DRC filovirus survivors (Ebola, Bundi and Marburg)

6. Clinical, Immunological and Genetic characterization of survivors Vs. asymptomatic infection Vs. vaccinees

7. To contribute to support community engagement activities in particular those to aimed to understand risk behaviour and risk management

8. To set in place a mechanism in DRC to facilitate the coordination of the research efforts related to Ebola

9. To coordinate the design and support the prompt implementation of efficacy trials to assess candidate therapeutics and the post-marketing evaluation of therapeutics for Ebola

10. To ensure prompt access and use of candidate Ebola rVSV vaccine through a ring vaccination strategy as part of the response to the outbreak, including in particular the evaluation of vaccine safety in target populations to better understand the risk of adverse events in outbreak settings

11. To conduct the evaluation of candidate multivalent filovirus vaccines in DRC for safety, immunogenicity, correlates of protection, and duration of immunity

12. Support coordination of data sharing and sample sharing in DRC

A. To improve and strengthen the surveillance system for the early detection of and response to VHF outbreaks in three pilot EVD affected Health Zones in DRC

Research outcomes

To improve and strengthen the surveillance system for the early detection of and response to VHF outbreaks in three pilot EVD affected Health Zones in DRC. This is critical for prompt implementation of research activities.

Partners providing support
Direction Nationale de Lutte contre les maladies
US CDC
Africa CDC
WHO
Univ of California, USA

Additional support required
Epidemiologists to adapt training materials and help conduct the training sessions.
In addition, expert support is welcome to evaluate the quality of surveillance in different areas.

Key Activities

1. Train key HCW (Doctors and nurses working in Referral General Hospital, in Referral Health Centers and in peripheral small clinics) in the selected Health Zones (HZ) to recognize a suspect case VHF

2. Train the key HCW in safe and proper collection of sample specimens from suspect cases of VHF for Rapid Testing and confirmation test in central lab

3. Train the Chief Medical Officer (CMO) of the HZ in timely investigation of suspect cases of VHF, in implementing initial isolation measures and in completing the notification form including list of contacts

4. Train the CMO of the Health Zone to properly prepare the shipment of the sample specimens from suspect case of VHF and to ship the samples with the completed notification form (including internet-based reporting system) to INRB in a timely manner.

5. Train the CMO to monitor the stock of supplies for samples collection material, PPE and Rapid Test in the health zone and to timely request replenish from INRB.

B. To better understand the epidemiology, the risk factors and the ecology of VHF in DRC

Research outcomes

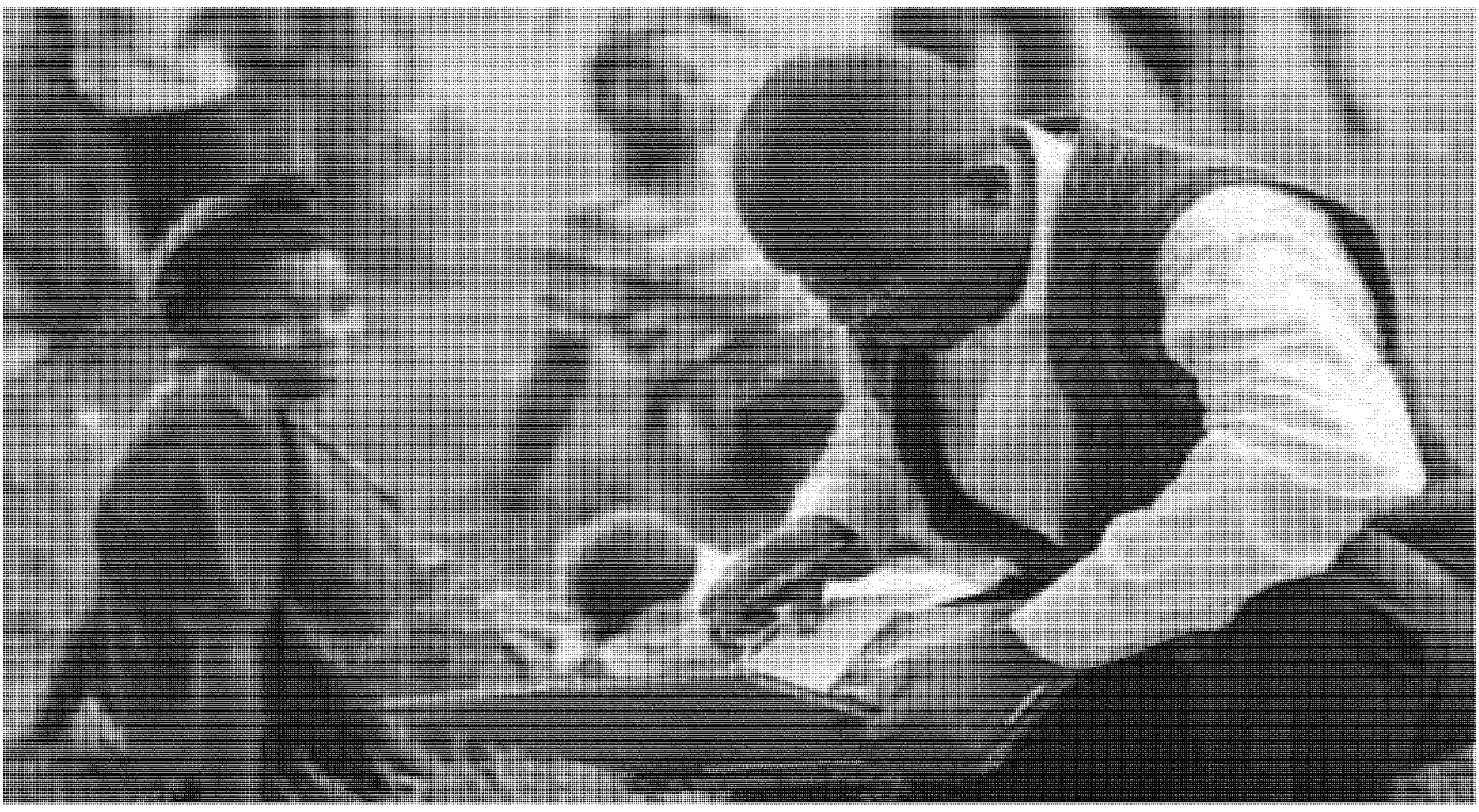
To better understand the epidemiology, the risk factors and the ecology of VHF in DRC

Partners providing support
USAMRIID
Robert Koch Institute, Germany
Public Health England, Porton Down
University of Montpellier
University of Laval, Canada
US NIH/NIAID

Additional support required
Technical support to develop detailed protocol for cohort studies is needed.
Financial support is required to complement costs of various studies

Key Activities

1. Mapping the distribution of VHF in DRC by conducting seroprevalence (using multiples antigen to increase specificity) studies for general population and high-risk population in outbreak zones as well as in non-outbreak zones.
2. Capacity development for local multiplex ELISA/protein array.
3. In regions with higher seroprevalence, conduct a detail risk behavior studies based on information collected during focus group.
4. Conduct cohort studies in identified high risk groups for detection of EBOV seroconversion (or increase of IgG titer) or EBOV.
5. Assess infection by Testing and for determination of associated risk factor (including contact with animals).
6. Screening animals identified as risk factor for Ebola infection using diverse method including non-invasive sampling and analysis of vertebrate genetic material ingested by invertebrates.



C. To strengthen the DRC capacities for safe handling, diagnosis and reporting of major VHF diseases in DRC.

Research outcomes

To strengthen the DRC capacities for safe handling, diagnosis and reporting of major VHF diseases in DRC.

Partners providing support
Bernard Nocht Institute, Germany
Public Health England, Porton Down
University of Leuven, Belgium
University of Montpellier, France
US NIH/NIAID
IP Dakar
US CDC
JICA

Additional support required
Need support from a reference laboratory to establish state of the art lab capacity in DRC.

Key Activities

1. Development of National Algorithm and strategies for the diagnostic of VHF in DRC or a guide for diagnostic

2. Establishment of state-of-the-art laboratory in molecular (including viral sequence) and serological techniques for diagnostics of VHF diseases but also arboviruses in Central laboratory (INRB)

3. Development of sequencing (both human and viral) center with training capacity

4. Strengthen provincial intermediate laboratories in diagnostic capacities (e.g. genexpert)

5. Evaluation of the performance of novel viral testing techniques including protein array and ELISA multiplex system that will enable rapid analysis of vaccinees and human blood samples for the surveillance and diagnostic of arboviruses and VHF viruses in DRC

D. To increase the capacity of DRC nationals to respond to EVD outbreak including the case management

Research outcomes

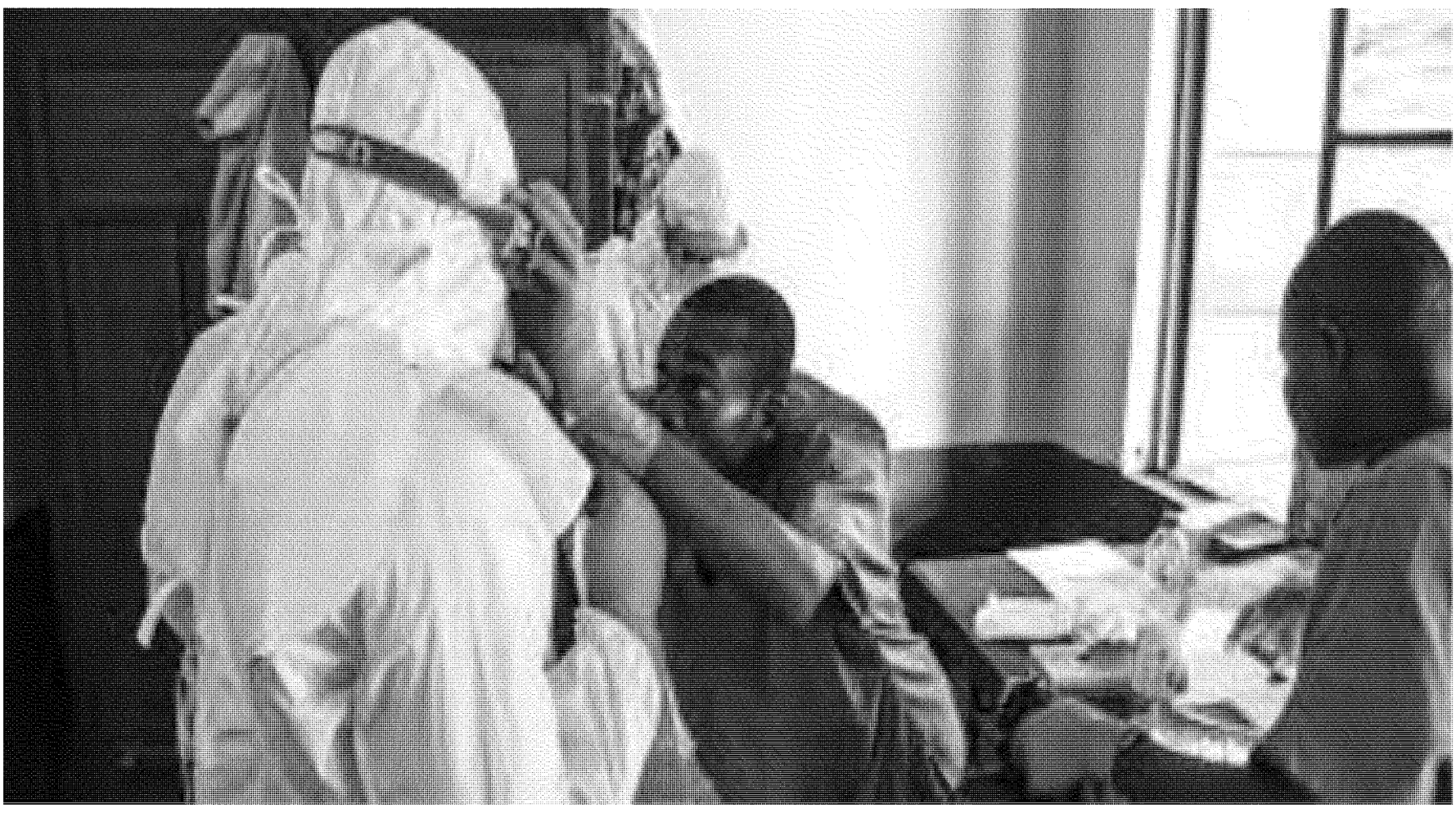
To increase the capacity of DRC nationals to respond to EVD outbreak including the case management

Partners providing support
MSF
GOARN research partners
EDCARN
ALIMA
US CDC

Additional support required
Expert clinicians to help develop training materials and to conduct training of national clinicians so that they work at an ETC in future outbreaks.

Key Activities

1. Implementation of national guidelines for cases management.
2. To create, train and support a DRC team for rapid ETC deployment.
3. To develop a basic stockpile of supplies and equipment required to start an ETC



E. To support the isolation and the GMP development of mAbs against other filovirus from DRC filovirus survivors (Ebola, Bundi and Marburg)

Research outcomes

To support the isolation and the GMP development of mAbs against other filovirus from DRC filovirus survivors (Ebola, Bundi and Marburg)

Partners providing support
US NIH/NIAID
University of Laval, Canada
AVAREF
WHO network of Bioethics collaborating centres.

Additional support required
Continued support is needed to develop capacity to isolate potent MAbs and to develop them as GMP products.

Key Activities

1. To develop Filo specific potent mAb from DRC survivors (Ebola, Bundi, Marburg) to be used to treat patients in DRC by reducing intellectual property restriction (Nagoya Protocol).

2. Support joint/ national NRA and ethics reviews of protocols for Dx, therapeutics and vaccines testing.

F. To perform clinical, immunological and genetic characterization of symptomatic and asymptomatic survivors, Ebola IgG positive individuals, and vaccinees.

Research outcomes

Better understanding of immune response among symptomatic and asymptomatic survivors, Ebola IgG positive individuals, and vaccinees

Partners providing support
US NIH
University of Oregon, USA
Bernard Knocht Institute, Germany
Robert Koch Institute, Germany
Public Health England

Additional support required
Continued support to the activities listed.

Key Activities

1. Ig G subclasses
2. Retrospective investigation of the current outbreak (epidemio and immuno)
3. Evaluate the durability of the response induced by the rVSV in DRC
4. Sera reactivity to GP forms (sGP, full length, delta Muc, Thermolysine cleaved)
5. Sera reactivity to other Ebola antigen (NP, VP40, ..)
6. Evaluation of long term sequelae of disease in ebola survivor including psycho neurological impairment
7. Assessing possible interaction between EVD and other endemic disease: cross reactivity with Monkeypox or malaria
8. Memory T cell characterization of survivors Vs asymptomatic infection and vaccinees
9. Genetic factor associate with disease susceptibility or resistance (HLA, NPC1)

.

G. To support the Ebola response, particularly through risk communication and community engagement activities with, better understanding of community context and practices.

Research outcomes

To contribute to support community engagement activities in particular those to aimed to understand risk behaviour and risk management

Partners providing support
University of Antwerp, Belgium
Institute of Tropical Medicine, Belgium
University of Kinshasa, DRC
University of Kisangani, DRC
SACIDS

Additional support required
Expert anthropologists to help develop training materials and to conduct training of national anthropologists so that they can contribute in future outbreaks

Key Activities

1. Operational research on community practices related to risk factor behaviours
2. Research on how best to offer psycho-social support to infected persons and their families
3. Anthropological research on perception and conception of disease
4. Research in knowledge, attitudes and practices (KAP) and social mobilisation and community engagement

H. To set in place a mechanism in DRC to facilitate the coordination of the research efforts related to Ebola

Research outcomes

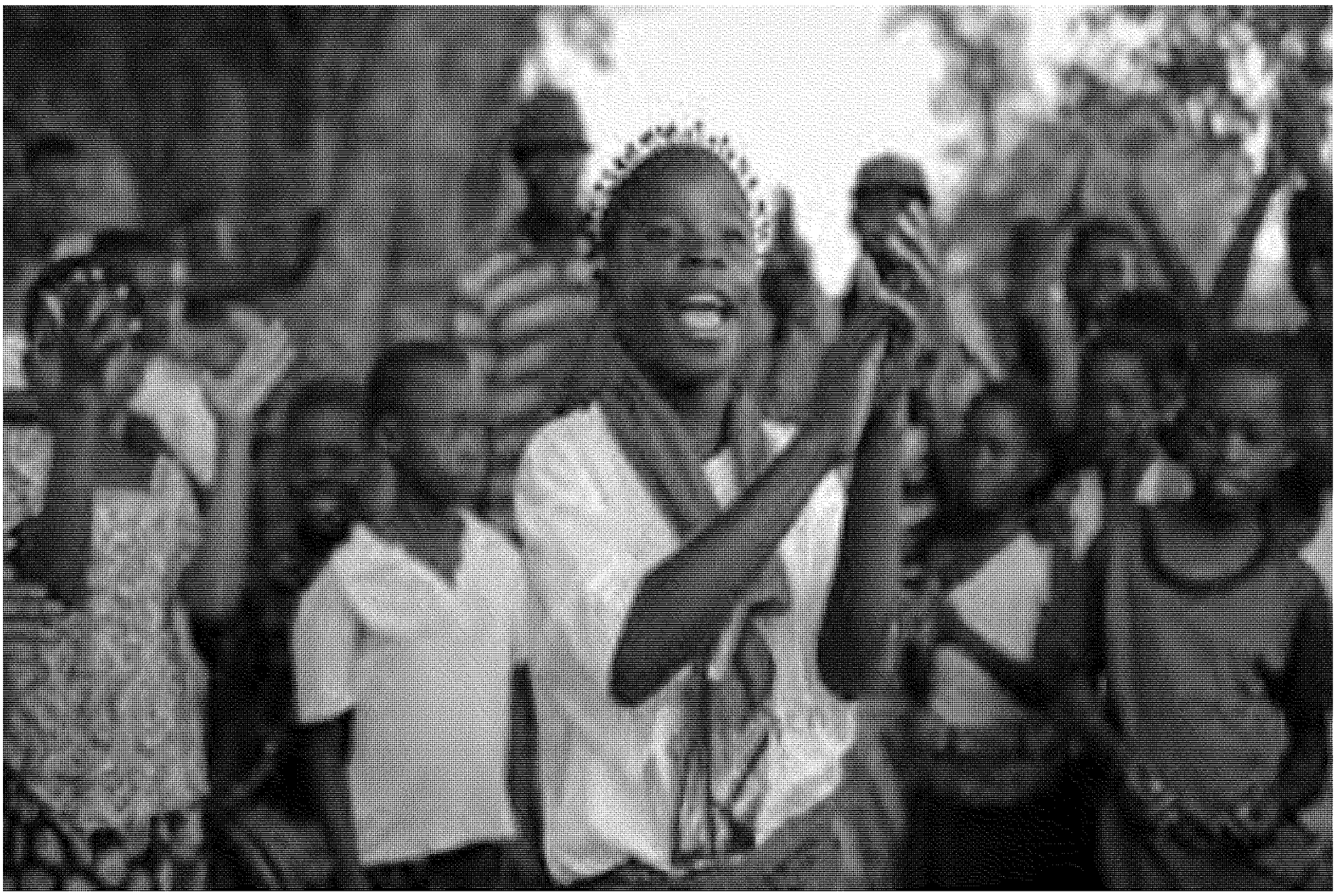
To set in place a mechanism in DRC to facilitate the coordination of the research efforts related to Ebola

Partners providing support
Wellcome/DFID
WHO

Additional support required
A multidisciplinary team at INRB will be critical to ensure the timely implementation and coordination of activities

Key Activities

1. Support to INRB for additional staff to ensure coordination and implementation
2. Support to ensure that the coordination team is operational and mobile.
3. Coordination workshop for research actors in DRC. Proactively build teams of Good Clinical Practice (GCP)-certified national researchers and pre-position clinical trial protocols approved by DRC NRA for future outbreaks



I. To coordinate the design and support the prompt implementation of efficacy trials to assess candidate therapeutics and the post-marketing evaluation of therapeutics for Ebola

Research outcomes

To coordinate the design and support the prompt implementation of efficacy trials to assess candidate therapeutics and the post-marketing evaluation of therapeutics for Ebola

Partners providing support

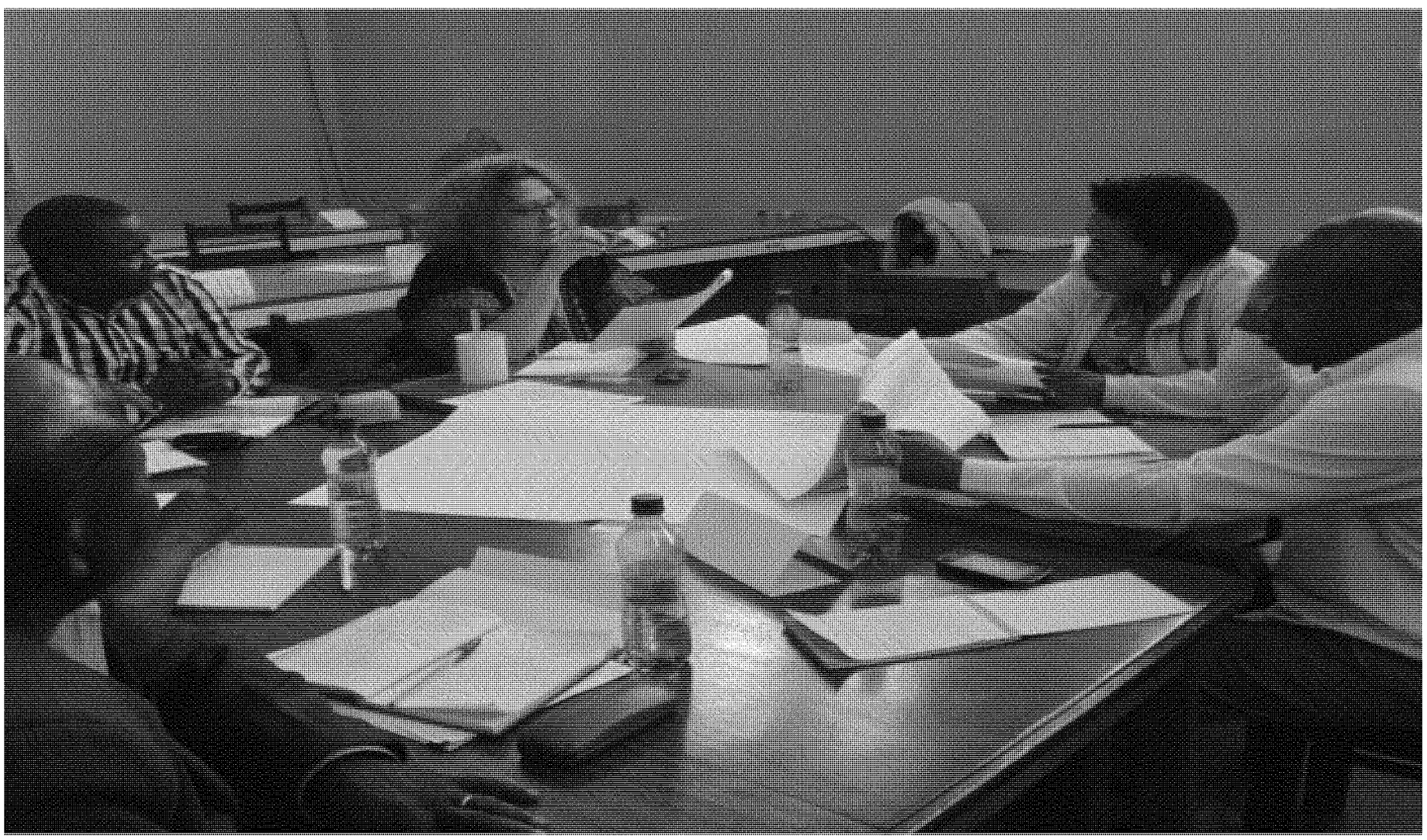
MSF
ALIMA
WHO
University of Kinshasa, DRC
Univ of Oxford, UK
WHO network of clinical trial experts
Developers donation.

Additional support required

Continued support from expert trialists to finalize protocol.

Key Activities

1. Design / Review of protocols for clinical trials
2. Good Clinical Practice (GCP) training of national researchers
3. Conduct testing of key candidate therapeutics
4. Coordination workshop in DRC



J. To ensure prompt access and use of candidate Ebola rVSV vaccine through a ring vaccination strategy as part of the response to the outbreak, including in particular the evaluation of vaccine safety in target populations to better understand the risk of adverse events in outbreak settings

Research outcomes

To ensure prompt access and use of candidate Ebola rVSV vaccine through a ring vaccination strategy as part of the response to the outbreak, including in particular the evaluation of vaccine safety in target populations to better understand the risk of adverse events in outbreak settings

Partners providing support
WHO
MSF
University of California, USA

Additional support required
No additional support is anticipated at this point in time.

Key Activities

1. Deployment under an Expanded Access/Compassionate Use protocol with individual informed consent and in compliance with GCP and all applicable ethical and regulatory requirements.

2. To further evaluate the immune response after rVSV vaccination in DRC.

K. To conduct the evaluation of candidate multivalent filovirus vaccines in DRC for safety, immunogenicity, correlates of protection, and duration of immunity

Research outcomes

To conduct the evaluation of candidate multivalent filovirus vaccines in DRC for safety, immunogenicity, correlates of protection, and duration of immunity

Partners providing support
WHO
NIH
WHO network of clinical trials experts

Additional support required
Continued support from expert trialists to finalize protocol.

Key Activities

1. Adapt and review of protocols for clinical trials to evaluate additional Ebola vaccines in DRC

L. Support coordination of data sharing and sample sharing in DRC

Research outcomes

Support coordination of data sharing and sample sharing in DRC

Partners providing support
Institute Pasteur, Senegal
WHO

Additional support required
Evaluation of feasibility for the establishment of a DRC VHF biobank. Training internationally of DRC scientists.

Key Activities

1. Support legal review of data and sample sharing provisions including MTA to allow for longer term storage and use of samples and wider sharing of data.
2. Support local capacity including for samples storage.
3. Implement plan for longer term storage of samples enabling exploration of research questions

Timeline

This timeline illustrate intended dates of start and completion of various activities.
A detailed micro-plan is being prepared.

	2018				2019				2020				2021			
Activity	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
A1 to A5																
B1																
B2																
B3																
B4																
B5																
B6																
C1 to C5																
D1 to D3																
E1 to E3																
F1																
G1 to G3																
H1 to H3																
I1 to I4																
J1 to J2																
K1 to K3																
L1 to L3																

RESEARCH PLAN for Ebola Virus Disease, Democratic Republic of Congo (DRC)

Prof Jean-Jacques Muyembe

Director, INRB

National Institute for Biomedical Research (INRB)

Clinical Trials Development

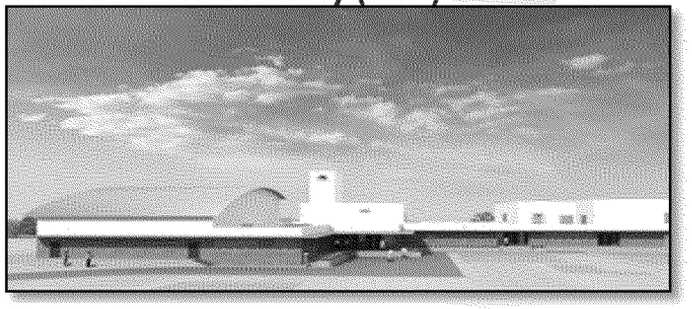
Ongoing:

-Clinical Immunology Laboratory
-Hospital pharmacy

Planned:

- INRB Clinical Center

INRB 2020 new facility (JICA)



Surveillance & Response Outbreak

Active Surveillance Labs

- Polio
- Measles/Rubella
- Influenza
- Ebola/Yellow Fever

Outbreak Response

- Epi Investigation
- Mobile Laboratory
- Clinical Care
- Training of staffs in the field

Biomedical Research

Fundamental, applied and operational research

- Sleeping sickness diagnostic kit commercialization
- Phytotherapy (Malaria)

Training

- Lab scientists
- Lab Tech
- Students (PhD, Msc..

Diagnostic Services

- Biochemical and microbiological analysis
- Pathological analysis
- Parasitological tests
- Serological tests

OBJECTIVES OF THE PLAN

- To expand knowledge about Ebola during the present outbreak and beyond
- To expand the existing research capacity in DRC
- To incorporate the numerous research suggestions by international partners in view of the country priorities, feasibility and other considerations

IMMEDIATE PRIORITIES OF THE PLAN

1. Urgently conduct a retrospective investigation on origins of the current outbreak
2. Develop national centre of excellence for molecular diagnostic, sequencing and immunology of VHF.
3. Create and train a local cadre of congolese physicians that can deploy rapidly with associated equipment and set up an ETC.

SHORT, MEDIUM AND LONG-TERM PRIORITIES

3 AREAS OF WORK, with 11 SETS OF ACTIVITIES are presented in the agreed research plan. These break down into short, medium and long-term priorities for DRC to better detect, prevent, control and treat Ebola infection and disease.

AREAS OF WORK	Priority research is proposed:
1. PREVENTION	1. To improve and strengthen the surveillance system for early detection and response to VHF outbreaks in 4 pilot areas (former Equateur, Oriental Province, Kasai and Bandundu).
	2. To better understand the epidemiology and risk factors and the ecology of VHF in the DRC
2. DETECTION	3. To strengthen the DRC capacities for safe handling, diagnosis and reporting of VHF diseases

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	4. To increase capacity to provide adequate standard of care and case management
	5. To support isolation and GMP development of mAbs against other filoviruses from DRC filovirus survivors
	6. To conduct Clinical, immunological and genetic characterization of survivors and asymptomatic infections and response in vaccinees
	7. To contribute to support community engagement activities in particular those aimed to understand risk behavior and risk management
	8. To set up a sustainable mechanism in DRC to facilitate the coordination of the research efforts related to Ebola

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	9. To coordinate the design and support the prompt implementation of efficacy trials to assess candidate therapeutics for Ebola and their post-marketing evaluation
	10. To ensure prompt access and use of candidate Ebola rVSV vaccine through a ring vaccination strategy as part of the response to the outbreak, including in particular the evaluation of vaccine safety in target populations to better understand the risk of adverse events in outbreak settings.
	11. To conduct the evaluation of candidate multivalent filovirus vaccines in DRC for safety, immunogenicity, correlates of protection, and duration of immunity.
	12. Support coordination of data sharing and sample sharing in DRC

AREAS OF WORK	Priority research is proposed:
1. PREVENTION	**1. To improve and strengthen the surveillance system for for early detection and response to VHF outbreaks in 3 pilot areas**
	2. To better understand the epidemiology and risk factors and the ecology of VHF in the DRC

KEY ACTIVITIES PREVENTION 1

Train key HCW (Doctors and nurses working in Referral General Hospital, in Referral Health Centers and in peripheral small clinics) in the selected Health Zones (HZ) to recognize a suspect case VHF

Train the key HCW in safe and proper collection of sample specimens from suspect cases of VHF for Rapid Testing and confirmation test in central lab

Train the Chief Medical Officer (CMO) of the HZ in timely investigation of suspect cases of VHF, in implementing initial isolation measures and in completing the notification form including list of contacts

Train the CMO of the Health Zone to properly prepare the shipment of the sample specimens from suspect case of VHF and to ship the samples with the completed notification form (including internet-based reporting system) to INRB in a timely manner.

Train the CMO to monitor the stock of supplies for samples collection material, PPE and Rapid Test in the health zone and to timely request replenish from INRB

AREAS OF WORK	Priority research is proposed:
1. PREVENTION	1. To improve and strengthen the surveillance system for for early detection and response to VHF outbreaks in 3 pilot areas
	2. **To better understand the epidemiology and risk factors and the ecology of VHF in the DRC**

KEY ACTIVITIES PREVENTION 2

Mapping the distribution of VHF in DRC by conducting seroprevalence (using multiples antigen to increase specificity) studies for general population and high risk population in outbreak zones as well as in non outbreak zones

Capacity development for local multiplex ELISA/protein array

In regions with higher seroprevalence, conduct a detail risk behavior studies based on information collected during focus group

Conduct cohort studies in identified high risk groups for detection of EBOV seroconversion (or increase of IgG titer) or EBOV infection by RTesting and for determination of associated risk factor (including contact with animals)

Screening animals identified as risk factor for Ebola infection using diverse method including non invasive sampling and analysis of vertebrate genetic material ingested by invertebrates

AREAS OF WORK	Priority research is proposed:
2. DETECTION	3. **To strengthen the DRC capacities for safe handling, diagnosis and reporting of VHF diseases**

Development of National Algorithm and strategies for the diagnostic of VHF in DRC or a guide for diagnostic

Establishment of state-of-the-art laboratory in molecular (including viral sequence) and serological techniques for diagnostics of VHF diseases but also arboviruses in Central laboratory (INRB)

Development of sequencing (both human and viral) center with training capacity

Strengthen provincial intermediate laboratories in diagnostic capacities (e.g genexpert)

Evaluation of the performance of novel viral testing techniques including protein array and ELISA multiplex system that will enable rapid analysis of vaccinees and human blood samples for the surveillance and diagnostic of arboviruses and VHF viruses in DRC

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	4. **To increase capacity to provide adequate standard of care and case management**
	5. To support isolation and GMP development of mABs against other filoviruses from DRC filovirus survivors

KEY ACTIVITIES 4

Implementation of national guidelines for cases management

Create, train, support a team in Kinshasa that could be rapidly deployed as an ETU

Provide needed materials for ETU in-situ

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	4. To increase capacity to provide adequate standard of care and case management
	5. **To support isolation and GMP development of mABs against other filoviruses from DRC filovirus survivors**

KEY ACTIVITIES 5

To develop Filo specific potent mAb from DRC survivors (Ebola, Bundi, Marburg) to be used to treat patients in DRC with local ownership, and favourable access and benefit provisions

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	**6. To conduct clinical, immunological and genetic characterization of survivors and asymptomatic infections and response in vaccinees**
	7. To contribute to support community engagement activities in particular those aimed to understand risk behavior and risk management
	8. To set up a sustainable mechanism in DRC to facilitate the coordination of the research efforts related to Ebola

KEY ACTIVITIES

Sera reactivity to GP forms

Sera reactivity to other Ebola antigen

Evaluation of long term sequelae of disease in ebola survivor including psycho neurological impairment

Assessing possible interaction between EVD and other endemic disease : cross reactivity with Monkeypox or malaria

Memory T cell charaterization of survivors Vs asymtomatic infection and vaccinees

Genetic factor associate with disease susceptibility or resistance

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	6. To conduct clinical, immunological and genetic characterization of survivors and asymptomatic infections and response in vaccinees
	7. To support the Ebola response, particularly through risk communication and community engagement activities, with better understanding of community contexts and practices
	8. To set up a sustainable mechanism in DRC to facilitate the coordination of the research efforts related to Ebola

KEY ACTIVITIES

Operational research on community practices related to risk factor behaviours

Research on how best to offer psycho-social support to infected persons and their families (Balayulu, University of Kinshasa)

Anthropological research on perception and conception of disease

Research in knowledge, attitudes and practices (KAP) and social mobilisation and community engagement

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	6. To conduct clinical, immunological and genetic characterization of survivors and asymptomatic infections and response in vaccinees
	7. To contribute to support community engagement activities in particular those aimed to understand risk behavior and risk management
	8. To set up a sustainable mechanism in DRC to facilitate the coordination of the research efforts related to Ebola

KEY ACTIVITIES

Support to INRB for additional staff to coordinate research

Activities and travels for the research coordinator

Coordination workshop for research actors in DRC.

Proactively build teams of Good Clinical Practice (GCP)-certified national researchers and pre-position approved clinical trial protocols by DRC authorities for future outbreaks

AREAS OF WORK	Priority research is proposed:
3. RESPONSE/ PREPAREDNESS	9. To coordinate the design and support the prompt implementation of efficacy trials to assess candidate therapeutics for Ebola and the post-marketing evaluation of the same.
	10. To ensure prompt access and use of candidate Ebola rVSV vaccine through a ring vaccination strategy as part of the response to the outbreak, including in particular the evaluation of vaccine safety in target populations to better understand the risk of adverse events in outbreak settings.
	11. To conduct the evaluation of candidate multivalent filovirus vaccines in DRC for safety, immunogenicity, correlates of protection, and duration of immunity.
	12. Support coordination of data sharing and sample sharing in DRC

KEY ACTIVITIES

Design / Review of protocols for clinical trials

Good Clinical Practice (GCP) training of national researchers

Conduct testing of key candidate therapeutics

Coordination workshop in DRC

Deployment under an Expanded Access/Compassionate Use protocol with individual informed consent and in compliance with GCP and all applicable ethical and regulatory requirements

Adapt and review of protocols for clinical trials to evaluate (Janssen) mutivalent filovirus vaccines in DRC

Support legal review of data and sample sharing provisions including MTA to allow for longer term storage and use of samples and wider sharing of data

Support local capacity including for samples storage

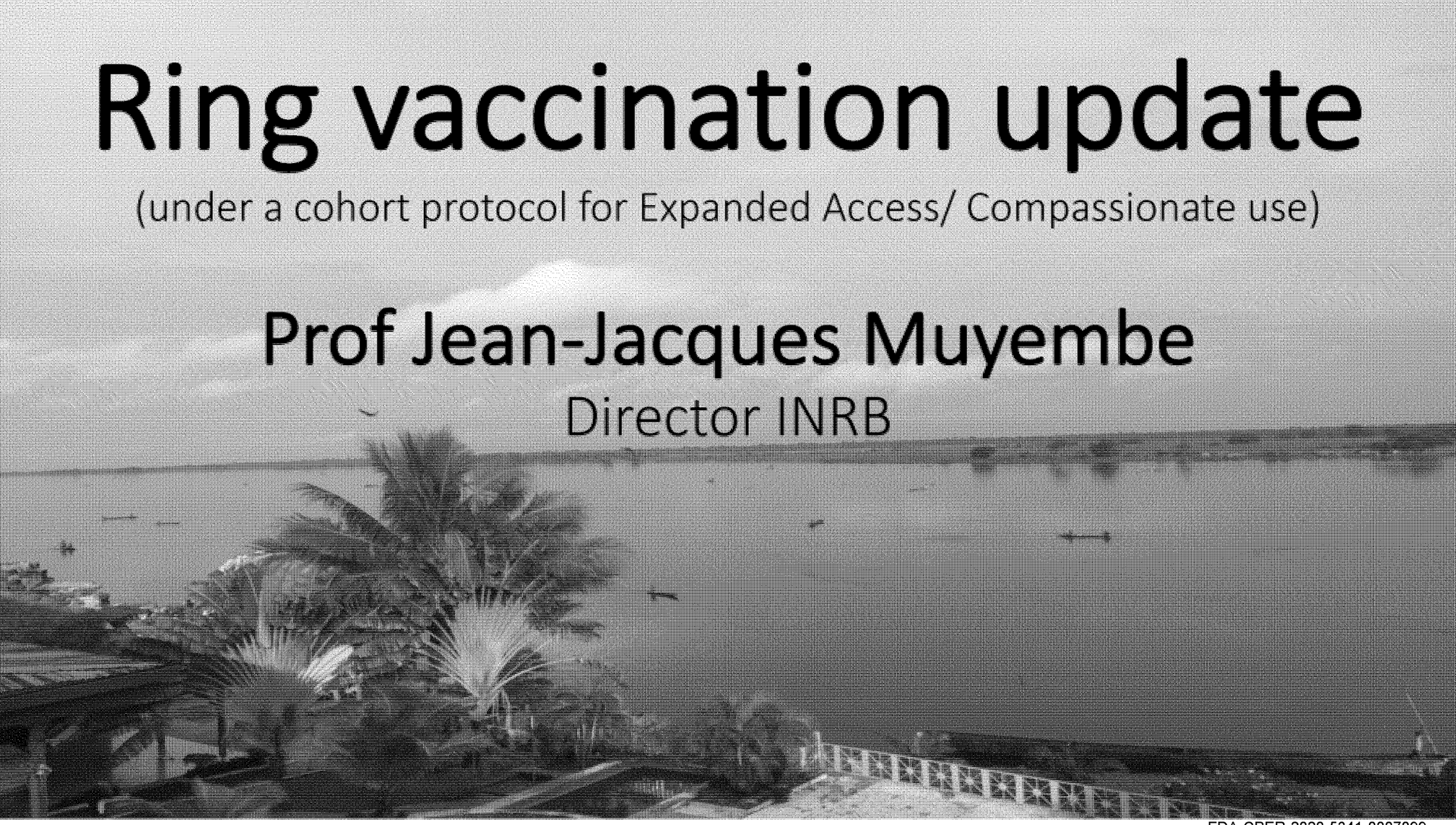
Implement plan for longer term storage of samples enabling exploration of research questions

Ring vaccination update

(under a cohort protocol for Expanded Access/ Compassionate use)

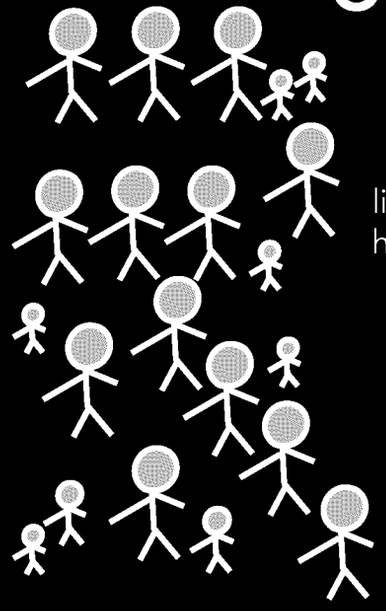
Prof Jean-Jacques Muyembe

Director INRB

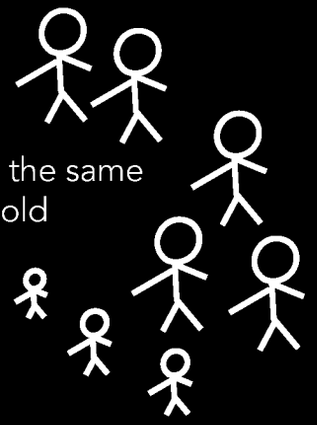


Who is offered Ebola vaccine in a ring vaccination?

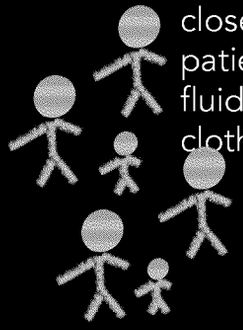
Contacts and contacts of contacts



extended family



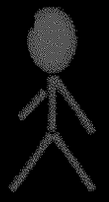
lived in the same household

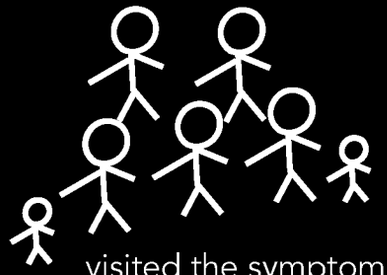


High risk contact: close contact with patient body or body fluids, linen, or clothes

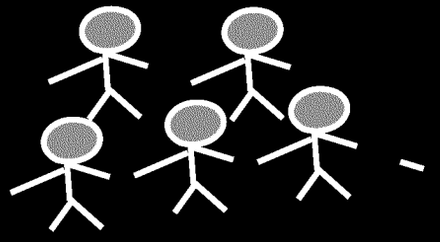
household members of high risk contacts

Lab confirmed EVD case



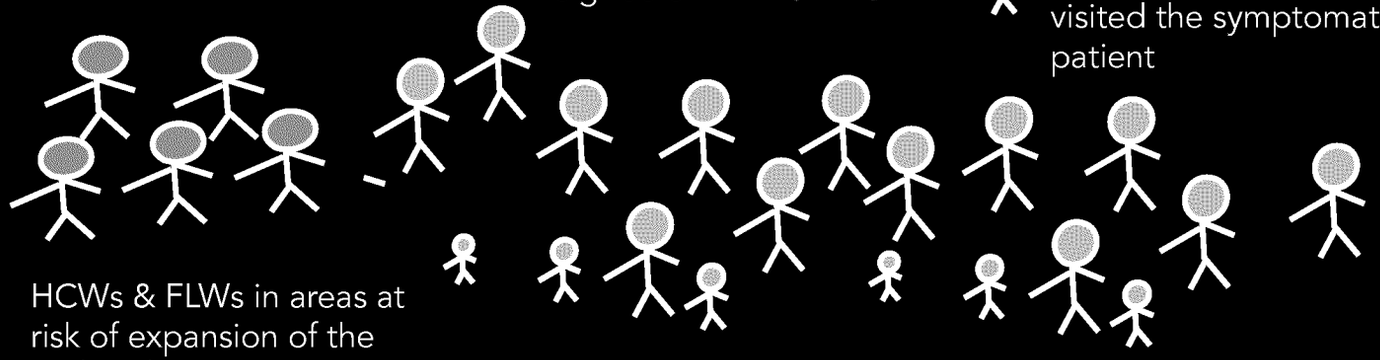


visited the symptomatic patient



local & international HCWs & FLWs in the affected areas

neighbors



HCWs & FLWs in areas at risk of expansion of the outbreak

Who is being offered the yet to be licensed Ebola vaccine?

- Children 1-17 years of age
- Adults 18 years and older

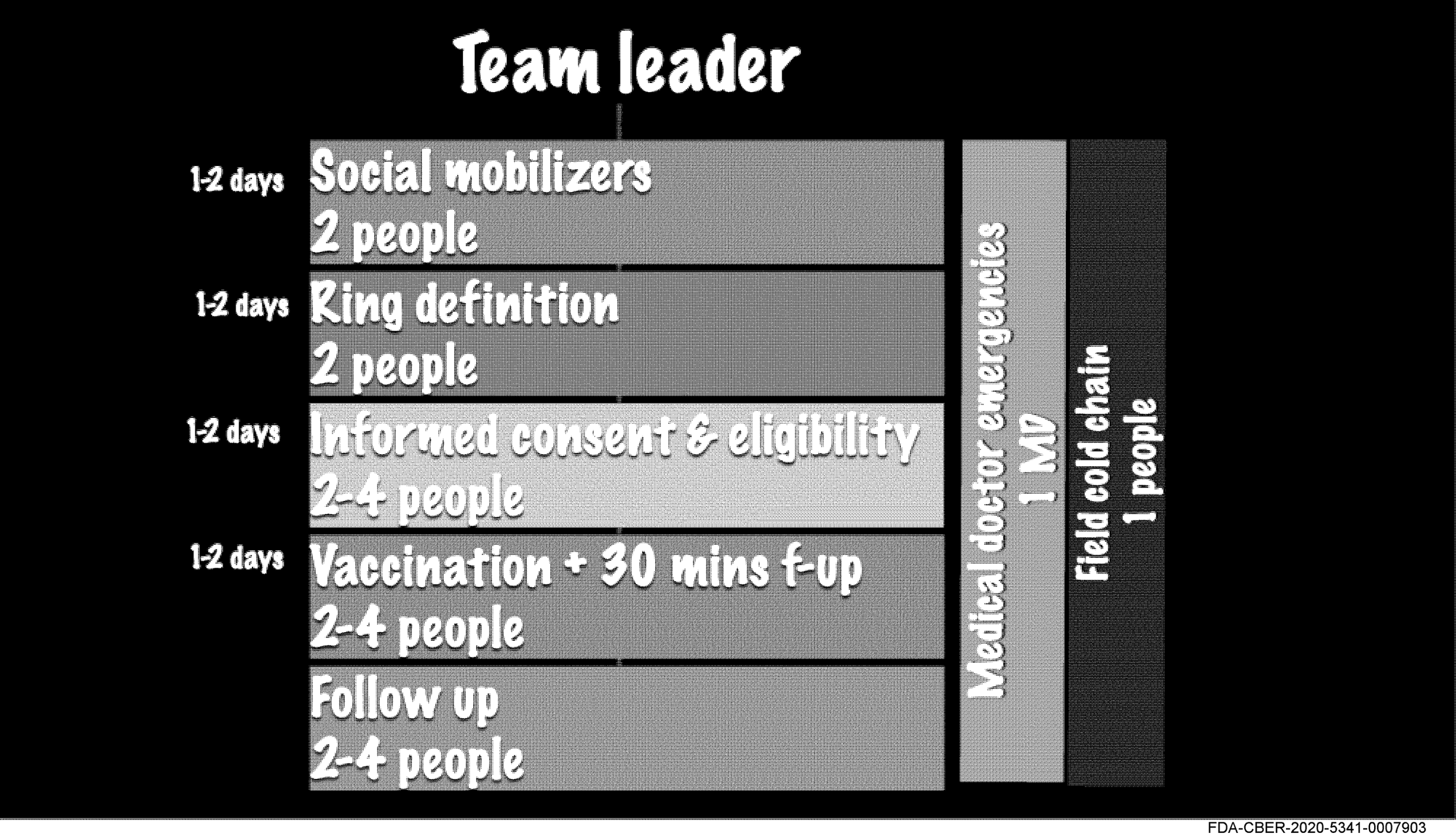
- Excludes pregnant women

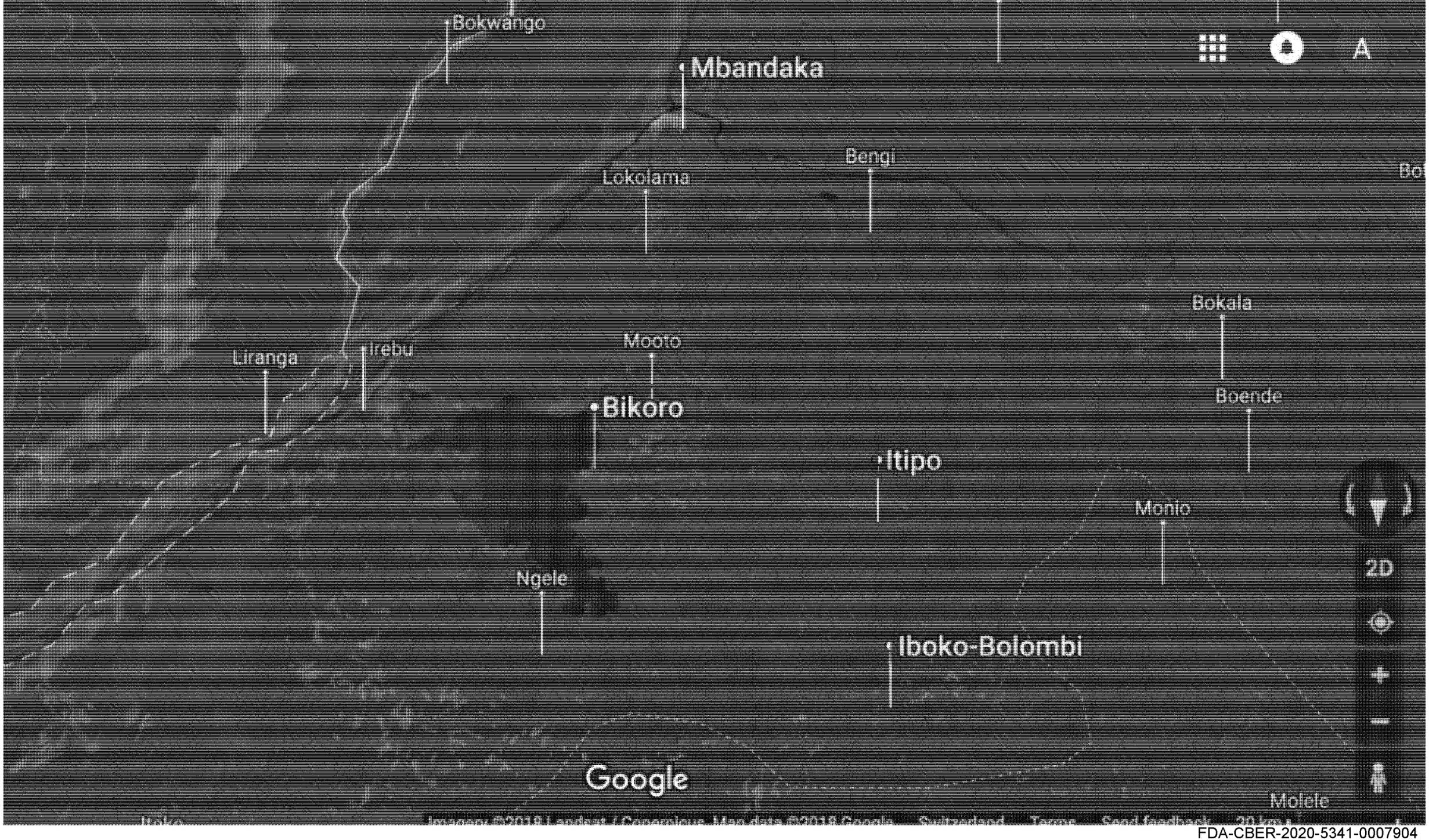
Who is implementing the ring vaccination?

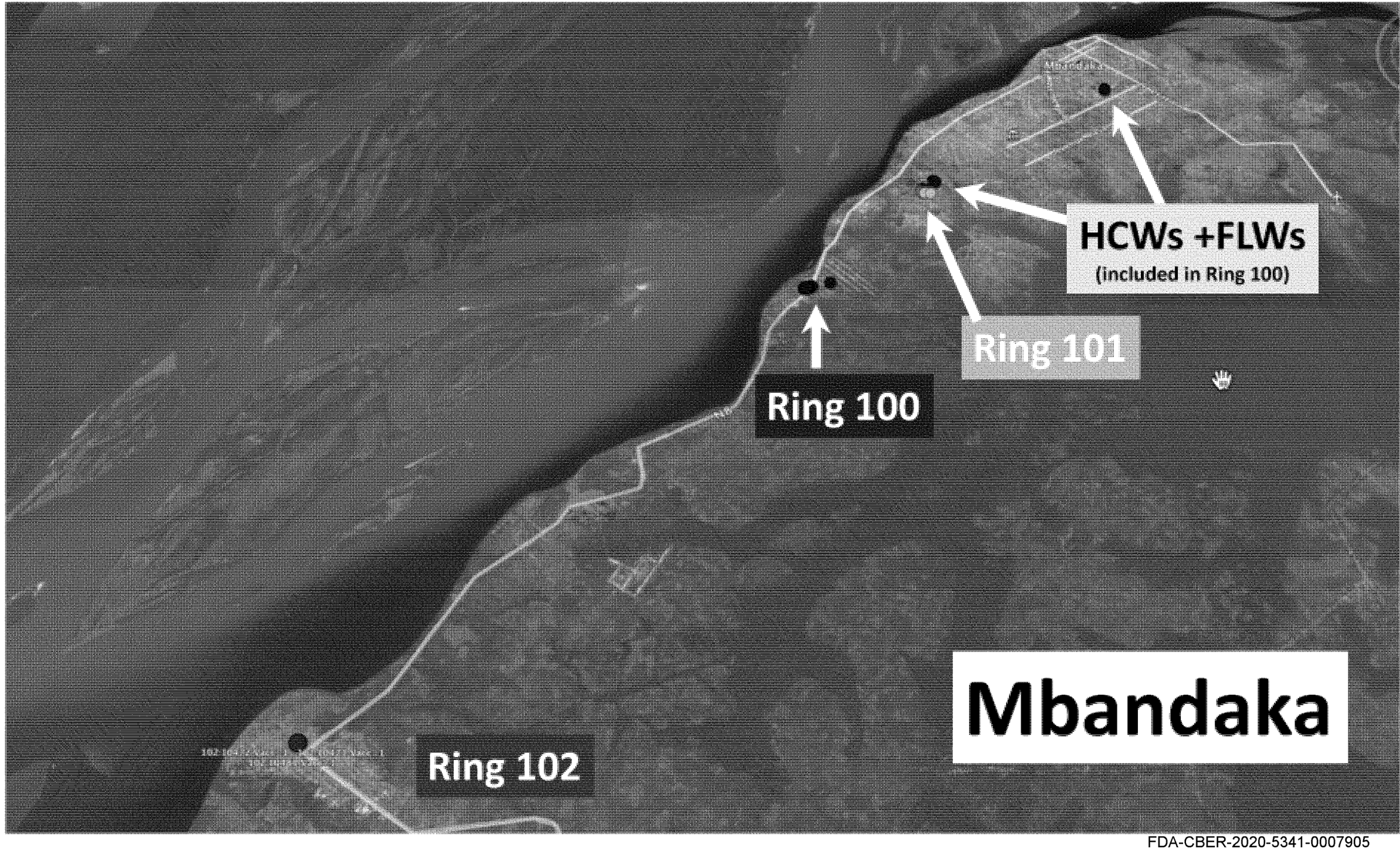
South to South collaboration of GCP trained and experienced Guineans and recently trained DRC colleagues

4 teams in Equator Province

1 team in Kinshasa

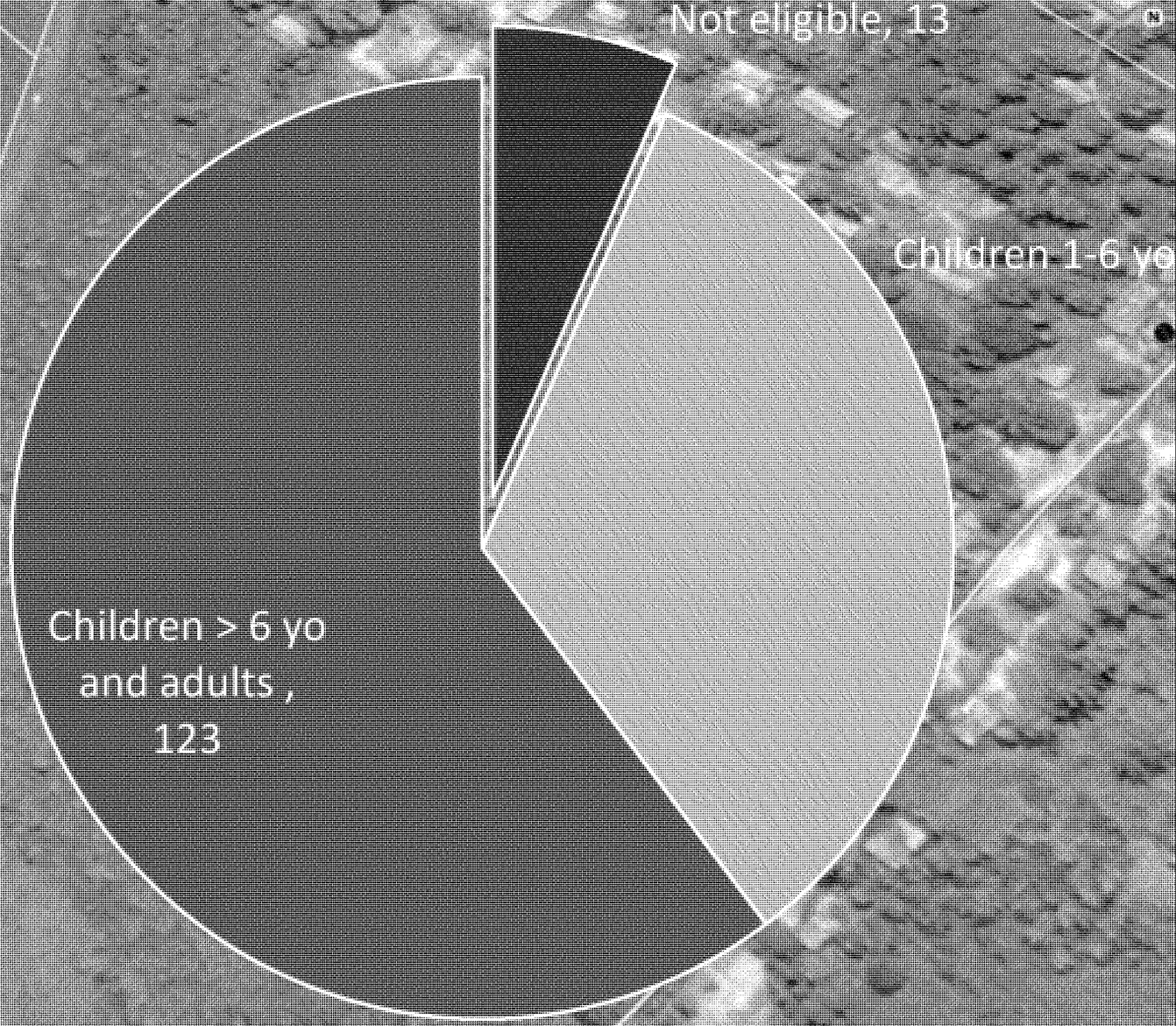



Bokwango
Mbandaka
Bengi
Lokolama
Bokala
Mooto
Liranga
Irebu
Bikoro
Boende
Itipo
Monio
Ngele
Iboko-Bolombi
Molele
2D
Google


HCWs +FLWs
(included in Ring 100)
Ring 101
Ring 100
Ring 102
Mbandaka

Ring 100

Contacts and contacts of contacts	206
Eligible	193
Consented and vaccinated	193

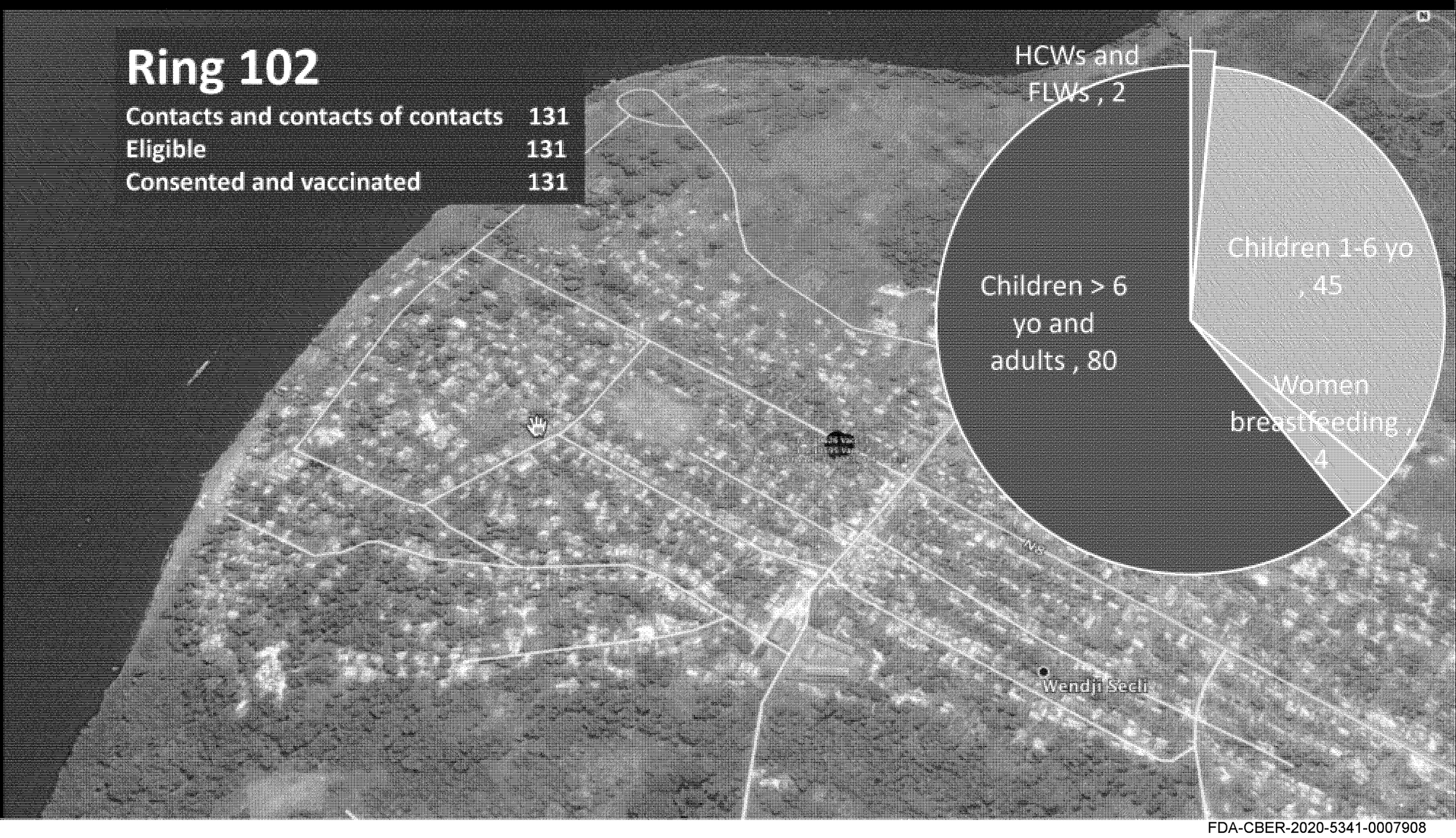


Ring 101

Contacts and contacts of contacts	160
Eligible	109
Consented and vaccinated	103

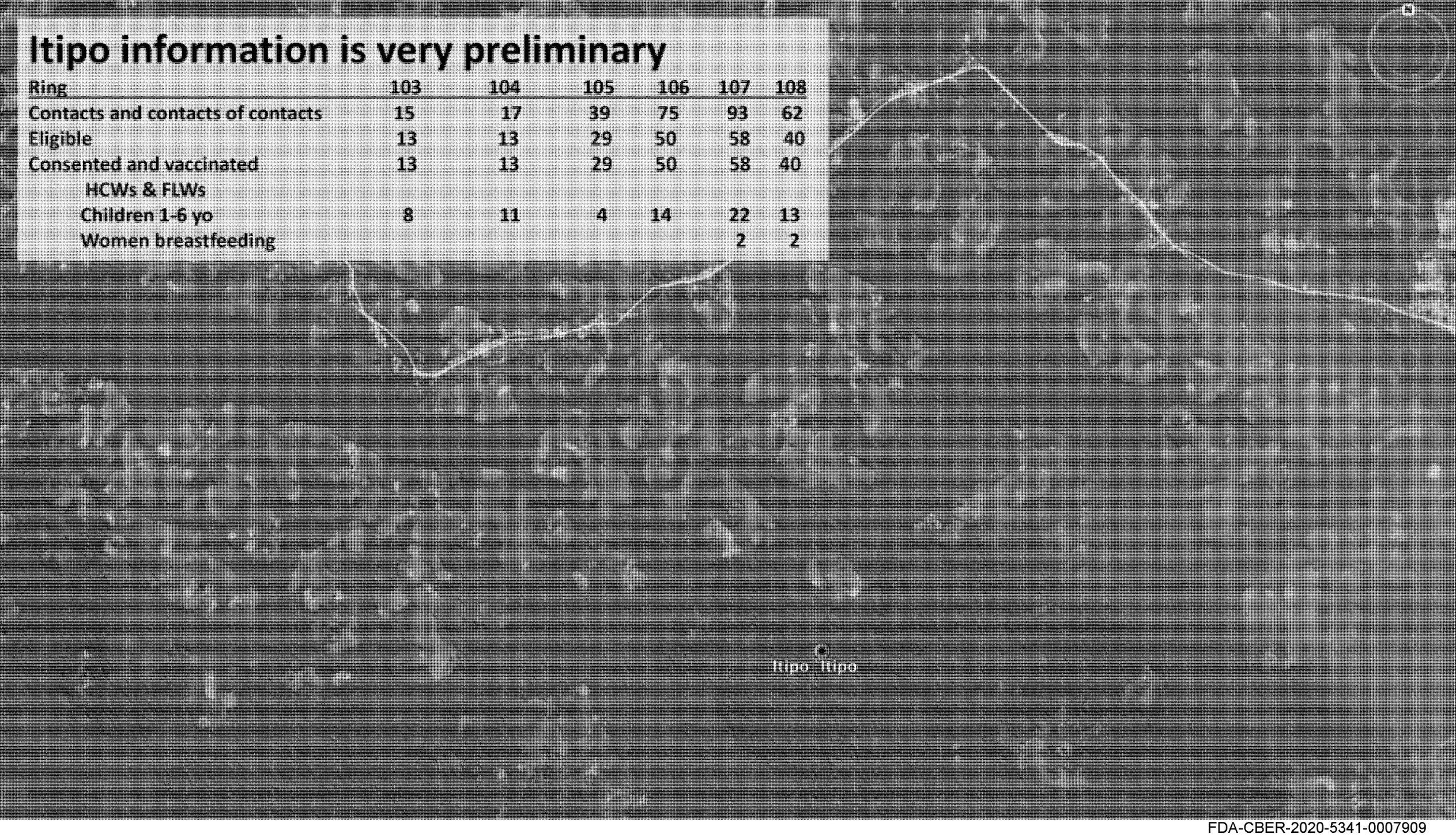
Ring 102

Contacts and contacts of contacts	131
Eligible	131
Consented and vaccinated	131



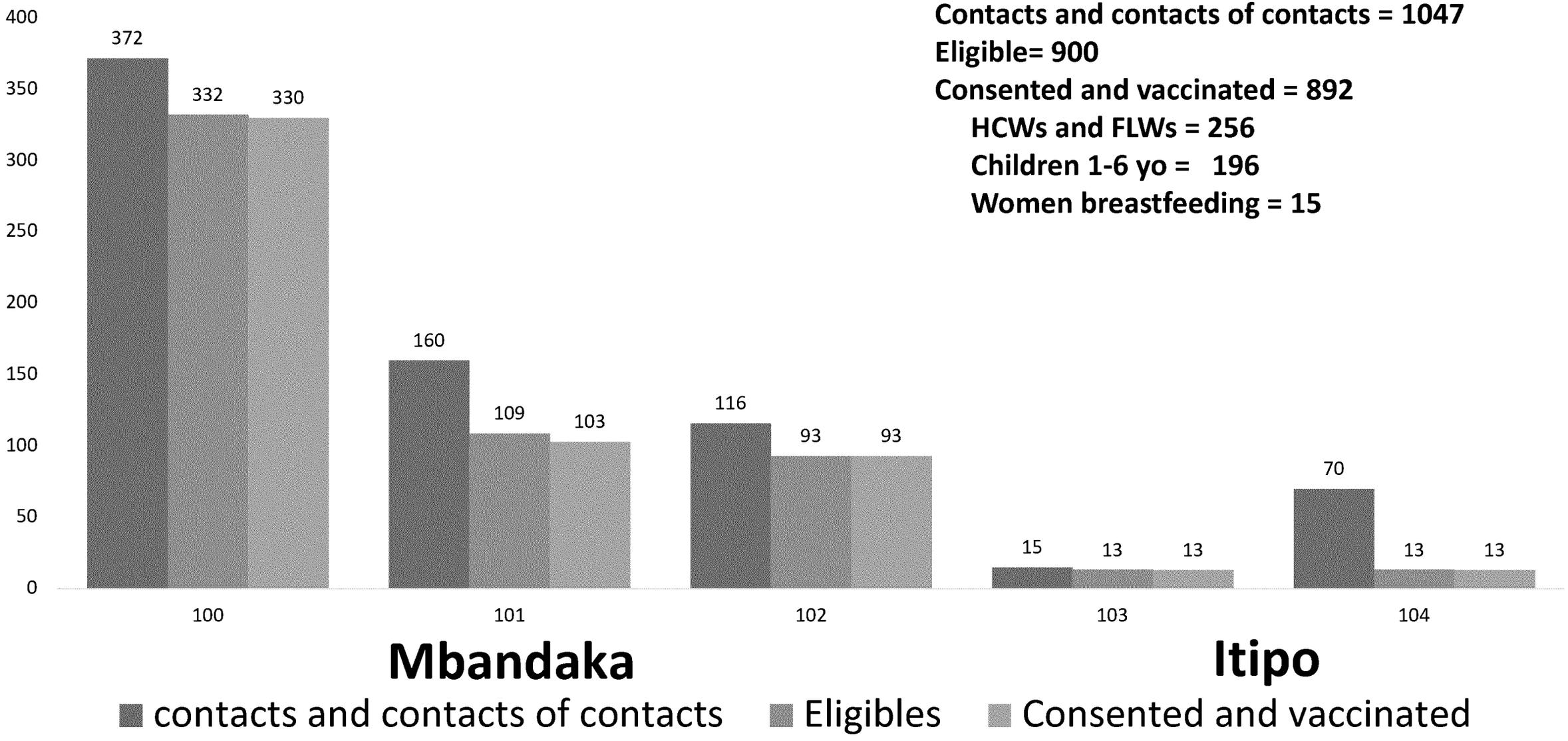
Itipo information is very preliminary

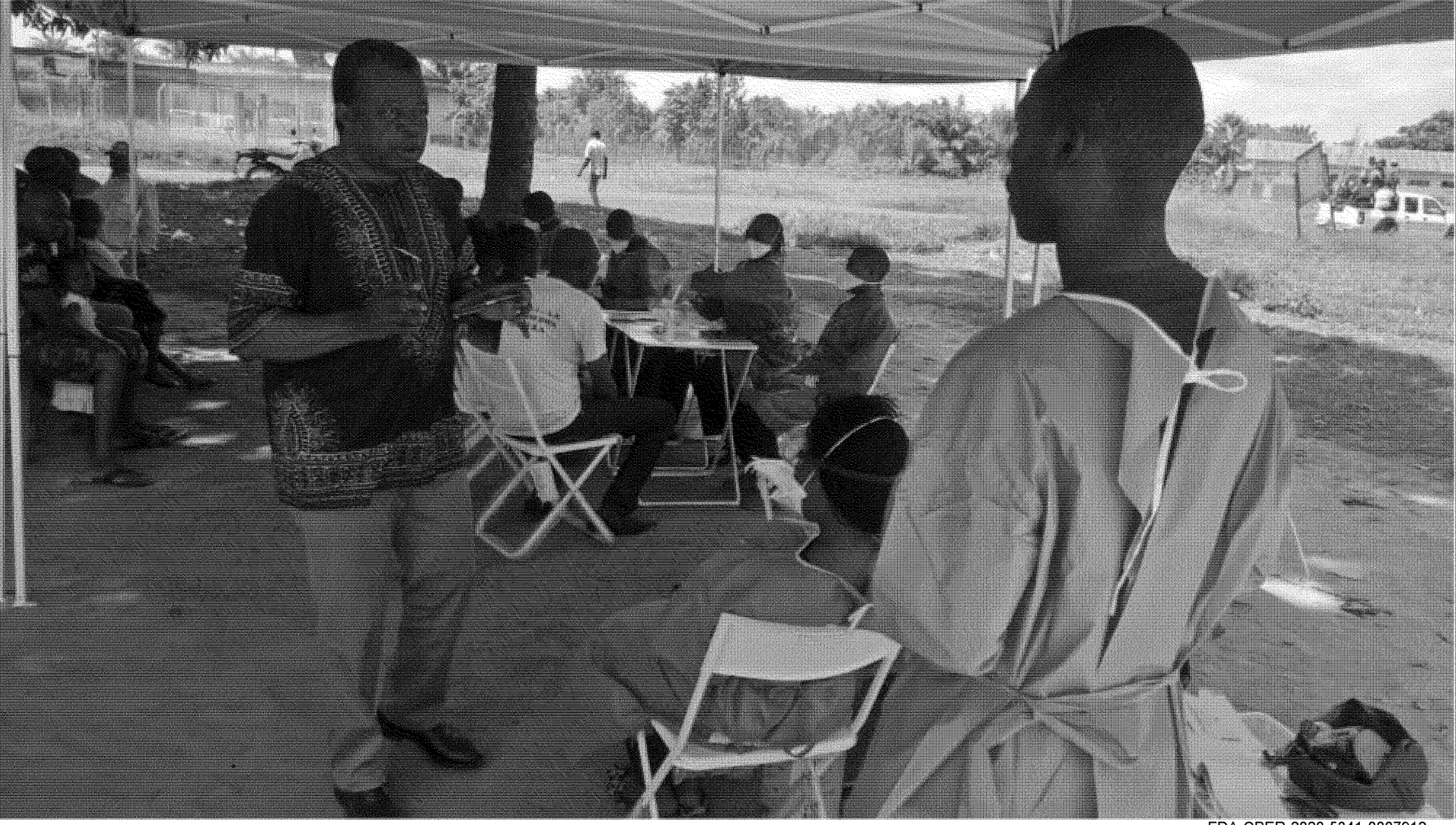
Ring	103	104	105	106	107	108
Contacts and contacts of contacts	15	17	39	75	93	62
Eligible	13	13	29	50	58	40
Consented and vaccinated	13	13	29	50	58	40
HCWs & FLWs						
Children 1-6 yo	8	11	4	14	22	13
Women breastfeeding					2	2

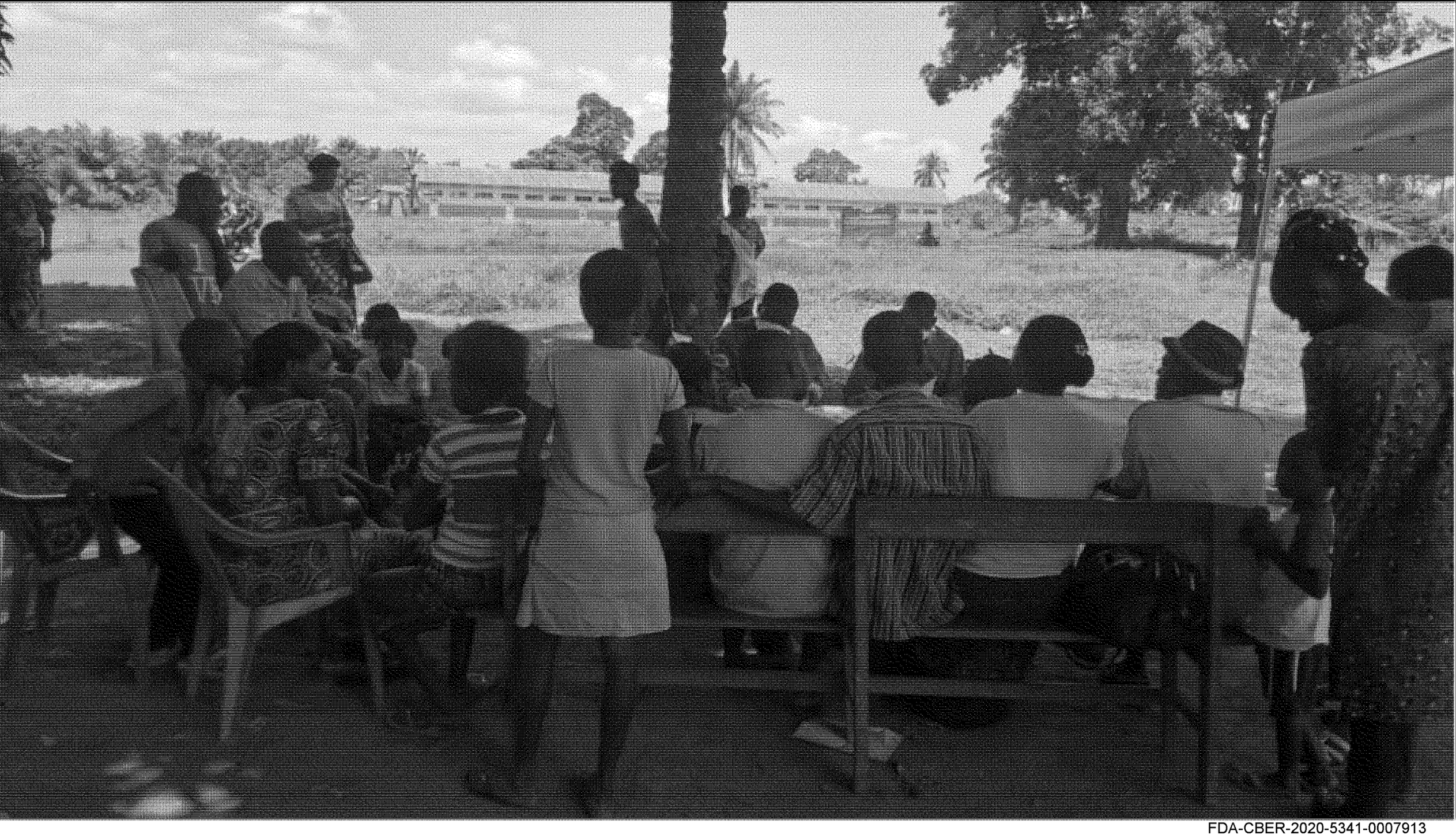


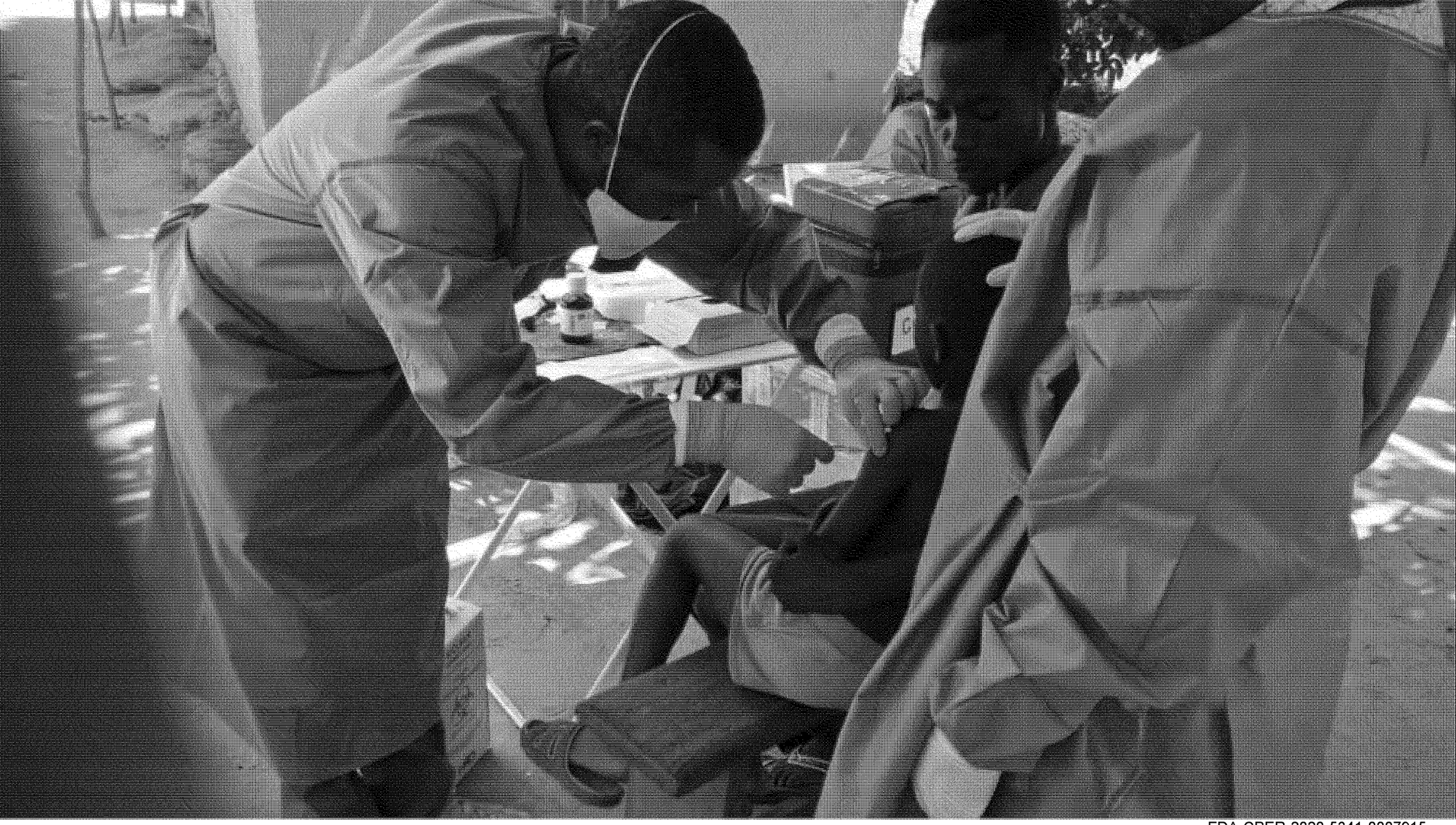
Preliminary results to date

Contacts and contacts of contacts = 1047
Eligible= 900
Consented and vaccinated = 892
HCWs and FLWs = 256
Children 1-6 yo = 196
Women breastfeeding = 15









WHO's ethical framework for decision-making on investigational therapeutics

World Health Organization

In outbreaks with high case fatality "monitored emergency use" may be appropriate if:

No licensed proven therapy exists

An appropriately qualified independent scientific committee reviews the evidence and deems that the benefits are likely to outweigh the harms

Risks can be minimized

Close monitoring is performed

Informed consent is obtained

Results are shared transparently with the scientific community

Protocols are reviewed and approved by a qualified ethics committee.

WHO's ethical framework for decision-making on investigational therapeutics

World Health Organization

Should any investigational therapeutics be highlighted for "monitored emergency use" this is only justified until clinical trial(s) can start.

May 17 scientific committee

World Health Organization

Against this background WHO constituted a scientific committee to review evidence on 5 agents that were highlighted to WHO from the start of the outbreak.

These agents were assessed (in order of data)

- Zmapp
- GS-5734
- REGN combination
- Favipiravir (questions about dose remain)
- mAb114

Situation as of 6 June

World Health Organization

4 investigational therapeutics are in DRC

Zmapp, GS-5734, REGN, mAb114

All have expanded access/compassionate use protocols approved by in-country authorities

Local treating physicians can decide to provide access to agents on a case by case basis, depending also on what is feasible in each treatment facility

Therapeutics to be administered in addition to standards of supportive care.

R&D Blueprint therapeutics trial design working group

World Health Organization

Agreement that clinical trial initiation is highly desirable

Agreement that placebo is not feasible/appropriate for current Ebola outbreak

Agreement that A vs B vs A + B is the methodologically most attractive option, but questions about its feasibility

Process of submission and review of preliminary master protocol underway.

Pre-positioning of RCT protocol will be important for next outbreak

World Health Organization

Ebola in the DRC

The research response timeline

Coordination ☐
R&D Blueprint product ☐
Vaccination ☐
Case management and Therapeutics ☐

08 May
WHO notified by the DRC MoH of confirmed cases of EVD

09 May
First deployments of teams to Bikoro

10 May
Distribution of Notes for the Record and circulation of draft research response plan

WHO, MoH DRC, MSF and Merck prepare for implementation of ring vaccination, pending support of DRC authorities

13 May
DRC formally asks to apply ring vaccination of Merck vaccine

13 May
WHO forms expert working group to prioritize candidate investigational Ebola therapeutics for MEURI

15 May
NIH support to vaccinate deployed frontline workers from USA

16-17 May
TCs on use of investigational therapeutic agents (NFR)

18 May
TC with GCM & SAG

21 May
Ring vaccination starts in Mbandaka

25 May
TC on clinical trial designs for assessing investigational therapeutic agents

25 May
TC on clinical trial designs for assessing vaccine candidates

28 May
Ring vaccination starts in Bikoro and Itipo

04-05 June
SAGE Working Group on Ebola vaccines

06 June
NFR for clinical trial designs for assessing investigational therapeutic agents finalized

Partner contributions
EDCTP has 2 networks (ALERRT/PANDORA) ready to provide support

GOARN research will support definition of the non-product R&D, including research to assess acceptability of experimental interventions.

09 May
R&D Blueprint Ebola Roadmap online for public consultation

09 May
TC between WHO, R&D Blueprint GCM and SAG, and the DRC MoH

10 May
Merck offers support to facilitate access of investigational vaccine under the framework of Expanded Access/Compassionate Use.

10-14 May
WHO approaches Sponsors of investigational therapeutics to access data for scientific assessment under WHO ethical framework.

WHO is working with MSF and DRC MoH to prepare to use those investigational therapeutics.

16 May
First shipment of vaccine arrives in DRC

16 May
WHO Global Health Ethics team launches the Ethics Platform

18 -19 May
Ultra Cold chain established

Guinean team arrives, begins vaccination training with MOH

25 May
TC with GCM & SAG

21 May- Ongoing
Discussions between WHO, MoH, and drug manufacturers to facilitate import and use of investigational therapeutics

04 June
Draft NFR from TC on clinical trial designs for assessing vaccine candidates circulated

06 June
Research meeting in Geneva

07 June
TC on clinical trial designs for assessing vaccine candidates

Planned activities
TC to discuss interpretation of lab results, EVD diagnostic tools, and laboratory capacity

TC on clinical management to discuss the standard of care, clinical core variables, and clinical evaluation

Clinical trial protocols for evaluating vaccines and therapeutics

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 6/6/2018 4:11:27 PM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Lim, Matt (STATE.GOV) [limml@state.gov]; Tracy Carson [CarsonTL@state.gov]
Subject: RE: [2018 Ebola DRC outbreak] - Research plan early draft
Attachments: Ebola-Marburg_Draft_Roadmap_publiccomment_MAY2018.pdf; Ebola-Marburg_Roadmap_Comment_Form.doc; LassaFever_Draft_Roadmap_publiccomment_MAY2018.pdf; LassaFever_Roadmap_Comment_Form.doc; Nipah_Draft_Roadmap_publiccomment_MAY2018.pdf; Nipah_roadmap_comm_form.doc

Dear Colleagues,

I wanted to send a gentle reminder that WHO has asked for feedback on their R&D Blueprint product development roadmaps for Ebola, Lassa and Nipah Viruses by the end of this week (June 8th). If you would like, I am happy to compile any edits (I have already received some) to send WHO/CIDRAP one document with HHS/USG combined edits. These roadmaps are separate, longer term work streams from the acute DRC Ebola outbreak research response, although WHO has leveraged some of the MCM landscape scoping work completed for the Ebola roadmap as they ramped up their response in DRC.

The links to the roadmaps are here and I have also attached them (as well as the WHO comment forms for each) to this email:
http://www.who.int/blueprint/priority-diseases/key-action/ebola/en/
http://www.who.int/blueprint/priority-diseases/key-action/lassa-fever/en/
http://www.who.int/blueprint/priority-diseases/key-action/nipah/en/

Best Regards,
Collin

From: Weinberger, Collin (OS/OGA) (CTR)
Sent: Thursday, May 10, 2018 10:16 AM
To: Handley, Gray (NIH/NIAID) [E] <handleygr@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Lane, Cliff (NIH/NIAID) [E] <CLANE@niaid.nih.gov>; Higgs, Elizabeth (NIH/NIAID) [E] <ehiggs@niaid.nih.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Schafer, Julie (OS/ASPR/BARDA) <Julie.Schafer@hhs.gov>; Helfand, Rita (CDC/OID/NCEZID) <rzh7@cdc.gov>; Craig, Allen (CDC/OID/NCIRD) <afc0@cdc.gov>; Vinter, Serena (CDC/CGH/OD) <uvv3@cdc.gov>; Kapil, Vikas (CDC/CGH/OD) <vck3@cdc.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Krause, Philip (FDA/CBER) <Philip.Krause@fda.hhs.gov>; Marinissen, Maria (OS/ASPR/OPP) <Maria.Marinissen@hhs.gov>; Moudy, Robin (OS/ASPR/OPP) <Robin.Moudy@hhs.gov>; Balliram, Richard (OS/ASPR/OPP) <Richard.Balliram@hhs.gov>; Barna, Lauren (OS/ASPR/OPP) <Lauren.Barna@hhs.gov>; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) <carl.c.holloway.civ@mail.mil>; Kishimori, Jennifer M COL USARMY OSD HA (US) <jennifer.m.kishimori.mil@mail.mil>; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil>; Korch, George (OS/ASPR/IO) <George.Korch@hhs.gov>
Cc: Yu, Anne (HHS/OS/OGA) <Anne.Yu@hhs.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Locus, Tiffany (OS/OGA) <Tiffany.Locus@hhs.gov>; Adeniyi-Jones, Samuel (HHS/OS/OGA) <Samuel.Adeniyi-Jones@hhs.gov>; Clarke, Elana (HHS/OS/OGA) <Elana.Clarke@hhs.gov>; Lim, Matt (STATE.GOV) <limml@state.gov>; Tracy Carson <CarsonTL@state.gov>
Subject: FW: [2018 Ebola DRC outbreak] - Research plan early draft

Dear Colleagues,

Several of you already received this earlier this morning directly from WHO, but in the interest of shared mutual awareness and to make sure all the relevant POCs have seen it, I wanted to pass the below note and attached early draft of the DRC Ebola outbreak research plan, which highlights key research needs. WHO is asking for feedback into the attached. In the interest of a speedy response, I recommend that each HHS and DoD division coordinate internally and send any inputs directly to Massi Si Mehand and the WHO R&D Blueprint team through the POCs on the below email from WHO.

In addition to the DRC research response plan, WHO has posted the R&D Blueprint roadmaps for Ebola, Lassa, and Nipah on their website for comment (see links in Dr. Si Mehand. WHO is accepting comments on the roadmaps through June 8 and I am happy to compile HHS/USG comments on the roadmaps and pass them along to the WHO team if folks will please send me their comments by Wednesday, June 6.

The roadmaps were developed in coordination with Michael Osterholm's group at CIDRAP and they will be holding several webinars on the roadmaps starting next week, the information for which I have pasted below underneath the email from Dr. Si Mehand at WHO. CIDRAP asks that you please RSVP if you plan to log in.

Best Regards,
Collin

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From: SI MEHAND, Massinissa [mailto:simehandm@who.int]
Sent: Thursday, May 10, 2018 3:52 AM
To: Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Erbelding, Emily (NIH/NIAID) [E] <emily.erbelding@nih.gov>; Helfand, Rita (CDC/OID/NCEZID) <rzh7@cdc.gov>; Weinberger, Collin (OS/OGA) (CTR) <Collin.Weinberger@hhs.gov>; george.w.christopher.civ@mail.mil; sina.bavari.civ@mail.mil; david.brett-major@usuhs.edu; kayvon.modjarrad.civ@mail.mil; nelson.l.michael2.mil@mail.mi; Cox, Edward M (FDA/CDER) <Edward.Cox@fda.hhs.gov>; Scherf, Uwe (FDA/CDRH) <Uwe.Scherf@fda.hhs.gov>; Sapsford, Kim E (FDA/CDRH) <Kim.Sapsford@fda.hhs.gov>; Roth, Kristian (FDA/CDRH) <Kristian.Roth@fda.hhs.gov>; gustavo.f.palacios.ctr@mail.mil
Cc: HENAO RESTREPO, Ana Maria <henaorestrepoa@who.int>; PREZIOSI, Marie-pierre <preziosim@who.int>; SATHIYAMOORTHY, Vaseeharan <moorthyv@who.int>; BENASSI, Virginia <benassiv@who.int>; FORMENTY, Pierre B.h. <formentyp@who.int>; LEGAND, Anais <leganda@who.int>; MURGUE, Bernadette <murgueb@who.int>
Subject: [2018 Ebola DRC outbreak] - Research plan early draft

Dear NIH/NIAID, CDC, OGA, DoD/WRAIR and FDA colleagues,

Following the declaration of a new Ebola outbreak in Bikoro in Equateur Province in the Democratic Republic of the Congo (RDC), WHO held a GCM call yesterday to provide a briefing of the situation and to identify/discuss key research activities to be conducted. Please find attached an early draft of a research plan, we will be grateful if you can give us your inputs.

Also, we are pleased to inform you that the draft R&D Roadmaps for Ebola/Marburg, Lassa and Nipah are now available online for a public call for comments, until Friday, 8 June 2018.

Please feel free to visit the dedicated pages (below) and provide your feedback. For each roadmap a comment form is available. However, should you prefer to send the comment directly to my colleague Virginia (cc'd : benassiv@who.int), please do not hesitate to do so.
http://www.who.int/blueprint/priority-diseases/key-action/ebola/en/
http://www.who.int/blueprint/priority-diseases/key-action/lassa-fever/en/
http://www.who.int/blueprint/priority-diseases/key-action/nipah/en/

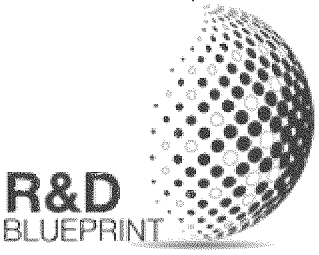
We would very much appreciate if you could share this email message with others in your networks who may be interested in reviewing the roadmaps.

Thannks a lot for your support.

Best wishes,

Massi.

Dr Massinissa Si Mehand
Technical Officer
Office of the Deputy Director General
Health Emergencies Programme
WHO R&D Blueprint



For information on the WHO R&D Blueprint:
http://www.who.int/csr/research-and-development/en/
Tel.: +41 22 791 1207
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Email: simehandm@who.int

From: Michael Osterholm [mailto:mto@umn.edu]
Sent: Wednesday, May 09, 2018 10:18 PM
To: mto@umn.edu
Subject: Informational Webinars for the Ebola/Marburg, Lassa fever, and Nipah WHO R&D roadmaps (May 15, 16, and 22)

Dear colleagues:
The Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota, with support from Wellcome Trust and in collaboration with the World Health Organization (WHO), will be hosting informational webinars on the following draft research and development (R&D) roadmaps, which were developed as part of the WHO R&D Blueprint initiative:

- Ebola/Marburg R&D Roadmap
- Lassa Fever R&D Roadmap
- Nipah R&D Roadmap

The informational one-hour webinars are intended to engage a broad audience in the review and further development of the draft roadmaps by offering opportunities for stakeholders who may not be familiar with the process to learn more about the goals for each roadmap and how to provide feedback. The three roadmaps are available on the WHO website for public comment through **8 June 2018** (see roadmaps webpages for Ebola/Marburg, Lassa, and Nipah).

The webinars will be held at the following times:

1. **Ebola/Marburg**: Tuesday, May 15, 2018 – 9:30 am Central Daylight Time (CDT) (3:30 pm British Summer Time [BST] / 4:30 pm Central European Summer Time [CEST])
2. **Lassa**: Wednesday, May 16, 2018 – 9:30 am CDT (3:30 pm BST / 4:30 pm CEST)
3. **Nipah**: Tuesday, May 15, 2018 – 8:00 pm CDT (Wednesday, May 16 at 2:00 am BST / 3:00 am CEST / 7:00 am Bangladesh Standard Time / 9:00 am Singapore Time)
4. **Nipah**: Tuesday, May 22, 2018 – 9:30 am CDT (3:30 pm BST / 4:30 pm CEST)

Pre-registration is required for webinar participation. Please visit the CIDRAP R&D Roadmaps Webinars information page to complete registration and for more details.

Please share this email message with others who may be interested in learning more about the draft roadmaps and participating in the webinars.

Sincerely,

Mike

Michael T. Osterholm, PhD, MPH
Regents Professor
McKnight Endowed Presidential Chair in Public Health
Director, Center for Infectious Disease Research and Policy
Distinguished University Teaching Professor
Environmental Health Sciences, School of Public Health
Professor, Technological Leadership Institute College of Science and Engineering
Adjunct Professor, Medical School
University of Minnesota

Ebola/Marburg Research and Development (R&D) Roadmap

Roadmap purpose: To provide a framework for identifying the vision, underpinning strategic goals, and prioritizing research areas and activities (from basic research to advanced development, licensure, manufacture, and deployment) for accelerating the collaborative development of medical countermeasures (MCMs)—diagnostics, therapeutics, and vaccines—against Ebola virus disease (EVD) and Marburg virus disease (MVD).

INTRODUCTION

Ebola virus disease (EVD) and Marburg virus disease (MVD), caused by several different filoviruses in the Filoviridae family, are severe hemorrhagic illnesses with similar clinical manifestations and high case-fatality rates. Sporadic outbreaks of EVD and MVD can occur following human contact with infected wild animal reservoirs. Subsequent human-to-human transmission may occur through contact with body fluids of infected persons. Filovirus diseases have significant epidemic potential in regions of Africa where there are reservoirs of the viruses in wild animal populations, including where human outbreaks have previously occurred, as well as in areas of Africa considered non-endemic but potentially at risk. Three highly virulent species of ebolavirus (Zaire, Bundibugyo, and Sudan) have been associated with large EVD outbreaks in sub-Saharan Africa, most recently the explosive 2014–2016 West African Ebola outbreak caused by the Zaire ebolavirus species. Two species of Marburg virus (Marburg and Ravn) have been associated with MVD outbreaks in sub-Saharan Africa, notably a recent outbreak in eastern Uganda.

The Ebola/Marburg R&D roadmap is a key component of the World Health Organization (WHO) R&D Blueprint for accelerating research and product development of MCMs to enable effective and timely emergency response to infectious disease epidemics. Ebola and Marburg viruses are identified in the Blueprint's initial list of priority pathogens (defined as pathogens that are likely to cause severe outbreaks in the near future and for which few or no MCMs exist). The WHO Blueprint calls for the development of R&D roadmaps for the priority pathogens to align and stimulate R&D of new or improved countermeasures, such as rapid diagnostic assays, novel therapeutics, and vaccines. The scope of R&D addressed in the roadmap ranges from basic research to late-stage development, licensure, manufacture, and early use of MCMs to prevent and control EVD/MVD outbreaks. The roadmap is organized into four main sections: cross-cutting topics and issues (for areas that apply to more than one MCM category), diagnostics, therapeutics, and vaccines.

In addition to the development of MCMs, other aspects of public health preparedness and response are critical for successful Ebola/Marburg disease prevention and control. Examples include well-equipped treatment units, improved personal-protective equipment, effective community engagement, and workforce development in at-risk regions. Many of these issues are beyond the scope of the R&D roadmap, but need to be addressed as part of a broader public-health control strategy.

VISION

Robust MCMs to detect, control, and prevent outbreaks of EVD and MVD that are available, affordable, and readily deployable when needed: (1) rapid, accurate, point-of-care diagnostics for Ebola/Marburg virus infection to inform treatment, outbreak detection, and clinical trials; (2) safe and effective treatment and post-exposure prophylaxis (PEP) to reduce morbidity and mortality from EVD/MVD; and (3) safe and effective vaccines to prevent EVD/MVD and stop filovirus transmission in human populations.

CROSS-CUTTING TOPICS AND ISSUES

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Commercial markets for Ebola/Marburg diagnostics, therapeutics, and vaccines are weak or nonexistent, given that EVD/MVD outbreaks occur episodically and unpredictably in low-income countries.
- Many of the critical resources for MCM development are scarce or limited, such as funding for research, stored biological samples, and high-biosafety level (BSL-4) containment facilities. Requirements for high-level biocontainment laboratory conditions, for example, pose a significant impediment and complicate Ebola/Marburg assay development and validation studies, as many assay reagents and assay validation materials must be generated in BSL-4 laboratories.
- Preparedness for conducting clinical trials quickly during future outbreaks poses a number of significant challenges, particularly since the location or timing of the next outbreak is unknown.
- Preclinical data are essential for licensing new therapeutics and vaccines via nontraditional regulatory pathways (e.g., the US Food and Drug Administration's [FDA's] Animal Rule) and for down-selecting promising therapeutic and vaccine candidates for human clinical studies. Nonhuman primates (NHPs) are regarded as the most relevant preclinical models for the development of filovirus therapeutics and vaccines, although high costs, insufficient standardization, ethical issues, and the need for BSL-4 facilities constrain their use.
- Insufficient data management capabilities in under-resourced areas may impede the sharing and reporting of clinical observations and study data regarding Ebola/Marburg diagnostic, therapeutic, and preventive interventions.
- Pharmacovigilance systems in affected regions may be inadequate to monitor and evaluate the safety, clinical benefit, delivery, and acceptability of licensed MCMs, as well as unlicensed therapeutic agents and vaccines deployed outside of clinical trials, e.g., via the WHO Emergency Use Assessment and Listing (EUAL) procedure or FDA Emergency Use Authorization (EUA).

Key needs

- Funding sources (such as public-private partnerships) and industry incentives and competitions for non-dilutive funding to encourage innovation and secure private-sector commitments to develop, manufacture, and stockpile critical filovirus MCMs.

- Strengthened scientific and regulatory capacity within the at-risk regions to enable greater input throughout the clinical development process for Ebola/Marburg MCMs.
- A collaborative and transparent process for prioritization of future preclinical and clinical studies, including sharing of biological samples, to optimize the use of limited resources and expedite the development of filovirus MCMs.
- An efficient, interoperable system for collecting data across study sites, reporting to WHO, analyzing results, and sharing information and outcome data to facilitate evaluation of filovirus MCMs during outbreak situations. (The Infectious Diseases Data Observatory's Ebola Data Sharing Platform provides a model for a novel platform for collecting, standardizing, and sharing clinical data under the authority of local leadership.)
- Standardized and validated assays, reagents, antibodies, nucleic acids, and stocks of challenge strains for research and development of Ebola/Marburg MCMs.
- Detailed planning and preparation for clinical trials before the next EVD/MVD outbreak to accelerate the evaluation of MCMs, including: (1) development of key components such as trial designs, protocols, and consent procedures; (2) obtaining ethical and regulatory approvals as far as possible in advance; and (3) prioritization of candidate MCMs for further study.
- Adequate supplies of experimental therapeutics and vaccines for future clinical trials and for expanded use, if clinical trials demonstrate efficacy.
- Adequate supplies of licensed filovirus therapeutics and vaccines for rapid deployment during outbreak situations.
- Development of material transfer agreements (MTAs) prior to outbreaks to expedite shipping and transfer of clinical samples during outbreak situations.
- Operational planning, coordinated by the WHO, to facilitate product-delivery contracts and establish, maintain, and deploy global stockpiles of licensed and experimental Ebola/Marburg MCMs.

Knowledge gaps

- Data to refine, standardize, and validate animal models for Ebola/Marburg infection and disease and to ensure that relevant animal models adequately recapitulate the clinical hallmarks of human infection and illness caused by filoviruses.
- Additional information on the immunology and pathogenesis of Ebola/Marburg viruses to develop a comprehensive understanding of the immune response to infection, which will facilitate development of filovirus MCMs. This includes evaluating immune responses in patients with natural immunity to these viruses, determining mechanisms of viral persistence in "sanctuary" sites in the body, identifying factors influencing the development of post-EVD syndrome, fully characterizing cell-mediated and humoral immune responses to filovirus infection, and identifying immune correlates of survival following infection.
- Additional research for development of MCMs specifically for Marburg virus; most research to date has focused on Ebola viruses.
- Integrated social science research on sociocultural and behavioral factors pertaining to the development and deployment of socially acceptable Ebola/Marburg MCMs.

Strategic Goals

1. Identify sources of funding (such as through public-private partnerships) and develop appropriate private-sector incentives and competitions to promote R&D of filovirus MCMs.
2. Conduct additional basic and preclinical research on Ebola/Marburg viruses to facilitate development of filovirus MCMs.
3. Develop standardized and validated animal models to enable licensure of Ebola/Marburg MCMs via nontraditional regulatory pathways.
4. Develop comprehensive plans and protocols for rapid implementation of clinical trials and field studies of promising MCMs during future filovirus outbreaks.

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Conduct** additional basic research on the immunology and pathogenesis of Ebola/Marburg viruses to inform the development and appropriate use of filovirus MCMs.
- **Generate** research tools to promote R&D of filovirus MCMs (i.e., standardized and validated assays, reagents, antibodies, nucleic acids, and stocks of Ebola/Marburg virus challenge strains).
- **Continue to research** promising filovirus MCM candidates.
- **Prioritize** preclinical/clinical studies and use of biological samples by research teams to ensure efficient use of limited resources.
- **Ensure** adequate preparation for clinical trials and field studies of promising MCMs in advance of EVD/MVD outbreaks to include the following:
    - **Agree** on preliminary trial designs, particularly regarding randomization and treatment arms, to be finalized at the time of an outbreak for specific products and outbreak settings.
    - **Identify** strategies for prioritizing MCMs for evaluation during future outbreaks, recognizing the challenge of achieving sufficient coordination of studies without stifling creativity.
    - **Develop** locally appropriate protocols, consent procedures, and ethics agreements.
    - **Promote** broad-based collaboration in planning and organizing clinical trials, e.g., by enhancing the involvement of healthcare providers, public health and community leaders, industry representatives, ethics committees, national regulatory officials in affected countries, and external regulatory agencies.
    - **Ensure** the eligibility of children and pregnant women in clinical trials (unless excluded for physiologic or metabolic reasons) to evaluate the safety, dosage, and toxicity of experimental filovirus MCMs.
    - **Develop** public communications in outbreak areas to enhance knowledge, acceptance, and support for clinical trials.

- **Engage** with local partners to build trust, particularly regarding sensitive sociocultural issues, such as drawing blood from trial participants and exporting samples for analysis.

Product development

- **Standardize and validate** relevant animal models that adequately recapitulate the clinical hallmarks of human infection and illness from Ebola/Marburg viruses to enable licensure of Ebola/Marburg MCMs via nontraditional regulatory pathways.
- **Obtain** in advance of future outbreaks, to the degree possible, MTAs and regulatory approvals.
- **Develop** plans for rapid development of MCMs specifically for Marburg virus.

Key capacities

- **Enhance** training for local clinical trial personnel.
- **Ensure** availability of institutional review boards in at-risk countries to facilitate approval of research studies during emergency situations.
- **Establish** an interoperable system to enhance capabilities for collecting, reporting, analyzing, and sharing data from clinical trials and field studies across different sites and outbreaks in resource-limited settings.
- **Ensure** that pharmacovigilance systems in affected areas are adequate for ongoing monitoring of licensed filovirus MCMs and unlicensed products administered via emergency-use procedures.

Policy and commercialization

- **Secure** funding (potentially through public-private partnerships) and promote use of incentives for private-sector R&D of filovirus MCMs.
- **Ensure** access to regulatory guidance, oversight, review, and authorization from appropriate regulatory agencies for filovirus MCMs, to include ongoing dialog with regulators during product development.
- **Promote** plans for adequate manufacturing and supply chains for the deployment of filovirus MCMs in at-risk areas.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

DIAGNOSTICS

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Ebola/Marburg diagnostic testing is critical for patient management (e.g., initial detection, disease confirmation, determination of infectivity, and post-treatment follow-up) as well as epidemic control (contact tracing and outbreak detection and surveillance for epidemiologic

analysis). Different diagnostic methodologies are appropriate for different use cases: (1) rapid, point-of-care (POC) testing, e.g., nucleic acid detection via automated real-time reverse transcriptase polymerase chain reaction (rRT-PCR) assays for initial identification of EVD/MVD cases; (2) laboratory-based molecular, serologic, antigenic, and virologic assays for case confirmation and clinical management; and (3) genomic analysis of Ebola/Marburg viruses, e.g., using portable, handheld real-time sequencing devices such as the MinION, for surveillance and epidemiologic analysis.

- The use of venipuncture blood samples from symptomatic individuals for Ebola/Marburg diagnostic testing poses safety and logistical challenges for collection and transport of specimens in under-resourced areas, requiring BSL-4 capabilities in regional or international reference laboratories, which may not be readily accessible.
- Laboratory-based confirmatory testing for Ebola/Marburg often requires long turnaround times, resulting in diagnostic delays that may lead to: (1) greater likelihood of exposure for the suspect case, if the suspect case is being held in a treatment unit with other suspected or confirmed cases; (2) greater likelihood of exposure for close contacts and healthcare providers, if the suspect case is being treated with routine (non-isolated) care; (3) delayed outbreak detection and response; and (4) delayed initiation of antiviral therapy (this may be more important as effective therapies are identified).
- Laboratory infrastructure, diagnostic capability, and adequately trained personnel in at-risk areas are often inadequate in Ebola/Marburg-affected countries. Building infrastructure and capacity requires dedicated commitment, prioritization in relation to other pressing public health issues, and sustained resources from international partners and in-country national health ministries.
- Differentiating EVD and MVD from other diseases that present with similar symptoms (e.g., malaria, Lassa fever, yellow fever, dengue, cholera, and typhoid) complicates clinical care and management in areas where the occurrence of such diseases overlaps.

Key needs

- Rapid and deployable POC and laboratory-based diagnostic testing for different use cases, such as: (1) detection of EVD/MVD outbreaks; (2) case identification for treatment, isolation, and infection control, including safe burials; and (3) epidemiologic control via genomic analysis of cases, contacts, and transmission chains.
- Regulatory clearance of standardized and validated EVD/MVD diagnostic assays, e.g., via the US FDA's premarket notification 510(k) process or European CE-Marking.
- Shared data on the performance characteristics of each assay and algorithms for test usage.
- An updated diagnostic Target Product Profile (TPP) that includes all relevant Ebola and Marburg virus species, primary methodologies, and diagnostic use cases (e.g., initial case identification, confirmation, ongoing clinical management, contact tracing, surveillance, and epidemiologic analysis). Key characteristics of the field-deployable EVD/MVD diagnostics include the following:
    - *Rapid turnaround times* for diagnostic results, contact tracing, and epidemiologic analysis during outbreak situations.

- *Minimal requirements* for laboratory infrastructure, sensitive sample handling (including cold-chain maintenance) prior to analysis, molecular biology expertise, electrical power, temperature-sensitive reagents, and specialized equipment, to enable deployment in remote locations.
- *Automated technologies and low-risk alternatives to obtaining specimens*, such as oral swabs, capillary blood sampling, or alternative methods for performing venipunctures, including for post-mortem diagnosis (which is particularly important for safe burial practices).
- *Infectivity testing*, e.g., for risk evaluation of potential exposures, assessment of patients being discharged from treatment centers, and measurement of viral persistence among survivors, including testing of alternative specimen types (such as seminal fluid).
- *Appropriate sensitivity and specificity of diagnostic testing*, corresponding to the use case (e.g., high test sensitivity to inform clinical management and high test specificity to improve outbreak detection).
- *High negative-predictive value* of testing to enable rapid exclusion of uninfected individuals from treatment units where they may be at increased risk of exposure.
- *Diagnostic algorithms* for high prevalence (outbreak) and low prevalence (surveillance) settings, particularly needed as more testing options and clinical validation data become available.
- *Detection of infection earlier in the clinical course*, prior to the onset of symptoms, to enhance control efforts and allow for earlier therapy (once antiviral treatments become available).
- *Potential development of combinations of diagnostic testing* (e.g., in multiplex assays or testing panels) that can detect EVD/MVD infection while simultaneously screening for the presence of other high-consequence or common pathogens (e.g., Lassa virus in West Africa) to facilitate wider usage of the diagnostic methodologies.

- Standardization and validation of diagnostic methodologies to enable comparability of data from different studies and diagnostic assays.
- Repositories of well-characterized clinical and preclinical specimens for diagnostic test development.
- Proficiency testing to monitor and evaluate performance of diagnostic assays in the field.
- Improvements in laboratory capacity in at-risk areas, including the availability of supplies and reagents, pre- and post-analytical processing, culture-independent confirmatory testing, training of local laboratory technicians in molecular diagnostic methodologies, and enhanced biosafety practices and quality control methods. Overall, an integrated and sustained laboratory infrastructure in at-risk areas should include the presence of strategically-placed supporting field laboratories that can perform rRT-PCR or other rapid diagnostic testing, access to regional laboratories for further confirmatory testing as necessary, and access to international reference laboratories.

- Ongoing clinical training to enhance early identification of EVD/MVD using rapid diagnostic technologies.

Knowledge gaps

- Identification and validation of host biomarkers correlated with patient prognosis and disease progression, such as viral load and transcriptomic signatures.
- Comparative data on commercially available rRT-PCR assays for Ebola infection to assess the performance of testing options in different situations and patient populations, such as patients with low viral loads (i.e., those who are very early in the clinical course or close to the point of recovery).

Strategic Goals

1. Expedite the development and evaluation of rapid, inexpensive, and highly sensitive and specific diagnostic testing methodologies with minimal requirements for biosafety precautions and staff training for POC or decentralized healthcare facility use in Ebola/Marburg affected areas.
2. Strengthen laboratory infrastructure and capacity in affected areas to ensure rapid identification of suspect cases in outbreak and non-outbreak settings.
3. Stimulate research into novel diagnostic approaches, including infectivity testing, prognostic biomarker analysis, and the development of alternatives to single Ebola/Marburg assays, such as broad testing panels, platforms, or multiplex assays for ongoing use between outbreaks.

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Further determine** the analytical characteristics (including sensitivity, specificity, and limits of detection) of novel diagnostic platforms and commercially available rRT-PCR assays for Ebola infection.
- **Research and validate** methods to identify host factors (biomarkers) associated with a high predictive value for survival or fatal outcomes to enhance clinical management of patients with EVD/MVD.
- **Explore** new diagnostic approaches that may enhance EVD/MVD diagnostic testing (e.g., by measuring infectivity, allowing earlier detection of infection, shortening turnaround time to results, and/or predicting outcome [survival or fatality]).

Product development

- **Continue to develop and evaluate** safe and accurate rapid POC diagnostic tests for use during EVD and MVD outbreaks.
- **Define** use cases for Ebola/Marburg diagnostics and determine optimal test characteristics that correspond to those use cases.

- **Develop** multiplex diagnostic assays to distinguish among fever-related illnesses and allow differentiation of EVD/MVD from other diseases that present with similar symptoms (e.g., Lassa fever for use in West Africa).

Key capacities

- **Create** international partnerships to fund, support, and promote enhanced laboratory capacity and infrastructure in at-risk areas for early disease detection and outbreak response.
- **Establish** a network of filovirus surveillance laboratories that can provide early warning for EVD/MVD outbreaks and enhance understanding of the epidemiology of filovirus diseases.
- **Develop** a database on the performance characteristics of available diagnostic assays and algorithms for test usage.

Policy and commercialization

- **Develop** additional guidance on the testing of alternative specimen types (such as seminal fluid) for viral persistence in EVD survivors.
- **Generate and update** new EVD diagnostic screening algorithms for high prevalence (outbreak) and low prevalence (surveillance) settings as additional diagnostic tests become available.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

THERAPEUTICS

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Efficacy data for therapeutic agents against EVD/MVD are lacking, particularly among special populations (e.g., children, pregnant women, immunocompromised patients), patients with late-stage disease, and EVD survivors with viral persistence.
- Ethical issues in therapeutic clinical trials need to be addressed, particularly regarding the assignment of patients to control (nontreatment) groups if preclinical data suggest potential efficacy of the experimental agent; alternative study designs for determining efficacy may be needed to address these concerns.

Key needs

- Development of a TPP that identifies optimal and desirable characteristics of EVD/MVD treatment interventions to guide the development of safe, effective, and appropriate treatment approaches.
- Safe and effective therapies to improve survival and decrease morbidity among patients with EVD/MVD.

- Safe, effective, and non-invasive (e.g., oral or intranasal) methods for PEP, including immune-stimulation via antibody therapy, to prevent EVD/MVD following exposure to filoviruses to protect healthcare workers, family caregivers, and burial teams, and to reduce transmission during outbreaks.
- Consistent standards for high-quality supportive care among Ebola/Marburg treatment centers.

Knowledge gaps

- Clinical data on the safety, tolerability, and efficacy of investigational treatments, including those evaluated during the Ebola epidemic in West Africa (e.g., ZMapp, TKM-130803, and favipiravir), including in special populations, such as pregnant women, immunocompromised persons, and children.
- Clinical data on the safety and effectiveness of administering combinations of treatment agents.
- Additional clinical data to inform the role of PEP in EVD/MVD outbreak control, including the development of a standard definition of PEP and guidance on the type of exposures that warrant such intervention and the most appropriate agents to administer.
- Research on the observed differences in outcome between NHP challenge studies and human trials of treatment candidates. This includes the evaluation of underlying factors such as biological differences between NHPs and humans, virus exposure routes, and infectious doses.
- Therapeutic options for eliminating persistent virus in the semen of EVD survivors, based on clinical evaluations of novel agents (such as the PREVAIL IV trial involving intravenous GS-5734).
- Research to characterize and validate biomarkers (e.g., transcriptomic signatures and multiplatform omics analysis) that can reliably predict the severity and outcome of illness in infected patients independent of viral load. The use of such biomarkers may enhance the design of therapeutic clinical trials and improve clinical care (e.g., through risk stratification).
- Additional research on the potential role of broadly protective filovirus immunotherapies. Priority agents include monoclonal antibodies (mAbs) that can recognize and neutralize viral targets (such as conserved elements of the virus's glycoprotein) and confer post-exposure protection. Key topics include analyzing cross-reactive and cross-neutralizing antibodies from Ebola survivors to address the challenge of achieving pan-Ebolavirus or pan-filovirus neutralization with mAbs targeting glycoprotein epitopes. Another key topic is evaluating the safety and efficacy of the "Trojan horse" strategy based on bi-specific antibodies (to neutralize ebolaviruses by co-opting viral particles themselves for endosomal delivery), potentially acting as broad antifilovirus immunotherapeutics.
- Additional research to optimize supportive care independent of specific EVD/MVD therapeutic agents. Key research areas include obtaining data on the safety and efficacy of various components of supportive care for EVD/MVD, such as optimal fluid resuscitation strategies, diagnosis of organ dysfunction, and the use of empiric antibiotics, antidiarrheal agents, NSAIDs, and vitamin K, to inform supportive care and best-practice guidelines. Clinical evaluation of various aspects of supportive care should focus on patients in at-risk regions to avoid extrapolating from conclusions based on patient outcomes in high-resource settings.

Strategic Goals

1. Develop a robust preclinical drug-development pipeline of potential therapeutic candidates with broad-spectrum activity against filovirus infection, relapse, post-Ebola syndrome, and viral persistence to expedite bridging studies in relevant animal models and clinical evaluation.
2. Complete preclinical and early-stage clinical studies of treatment and PEP approaches during inter-epidemic periods to facilitate the licensing/registration of safe and efficacious new agents and the prompt implementation of efficacy trials and post-marketing evaluation during future Ebola/Marburg outbreaks.
3. Determine optimal strategies for supportive care of patients with EVD/MVD disease.

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Continue to research** the safety, tolerability, and efficacy of investigational therapies for EVD/MVD, including those evaluated during the Ebola epidemic in West Africa. In the absence of outbreaks, this work can include animal studies, pharmacokinetics and pharmacodynamics evaluation, definition of optimal dosage, and phase 1/2 clinical trials to assess safety and tolerability.
- **Determine** the safety and efficacy of promising new therapeutic and PEP approaches (such as pan-filovirus mAbs) with demonstrated efficacy in NHP models for treatment of MVD.
- **Identify and validate** host biomarkers in patients with early stage EVD/MVD to improve clinical management and predict the likelihood of survival.
- **Research** optimal supportive care for infected patients in outbreak settings and determine best-practice guidelines.
- **Conduct** research on the mechanisms of viral persistence in immune-privileged sites to help identify further treatment options.

Product development

- **Generate** a TPP for Ebola/Marburg therapeutics.
- **Continue** to develop safe and effective therapeutic agents for treatment of EVD/MVD.
- **Identify** immunotherapeutic approaches for PEP that are broadly active against multiple species of filoviruses and can be administered via non-invasive methods.
- **Research** discrepancies in efficacy outcomes between NHP challenge studies and human trials of treatment candidates.

Key capacities

- **Develop** a database of preclinical studies regarding EVD/MVD therapeutic agents.

Policy and commercialization

- **Develop** clinical guidance as research demonstrates the safety and efficacy of new therapies.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

VACCINES

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Filovirus vaccines are needed for multiple indications, including vaccines for rapid onset of immunity against a specific outbreak strain and vaccines to confer long-lasting immunity against one or more filoviruses.
- The availability of one or more licensed Ebola vaccines complicates the evaluation of other Ebola vaccine candidates, owing to ethical issues and challenges with efficacy trial design.
- Cold-chain requirements for some of the current Ebola vaccine candidates create challenges for vaccine deployment in clinical trials in affected regions.
- Side-effect profiles (e.g., vaccine-induced fever) of some of the current Ebola vaccine candidates, which mimic the symptoms of early EVD, complicate the evaluation of the vaccines and create diagnostic challenges among exposed persons.
- Time of onset of effective immunity following vaccination is unclear, which complicates the determination of appropriate vaccination strategies in outbreak situations.
- Vaccine skepticism, suspicion of outsiders, and suspicion of research during outbreaks are potential obstacles to community support for EVD/MVD vaccine clinical trials.
- Limited manufacturing capacity creates a risk of inadequate supplies of vaccines.
- The lack of field efficacy data and the uncertainties regarding the evidence from NHP data that would underpin the use of nontraditional approval pathways could create difficulties in licensing vaccines.

Key needs

- Broad-spectrum filovirus vaccines or multiple monovalent vaccines capable of inducing cross-reactive antibodies that can neutralize one or more Ebola/Marburg species.
- Additional guidance on vaccination strategies for preventive and reactive use. The WHO's Strategic Advisory Group of Experts (SAGE) on Immunization concluded in April 2017 that current evidence is insufficient to recommend population-based vaccination or prophylactic Ebola vaccination of healthcare workers in the absence of an outbreak. The SAGE has recommended a ring vaccination approach using the unlicensed rVSVΔG-ZEBOV-GP (Merck) vaccine candidate under expanded-access protocols in case of another Ebola outbreak; additional guidance is needed regarding vaccination of contacts and the role of PEP among contacts exposed to Ebola virus. Additional vaccination strategies for the Merck vaccine and other products need to be defined, following regulatory review and in coordination with SAGE

policy recommendations and the Global Ebola Vaccine Implementation Team (GEVIT) operational guidance for use of licensed vaccines, in case outbreaks occur in densely populated regions or megacities where ring vaccination would not be feasible.

- Bridging of vaccine outcome data between preclinical and clinical studies. Standardized assays are needed to compare vaccine-induced humoral immunogenicity, such as qualitative and quantitative differences between antigen-specific binding antibody responses.
- Guidance regarding the use and deployment in outbreak settings of two monovalent, prime-boost Ebola vaccines that have been approved in their countries of origin: the GamEvac-Combi rVSV/Ad5-vectored vaccine licensed in Russia in 2016 and the Ad5-vectored vaccine licensed in China in 2017.

Knowledge gaps

- Additional research to identify specific vaccine-induced immune responses (including binding antibody, neutralizing antibody, and/or cell-mediated immune responses) that can serve as biomarkers for clinical protection against EVD/MVD and predict the level of vaccine efficacy.
- Enhanced understanding of humoral and cell-mediated immune responses to Ebola/Marburg vaccines. Key topics include evaluating the protective roles of vaccine-induced neutralizing antibodies, glycoprotein-specific T-cells, and cytokine-producing peripheral blood mononuclear cells (PBMCs); and comparing naturally acquired immunity (such as among EVD survivors and individuals with asymptomatic Ebola virus infection) with vaccine-induced immune responses.
- Specific correlates of protection to facilitate clinical research on promising filovirus vaccine candidates and expedite licensing through nontraditional regulatory pathways, such as the FDA's Animal Rule and accelerated approval.
- Evaluation of vaccine safety in target populations to better understand the risk of adverse events in outbreak settings.
- Direct evaluation of Marburg vaccines, without relying on data extrapolated from Ebola preclinical or clinical studies. Further research is needed to determine the utility of potential platform technologies for the development of rapid, low-cost vaccines to protect against novel or multiple emerging Ebola/Marburg viruses. Suitable platform technologies require: (1) guidance on immune bridging from NHP data for each filovirus; (2) pre-established safety, reactogenicity, immunogenicity profiles in various at-risk age groups and special populations; and (3) plans for manufacturing, stockpiling, and deployment in field efficacy trials when outbreaks occur.
- Data on the duration of protective immunity for each type of vaccine and vaccination strategy (including single shot and prime-boost strategies) in different population groups.
- Data on the stability of different vaccine types and formulations under field conditions in at-risk regions.

Strategic Goals

1. Complete the evaluation of candidate Ebola and multivalent vaccines for safety, immunogenicity, correlates of protection, and duration of immunity to achieve licensure/registration of the vaccines

for different indications (e.g., monovalent, pathogen-specific vaccines for rapid onset of immunity against specific outbreak strains and multivalent filovirus vaccines for long-lasting immunity against multiple Ebola and Marburg virus strains).

2. Accelerate the development of safe and effective filovirus vaccines by integrating advanced R&D activities into the public-health response to future outbreaks, as guided by the WHO R&D Blueprint process, for planning and conducting phase 3 trials (or other evaluation strategies) of investigational products and other vaccines potentially approved through nontraditional regulatory pathways.
3. Develop comprehensive plans for emergency use of Ebola/Marburg vaccines in future outbreaks. Key priorities include clarifying public health and regulatory requirements to authorize and deploy unlicensed vaccines (particularly in countries that do not have EUA procedures), developing scenario-based reactive vaccination strategies specific to the needs and resources of the affected countries, protecting healthcare/frontline workers and other vulnerable groups, scaling up manufacturing, managing stockpiles, and addressing issues regarding vaccine delivery such as shelf-life and cold-chain requirements.

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Determine** the mechanisms of humoral and cell-mediated immune responses to Ebola/Marburg vaccines.
- **Identify** correlates of protection, which are specifically needed for ongoing vaccine research.
- **Determine** the duration of protective immunity for each type of vaccine and vaccination strategy.
- **Conduct** research aimed at the development and evaluation of Marburg vaccines.
- **Conduct** further research to assess safety profiles of filovirus candidate vaccines in target populations to better understand the risk of adverse events in outbreak settings.
- **Continue to conduct** social science research to address issues related to vaccine skepticism and concerns related to participation in research involving filovirus vaccines.

Product development

- **Develop**, clinically evaluate, and license filovirus vaccines, including multiple monovalent, multivalent, or pan-filovirus vaccines that provide protection against Ebola and Marburg virus species.
- **Develop** thermostable formulations of filovirus vaccines.
- **Determine** the utility of potential platform technologies for enhancing the rapid development of safe and effective low-cost vaccines.

Key capacities

- **Promote** the development of adequate manufacturing capacity to ensure adequate supplies of vaccines.

- **Establish and maintain** global stockpiles of filovirus vaccines (licensed and unlicensed) for rapid outbreak response.

Policy and commercialization

- **Develop** comprehensive plans for emergency use of Ebola/Marburg vaccines in future outbreaks.
- **Provide** additional guidance on vaccination strategies for potential reactive and prophylactic scenarios.
- **Develop** guidance on the evaluation and use of currently licensed Ebola vaccines, including the GamEvac-Combi rVSV/Ad5-vectored vaccine licensed in Russia in 2016 and the Ad5-vectored vaccine licensed in China in 2017.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

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Comments and Suggestions from Reviewer for

Ebola/Marburg Research and Development (R&D) Roadmap

Deadline for receiving comments: Tuesday, 5 June 2018

Reviewer Contact Information
Name:
Position:
Organization:
Email Address:
Telephone Number (including country code):

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
Roadmap purpose					
INTRODUCTION					
VISION					
CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					

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CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
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CROSS-CUTTING TOPICS AND ISSUES: Strategic Goals					
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Research***					
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CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Key capacities***					

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CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Policy and commercialization***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					
DIAGNOSTICS: Strategic Goals					
DIAGNOSTICS: Priority Areas/Activities – ***Research***					

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DIAGNOSTICS: Priority Areas/Activities – ***Product development***					
DIAGNOSTICS: Priority Areas/Activities – ***Key capacities***					
DIAGNOSTICS: Priority Areas/Activities – ***Policy and commercialization***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					

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THERAPEUTICS: Strategic Goals					
THERAPEUTICS: Priority Areas/Activities – ***Research***					
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THERAPEUTICS: Priority Areas/Activities – ***Policy and commercialization***					
VACCINES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					

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VACCINES: Priority Areas/Activities – ***Policy and commercialization***					
BACKGROUND INFORMATION					
ANY OTHER COMMENTS					

Lassa Fever Research and Development (R&D) Roadmap

Roadmap purpose: To provide a framework for identifying the vision, underpinning strategic goals, and prioritizing areas and activities (from basic research to advanced development, licensure, manufacture, and deployment) for accelerating the collaborative development of medical countermeasures (MCMs)—diagnostics, therapeutics, and vaccines—against Lassa fever.

INTRODUCTION

Lassa fever is a zoonotic disease caused by Lassa virus (LASV) and is endemic in several West African countries, including Guinea, Liberia, Nigeria, and Sierra Leone; disease occurs both sporadically and as outbreaks. Population studies demonstrating serologic evidence of LASV infection and the presence of occasional sporadic Lassa fever cases in additional West African countries (i.e., Benin, Burkina Faso, Ghana, the Ivory Coast, Mali, and Togo) indicate that other areas of the region also may be at risk. LASV exhibits marked genetic heterogeneity and strains have been phylogenetically placed into four established lineages—three in Nigeria (lineages I-III) and one in the Mano River Union countries of Guinea, Liberia, and Sierra Leone (lineage IV). Three more lineages have been proposed—one in Mali and the Ivory Coast, one found among *Hylomyscus pamfi* rodents in Nigeria, and one in Togo. *Mastomys natalensis* (i.e., the multimammate mouse which also is known as the multimammate rat) has long been considered the sole natural reservoir of LASV, but additional rodent reservoirs (*M. erythroleucus* and *H. pamfi*) recently have been discovered and may affect the distribution of Lassa fever. Primary transmission of the virus from animal hosts to humans typically occurs via exposure to excreta (urine or feces) or blood from LASV-infected rodents. Person-to-person and laboratory transmissions occur to a lesser extent and result from direct contact with the blood, tissue, urine, feces, or bodily secretions of an LASV-infected individual or reuse of contaminated medical equipment.

Although public health officials often cite annual case estimates of 100,000 to 300,000 LASV infections and up to 5,000 deaths, these numbers are extrapolations from a single longitudinal study conducted over 30 years ago in Sierra Leone. The true public health burden of Lassa fever is unknown and represents a crucial gap in understanding the relative impact of Lassa fever in the affected West African countries. Existing Lassa fever surveillance data are limited and/or biased because they typically have been collected in conjunction with biomedical research projects located in areas where the disease already is recognized to be endemic. In contrast, seroprevalence studies in non-endemic areas have suggested high numbers of previously unrecognized infections, and more recent surveillance reports have observed substantial increases in the number and geographic spread of cases. Thus, the true incidence and spatial distribution of Lassa fever may be significantly underestimated. LASV infection causes a wide spectrum of clinical manifestations; an estimated 80% of people with LASV infections have no or mild symptoms (and often are unrecognized and unreported), while the remaining 20% may progress to severe and life-threatening disease requiring hospitalization. Among survivors, the most common long-term sequela of Lassa fever is sensorineural hearing loss. The onset of Lassa fever is gradual and nonspecific with an incubation period ranging from 2 to 21 days; thus, it is clinically difficult

to distinguish Lassa fever from other febrile illnesses that occur in West Africa such as malaria, typhoid, yellow fever, dengue, and Ebola virus disease (EVD).

The R&D roadmap for Lassa fever is an integral component of the WHO R&D Blueprint initiative for accelerating research and product development of MCMs to enable effective and timely emergency response to infectious disease epidemics. LASV is identified in the Blueprint's list of "priority pathogens" (defined as pathogens that are likely to cause severe outbreaks in the near future and for which few or no MCMs exist). The Blueprint calls for the creation of R&D roadmaps for the priority pathogens to align and stimulate R&D of new or improved countermeasures, such as rapid diagnostic assays, novel therapeutics, and vaccines. Furthermore, the Blueprint considers product R&D for all three of these categories of MCMs to be a high priority for Lassa fever. The scope of R&D addressed in the roadmap ranges from basic research to late-stage development, licensure, manufacture, deployment, and early use of MCMs to prevent and control Lassa fever outbreaks and endemic disease. The roadmap is organized into four main sections: cross-cutting topics and issues (for areas that apply to more than one MCM category), diagnostics, therapeutics, and vaccines.

Other aspects of public health preparedness and response, in addition to R&D for MCMs, are critical to successful Lassa fever prevention and control. Examples include understanding the drivers and dynamics of zoonotic transmission from rodents to humans, programs and activities to prevent zoonotic transmission (such as rodent control), access to high-quality personal protective equipment (PPE) for healthcare workers, implementation of adequate infection prevention and control practices in healthcare settings, and availability of guidelines to reduce nosocomial transmission. Many of these issues are beyond the scope of the R&D roadmap, but need to be addressed as part of a broader public health control strategy.

VISION

Robust MCMs to detect, control, and prevent Lassa fever that are readily available and accessible for use in at-risk areas for both endemic and outbreak-related disease. These MCMs include: (1) rapid, accurate, point-of-care diagnostics for Lassa fever; (2) safe and effective treatment, pre-exposure prophylaxis (PrEP), and post-exposure prophylaxis (PEP) for Lassa fever; and (3) safe and effective vaccines to prevent disease, disability, and death from Lassa fever and stop person-to-person transmission of LASV.

CROSS-CUTTING TOPICS AND ISSUES

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- The diversity of LASV strains and propensity of these strains to evolve over time complicate the development of effective MCMs for Lassa fever, especially for diagnostics and vaccines. In addition, the different LASV lineages may vary in their pathogenicity, virulence, and disease

manifestations, which necessitates that research be completed in parallel for the different lineages, particularly in animal models.

- Maximum biologic containment is required for LASV and may pose an impediment to R&D of Lassa fever MCMs, as certain materials must be generated and/or tested under the highest biosafety level (BSL-4) conditions.
- The development of animal models for R&D of Lassa fever MCMs is associated with a number of issues, including: (1) a limited number of BSL-4 facilities and limited space within those facilities, resulting in backlogs for animal research use; (2) the difficulty and costs in procuring animals, particularly non-human primates (NHPs); (3) increased regulations, restrictions, and ethical concerns regarding animal research, especially for NHPs; (4) regulations for transport of materials; (5) appropriate experimental design (e.g., challenge strain, route of challenge, timing of challenge, and challenge dose); and (6) the need to better understand the adequacy of current animal models and clarify whether or not additional animal models are required. Some of these issues necessitate down-selection of MCM candidates from rodent models prior to conducting further research in NHPs under BSL-4 conditions; however, these decisions are complicated by inherent limitations of the rodent models.
- The absence of diagnostic assays to distinguish between acute illness, prior infection, and response to vaccination hinders Lassa fever patient management, disease surveillance efforts, epidemiologic research on LASV infection and disease in West Africa, and clinical research on promising Lassa fever treatments and vaccines.
- The West African region continues to experience the loss of physicians and scientists to more lucrative jobs elsewhere, and this weakens in-country clinical, laboratory, research, public health, and regulatory capacity. The 2014-2016 EVD epidemic in this region also resulted in further workforce reductions owing to the deaths of numerous healthcare workers, including those with Lassa fever expertise.
- Funding for Lassa fever research is insufficient and economic incentives to invest in such research are not readily apparent, as the disease is endemic in the under-resourced West African region. Development of a sustainable value proposition and international philanthropic-public-private partnerships and innovative methods are needed to secure funding to complete development, licensure, manufacture, deployment, and use of affordable Lassa fever MCMs.
- A number of important obstacles exist with regard to conducting clinical trials of novel therapeutic agents and vaccines for Lassa fever in the endemic area. Examples include: (1) the lack of accurate disease burden estimates to guide the selection of clinical trial sites; (2) challenges in identifying and equipping clinical sites with the administrative, research, clinical, and laboratory infrastructure and workforce capacity to conduct clinical trials; (3) the lack of dependable water and electricity sources, which impact clinical care and laboratory services, as well as safe storage of therapeutics and vaccines; (4) the remote and sometimes politically unstable nature of the endemic area, which can make clinical research difficult; (5) issues in excluding vulnerable populations from clinical trials (such as pregnant women, children, and immunocompromised persons), although they are at risk, or even at increased risk, of mortality from Lassa fever; and (6) challenges in patient recruitment owing to socioeconomic constraints and skepticism of Western research and medicine.

- Insufficient and/or ineffective community awareness, sensitization, and education programs, which are needed to strengthen community participation and ownership for the prevention, detection, and treatment of Lassa fever.

Key needs

- Standardized and validated assays (including assays to compare immunogenicity of different vaccines), reagents, antibodies, nucleic acids, and stocks of LASV challenge strains for R&D of MCMs for Lassa fever, including the availability of validated diagnostic assays for use in epidemiologic research, surveillance activities, and clinical trials of therapeutics and vaccines for Lassa fever.
- Ongoing availability of current circulating LASV strains as reference samples for MCM development.
- Epidemiologic studies and ongoing surveillance infrastructure and capacity to determine Lassa fever incidence and LASV infection seroprevalence in affected countries utilizing standardized, highly sensitive and specific diagnostic tests with uniform testing algorithms and case definitions across affected countries. These data are needed to better understand the burden of disease and to monitor the effectiveness of Lassa fever MCMs.
- Coordination of preclinical and clinical research for R&D of Lassa fever MCMs.
- A sufficient workforce of clinical, laboratory, research, public health, and regulatory personnel in West Africa who are qualified by education, training, and experience.
- Early and recurrent communication between product developers and the appropriate national regulatory authorities (NRAs), including those in West Africa, to obtain clarity and guidance on regulatory pathways, requirements, and other considerations for new Lassa fever MCMs during the pre-licensure and post-licensure periods.
- A determination regarding the feasibility of conducting clinical trials of Lassa fever therapeutics and vaccines, which is needed before considering alternative regulatory pathways for licensure (such as the United States Food and Drug Administration's Animal Rule).
- Enhanced good clinical practice capabilities, as well as capacity for data reporting and analysis to support collaborative clinical research, including methods for collecting, standardizing, and sharing clinical data under the authority of local leadership.
- Prioritization of Lassa fever therapeutics and vaccines that should be moved forward into clinical trials versus those that need additional preclinical research. Head-to-head comparisons of candidate MCMs may be needed to enable these decisions.
- Evaluation of the safety of candidate therapies and vaccines for Lassa fever in animal models prior to clinical trials in vulnerable populations such as pregnant women, children, and immunocompromised persons (including those with HIV infection or malnutrition).
- Increased infrastructure and capacity for post-marketing surveillance of safety and effectiveness for licensed Lassa fever therapeutics and vaccines.
- Clarification regarding the potential for and possible strategies to promote technology transfer to at-risk areas for Lassa fever MCMs.
- Identification of effective community engagement strategies for prevention, detection, and treatment of Lassa fever.

Knowledge gaps

- Additional research on animal models is needed to: (1) identify or adapt, refine, and validate relevant animal models (e.g., guinea pig, common marmoset, and macaque models) for the multiple LASV lineages; (2) define their role in supporting basic research on the pathogenesis and immunology of Lassa fever and Lassa fever-associated sequelae; and (3) allow evaluation of new Lassa fever MCMs. In addition, efforts are needed to establish benchmark parameters (such as challenge strain, route of challenge, timing of challenge, and challenge dose) for testing in animals.
- A better understanding of the natural history of Lassa fever is needed in order to inform R&D of MCMs.
- Further research is needed on the pathogenesis and immunology of LASV infections (including the timing and duration of the viremic phase) to support the development and appropriate use of MCMs for LASV infection and Lassa fever. (For example, detailed knowledge of the innate, cell-mediated, and humoral immune responses that constitute protective immunity against Lassa fever is needed to identify specific vaccine-induced immune responses that can serve as biomarkers for clinical protection against Lassa fever and predict the level of vaccine efficacy.)
- The determinants of LASV infection and disease severity in West Africa, particularly pathogen versus host factors, have not been well-characterized. More data are needed to better understand Lassa fever disease severity (asymptomatic, mild, and severe) and Lassa fever-associated sequelae by LASV lineage, geographic area, and other population demographics.
- Successful R&D, deployment, and assessment of MCMs are dependent on current and accurate descriptive epidemiologic information on Lassa fever incidence and LASV seroprevalence by lineage, geographic area, and other population demographics. Detailed information about Lassa fever incidence and LASV seroprevalence by geographic area is needed to identify those communities with and without ongoing transmission within the endemic countries in West Africa.
- Ecologic research and modelling are needed to assess the impacts of climate, environmental, demographic, and socioeconomic changes occurring in West Africa on the rodent reservoir to improve forecasting for Lassa fever.
- Social science research is needed to: (1) assess the socioeconomic impact of Lassa fever; and 2) understand how best to engage the West African population (including vulnerable populations) to promote awareness and sensitization about Lassa fever symptoms and prevention programs, participation in clinical trials, and acceptance of Lassa fever MCMs.

Strategic Goals

1. Develop a sustainable value proposition and identify funding sources to promote R&D, availability, and accessibility of Lassa fever MCMs.
2. Improve understanding of the pathogenesis, immunology, and clinical diagnosis of LASV infections to inform the development of MCMs.
3. Support research and surveillance with appropriate sampling methodologies to accurately characterize the current epidemiology and disease burden of Lassa fever in West Africa.

4. Strengthen the clinical, laboratory, public health, and regulatory infrastructure and workforce in the endemic area for Lassa fever to: (1) promote awareness and education about Lassa fever; (2) improve capacity for early and accurate diagnosis; (3) promote optimal case management and clinical care, including the availability of critical care and enhanced supportive care in strategically located healthcare facilities; (4) provide capacity for conducting clinical trials and other field studies applicable to MCM development; and (5) allow assessment and licensure of new MCMs for Lassa fever.

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Conduct** basic research on the immunology and pathogenesis of LASV infections (including the timing and duration of viremia) to inform the development and appropriate use of MCMs for LASV infection and Lassa fever.
- **Determine** the innate, cell-mediated, and humoral immune responses that contribute to protective immunity against Lassa fever.
- **Generate** research tools to promote R&D of MCMs for Lassa fever (i.e., standardized and validated assays, reagents, antibodies, nucleic acids, and stocks of LASV challenge strains).
- **Refine and validate** animal models for assessment of promising Lassa fever therapeutic and vaccine candidates.
- **Conduct** ongoing research and surveillance to obtain accurate and up-to-date epidemiologic data on Lassa fever incidence and LASV seroprevalence by lineage, geographic area, and other population demographics and to assess the impact of certain Lassa fever MCMs, such as vaccines, over time.
- **Conduct** research on ecologic issues influencing the natural reservoirs for LASV to better forecast disease occurrence in human populations.
- **Conduct** social science research for Lassa fever to assess socioeconomic impact and determine effective community engagement strategies, as well as strategies for acceptability of treatments and vaccines.

Product development

- **Promote** communication between developers and appropriate NRAs for clarity and guidance on the regulatory pathways, requirements, and other considerations for Lassa fever MCM development.

Key capacities

- **Ensure** adequate infrastructure, workforce, and capability for conducting clinical trials of promising Lassa fever therapeutics and vaccines in the endemic area.

- **Strengthen** regulatory capacity in areas at risk for Lassa fever to enhance the ability of in-country NRAs to work with researchers and product developers toward evaluating and licensing Lassa fever MCMs.
- **Develop** good clinical practice capabilities, including standardized data collection and sharing methods to facilitate clinical research into potential therapeutic agents and vaccines for Lassa fever.
- **Strengthen** infrastructure and capacity for post-marketing surveillance of safety and effectiveness for licensed Lassa fever therapeutics and vaccines.
- **Create** strategies to promote community awareness, sensitization, and education to strengthen community participation and ownership for the prevention, detection, and treatment of Lassa fever.

Policy and commercialization

- **Establish** a sustainable value proposition and **secure** funding to complete development, licensure, manufacture, deployment, and use of affordable Lassa fever MCMs.
- **Explore** methods (such as priority review vouchers) to incentivize developers to perform R&D for Lassa fever MCMs.
- **Ensure** access to regulatory guidance, oversight, review, and authorization from appropriate NRAs for Lassa fever MCMs.
- **Promote** plans for adequate manufacturing and robust supply chains for subsequent deployment and use of Lassa fever MCMs in endemic and at-risk areas.
- **Clarify** potential for and possible strategies to promote technology transfer for Lassa fever MCMs.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

DIAGNOSTICS

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- LASV strain variability poses major challenges for Lassa fever diagnostic assay development and validation.
- Differentiating Lassa fever from other conditions with similar presenting symptoms (e.g., malaria, typhoid, yellow fever, dengue, and EVD) poses challenges in clinical care and management of patients with febrile illness in West Africa. Antimalarial and antibiotic therapies usually are given first, and Lassa fever is considered only after patients fail to improve, which can lead to delays in diagnosis, treatment, isolation, and contact follow-up. Another

complicating factor is that patients may present with co-infections (e.g., malaria and Lassa fever) and some existing case definitions for Lassa fever require exclusion of other diseases.

- The broad disease spectrum, which encompasses asymptomatic LASV infection through severe Lassa fever, and the associated variations in viremia levels, immune responses, and symptoms pose challenges for diagnostic tests and the timing of their use. No single reference test (i.e., a gold standard) currently exists to definitively determine who has Lassa fever.
- In Lassa fever survivors, the virus may persist for extended periods of time in immunologically protected sites such as the kidney and gonads. The presence and levels of virus in these immunologically protected sites typically are unknown; thus, this can result in secondary transmission of LASV.
- Diagnostic testing for Lassa fever using blood, serum, or tissue from symptomatic individuals poses safety and logistical challenges for collection, handling, and transport of specimens in under-resourced areas.
- A limited number of facilities exist for confirmatory laboratory diagnosis and treatment of Lassa fever in a region comprising over 5 million square kilometers. This can lead to prolonged delays in diagnosis and initiation of therapy, as well as implementation of infection control measures and public health interventions. While some efforts have been made to enhance laboratory and diagnostic capacity, building infrastructure requires: (1) dedication and ongoing commitment, (2) prioritization in relation to other competing public health needs, and (3) sustained resources from international partners and in-country national health ministries.

Key needs

- A target product profile (TPP) for Lassa fever diagnostics, identifying optimal and desirable characteristics to guide the development of promising diagnostic assays.
- Clear diagnostic criteria and case definitions (for suspect, probable, and confirmed Lassa fever cases) for clinical management of patients, clinical trials, and surveillance activities.
- Clarification regarding the use cases for different Lassa fever diagnostic assays, since the corresponding performance, validation, and regulatory approval requirements may differ depending on whether the test will be used for differential diagnosis, confirmation of diagnosis, preclinical and clinical R&D of therapeutics and vaccines, or surveillance activities. (For example, it may be desirable to have a point-of-care screening test that is highly sensitive and a confirmatory test that is highly specific.)
- Assays that allow accurate diagnosis across the full disease spectrum, ranging from asymptomatic LASV infection to advanced Lassa fever.
- Lassa fever point-of-care diagnostic assays that detect genetically diverse LASV strains in a timely manner. In addition to antigen- and antibody-based rapid diagnostic tests (RDTs), these include improved molecular detection methods such as industry-standard real-time polymerase chain reaction (PCR) assays and all-in-one cartridge-based PCR systems that can be used with and without molecular diagnostic laboratory infrastructure, respectively.
- A gold standard test for validation of Lassa fever candidate assays.
- Access to a large reference panel comprised of qualified acute and convalescent samples from across the West African region and representing the multiple LASV lineages for assay validation.

- Continuing improvements in clinical and laboratory capacity for diagnosis of Lassa fever in West Africa. Capacity enhancement should ensure that more referral hospitals in endemic and at-risk areas have both point-of-care and laboratory capability to perform diagnostic testing for Lassa fever, including: (1) a high index of suspicion and tools to enable differential diagnosis; (2) the availability of diagnostic tests; (3) the skills and mechanisms to appropriately collect, transport, process, and test specimens; and (4) the ability to interpret test results. Such hospitals will need guidance, equipment, and training of personnel for required diagnostic methodologies, enhanced biosafety practices, quality standards, and quality control methods. Additionally, more in-country reference laboratories are needed for confirmatory testing.
- Guidance on forward deployment and best practices for using rapid and confirmatory tests to diagnose Lassa fever.
- Guidance on testing of alternative specimen types (such as seminal fluid) for viral persistence in Lassa fever survivors.
- If feasible and as a long-term goal, multiplex assays that can detect LASV infection, while simultaneously screening for the presence of other high-consequence pathogens.

Knowledge gaps

- Additional field validation data are needed to assess performance characteristics of Lassa fever diagnostic assays against the multiple lineages of LASV that can be found across West Africa.
- Ongoing molecular characterization (i.e. sequencing) of LASV isolates from both rodent reservoirs and humans is needed to map the geographic distribution of various strains across West Africa and to continually monitor genetic changes in LASV strains over time so that diagnostics assays can be updated and refined as needed. Additionally, a system is needed for communicating sequencing results to key stakeholders.

Strategic Goals

1. Promote the development and assessment of affordable, point-of-care, immunologic- and nucleic acid-based Lassa fever RDTs that capture the wide genetic diversity of LASV strains.
2. Develop guidance on forward deployment and best practices for using rapid and confirmatory tests to diagnose Lassa fever.
3. Create a network of laboratories to perform molecular characterization (sequencing) of LASV strains isolated from rodents and humans to assess genetic changes over time and by geographic region in endemic and at-risk areas.

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Determine** performance characteristics for promising new assays for Lassa fever diagnosis and **develop** appropriate standards, including rapid evaluation of assays against existing samples (from biobanks or other repositories).
- **Conduct** field evaluation of new diagnostic tests for Lassa fever.
- **Perform** molecular characterization (i.e., sequencing) of LASV strains to assess genetic changes geographically and over time so that diagnostic assays can be updated and refined as needed.

Product development

- **Generate** a TPP for Lassa fever diagnostics.
- **Define** use cases for Lassa fever diagnostic assays, including for screening and confirmatory diagnostic purposes and for conducting clinical trials of therapeutics and vaccines.
- **Build** biobanks of reference samples for validation of Lassa fever diagnostic assays via prospective studies using standardized methods.
- **Establish** a gold standard test for definitive diagnosis of Lassa fever and validation of other candidate assays.
- **Develop, evaluate, and validate** Lassa fever point-of-care immunologic- and nucleic acid-based RDTs that are affordable and can capture: (1) the full spectrum of disease associated with LASV infection and (2) the wide genetic diversity of LASV strains in the endemic and at-risk areas.
- **Develop** multiplex diagnostic assays that can distinguish between specific fever-related illnesses to allow differentiation of Lassa fever from other infectious diseases that present with similar symptoms (if feasible and as a long-term goal).

Key capacities

- **Create** mechanisms and protocols for collecting, shipping, and sharing of clinical samples.
- **Create** international partnerships to fund, support, and promote enhanced laboratory, clinical, and surveillance capacities and infrastructure for detection of LASV infection and Lassa fever in endemic and at-risk areas of West Africa.
- **Establish** a network of LASV surveillance laboratories that can perform ongoing molecular characterization (i.e., sequencing) of LASV strains isolated from rodents and humans over time and by geographic region in endemic and at-risk areas.
- **Construct** a communication infrastructure and plan to notify key stakeholders of sequencing results, especially about the evolution of LASV strains and the identification of additional LASV lineages.

Policy and commercialization

- **Create** Lassa fever diagnostic algorithms and case definitions, and revise them as new diagnostic methods become available.
- **Provide** guidance on testing of alternative specimen types for viral persistence in Lassa fever survivors.

- **Develop** guidance on forward deployment and use of Lassa fever RDTs and confirmatory assays in endemic-disease and outbreak situations, taking into consideration the occurrence of other febrile illnesses, which may vary by geographic area.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

THERAPEUTICS

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Supportive care and ribavirin are common therapies used for Lassa fever. Ribavirin (a broad-spectrum antiviral) appears to be most effective in reducing mortality from Lassa fever if given within the first 6 days of illness and when administered intravenously rather than orally; however, scant efficacy data are available for ribavirin and its significant cost and difficulty in procurement present operational challenges for treatment in West Africa.
- Case management and clinical care quality is positively associated with the outcome of Lassa fever (i.e., survival versus death). Not only does West Africa have an insufficient number of healthcare facilities for treatment of Lassa fever but very few facilities have the capability to provide critical care or enhanced supportive care.
- Specific challenges for clinical trials of candidate therapeutics in the endemic area include: (1) delayed presentation of Lassa fever cases to healthcare facilities, which may preclude appropriateness for patient enrollment in clinical research; (2) difficulties in rapidly and accurately diagnosing Lassa fever for prompt initiation of treatment (ribavirin or novel therapies), which may affect evaluation of efficacy; (3) the wide variability in quality of supportive care, which makes the individual evaluation and comparison of therapies difficult; and (4) the availability of ribavirin (appearing on the WHO Model List of Essential Medicines) as an off-label widely used therapy for Lassa fever, which raises potential ethical and sociologic issues for placebo-controlled trials using other therapeutic agents, despite its limitations.

Key needs

- A TPP for Lassa fever therapeutic agents, identifying optimal and desirable characteristics to guide the development of promising treatment approaches.
- Safe, easily administered, well-tolerated, therapeutic agents effective against the multiple LASV lineages, including viable treatment alternatives to ribavirin, for treatment of Lassa fever and prevention of Lassa fever-associated sequelae to improve survival and decrease morbidity and long-term disability.

- Safe and effective PrEP and/or PEP to prevent Lassa fever for high-risk exposure to LASV and guidance on PrEP/PEP use. Such countermeasures are important tools to protect healthcare workers, family caregivers, and burial teams, and to reduce transmission.
- Uniform patient management and minimum standards for supportive care in the West African region to facilitate the evaluation of new therapies via clinical trials.

Knowledge gaps

- Development of optimal therapeutic agents will require additional research to: (1) understand how Lassa fever develops following LASV infection and the reasons for the substantial variation in disease severity, (2) further characterize both cell-mediated and humoral immune responses, (3) identify factors influencing the development of permanent sequelae, and (4) determine mechanisms of viral persistence in immunologically-protected body sites.
- Treatment of Lassa fever with ribavirin has been evaluated in only a single nonrandomized clinical trial and in field studies utilizing retrospective analyses. Additional animal and/or human studies of the efficacy of ribavirin against the multiple LASV lineages and at various stages of Lassa fever disease progression are needed, as well as equivalency trials for alternative administration routes and dosing regimens of ribavirin.
- Several therapeutic agents have demonstrated protection against lethal Lassa fever challenge in animal models (i.e., antivirals such as favipiravir, small-molecule inhibitors such as ST-193, and immune-based agents such as convalescent plasma with high titers of neutralizing antibodies and human monoclonal antibodies); however, additional studies of these and other agents in relevant animal models may be needed before moving into clinical trials to obtain data on efficacy for the multiple LASV lineages, pharmacokinetics, pharmacodynamics, barriers to resistance, and dose and regimen selection. Preclinical data on treatment effectiveness by time of treatment initiation also are needed for these agents.
- Further research is needed on the efficacy of convalescent blood products (including convalescent whole blood, convalescent plasma, convalescent serum, pooled or high-titer immunoglobulin, and polyclonal or monoclonal antibodies) and exchange blood transfusion, for treatment of severely ill Lassa fever patients.
- Additional research would be of value to identify broad-spectrum agents for Lassa fever and to examine therapeutics in the R&D pipeline for other pathogens (such as influenza) that also may protect against Lassa fever. Such approaches may assist with funding, logistics, and technical aspects of research, and provide long-term market potential.
- Clinical trial data are needed on the safety, tolerability, and efficacy against the multiple LASV lineages for the most promising novel Lassa fever therapies, used alone or in combination with other therapies, such as ribavirin. Understanding the disease kinetics and the efficacy of treatment at various stages of disease progression are important considerations when conducting such clinical trials.
- Additional data are needed to inform development of guidance on the use of PrEP/PEP and the most appropriate agents to administer to prevent Lassa fever.
- Clinical evaluations of novel agents are needed to identify therapeutic options for eliminating persistent virus in the urine and semen of Lassa fever survivors.

- Research is needed to clarify the clinical and virologic determinants of Lassa fever outcomes and to identify clinical presentation criteria and/or measureable biomarkers that can reliably predict the severity and outcome of illness in infected patients. Identification of such criteria and/or biomarkers, and other methods to quantify viral loads, could lead to evidence-based approaches to reduce mortality from Lassa fever and may enhance clinical research into new therapeutic agents and PrEP/PEP countermeasures.
- Patients may benefit from optimal supportive care independent of treatment with specific Lassa fever therapeutic agents. Key research areas include obtaining data on the safety and efficacy of supportive care approaches for Lassa fever to inform best-practice guidelines, such as ideal fluid, electrolyte, and blood pressure management; proper blood oxygen saturation; prompt diagnosis of organ dysfunction; appropriate triage of other secondary complications; and judicious use of empiric antibiotics and antiparasitics, antiemetics, antidiarrheal agents, and/or vitamin K. Clinical evaluation of various aspects of supportive care should focus on patients in the endemic area to avoid extrapolating from conclusions based on patient outcomes in high-income countries.

Strategic Goals

1. More fully evaluate ribavirin for treatment of Lassa fever and determine the appropriate role of ribavirin in clinical trials of new therapeutics.
2. Develop, evaluate, and license new and improved affordable therapeutic agents for treatment of Lassa fever and prevention of Lassa fever-associated sequelae, as well as for PrEP/PEP to prevent LASV infection, for the multiple LASV lineages.
3. Determine best strategies for treatment with therapeutic agents and supportive care for Lassa fever patients and develop applicable guidelines.
4. Continue to stimulate research into areas that will enhance prognostic capabilities for Lassa fever, such as use of clinical presentation criteria and/or measurable biomarkers (such as quantitative assays for measuring viral load).

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Continue to research** the safety, tolerability, and efficacy of ribavirin, favipiravir, and other investigational therapies for Lassa fever via animal studies; and determine which of these therapies warrant further clinical evaluation.
- **Conduct** clinical trials for the most promising therapeutic candidates (including early trials in affected countries) to determine dose regimen and assess safety, tolerability, and efficacy.
- **Research** optimal strategies for supportive care for Lassa fever patients and determine best-practice guidelines.

- **Identify, assess, and validate** clinical presentation criteria and/or measureable biomarkers that can reliably predict the severity and outcome of illness in infected patients (such as quantitative assays to measure LASV viral load).

Product development

- **Generate** a TPP for Lassa fever therapeutics.
- **Develop, clinically evaluate, and license** safe and effective therapeutic agents for treatment of Lassa fever that are broadly active against the multiple lineages of LASV.
- **Identify** therapeutic approaches for PrEP/PEP that are broadly active against the multiple lineages of LASV.

Key capacities

- **Ensure** that a coordinated process is in place to assess promising therapeutic (including broad-spectrum agents), and that strategies are created to move them forward.
- **Promote** enhancements to the healthcare delivery systems in affected areas to improve and standardize clinical management and supportive care of Lassa fever patients, including the ability to provide critical care and enhanced supportive care.

Policy and commercialization

- **Create** guidelines for patient management and minimum standards for supportive care to facilitate clinical research of novel treatments.
- **Develop** treatment and PrEP/PEP guidance as new therapies become available.
- **Develop** a consensus approach for how to address ethical and sociologic issues regarding the role of ribavirin in future clinical trials of new therapeutic agents.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

VACCINES

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- The multiple lineages of LASV present considerable challenges for vaccine development and evaluation.
- The lack of systematic estimates for Lassa fever incidence and LASV seroprevalence creates challenges in monitoring the impact of vaccination on the public health burden of disease.
- The scientific basis is limited for guiding vaccine research. (For example, more information is needed about which biomarkers are associated with Lassa fever immunologic responses and survival.)

- One vaccine may not be suitable for all uses. (For example, a vaccine for preventive use or for use in vulnerable populations will likely need to have a relatively low risk profile for adverse reactions, whereas the risk profile may be different if a vaccine is targeted for reactive use in an outbreak situation.)
- A specific challenge for clinical research on LASV vaccine candidates in the endemic area is the need for a high enough incidence of disease to conduct clinical efficacy trials, which may require implementing trials only during large Lassa fever outbreaks. If clinical trials are planned for implementation during outbreaks, a number of additional challenges will need to be addressed, such as ensuring advance development and regulatory/ethical approval of clinical trial protocols and adequate stockpiles of vaccines. If clinical trials are not feasible, alternative pathways to licensure will be needed.

Key needs

- Vaccines with many of the optimal and desirable characteristics outlined in the TPP for LASV vaccines, and capable of inducing immunity to genetically diverse LASV strains.
- Specific correlates of protection (or causally related surrogates for correlates of protection) to facilitate research on promising LASV vaccine candidates.
- Well-defined endpoints for LASV vaccine efficacy trials (i.e., clinical disease, infection, or correlates of protection) and diagnostic algorithms and laboratory methods for case verification.
- An assessment of the feasibility of conducting clinical vaccine trials in non-outbreak situations versus conducting trials only during large outbreaks of disease. If clinical trials will be conducted primarily when outbreaks occur, then plans and approvals for emergency use of candidate vaccines will need to be in place to ensure research preparedness.
- Guidance on vaccination strategies (particularly determining preventive and reactive/outbreak approaches), if and when approved LASV vaccines become available.

Knowledge gaps

- Further research is needed to determine the mechanisms of and the differences between naturally acquired immunity (such as among Lassa fever survivors and individuals with asymptomatic LASV infection) and vaccine-induced immunity.
- Additional knowledge gaps include: (1) determining the duration of protective immunity for promising vaccine candidates, (2) identifying optimal vaccination strategies for different vaccines in different population groups and geographic areas, and (3) measuring the ability of different vaccine types and formulations to remain stable in field conditions in at-risk regions.
- Social science research is needed to determine: (1) community attitudes and barriers towards vaccination, (2) issues pertinent to vaccine strategy implementation, and (3) best mechanisms of community engagement to ensure successful implementation of vaccination programs.
- Mathematical modelling may be useful in estimating the potential impact of LASV vaccines and in simulating various epidemiologic scenarios that may affect vaccine use, particularly when paired with more accurate incidence data from additional epidemiologic studies and surveillance activities.

Strategic Goals

1. Develop, evaluate, and license affordable LASV vaccines that protect against the multiple LASV lineages for preventive and reactive/outbreak use in Lassa fever endemic and at-risk areas.
2. Identify vaccination strategies that: (1) optimize the potential public health impact of LASV vaccines, (2) consider the regional epidemiology of Lassa fever in at-risk regions, and (3) take into account the vaccine attributes for the specific vaccines that become available.

Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Determine** the mechanisms of cell-mediated and humoral immune responses to LASV vaccines.
- **Identify** immune correlates of protection that can be used to assess candidate vaccines across different studies.
- **Study** the duration of protective immunity for each type of LASV vaccine and vaccination strategy.
- **Complete** preclinical evaluation of candidate LASV vaccines for safety, tolerability, immunogenicity, efficacy, correlates of protection, and duration of immunity and identify the most promising candidates to move forward.
- **Conduct** clinical trials of promising vaccine candidates (including early trials in affected countries) to determine dose regimen and assess safety, tolerability, and efficacy in various groups, including vulnerable populations.

Product development

- **Determine** appropriateness of traditional and alternative pathways to licensure for LASV vaccines, as the pathway used will impact development activities.
- **Develop, clinically evaluate, and license** safe and effective LASV vaccines that protect against the multiple LASV lineages for preventive and reactive/outbreak use.

Key capacities

- **Establish and maintain** stockpiles of LASV vaccines for use during large Lassa fever outbreaks.
- **Improve** surveillance capabilities in endemic areas to assess the impact of vaccination strategies once vaccines become available.
- **Plan** for clinical vaccine trials to be conducted, including determining the feasibility of conducting trials in non-outbreak versus outbreak settings. If clinical trials will be conducted primarily when outbreaks occur, then develop advance plans for emergency use and evaluation of candidate vaccines.

Policy and commercialization

- **Provide** guidance on vaccination strategies for various target populations, geographic areas, and epidemiologic scenarios, once LASV vaccines are available.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

BACKGROUND INFORMATION

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Comments and Suggestions from Reviewer for

Lassa Fever Research and Development (R&D) Roadmap

Deadline for receiving comments: Friday, 8 June 2018

Reviewer Contact Information
Name:
Position:
Organization:
Email Address:
Telephone Number (including country code):

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
Roadmap purpose					
INTRODUCTION					
VISION					
CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					
CROSS-CUTTING TOPICS AND ISSUES: Strategic Goals					
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Research***					
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Product development***					
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Key capacities***					

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CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Policy and commercialization***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					
DIAGNOSTICS: Strategic Goals					
DIAGNOSTICS: Priority Areas/Activities – ***Research***					

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DIAGNOSTICS: Priority Areas/Activities – ***Product development***					
DIAGNOSTICS: Priority Areas/Activities – ***Key capacities***					
DIAGNOSTICS: Priority Areas/Activities – ***Policy and commercialization***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
THERAPEUTICS: Strategic Goals					
THERAPEUTICS: Priority Areas/Activities – ***Research***					
THERAPEUTICS: Priority Areas/Activities – ***Product development***					
THERAPEUTICS: Priority Areas/Activities – ***Key capacities***					
THERAPEUTICS: Priority Areas/Activities – ***Policy and commercialization***					
VACCINES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					

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VACCINES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
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VACCINES: Priority Areas/Activities – ***Policy and commercialization***					
BACKGROUND INFORMATION					
ANY OTHER COMMENTS					

Nipah Research and Development (R&D) Roadmap

Roadmap purpose: To provide a framework for identifying the vision, underpinning strategic goals, and prioritizing areas and activities (from basic research to advanced development, licensure, manufacture, and deployment) for accelerating the collaborative development of medical countermeasures (MCMs)—diagnostics, therapeutics, and vaccines—against Nipah virus infection.

INTRODUCTION

Nipah virus (NiV) is a paramyxovirus that was first identified as a zoonotic pathogen after an outbreak involving severe respiratory illness in pigs and encephalitic disease in humans occurred in Malaysia and Singapore in 1998 and 1999. As part of that outbreak, 265 human cases were identified in Malaysia, and 11 abattoir workers in Singapore became ill following contact with imported pigs, with an overall case fatality rate of 40%. No new outbreaks have been reported in these countries since May 1999. NiV infection was subsequently recognized, however, in Bangladesh in 2001 and nearly annual outbreaks have occurred in that country since, with disease also identified periodically in eastern India; case fatality rates during outbreaks in these countries have ranged from 75% to 100%. Other regions may be at risk for NiV infection, as serologic evidence for NiV has been found in the known natural reservoir (Pteropus bat species) and several other bat species in a number of other countries, including Cambodia, Thailand, Indonesia, Madagascar, Ghana, and the Philippines. In the 1998-99 Malaysia outbreak, NiV spillover occurred from bats to pigs, which led to pig-to-pig, pig-to-human, and suspected, although limited, human-to-human NiV transmission. Additionally, several other domestic animal species were found to be infected with NiV on the farms involved in the outbreak, including horses, cats, and dogs. In the outbreaks in Bangladesh, intermediary hosts between bat and human have not played a major role, with the primary modes of NiV transmission being human consumption of bat-contaminated raw date palm sap and subsequent person-to-person transmission.

The zoonotic potential of NiV is significant, particularly because of its ability to amplify in livestock, which can serve as a source of exposure to humans. NiV is part of the Henipavirus genus; this genus also includes another zoonotic pathogen (Hendra virus [HeV]), which predominantly causes infection in horses and also can lead to human disease (usually following contact with infected horses). HeV was initially recognized in 1994, following an outbreak of fatal cases of severe respiratory disease in horses and humans in the Brisbane suburb of Hendra in Queensland, Australia. To date, confirmed HeV disease has been confined to Australia. An outbreak of an unidentified henipavirus (possibly NiV or a closely related virus) occurred among horses and humans in the Philippines in 2014. This outbreak likely involved spillover of NiV into horses and subsequent disease in humans following consumption of contaminated horsemeat and in healthcare workers who cared for NiV-infected patients. Detailed genomic information for this virus is limited.

In humans, NiV infection results in neurologic and respiratory syndromes, with fever, headache, altered mental state or unconsciousness, dizziness, cough, and vomiting as the primary presenting clinical features. NiV infection may result in late-onset encephalitis and relapsing encephalitis, and survivors

may experience long-term neurological sequelae. Genomic sequencing has demonstrated that there are multiple strains of NiV. For example, the strain responsible for the outbreak in Malaysia is different from those identified in Bangladesh and India; these strains provoke distinct but overlapping clinical features in both humans and experimentally infected non-human primates.

The R&D roadmap for NiV infection is a key component of the WHO R&D Blueprint initiative for accelerating research and product development of medical countermeasures to enable effective and timely emergency response to infectious disease epidemics. NiV is identified in the Blueprint's list of "priority pathogens" (defined as pathogens that are likely to cause severe outbreaks in the near future and for which few or no MCMs exist). The Blueprint calls for the development of R&D roadmaps for the priority pathogens to align and stimulate R&D of new or improved countermeasures, such as rapid diagnostic assays, novel therapeutics, and effective vaccines. The scope of R&D addressed in the roadmap ranges from basic research to late-stage development, licensure, and early use of MCMs to prevent and control NiV outbreaks and endemic disease.

Other aspects of public health preparedness and response, in addition to R&D for MCMs, are critical to successful NiV infection prevention and control. Examples include enhanced surveillance systems, minimizing zoonotic NiV transmission, improved personal protective equipment (PPE), effective community engagement, adequate infection prevention and control practices, and workforce development and training in endemic and at-risk regions. Many of these issues are beyond the scope of the R&D roadmap, but need to be addressed as part of a broader public health control strategy.

VISION

Robust MCMs to detect, prevent, and control outbreaks of NiV infection (and other closely related henipaviruses) that are readily available and accessible for use in areas of known or potential NiV spillover. These MCMs include: (1) rapid, accurate, point-of-care diagnostics; (2) safe and effective treatment and post-exposure prophylaxis (PEP); and (3) safe and effective vaccines to prevent disease, disability, and death.

CROSS-CUTTING TOPICS AND ISSUES

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Economic incentives to invest in Nipah research are not readily apparent, as the disease primarily occurs in under-resourced areas of South Asia and disease incidence is low; therefore, securing funding for Nipah research represents a substantial challenge. The development of a sustainable value proposition for industry and international philanthropic public-private partnerships are needed to secure funding to complete development, licensure, manufacture, and deployment of NiV MCMs. The value proposition would ideally be informed by a robust assessment of the risk of future outbreaks, and will likely require new systematic surveillance studies in humans and susceptible animal hosts in affected areas to strengthen the evidence base.

- Regulatory approval pathways for MCMs can be prohibitively expensive for product developers in the absence of a predictable demand. For example, obtaining regulatory approval for diagnostic tests through the premarket approval (PMA) process is costly, but may be necessary when an Emergency Use Authorization (EUA), which is associated with lower approval costs, is not applicable. Furthermore, licensure of vaccines and therapeutics using alternative regulatory pathways also can be very costly, given the regulatory requirements for such approval.
- High-level biocontainment requirements may pose an impediment to research on NiV pathogenesis and development of MCMs, as certain materials must be generated under the highest biosafety level (BSL-4) conditions. This raises the cost of MCM development.
- To date, NiV spillovers to human communities have occurred almost exclusively in rural communities in Bangladesh and East India; the healthcare facilities that serve these communities have limited laboratory and clinical infrastructure for diagnosis and treatment.
- The natural reservoir for NiV is fruit bats of the Pteropus genus; these bats have a wide geographic range that stretches across much of the Western Pacific region, Southeast and South Asia, and Madagascar. Evidence also suggests that other fruit bats of the Pteropodidae family may harbor NiV; such bats can be found across Africa and parts of the Middle East. This broad host range increases the likelihood of additional spillover events from bats to humans or livestock in new areas where the disease has not yet been detected, which may make accurate and timely diagnosis, disease recognition, and treatment more difficult owing to lack of clinical experience with the condition, lack of available laboratory testing, and the occurrence of other diseases that have similar clinical presentations.
- Because NiV infection results in low mortality rates in livestock (e.g., approximately 1% to 5% in pigs), infection in animal herds may not be recognized until after human cases are identified. This delay in diagnosis may lead to an entire herd being infected before livestock are tested for NiV, which could cause large financial losses for livestock owners and increases the likelihood of NiV infection in exposed animal husbandry workers.
- While ferrets, Syrian hamsters, and IFNAR-KO mice are well-established animal models for NiV research applicable to humans, the African green monkey (AGM) is regarded as the most relevant animal model for evaluation of candidate therapeutics and vaccines. Additionally, studies involving the AGM model may be required for licensure of MCMs via alternative regulatory pathways. Costs, space requirements (particularly in BSL-4 containment facilities), and ethical concerns constrain the use of AGMs.
- Conducting phase 1 and phase 2 clinical trials is potentially feasible in endemic regions. However, because NiV infection occurs as relatively small, focal outbreaks, the low disease incidence poses a major challenge for conducting phase 3 clinical trials, in terms of achieving a sufficient sample size to estimate MCM efficacy with adequate statistical power. Therefore, alternative regulatory pathways and/or innovative study designs (e.g., including combining clinical trial data across outbreaks over time) may need to be considered for licensure of NiV vaccines or therapeutics, if classic clinical trial designs (e.g., randomized controlled trials [RCTs]) are not applicable.

Key needs

- Enhanced clinical, laboratory, and public health infrastructure in endemic and at-risk areas to promote early diagnosis, treatment, and implementation of vaccination programs for NiV prevention and control.
- Additional prospective serosurveillance data from susceptible animal species and proximate human populations in areas of predicted risk to determine the level of human spillover and to build preparedness for detection of human cases and for limiting exposure. This is particularly important in areas where public health surveillance programs are not feasible or justifiable.
- Standardized and validated assays, reagents, antibodies, nucleic acids, and stocks of NiV challenge strains for R&D of MCMs for NiV infection. (Assays that can be used at lower biosafety levels are an important priority.)
- Clear criteria for down-selection and prioritization of candidate MCMs to move forward into clinical trials versus those that need additional preclinical research. Such criteria should align with desired characteristics outlined in the target product profiles (TPPs) and should address aspects of sustainable MCM production, stockpiling, and access.
- A determination regarding the feasibility of conducting clinical trials of therapeutics and vaccines for NiV infection, which is needed before considering alternative regulatory pathways for licensure (such as the United States Food and Drug Administration's [FDA's] Animal Rule).
- Early and recurrent communications between product developers and the appropriate national regulatory authorities (NRAs) to obtain clarity and guidance on clinical trial requirements, regulatory pathways and requirements, and other considerations for NiV MCMs during the pre-licensure and post-licensure periods. Regulatory pathways and NRA capabilities may vary between countries; therefore, early engagement is essential to identify country-specific considerations.
- Outreach and education to clinicians to improve NiV awareness and training, and to ensure availability of diagnostic tools in endemic areas to increase the likelihood of accurate and timely diagnosis and treatment of NiV infection.
- Enhanced capacity for data sharing and analysis (particularly of NiV sequence data) to support collaborative clinical research, including methods for collecting, standardizing, and sharing clinical data under the authority of local leadership.
- Collaboration between public health authorities in endemic and at-risk areas and international development partners to support NiV surveillance and facilitate effective communication with communities regarding disease prevention activities. Human health, animal health, and wildlife officials should be engaged as part of a long-term collaborative effort.
- Clarification regarding the potential for and possible strategies to promote technology transfer for NiV MCM development and manufacturing to endemic and at-risk areas.

Knowledge gaps

- Continued R&D, manufacture, deployment, and assessment of MCMs, as well as other preventive measures, are dependent on accurate and current information on the ecology and epidemiology of NiV infection, using a One Health approach. Improved surveillance (or dedicated prospective research with a surveillance focus) is needed to determine the true

incidence of disease in endemic areas and to monitor the occurrence of spillover incidents from bats to humans or livestock in new geographic areas. Additionally, continued research is needed to better define and assess the occurrence of NiV and other henipaviruses, including drivers of infection, in the natural reservoir of Pteropus bats and potentially other bat species.

- Additional research is needed to refine, standardize, and validate relevant animal challenge models (e.g., ferret, Syrian hamster, IFNAR-KO mouse, and AGM models) to define their role in supporting basic research on the pathogenesis and immunology of NiV infection, which is essential for development and evaluation of MCMs. For example, efforts are needed to: (1) determine the appropriate animal model(s) for screening assay development; (2) standardize the challenge strain and dose, and determine the most appropriate lethal NiV dose for MCM development; (3) determine when MCMs should be administered in animal models to best mimic realistic timing of MCM use in humans; (4) bridge NiV MCM data between animal models and humans, such as identifying thresholds of vaccine protection; and (5) identify the best models for studying chronic (relapsing) infection, particularly if investigators use the US FDA's Animal Rule to obtain regulatory approval.
- Additional information is needed on the virology, immunology, and pathogenesis of NiV in humans and animals to inform development of NiV MCMs. This includes evaluating the pathophysiologic differences between different NiV strains, determining the mechanisms that allow NiV to escape immunological clearance and cause delayed onset or recurrent encephalitis, identifying factors influencing the development of permanent neurological sequelae, and further characterizing cell-mediated and humoral immune responses to NiV infection. In addition, identifying aspects of the immune response that are absent or counter-effective during human NiV infection may lead to the development of novel targeted intervention strategies.
- Ongoing phylogenetic and evolutionary analyses of NiV strains are needed to monitor viral heterogeneity and antigenic changes over time that may impact the epidemiologic and clinical features of disease, and thereby influence MCM development.
- Further research is needed to better understand viruses in the Henipavirus genus, including their reservoir hosts and pathogenicity.
- Additional studies applying whole genome sequencing of NiV viruses are needed to generate a comprehensive phylogenetic mapping of the global genetic variability among henipaviruses.
- Sociological and anthropological research is needed to understand how to best engage at-risk populations (including vulnerable populations such as children, immunocompromised individuals, and pregnant women) for participation in clinical trials and to ensure acceptance of new NiV MCMs, especially if therapeutics and vaccines do not consistently prevent disease. Efforts are needed to: (1) assess potential barriers for conducting clinical trials, (2) assess MCM acceptability in at-risk populations, (3) determine culturally appropriate messaging to enhance MCM acceptance, and (4) identify public health strategies to promote vaccine use.

Strategic Goals

1. Identify sources of funding and develop appropriate private-sector incentives and competitions to promote R&D of NiV MCMs.

2. Undertake surveillance activities (including research studies) to estimate the relative risk and global spread of NiV outbreaks and public value of MCM development
3. Stimulate and support basic science research for better understanding of NiV virology, pathogenesis, and the immune response to infection in humans and animals.
4. Strategically strengthen laboratory, clinical, and public health infrastructure and capacity at the local and national levels in areas of known or potential NiV spillover.
5. Engage NRAs (particularly in endemic and at-risk areas) to gain guidance on requirements for clinical trials, regulatory pathways, and other considerations that will impact MCM development, acceptance, and post-licensure surveillance.

Landmark Goals/Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Expand** research to further understand the ecology and epidemiology of NiV and other pathogenic henipaviruses in human and animal populations (wild and domestic) over time and across geographic areas, using a One Health approach.
- **Continue to perform** phylogenetic and evolutionary analyses of NiV strains to monitor antigenic changes and characterize genetic diversity over time.
- **Conduct** basic science research on the virology, pathogenesis, and immunology of NiV infections to inform development of MCMs.
- **Determine** key differences in pathogenesis for different NiV strains that may have implications for the development of safe and effective NiV vaccines or therapies.
- **Refine, validate, and standardize** relevant animal models to support the development and evaluation of NiV MCMs.
- **Generate** research tools to promote R&D of MCMs for NiV infection (i.e., standardized and validated assays, reagents, antibodies, nucleic acids, and stocks of NiV challenge strains), particularly those that can be used at lower biosafety levels.
- **Conduct** research studies to enable a more comprehensive mapping of genetic variability henipaviruses in order to improve understanding of their global distribution.
- **Determine** the feasibility of conducting phase 3 clinical trials or identify alternative approaches for assessing efficacy of new NiV vaccines and therapeutics, in coordination with the appropriate NRAs.
- **Establish** a plan for conducting phase 3 clinical trials in endemic regions in coordination with local government agencies, if clinical trials are considered to be a feasible option for efficacy assessment.
- **Conduct** social science research to determine strategies for engaging communities for participation in clinical trials and to support acceptance of MCMs for NiV infection as they become available.

Product development

- **Define** criteria for down-selection and prioritization of candidate MCMs that should be moved forward.
- **Promote** early communication between developers and appropriate NRAs for clarity and guidance on the regulatory aspects of MCM development for NiV infection.

Key capacities

- **Create** international partnerships to fund, support, and promote enhanced laboratory capacity, public health surveillance capacity, and infrastructure in endemic and at-risk areas to promote early diagnosis, treatment, and implementation of vaccination programs for NiV prevention and control.
- **Improve** active and passive surveillance capacity to: (1) better define the incidence of disease in NiV-endemic and at-risk areas and (2) promote targeted research in non-endemic areas to identify evidence of spillover of NiV or other related henipaviruses from the natural reservoir to human or animal populations.
- **Develop** a shared data platform to facilitate sharing of NiV sequence and strain data.
- **Collaborate** with local government authorities (including human health, animal health, and wildlife representatives) to support NiV surveillance and disease prevention activities in endemic and at-risk areas.
- **Promote** community-based outreach programs that transfer skills and knowledge for the prevention and early recognition of NiV disease in areas of known or potential NiV spillover risk.
- **Strengthen** infrastructure and capacity for post-marketing pharmacovigilance of licensed NiV therapeutics and vaccines.

Policy and commercialization

- **Establish** a sustainable value proposition and **secure** funding to complete development, licensure, manufacture, deployment, and use of affordable MCMs for NiV infection.
- **Support** plans for adequate manufacturing and subsequent distribution of NiV diagnostics, therapeutics, and vaccines to endemic and at-risk areas.
- **Ensure** access to regulatory guidance, oversight, review, and authorization from appropriate NRAs for NiV MCMs. This should be done when clinical trials and approaches for regulatory approval are being determined.
- **Clarify** the potential for and possible strategies to promote technology transfer for development and manufacturing of MCMs for NiV infection.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

DIAGNOSTICS

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Initial signs and symptoms of NiV infection are nonspecific and the diagnosis often is not suspected at the time of presentation. This can hinder accurate diagnosis and creates challenges in outbreak detection and institution of effective and timely infection control measures and outbreak response activities. Additionally, latent disease can occur months to years after initial infection.
- Laboratory infrastructure and diagnostic capabilities in endemic and at-risk areas are often limited, and etiologic diagnosis is not always pursued; these issues can lead to delays in diagnosis and outbreak investigation and response.
- Clinical sample quality, quantity, type, timing of collection, and the time necessary to transfer the sample from the patient to the laboratory can affect the accuracy of laboratory results.
- Various types of test methods and platforms are required to test patients at different phases of NiV infection, which can complicate diagnostic needs and capabilities.
- Owing to the biosafety precautions necessary when working with the NiV virus, diagnostic testing of clinical specimens for NiV poses safety and logistical challenges in under-resourced areas with regard to collection, handling, transport, and laboratory analysis.
- The time required to perform diagnostic testing using conventional laboratory methods poses challenges, given the rapid disease progression of NiV infection.
- Pteropus bat species (and perhaps other bat species) appear to carry other henipaviruses (in addition to NiV and HeV), some of which may prove to be pathogenic in humans and livestock. Antibodies to different henipaviruses are highly cross-reactive, making it difficult to discriminate which henipaviruses are in circulation using serologic assays. Capacity to identify additional pathogenic henipaviruses is an important challenge for ensuring diagnostic preparedness to respond to future outbreaks.

Key needs

- A TPP for NiV diagnostics, identifying optimal and desirable characteristics to guide the development of promising diagnostic assays.
- A biobank of human and animal clinical samples to assess and validate diagnostic tests and a process for how best to judiciously use the samples. A clear approach is needed to: (1) determine what clinical samples should be collected, based on what would be most useful (e.g., plasma, whole blood, urine, cerebrospinal fluid, etc.); (2) outline the purposes of sample collection; (3) identify who would have access to the samples; and (4) prioritize use of samples and sample distribution.
- Clarification regarding the use cases for different diagnostic assays and what viruses are targeted (i.e., NiV, NiV and HeV, or all henipaviruses), since the corresponding performance, validation, and regulatory approval requirements may differ depending on how and in which population (i.e., human or animal) the test will be used. For example, it may be desirable to have a point-of-care screening test that is highly sensitive and a confirmatory test that is highly

specific. In animals, it may be desirable to have a diagnostic test with high sensitivity to screen reservoir populations and a highly specific test for livestock. Diagnostic use cases need to be considered in tandem with the use of therapeutics and other interventions.

- Rapid point-of-care diagnostic tests for NiV that involve minimal requirements for laboratory infrastructure, can detect disease early in the clinical course, are robust for use under a variety of conditions (e.g., varying humidity, temperature, etc.), can be applied in both human and animal populations, and have a high degree of sensitivity and specificity for different NiV strains.
- Optimal deployment strategies for diagnostics in different geographic areas based on the risk and epidemiology of NiV infection.
- International reference standards to calibrate diagnostic assays.
- Validation of promising diagnostics in endemic and at-risk geographic regions.
- Diagnostic preparedness to detect NiV, HeV, and other emergent henipaviruses in humans and animals as they arise.
- In-country laboratories able to conduct proficiency testing to monitor reproducibility and performance of NiV diagnostic assays in the field.
- A sufficient number of laboratories committed to using the diagnostics on a regular basis to support the business case for Nipah diagnostics, given the costs of regulatory approval.
- If feasible, multiplex syndrome-based assay panels for use in humans and animals that can detect NiV infection while simultaneously screening for the presence of other henipaviruses or other pathogens of public health concern that may cause similar clinical syndromes in endemic or at-risk areas. Since validation and regulatory approval of multiplex assays can prove challenging, an alternate approach would be the development of multiple single assays that can be run in parallel.
- If NiV or HeV vaccines become widely used in livestock, serological testing to differentiate vaccinated animals from infected animals (such as the Differentiating Infected from Vaccinated Animals (DIVA) test) will be needed.

Knowledge gaps

- Further research is needed on the kinetics of NiV detection in cerebrospinal fluid, blood, saliva, other body fluids (e.g., urine and respiratory secretions), and tissue samples to enhance the ability to diagnose infection at different stages of disease. Additionally, further research on the kinetics of NiV in the animal reservoirs is needed.
- More information is needed regarding the performance characteristics (including sensitivity, specificity, limits of detection, cross-reactivity, and quantitative vs. qualitative data) for NiV assays, particularly for newer tests (such as pseudotyped neutralization assays and antigen-capture ELISAs) and tests that are designed to detect more than one henipavirus. Further testing of diagnostics should be conducted in animal models before field trials in humans are pursued.
- A clear understanding is needed of the potential for cross-reactivity of diagnostic tests in animal populations to allow accurate interpretation of test results, since substantive economic consequences (such as trade restriction for livestock) could be triggered by positive results.

Strategic Goals

1. Obtain a better understanding of the kinetics of NiV detection at various points during the clinical course of illness to allow improved diagnostic capability across the disease spectrum.
2. Develop and assess affordable, highly sensitive and specific, point-of-care NiV diagnostic tests for use in humans and animals that are sufficiently robust for the conditions in which they will be used and that have minimal requirements for biosafety precautions and staff training. Consideration also should be given to development of multiplex assays that can detect related henipaviruses, in addition to NiV, or that can detect other pathogens of concern in endemic and at-risk areas.
3. Generate guidance on deployment strategies and use of diagnostic tests for NiV detection in areas of known or potential henipavirus spillover risk.
4. Enhance diagnostic preparedness in areas of known or potential henipavirus spillover risk to promote early detection of NiV, HeV, and other emergent henipaviruses in humans and animals.

Landmark Goals/Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Explore** new diagnostic approaches that may allow for earlier detection of infection.
- **Further evaluate** the kinetics of NiV detection in cerebrospinal fluid, blood, saliva, other body fluids, and tissue samples to enhance the ability to diagnose NiV infection at different stages of disease.
- **Determine** performance characteristics for promising new assays for diagnosis of NiV infection and **develop** appropriate standards for their use in different contexts.
- **Conduct** field evaluation studies to assess and validate new diagnostic tests for NiV infection.
- **Create** a biobank of clinical human and animal samples for use in researching new diagnostic agents.
- **Continue to research** cross-reactivity of diagnostic tests in animal populations.

Product development

- **Generate** a TPP for NiV diagnostics.
- **Define** use cases for diagnostic assays.
- **Develop, evaluate, and validate** point-of-care rapid diagnostic tests for NiV infection that are affordable, highly sensitive and specific, available for use in humans and animals, and can capture antigenically diverse strains of the virus and be performed accurately and safely in remote areas under a variety of circumstances.
- **Develop** multiplex syndrome-based assay panels that can detect NiV infection while simultaneously screening for the presence of other henipaviruses or other pathogens of concern in the geographic region that cause similar clinical syndromes.

- **Develop** diagnostics applicable to mass testing in livestock to identify NiV infection early and to reduce the likelihood of transmission of NiV from livestock to humans.
- **Develop** serologic testing to differentiate vaccinated from infected animals (such as a DIVA test), if NiV or HeV vaccines become widely used (long-term consideration).

Key capacities

- **Generate** international reference standards to calibrate diagnostic assays.
- **Support** in-country laboratories in monitoring performance of NiV diagnostics in the field.
- **Enhance** diagnostic preparedness in areas of known or potential henipavirus spillover risk to promote early detection of NiV, HeV, and other emergent henipaviruses in humans and animals.

Policy and commercialization

- **Develop** guidance on optimal strategies for deployment and use of new NiV diagnostic tests across different geographic areas, as such tests become available.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

THERAPEUTICS

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Patients typically present late in the clinical course of disease, which decreases the likelihood of successful treatment.
- The absence of improved diagnostic assays for timely diagnosis of infection creates an important challenge in providing early treatment and PEP to exposed persons.
- In the NiV-endemic region of Bangladesh, hundreds of patients are admitted to hospitals annually with a diagnosis of encephalitis, but do not have NiV infection. In the absence of confirmatory testing, treating all patients with encephalitis and their contacts for NiV infection would be costly and labor intensive, with relatively little benefit; therefore accurate and rapid diagnosis is critical.
- Studies in animals often evaluate usefulness of therapeutics when delivered prior to disease onset or early during the disease course. Patients with NiV infection often are detected later in the clinical course, which creates challenges for predicting how well an agent will work in the field.
- Nipah virus can infect the central nervous system (CNS), which creates challenges for generating therapeutic agents that cross the blood-brain barrier to inhibit viral replication and prevent severe neurologic disease.

- Healthcare systems in endemic countries often do not have adequate infection control systems in place to prevent person-to-person transmission. They also lack the ability to rapidly identify contacts most likely to benefit from PEP therapy.

Key needs

- A TPP for NiV therapeutic agents, identifying optimal and desirable characteristics to guide the development of promising treatment approaches in the context of individual and community priorities.
- Safe, easily administered, well-tolerated, and effective therapeutic agents that treat acute NiV infection to improve survival and decrease associated morbidity and long-term disability.
- Safe, easily administered, well-tolerated, and effective therapeutic agents that treat chronic (relapsing) NiV infection to decrease associated long-term disability.
- Safe and effective PEP to prevent infection following exposure to NiV and guidance on PEP use. PEP could be used to prevent illness in healthcare workers, family caregivers, and persons exposed to infected livestock.
- Improved patient care in endemic areas (such as the ability to provide ventilator support for seriously ill patients).

Knowledge gaps

- Ribavirin may be an option for treatment of NiV infection, but animal studies in hamsters and AGMs have not supported efficacy for ribavirin. Further research into the potential effectiveness of ribavirin for NiV infection may be warranted.
- The human monoclonal antibody (mAb) m102.4 has demonstrated protection against lethal NiV challenge in animal models and has been provided as a compassionate use for a small number of individuals exposed to either HeV or NiV. Recently, a phase 1 clinical trial for m102.4 with 40 human participants was completed in Australia, but results are not yet available. Additional animal studies using different NiV strains and clinical trials in endemic areas are needed to assess the safety, tolerability, and efficacy of m102.4 (and possibly other mAbs) for PEP and potentially early treatment of clinical disease.
- Additional research is needed regarding the likelihood of escape mutants with mAb use. While evidence of escape mutants has not been found to date with mAb 102.4, it may be necessary to consider mAb cocktails.
- Preclinical and clinical data are needed on the safety, tolerability, and efficacy of the most promising novel treatments (such as fusion inhibitory peptides, antifusion peptides, and GS-4734 [a broad-spectrum agent being used to treat Ebola virus disease survivors]), used alone or in combination with other therapies. Additionally, the therapeutic windows of each therapy should be determined for different NiV strains, as highlighted by a recent study in AGMs that showed the therapeutic window for m102.4 against a strain from Bangladesh/India to be shorter than for a strain from Malaysia.
- Further research is needed to broaden the number of novel antiviral candidates for treatment of NiV infection.
- Additional data are needed to establish the pharmacokinetic/pharmacodynamics (PK/PD) relationship of promising therapeutic candidates.

- Additional studies, as needed, of therapeutic candidates in the AGM model, followed by human clinical trials for safety, feasibility, and efficacy.
- Additional data are needed to determine the role of PEP and to inform development of guidance on the types of exposures that warrant such intervention and the most appropriate agents to administer. This determination should include feasibility for PEP distribution in both endemic and at-risk areas, including Bangladesh, which has hundreds of potentially-exposed persons annually that could be candidates for PEP.
- Patients may benefit from optimal supportive care independent of treatment with specific NiV therapeutic agents. Key research areas include obtaining data on the safety and efficacy of components of supportive care for NiV, such as optimal fluid and respiration management strategies, diagnosis and treatment of organ dysfunction, and the use of empiric antibiotics and/or antimalarials, to inform best-practice guidelines.

Strategic Goals

1. Develop, evaluate, and license therapeutic agents for treatment of NiV infection and for PEP to prevent NiV infection, and ensure that therapies are readily available, affordable, and accessible in areas of known or potential NiV spillover.
2. Develop guidance for the use of therapeutics for disease treatment and PEP as new therapies become available.

Landmark Goals/Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Continue to research** the safety, tolerability, and efficacy of investigational therapies (such as ribavirin and m102.4) for treating and preventing NiV infection, including conduct of animal studies and clinical trials as appropriate and feasible.
- **Continue to identify** new therapeutic options for treating and preventing NiV infection that should undergo further evaluation.
- **Research** optimal treatment and supportive care strategies for NiV infection and determine best-practice guidelines.

Product development

- **Generate** a TPP for NiV infection therapeutics.
- **Develop, evaluate, and license** safe and effective therapeutic agents for treatment of NiV infection that are active against different NiV strains and other henipaviruses, and that can cross the blood-brain barrier to treat or prevent CNS disease.
- **Identify** therapeutic approaches for PEP that are broadly active against different NiV strains and other pathogenic henipaviruses that may emerge.

Key capacities

- **Promote** enhancements to the healthcare delivery systems in impacted areas to improve clinical management and supportive care of patients with NiV infection.
- **Ensure** that mechanisms are in place to finance, generate, and maintain stockpiles of NiV therapeutics for outbreak control.

Policy and commercialization

- **Identify** a company to advance therapeutic use of m102.4 and **secure** financing for its manufacture and distribution.
- **Develop** guidance for the use of therapeutics for disease treatment and PEP, as new therapies become available.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

VACCINES

Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Sociocultural issues may hinder trust in the formal human, veterinary, and public health systems, which could impact acceptance of NiV vaccines for use in humans or animals.
- The absence of improved diagnostic assays for timely diagnosis of infection creates an important challenge in implementing a rapid reactive vaccination strategy for NiV outbreak control.

Key needs

- Nipah vaccines that can protect against different NiV strains in humans and animals, and that provide rapid onset of an immune response to adequately prevent and control outbreaks.
- Guidance on use of NiV vaccines (or broader henipavirus vaccines) to include vaccination strategies, potentially in both humans (including special populations such as children, immunocompromised individuals, and pregnant women) and animals, for different epidemiologic scenarios and different vaccine attributes.
- Once vaccines are available, enhanced surveillance capacity to assess the impact of vaccination programs and to refine vaccination strategies over time.

Knowledge gaps

- While neutralizing antibodies are likely a primary mediator of protection against NiV infection, cellular immunity appears to also play a role. Additional research is needed regarding the innate, cell-mediated, and humoral immune responses that constitute protective immunity against NiV.
- Further research is needed to clarify vaccine attributes (such as time from administration to immune protection, duration of immunity, and the need for booster doses) and to determine safety profiles of candidate vaccines.

- Further research is needed to determine the cross-protection efficacy for NiV of the HeV-sG subunit vaccine (i.e., the recombinant subunit vaccine Equivac® HeV from Zoetis).
- Additional research is needed to determine if vaccine candidates are cross-protective between different NiV strains, including recently identified strains; only a few studies demonstrating cross-protection have been performed to date.
- The identification of specific correlates or surrogates of protection in humans and animals and standardized assays for measuring immune correlates are needed to facilitate research on promising NiV vaccine candidates, and expedite possible licensing through nontraditional regulatory pathways, such as the US FDA's Animal Rule and accelerated approval mechanisms.
- Evaluation of vaccine safety in target populations is needed to better understand the risk of adverse incidents associated with vaccine use.
- If evidence at some point supports the need for a broader, population-based vaccination strategy (beyond reactive use for outbreak control in affected communities), additional research may be warranted on the development of multivalent vaccines that protect against more than one infection (such as a combined vaccine against NiV and HeV or NiV and measles virus [MV]) for use in NiV endemic areas.
- Mathematical modelling may be useful in: (1) assessing whether or not disease incidence is high enough in endemic areas for conducting clinical trials of candidate vaccines, (2) simulating various epidemiologic scenarios for development of vaccination strategies, (3) estimating the potential impact of NiV vaccines (once vaccines become available), and (4) estimating the vaccine quantity that may be necessary to maintain vaccine stockpiles.
- Because livestock (e.g., pigs and horses) are intermediary hosts for NiV and HeV, vaccination of livestock populations has been suggested as a possible mitigation strategy for preventing secondary transmission to humans. Currently, one HeV vaccine is available for horses and available evidence suggests this vaccine is cross-protective against NiV. Ongoing research into developing NiV/HeV vaccines for livestock (or other animals) and the potential for their use in endemic regions is needed to further assess the merit of this potential control strategy.
- Additional research is needed to determine if development of multivalent vaccines for animals (that protect against more than one disease) would increase the likelihood of vaccine uptake by food animal producers and the broader veterinary community.

Strategic Goals

1. Develop, evaluate, license, and deploy NiV vaccines for use in humans and potentially animals (e.g., livestock, companion animals).
2. Continue to research cross-protection of candidate vaccines against NiV and HeV (and potentially other emergent henipaviruses as needed).
3. Develop and refine guidance on vaccine use in humans and animals that aligns with current NiV epidemiology and takes into consideration attributes of new vaccines as they become available.

Landmark Goals/Milestones

[TBD once the strategic goals have been determined.]

Priority Areas/Activities

Research

- **Determine** the innate, cell-mediated, and humoral immune responses that contribute to protective immunity against NiV infection for use in developing and evaluating NiV vaccines.
- **Identify and standardize** correlates and/or surrogates of protection, which are necessary for ongoing research into candidate vaccines and also may be important for vaccine licensure.
- **Complete** preclinical evaluation of promising candidate NiV vaccines for safety, immunogenicity, efficacy in animal models, correlates of protection, and durability.
- **Further study** cross protection of various vaccine candidates against different NiV strains, and between NiV strains and HeV strains.
- **Perform** clinical trials to assess safety and immunogenicity in phase 1 and 2 trials, and undertake animal studies for immune bridging to facilitate regulatory licensing.
- **Explore** whether multivalent vaccines for animal populations would increase vaccine acceptability and uptake by food-animal producers and the broader veterinary community.
- **Conduct** mathematical modelling to estimate the potential impact of NiV vaccines and inform strategies for vaccine use.

Product development

- **License** safe and effective monovalent NiV vaccines for humans and animals.
- **License** safe and effective multivalent vaccines for use in humans that protect against more than one disease for use in human populations (e.g., vaccines that protect against both NiV and MV or HeV), if broader population-based vaccination is warranted at some point in the future.
- **Develop, clinically evaluate, and license** safe and effective multivalent vaccines that protect against more than one disease for use in animal populations, if this is deemed to be a sustainable approach.

Key capacities

- **Improve** surveillance capabilities to assess the impact of vaccine use and vaccination strategies (once vaccines become available).
- **Prepare** clinical trial sites and NRAs in affected countries for future clinical trials with NiV vaccines.
- **Support** plans for adequate manufacturing and stockpiling of licensed NiV vaccines for use when outbreaks occur.

Policy and commercialization

- **Provide** guidance on vaccination strategies for various target populations and epidemiologic scenarios that align with vaccine attributes, once vaccines are available.
- **Consider** development of a strategy for vaccine surge capacity to rapidly ramp up the vaccine supply, if NiV is used as a bioterrorism agent, or if an NiV strain emerges with increased capacity for person-to-person transmission, and thus more rapid spread.

Schedule of Resources, Coordination, and Implementation

[TBD; will obtain input later in the process.]

Critical Path Analysis

[TBD once the primary activities have been vetted by subject matter experts.]

BACKGROUND INFORMATION

World Health Organization R&D Roadmap documents and guidance:

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Other Publications:

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Comments and Suggestions from Reviewer for

Nipah Research and Development (R&D) Roadmap

Deadline for receiving comments: Friday, 8 June 2018

Reviewer Contact Information

Name:
Position:
Organization:
Email Address:
Telephone Number (including country code):

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
Roadmap purpose					
INTRODUCTION					
VISION					
CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
CROSS-CUTTING TOPICS AND ISSUES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					
CROSS-CUTTING TOPICS AND ISSUES: Strategic Goals					
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Research***					
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Product development***					
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Key capacities***					

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
CROSS-CUTTING TOPICS AND ISSUES: Priority Areas/Activities – ***Policy and commercialization***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
DIAGNOSTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					
DIAGNOSTICS: Strategic Goals					
DIAGNOSTICS: Priority Areas/Activities – ***Research***					

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
DIAGNOSTICS: Priority Areas/Activities – ***Product development***					
DIAGNOSTICS: Priority Areas/Activities – ***Key capacities***					
DIAGNOSTICS: Priority Areas/Activities – ***Policy and commercialization***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
THERAPEUTICS: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Knowledge gaps***					

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
THERAPEUTICS: Strategic Goals					
THERAPEUTICS: Priority Areas/Activities – ***Research***					
THERAPEUTICS: Priority Areas/Activities – ***Product development***					
THERAPEUTICS: Priority Areas/Activities – ***Key capacities***					
THERAPEUTICS: Priority Areas/Activities – ***Policy and commercialization***					
VACCINES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Primary challenges***					

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VACCINES: Current Primary Challenges, Key Needs, and Knowledge Gaps – ***Key needs***					
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VACCINES: Priority Areas/Activities – ***Key capacities***					

Page #	Line #	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
VACCINES: Priority Areas/Activities – ***Policy and commercialization***					
BACKGROUND INFORMATION					
ANY OTHER COMMENTS					

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 5/10/2018 10:16:10 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Clarke, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=29f1610b5b03444eac88f814312fb2e0-HHS-Elana.C]; Lim, Matt (STATE.GOV) [limml@state.gov]; Tracy Carson [CarsonTL@state.gov]
Subject: FW: [2018 Ebola DRC outbreak] - Research plan early draft
Attachments: DRC plan_DRAFT_08May2018_for review.xlsx

Dear Colleagues,

Several of you already received this earlier this morning directly from WHO, but in the interest of shared mutual awareness and to make sure all the relevant POCs have seen it, I wanted to pass the below note and attached early draft of the DRC Ebola outbreak research plan, which highlights key research needs. WHO is asking for feedback into the attached. In the interest of a speedy response, I recommend that each HHS and DoD division coordinate internally and send any inputs directly to Massi Si Mehand and the WHO R&D Blueprint team through the POCs on the below email from WHO.

In addition to the DRC research response plan, WHO has posted the R&D Blueprint roadmaps for Ebola, Lassa, and Nipah on their website for comment (see links in Dr. Si Mehand. WHO is accepting comments on the roadmaps through June 8 and I am happy to compile HHS/USG comments on the roadmaps and pass them along to the WHO team if folks will please send me their comments by Wednesday, June 6.

The roadmaps were developed in coordination with Michael Osterholm's group at CIDRAP and they will be holding several webinars on the roadmaps starting next week, the information for which I have pasted below underneath the email from Dr. Si Mehand at WHO. CIDRAP asks that you please RSVP if you plan to log in.

Best Regards,
Collin

Collin Weinberger, MPH
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(O): (202) (b)(6) (M): (b)(6)
collin.weinberger@hhs.gov

From: SI MEHAND, Massinissa [mailto:simehandm@who.int]
Sent: Thursday, May 10, 2018 3:52 AM
To: Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Erbelding, Emily (NIH/NIAID) [E] <emily.erbelding@nih.gov>; Helfand, Rita (CDC/OID/NCEZID) <rzh7@cdc.gov>; Weinberger, Collin (OS/OGA) (CTR) <Collin.Weinberger@hhs.gov>; george.w.christopher.civ@mail.mil; sina.bavari.civ@mail.mil; david.brett-major@usuhs.edu; kayvon.modjarrad.civ@mail.mil; nelson.l.michael2.mil@mail.mi; Cox, Edward M (FDA/CDER) <Edward.Cox@fda.hhs.gov>; Scherf, Uwe (FDA/CDRH) <Uwe.Scherf@fda.hhs.gov>; Sapsford, Kim E (FDA/CDRH) <Kim.Sapsford@fda.hhs.gov>; Roth, Kristian (FDA/CDRH) <Kristian.Roth@fda.hhs.gov>; gustavo.f.palacios.ctr@mail.mil
Cc: HENAO RESTREPO, Ana Maria <henaorestrepoa@who.int>; PREZIOSI, Marie-pierre <preziosim@who.int>; SATHIYAMOORTHY, Vaseeharan <moorthyv@who.int>; BENASSI, Virginia <benassiv@who.int>; FORMENTY, Pierre B.h. <formentyp@who.int>; LEGAND, Anais <leganda@who.int>; MURGUE, Bernadette <murgueb@who.int>
Subject: [2018 Ebola DRC outbreak] - Research plan early draft

Dear NIH/NIAID, CDC, OGA, DoD/WRAIR and FDA colleagues,

Following the declaration of a new Ebola outbreak in Bikoro in Equateur Province in the Democratic Republic of the Congo (RDC), WHO held a GCM call yesterday to provide a briefing of the situation and to identify/discuss key research activities to be conducted. Please find attached an early draft of a research plan, we will be grateful if you can give us your inputs.

Also, we are pleased to inform you that the draft R&D Roadmaps for Ebola/Marburg, Lassa and Nipah are now available online for a public call for comments, until Friday, 8 June 2018.

Please feel free to visit the dedicated pages (below) and provide your feedback. For each roadmap a comment form is available. However, should you prefer to send the comment directly to my colleague Virginia (cc'd : benassiv@who.int), please do not hesitate to do so.
http://www.who.int/blueprint/priority-diseases/key-action/ebola/en/
http://www.who.int/blueprint/priority-diseases/key-action/lassa-fever/en/
http://www.who.int/blueprint/priority-diseases/key-action/nipah/en/

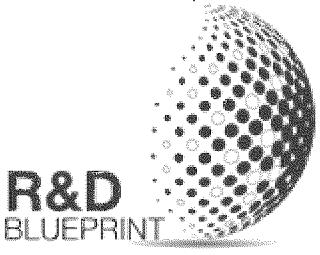
We would very much appreciate if you could share this email message with others in your networks who may be interested in reviewing the roadmaps.

Thannks a lot for your support.

Best wishes,

Massi.

Dr Massinissa Si Mehand
Technical Officer
Office of the Deputy Director General
Health Emergencies Programme
WHO R&D Blueprint



For information on the WHO R&D Blueprint:
http://www.who.int/csr/research-and-development/en/
Tel. : +41 22 791 1207
Mobile: (b)(6)
Email: simehandm@who.int

From: Michael Osterholm [mailto:mto@umn.edu]
Sent: Wednesday, May 09, 2018 10:18 PM
To: mto@umn.edu
Subject: Informational Webinars for the Ebola/Marburg, Lassa fever, and Nipah WHO R&D roadmaps (May 15, 16, and 22)

Dear colleagues:
The Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota, with support from Wellcome Trust and in collaboration with the World Health Organization (WHO), will be hosting informational webinars on the following draft research and development (R&D) roadmaps, which were developed as part of the WHO R&D Blueprint initiative:

- Ebola/Marburg R&D Roadmap
- Lassa Fever R&D Roadmap
- Nipah R&D Roadmap

The informational one-hour webinars are intended to engage a broad audience in the review and further development of the draft roadmaps by offering opportunities for stakeholders who may not be familiar with the process to learn more about the goals for each roadmap and how to provide feedback. The three roadmaps are available on the WHO website for public comment through **8 June 2018** (see roadmaps webpages for Ebola/Marburg, Lassa, and Nipah).

The webinars will be held at the following times:

1. **Ebola/Marburg**: Tuesday, May 15, 2018 – 9:30 am Central Daylight Time (CDT) (3:30 pm British Summer Time [BST] / 4:30 pm Central European Summer Time [CEST])
2. **Lassa**: Wednesday, May 16, 2018 – 9:30 am CDT (3:30 pm BST / 4:30 pm CEST)
3. **Nipah**: Tuesday, May 15, 2018 – 8:00 pm CDT (Wednesday, May 16 at 2:00 am BST / 3:00 am CEST / 7:00 am Bangladesh Standard Time / 9:00 am Singapore Time)
4. **Nipah**: Tuesday, May 22, 2018 – 9:30 am CDT (3:30 pm BST / 4:30 pm CEST)

Pre-registration is required for webinar participation. Please visit the CIDRAP R&D Roadmaps Webinars information page to complete registration and for more details.

Please share this email message with others who may be interested in learning more about the draft roadmaps and participating in the webinars.

Sincerely,

Mike

Michael T. Osterholm, PhD, MPH
Regents Professor
McKnight Endowed Presidential Chair in Public Health
Director, Center for Infectious Disease Research and Policy
Distinguished University Teaching Professor
Environmental Health Sciences, School of Public Health
Professor, Technological Leadership Institute College of Science and Engineering
Adjunct Professor, Medical School
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Document produced natively.

From: Weinberger, Collin (OS/OGA) (CTR) [Collin.Weinberger@hhs.gov]
Sent: 6/14/2018 11:20:50 AM
To: Handley, Gray G (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c028db015f1f4544ab4c265ec05ad834-HHS-handley]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Helfand, Rita (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae435981a2b14a1d8b16cfd4c954575f-HHS-rzh7-cd]; Craig, Allen (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=258003fd08cc4d1ba85dc4e70ec3b708-HHS-afc0-cd]; Vinter, Serena (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=994f0f1af6d6491fae1d0788b3667454-HHS-uvv3-cd]; Kapil, Vikas (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b24fd89e78a64022875d565407d5c30a-HHS-vck3-cd]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Krause, Philip [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00c6330fea0042fdb5571c3fdef792ed-krause]; Marinissen, Maria Julia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bad48dfabf84875995b2cad6a6bf46f-HHS-Maria.M]; Moudy, Robin (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad66e2f809804b82b5f35f68d60fbde4-HHS-Robin.M]; Balliram, Richard (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=84c90e08bdbe475889893cf95db919bf-HHS-Richard]; Barna, Lauren (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=271142eac37342bf97e640c7903bb7a1-HHS-Lauren.]; Holloway, Carl C (Clay) CIV USARMY DOD JPEOCBD (US) [carl.c.holloway.civ@mail.mil]; Kishimori, Jennifer M COL USARMY OSD HA (US) [jennifer.m.kishimori.mil@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; LeButt, Kimberly A CIV OSD OUSD ATL (US) [kimberly.a.lebutt.civ@mail.mil]
CC: Yu, Anne (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d80d118c6f7e42eea77511b04486f1fd-HHS-Anne.Yu]; Kerr, Lawrence (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0920fe6d7b54496b84446fee6a21ddea-HHS-Lawrenc]; Locus, Tiffany (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7bcc86804dc449c18c21be6469f0ee86-HHS-Tiffany]; Adeniyi-Jones, Samuel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4d4fcfef92d4d08be98c52ea3445102-HHS-Samuel.]; Ekpenyong, Elana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4cb339b79b904f62a6506370cef1ec59-HHS-Elana.E]; Lim, Matt (STATE.GOV) [limml@state.gov]; Tracy Carson [CarsonTL@state.gov]
Subject: FW: [R&D Blueprint GCM] DRC Ebola research plan meeting June 6th
Attachments: NFR Ebola research meeting 6 June.pdf

Dear All,

Please find attached WHO's notes for the record from the June 6th meeting in Geneva on the DRC Ebola research plan and research priorities.

Best Regards,
Collin

Collin Weinberger, MPH
Senior Global Health Officer, Office of Pandemics and Emerging Threats
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From: GSELL, Pierre [mailto:gsellp@who.int]
Sent: Thursday, June 14, 2018 10:52 AM
Cc: HENAO RESTREPO, Ana Maria <henaorestrepoa@who.int>; PREZIOSI, Marie-pierre <preziosim@who.int>; SATHIYAMOORTHY, Vaseeharan <moorthyv@who.int>
Subject: FW: [R&D Blueprint GCM] DRC Ebola research plan meeting June 6th

Dear All,

Please find attached NFRs from the DRC Ebola national research plan meeting, held June 6th.
Many thanks for your continuous support and contributions to this important development.
A new iteration of the plan will follow.

Kind regards

Pierre on behalf of the Secretariat

From: Pierre GSELL <gsellp@who.int>
Date: Thursday, 31 May 2018 at 20:38
Cc: Ana HENAO RESTREPO <henaorestrepoa@who.int>, "preziosim@who.int" <preziosim@who.int>, Vaseeharan SATHIYAMOORTHY <moorthyv@who.int>, "MAFUNGA, Neddy" <mafungan@who.int>
Subject: [R&D Blueprint GCM] DRC Ebola research plan meeting June 6th

This message is sent to the R&D Blueprint GCM and SAG members

Dear All,

Institut National de Recherche Biomédicale is the lead entity in DRC for the Ebola research response, as designated by DRC Ministry of Health.
During a mission by the Blueprint leadership team to DRC, INRB articulated the local research priorities for better detection, prevention, treatment and control of the current outbreak and future DRC Ebola outbreaks.
Professor Muyembe, DG of INRB, has been a leading global figure in the fight against Ebola since 1976, and is one of the foremost health researchers in Africa.
WHO invites you to take part in a meeting on June 6th in Geneva, where Professor Muyembe will discuss the research priorities for Ebola response and preparedness in DRC.
At this meeting the Ebola DRC research plan developed by INRB will be presented to partners, and there will be a discussion about how best to coordinate support to address these priorities.

At such short notice we understand that very few of you will be able to attend, and TC/VC participation will be possible for those unable to attend in person.
If you are able to attend in person **please liaise with Ms Neddy Mafunga** – mafungan@who.int - on administrative arrangements.
The meeting will start at 11am on **Wednesday June 6th at CICG, Geneva.**

With best regards,

Blueprint technical leadership team

From: AL-SHORBAJI, Farah
Sent: 25 May 2018 09:47
To: AL-SHORBAJI, Farah
Subject: Invitation to GCM call TODAY
Importance: High

This message is sent to the R&D Blueprint GCM and SAG members

Dear all,

We would like to invite you for a teleconference to update you on the research response to the Ebola outbreak in DRC, **this afternoon Friday 25 May at 14.00 Geneva time**.

With apologies for the short notice, this is the only available time for our colleagues in DRC. An agenda will follow shortly, and dial in details are below.

Dial in details:
(b)(6) / **Participant code:** (b)(6)

Best wishes,
Farah

Dr Farah Al-Shorbaji
Technical Officer
WHO R&D Blueprint

Phone: +41 2279 12786

R&D BLUEPRINT

For information on the WHO R&D Blueprint:
http://www.who.int/csr/research-and-development/en/

World Health Organization

Note for the Record

R&D Blueprint – Global Coordination Mechanism Meeting on DRC National Ebola research plan, 6 June 2018, Geneva

Attendees (in alphabetical order) (b)(6)

(b)(6)

Invited but unable to attend: (b)(6)

(b)(6)

1. **Introduction**
   - Professor Jean-Jacques Muyembe and Dr Cliff Lane opened the meeting by thanking everyone for attending on such short notice, and presenting the aims of the workshop. They noted that this Ebola outbreak has been markedly different to previous epidemics, with a more rapid response that has included research from the beginning.
   - The goal of this meeting is to establish top research priorities for Ebola virus disease in the DRC. During the meeting, a new way of looking at Ebola was proposed: as a seasonal epidemic with acute phases of reemergence rather than isolated outbreaks. This long term perspective may enable research efforts to continue in the interim between cases and resume smoothly, with partnerships and specific protocols already agreed in advance.
   - The draft national research plan for EVD is attached, and was reviewed and discussed.

2. **Epidemiological update – DRC Ebola outbreak**
   - Dr Brett Archer from WHE presented the latest epidemiological situation to the group. This is still considered an active outbreak, although the last confirmed case was on 28 May [since the meeting there has been a confirmed case on 7 June]. There is strong evidence that all confirmed cases are epidemiologically linked.
   - The location of the outbreak and logistical challenges contribute to the risk of spread, making this one of the most complex outbreak responses to date. There remains concern over more cases surfacing in Mbandaka, especially after two patients left the ETC. All 19 of their contacts have been identified and are being monitored. Cases from Itipo are transferred to Bikoro where there is an MSF ETU.
   - The Ministry of Health is providing daily updates via Twitter (https://twitter.com/MinSanteRDC).

3. **Research activities ongoing in DRC**
   - The ring vaccination protocol begun its implementation within two weeks of the outbreak being declared.
   - The process for therapeutics has been accelerated too (two weeks to obtain authorizations and import the treatments into the DRC). Current efforts to develop specific RCT protocols while the urgency is maintained may mean that the process to conduct RCTs in the future would be much more rapid (see below).

4. **Ring Vaccination protocol with rVSV**
   - Vaccination with rVSV-ZEBOV began within two weeks of the outbreak being reported to WHO on 8 May, under an Expanded Access Protocol with Professor Muyembe as the PI. This has been possible due to the strong collaboration between WHO, MSF, INRB and the MoH, and to date has been successful.
   - WHO and MSF are using the same protocol to vaccinate eligible people. All contacts and contacts of contacts aged 1 and above are eligible (regardless of when they came into contact with the confirmed case). HCWs and FLWs are also being vaccinated, and all vaccinated people are followed up on days 3, 14, and 21. Some breakthrough cases are expected where infection has already occurred before vaccination. The ethics committee declined the proposed amendment to include pregnant women.
   - Nearly 250 HCWs have been vaccinated in total, and there is a team in Kinshasa offering the vaccine to HCWs there. International HCWs are also being vaccinated in three locations (NIH, Emory University, and PHAC Winnipeg).
   - Most of the FLWs vaccinated are also contacts of the confirmed cases, and the different groups will be identified at a later date. There are no limiting inclusion criteria for FLWs (including traditional healers, taxi drivers, etc.).
   - Vaccination teams include social mobilisers who are gradually and successfully building community acceptance of the vaccine.

- The SAGE Ebola Working Group met on 4-5 June and reviewed 11 candidates. They will be proposing a set of recommendations to SAGE for consideration.
- The participants agreed that having more than one licensed vaccine for Ebola is important- for complementarity of approaches (e.g. reactive use versus long term protection) and to ensure that more than one manufacturer is able to produce effective vaccines. The Blueprint has convened an expert working group to discuss trial designs for evaluating other vaccines, and will be sharing the outcomes of these discussions with everyone for additional inputs.

5. The DRC Ebola Research Plan

Priorities

Prof Muyembe and Dr Mulangu presented the highlights of the national research plan. They stated that their number one priority is to build clinical research capacity in country, as well as improve lab capacity and diagnostic tests to strengthen surveillance systems and enable rapid detection of Ebola and other VHF, not only in Kinshasa but in all provinces.

The full list of research questions and capacity building activities can be found in the draft document which was circulated during the meeting, and covers a broad scope. Executing this plan will need joint efforts led by INRB. It will be crucial to integrate a longer term capacity building plan while still in response mode.

- Immediate priorities include:
    - A retrospective study on the origin of the outbreak;
    - Standardized data collection between ETCs using checklists etc.(GOARN partners are working on compiling key questions);
    - Building a research centre for molecular biology, diagnostics and immunology and training national physicians and scientists.
- Key long term priorities include:
    - To better understand the epidemiology, risk factors including behavior and cultural practices, and ecology of Ebola;
    - To improve patient care and develop effective treatments, not only for Zaire Ebola;
    - To better understand the clinical course of infection and the immunology of survivors;
    - To understand the effects of asymptomatic patients on transmission.

Below are excerpts of some of the detailed possible research questions included in the DRC national research plan that were presented by the INRB team and discussed during the meeting.

Ecological:

- **What is the ecologic reservoir/ animal host for Ebola virus?**

Epidemiology:

- **What is the prevalence of Ebola virus infection in the DRC?**
- **What are the socioeconomic and behavioral factors associated with Ebola virus infection?**

Serosurveys are one area where support is needed to increase country capacity and to tackle a huge area. It could be useful to consider using existing serosurveys done at the village level that could be leveraged for Ebola surveillance in order to map areas at high risk of transmission. This will be a significant challenge in itself. Suggestions for narrowing this down included focusing on areas where outbreaks have previously occurred, or targeting serosurveys at subsets of the population deemed as high risk (although this may overlook unknown risk factors).

Once areas at high risk of transmission are identified, risk assessments can be done on social and cultural factors, human-animal contact etc. to determine if high seroprevalence is associated with any behavioural or other patterns.

Integrating social science and cultural aspects into study protocols will inform the knowledge base much more. There are previous protocols that can be used as a base, and partners willing to share these protocols. Such a study would combine seroprevalence studies, risk assessment, and social factors.

Diagnosis:

- **What is the best diagnostic test for Ebola virus infection?**

Determining the best way to screen for and diagnose Ebola will be an important step, i.e. defining the appropriate algorithms for use of the RDT versus molecular testing. It will be critical to strengthen the DRC capacities for safe handling, diagnosis and reporting of major VHF diseases.

Another aspect which was briefly discussed was the sharing of samples and genetic sequencing. The idea of a sample bank as part of a wider research proposal and long-term plan was proposed. A longer-term priority for the DRC is to build capacity in country for molecular epidemiology, using sequencing to understand the spread of Ebola and evaluate interventions, etc. Support in building this capacity was offered by UK PHE and Bernard Knock Institute

Pathogenesis:

- **What are the long-term consequences of Ebola virus infection?**

There are several ongoing studies of long term consequences and sequelae of Ebola in survivors of the West Africa outbreak. They are looking at a range of outcomes including persistence of viral shedding in semen, immunology and clinical symptoms/sequelae. The study protocols, assays and standards should be shared with INRB, highlighting what worked and what didn't so that results between them and future studies could be comparable.

Prevention:

- **What are the characteristics of the immune response to Ebola virus vaccination?**

The INRB and UCLA have developed a protocol for a seroconversion study and plan to begin collecting samples to learn more about the antibody immune response in vaccinated people. Prof Muyembe noted they are willing to receive comments on how correlates of protection and risk could be measured across outbreaks. Collecting this data will support the process for licensure of the vaccine, and there are existing validated assays for antibodies and T cells.

Treatment:

- **What is the best treatment for Ebola virus infection?**

WHO convened a group of independent scientific experts to evaluate the evidence for five investigational EVD therapeutics, and make recommendations for Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI). A key component of MEURI is standardized data collection in order to monitor use and effects of a treatment from time of admission to discharge.

The expert group prioritized the available treatments based on the current evidence. While WHO cannot publicly state the available number of treatment courses for each product, there is a sufficient number to treat new confirmed cases, and stocks can be renewed within three days if needed. Four of the five treatments are currently in the DRC.

A committee of clinical experts in Kinshasa has been set up and will provide guidance to clinicians in the ETCs on what treatments can be used given the evidence and capacity of each ETU (which vary between locations). The ultimate choice of which treatment will be administered will be up to the treating physicians on site.

Randomized clinical trials will be critical to learning more about the safety and efficacy of each investigational product, and the expert group supported the transition of MEURI into a trial if the outbreak continues. It was also recognized that this will be challenging, especially with small numbers of cases who differ in when they are admitted, the capacity of the health facility, and the availability of interventions and care.

WHO is coordinating between members of the scientific community, ethicists, the responders on the ground, and most importantly country authorities and the INRB to continue the dialogue on a protocol that is ethical and methodologically robust. WHO aims to be as inclusive and transparent as possible during this process. Due to the urgency of the situation, it is important to move quickly to mobilize and engage a critical mass of available people.

A draft generic protocol for a three arm trial (A, B, A+B) has been developed with methodologists and regulatory agencies, and a summary will be posted online shortly. It has been submitted to the national Ethics Review Board for preliminary feedback on the methodology as the final protocol is prepared. Currently it does not preclude any drugs, only outlines the design of the randomized trial, with primary endpoint of mortality at day 14, and secondary endpoints on disease features and viral load, with a follow up after 1 year. The summary also outlines options for extending the trial across multiple epidemics. There remain concerns over including the A+B arm, for feasibility and safety reasons which were noted during the meeting.

The protocol will be finalized and will include the feedback from the ERB is received, specifying which therapeutics could be included. The aim is to have this complete by the end of June 2018, to be used in this outbreak if pertinent or in a future outbreak of EVD. A face to face meeting of relevant stakeholders has been proposed to achieve this consensus. Some partners have suggested that the protocol should have an adaptive design that allows for treatment centres to be flexible based on feasibility. Attendees highlighted the importance of developing a specific protocol as soon as possible, so it will be ready to be used immediately in a future outbreak.

The difficulty of initiating research for the immediate response needs compared with the longer term needs was noted.

Other critical research questions:

It will also be important to carry out anthropological studies of how communities react to Ebola outbreaks and behaviours/attitudes change over time. This may impact how community response is mobilized in the future (prevention, disease control, operational response, engagement, disinfection practices, etc.).

There is an opportunity to collect what has been learned from previous outbreaks, and develop consensus study protocols to address various of the above noted research questions rather than developing in parallel multiple different protocols from various parties. This would support the sharing of best practices between partners and enable more rapid progress. Traditionally, many activities done in the field as part of the response are not thought of as research, but certainly can be tailored to be useful for knowledge generation

6. A long term vision and the need for national capacity building

The DRC national research plan includes critical capacity building activities required to be able to implement the research questions depicted above.

A new way of thinking about Ebola outbreaks as a set of periodic event was proposed, with an initial five year continuous research program that could lead to increasing research capacity and implementation of a national research agenda from one epidemic to another. Wellcome Trust indicated their interest in principle to fund such national research plan. Key research funders can bring partners together to endorse a well-rounded and complete national research program that includes elements like data and sample sharing, supply chain, and training with a long term funding strategy. For Ebola, this long term program could consist of international group of funders providing resources to the research plan under the leadership of the INRB, focusing on different elements of the research plan and developing concrete proposals now to prepare for the next outbreak.

7. Next steps

- Prof Muyembe noted that Ebola is often accompanied by panic and fear, and there is still much to learn about the disease. He acknowledged that the meeting demonstrated the global interest in Ebola research and in building critical research capacity in DRC. *"Today is not each one flag that is being planted but the flag of DRC in an effort to help us better prepared".* He thanked everyone and stated that INRB looks forward to working with everyone to build DRC's research capacity.
- INRB welcomes the coordinated approach and the partnership of the different organizations under the leadership of the DRC and INRB. The research plan will be updated by INRB in view of the suggestions received with support from WHO, and will be recirculated.
- WHO will continue implementing the outcomes of the Ebola R&D roadmap and convening clinical trial methodologists to help inform the design of the protocols.
- WHO will also work closely with GOARN research to ensure that all aspects of expert support needs as highlighted in the DRC national research plan are addressed.
- WHO will continue to facilitate interactions between INRB and various partners and implement a follow up on the main proposals discussed today, with the aim of developing a revised national research plan and protocols by the end of this month.
- WHO will develop a log/registry of what studies are ongoing and planned, including outcomes, sample sizes, locations, results, etc. This will inform the development of a research partner mapping tool similar to the one developed for Lassa fever.
- Wellcome Trust, NIH, WHO and other partners will continue to discuss approaches for a sustainable long term funding strategy in support if the DRC national research plan, looking at Ebola research as a 5 year continuous investment.
- WHO thanked all who participated in this meeting and stated that it continues to be a pleasure to work with the capable INRB team.

From: Aviles, Natalie (OS/ASPR) [Natalie.Aviles@hhs.gov]
Sent: 1/22/2018 11:58:14 AM
To: Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]
CC: Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]
Subject: STATUS: Innovation Initiative: Mining the Pathogen-Host Interactome - January 31, 2018

Importance: High

Dear Colleagues,

In light of the uncertainty of when normal government operations will resume, we are taking the following approach regarding the upcoming "ASPR Innovation Initiative: Mining the Pathogen-Host Interactome" meeting currently scheduled for 31 January 2018. Should the current situation persist up this coming Sunday, January 28th, we will then need to reschedule the meeting to a date that we hope will be convenient for everyone later in February. If operations resume before this Sunday, please continue to plan on attending.

Very respectfully,

Natalie Avilés
Program Analyst
U.S. Department of Health & Human Services (HHS)
Assistant Secretary for Preparedness & Response (ASPR)
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From: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]
Sent: 1/13/2018 9:19:42 AM
To: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew (matthew.hepburn@darpa.mil) [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; 'kimberly.a.lebutt.civ@mail.mil' [kimberly.a.lebutt.civ@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared (paragas1@llnl.gov) [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil) [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; 'robert.g.ulrich.civ@mail.mil' [robert.g.ulrich.civ@mail.mil]; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]

Subject: SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Location: O'Neill House Office Building - Washington, D.C.

Start: 1/31/2018 9:00:00 AM

End: 1/31/2018 1:30:00 PM
Show Time As: Busy

Required Attendees: Korch, George (OS/ASPR/IO); Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA) (Joseph.Larsen@hhs.gov); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E] (ccoleman@mail.nih.gov); Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID) (iad7@CDC.GOV); Merlin, Toby (CDC/OID/NCEZID) (tfm5@CDC.GOV); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC) (carmen.maher@fda.hhs.gov); Mair, Michael (FDA/OC) (Michael.Mair@fda.hhs.gov); Bryant, Paula (NIH/NIAID) [E] (paula.bryant@nih.gov); Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E] (michael.kurilla@nih.gov); Hepburn, Matthew (matthew.hepburn@darpa.mil); Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil); Paragas, Jason Jared (paragas1@llnl.gov); cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil); jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH)

From: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]
Sent: 1/13/2018 9:19:42 AM
To: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew (matthew.hepburn@darpa.mil) [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; 'kimberly.a.lebutt.civ@mail.mil' [kimberly.a.lebutt.civ@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared (paragas1@llnl.gov) [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil) [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; 'robert.g.ulrich.civ@mail.mil' [robert.g.ulrich.civ@mail.mil]; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]; Kadlec, Robert P (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=70539a2f88924cc8913781ea74278b12-HHS-Robert.]; Stephan, Briana (OS)

	[/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86b3179b17604efa9818a549ef7e3fa0-HHS-Briana.]; Ford-Barnes, Arwenthia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=38db99da9c0f4495b790adda00040fe7-HHS-Arwenth]
CC:	Williams, David (Dave) CIV USARMY DOD JPEOCBD (US) [david.williams8.civ@mail.mil]
Subject:	SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Location:	O'Neill House Office Building - Washington, D.C.
Start:	1/31/2018 9:00:00 AM
End:	1/31/2018 1:30:00 PM
Show Time As:	Busy
Required Attendees:	Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E]; Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID); Merlin, Toby (CDC/OID/NCEZID); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC); Mair, Michael (FDA/OC); Bryant, Paula (NIH/NIAID) [E]; Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E]; Hepburn, Matthew; Hann, Ronald K Jr SES DTRA (US); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US); Paragas, Jason Jared; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil'; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH); bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto); Patel, Jean (CDC/OID/NCEZID); McDonald, Clifford (CDC/OID/NCEZID); Kadlec, Robert (OS/ASPR/IO); Stephan, Briana (OS/ASPR/IO); Ford-Barnes, Arwenthia (HHS/ASPR/IO)
Optional Attendees:	Williams, David (Dave) CIV USARMY DOD JPEOCBD (US)

From: Aviles, Natalie (OS/ASPR) [Natalie.Aviles@hhs.gov]
Sent: 1/30/2018 4:04:13 PM
To: Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]; Kadlec, Robert P (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=70539a2f88924cc8913781ea74278b12-HHS-Robert.]; Stephan, Briana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86b3179b17604efa9818a549ef7e3fa0-HHS-Briana.]; Ford-Barnes, Arwenthia

(OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=38db99da9c0f4495b790adda00040fe7-HHS-Arwenth]; Sundaram, Shivshankar [sundaram1@llnl.gov]; Reichert, Erin D CIV (US) (erin.d.reichert.civ@mail.mil) [erin.d.reichert.civ@mail.mil]; david.m.hone2.civ@mail.mil

CC: Williams, David (Dave) CIV USARMY DOD JPEOCBD (US) [david.williams8.civ@mail.mil]; Shuren, Jeff [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=44335a0c2f834535bc8713dfd643905e-Jeff.Shuren]; Johnson, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9c7eb3a419464ea2917f9d1e3f6e57a4-HHS-Robert.]; Maisel, William [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a1173dcb42794e11805d85993d1f9797-WZM]; Dorsey, Christopher B CIV USARMY DOD JPEOCBD (US) [christopher.b.dorsey2.civ@mail.mil]

Subject: SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Location: O'Neill House Office Building - Washington, D.C.

Start: 1/31/2018 9:00:00 AM
End: 1/31/2018 1:30:00 PM
Show Time As: Tentative

Required Attendees: Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E]; Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID); Merlin, Toby (CDC/OID/NCEZID); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC); Mair, Michael (FDA/OC); Bryant, Paula (NIH/NIAID) [E]; Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E]; Hepburn, Matthew; Hann, Ronald K Jr SES DTRA (US); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US); Paragas, Jason Jared; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil'; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH); bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto); Patel, Jean (CDC/OID/NCEZID); McDonald, Clifford (CDC/OID/NCEZID); Kadlec, Robert (OS/ASPR/IO); Stephan, Briana (OS/ASPR/IO); Ford-Barnes, Arwenthia (HHS/ASPR/IO); Sundaram, Shivshankar; Reichert, Erin D CIV (US) (erin.d.reichert.civ@mail.mil); david.m.hone2.civ@mail.mil

Optional Attendees: Williams, David (Dave) CIV USARMY DOD JPEOCBD (US); Shuren, Jeff (FDA/CDRH); Johnson, Robert (OS/ASPR/BARDA); Maisel, William (FDA/CDRH); Dorsey, Christopher B CIV USARMY DOD JPEOCBD (US)

From: Aviles, Natalie (OS/ASPR) [Natalie.Aviles@hhs.gov]
Sent: 1/25/2018 4:25:51 PM
To: Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]; Kadlec, Robert P (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=70539a2f88924cc8913781ea74278b12-HHS-Robert.]; Stephan, Briana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86b3179b17604efa9818a549ef7e3fa0-HHS-Briana.]; Ford-Barnes, Arwenthia

(OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=38db99da9c0f4495b790adda00040fe7-HHS-Arwenth]

CC: Williams, David (Dave) CIV USARMY DOD JPEOCBD (US) [david.williams8.civ@mail.mil]

Subject: SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Location: O'Neill House Office Building - Washington, D.C.

Start: 1/31/2018 9:00:00 AM
End: 1/31/2018 1:30:00 PM
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Required Attendees: Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E]; Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID); Merlin, Toby (CDC/OID/NCEZID); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC); Mair, Michael (FDA/OC); Bryant, Paula (NIH/NIAID) [E]; Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E]; Hepburn, Matthew; Hann, Ronald K Jr SES DTRA (US); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US); Paragas, Jason Jared; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil'; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH); bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto); Patel, Jean (CDC/OID/NCEZID); McDonald, Clifford (CDC/OID/NCEZID); Kadlec, Robert (OS/ASPR/IO); Stephan, Briana (OS/ASPR/IO); Ford-Barnes, Arwenthia (HHS/ASPR/IO)

Optional Attendees: Williams, David (Dave) CIV USARMY DOD JPEOCBD (US)

From: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]
Sent: 1/13/2018 9:19:42 AM
To: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew (matthew.hepburn@darpa.mil) [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; 'kimberly.a.lebutt.civ@mail.mil' [kimberly.a.lebutt.civ@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared (paragas1@llnl.gov) [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil) [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; 'robert.g.ulrich.civ@mail.mil' [robert.g.ulrich.civ@mail.mil]; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]

Subject: SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Attachments: Meeting Agenda 20170131.pdf
Location: O'Neill House Office Building - Washington, D.C.

Start: 1/31/2018 9:00:00 AM
End: 1/31/2018 1:30:00 PM
Show Time As: Tentative

Required Attendees: Korch, George (OS/ASPR/IO); Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA) (Joseph.Larsen@hhs.gov); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E] (ccoleman@mail.nih.gov); Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID) (iad7@CDC.GOV); Merlin, Toby (CDC/OID/NCEZID) (tfm5@CDC.GOV); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC) (carmen.maher@fda.hhs.gov); Mair, Michael (FDA/OC) (Michael.Mair@fda.hhs.gov); Bryant, Paula (NIH/NIAID) [E] (paula.bryant@nih.gov); Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E] (michael.kurilla@nih.gov); Hepburn, Matthew (matthew.hepburn@darpa.mil); Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil); Paragas, Jason Jared (paragas1@llnl.gov); cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil); jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH)

U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: Mining the Pathogen-Host Interactome

Dear Colleagues:

We would like to invite you to an interagency meeting and discussion regarding the development of an ASPR Innovation Initiative, which will explore current efforts and envision future programs to help develop medical countermeasures against present and future threats. The framework for this discussion will be linked to opportunities that might be realized through recognition and deeper understanding of the pathogenesis patterns that could emerge from the host-pathogen interactome. A short white paper will be provided before the meeting to add further context.

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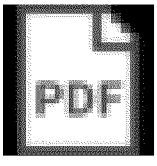

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200 C Street Southwest

Washington, D.C. 20515
Willow Conference Room
Sub-Basement Level

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U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: *Mining the pathogen-host interactome*

Tip O'Neill House Office Building
200 C Street Southwest
Washington, D.C. 20515
Sub-Basement Level – Willow Conference Room

January 31, 2018
9:00AM – 1:30PM EST

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9:20 – 9:50	Current federal efforts *(5 min brief overview from each agency, if applicable) Capturing current or recent federal programs that engage this approach*

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- Defense Advanced Research Project Agency (DARPA)
- *Biomedical Advanced Research and Development Authority (BARDA): 1) On-Demand Availability, 2) Non-Clinical Studies, 3) Earlier Indication (Rick Bright)*
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- *Other potential contributors (USDA, DOD)*

Facilitated Open Discussion: Joe Hamel (HHS/ASPR)

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1:10 – 1:30	Next Steps & Closing Remarks

From: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]
Sent: 1/13/2018 9:19:42 AM
To: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew (matthew.hepburn@darpa.mil) [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; 'kimberly.a.lebutt.civ@mail.mil' [kimberly.a.lebutt.civ@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared (paragas1@llnl.gov) [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil) [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; 'robert.g.ulrich.civ@mail.mil' [robert.g.ulrich.civ@mail.mil]; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]; Kadlec, Robert P (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=70539a2f88924cc8913781ea74278b12-HHS-Robert.]; Stephan, Briana (OS)

	[/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86b3179b17604efa9818a549ef7e3fa0-HHS-Briana.]; Ford-Barnes, Arwenthia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=38db99da9c0f4495b790adda00040fe7-HHS-Arwenth]
CC:	Williams, David (Dave) CIV USARMY DOD JPEOCBD (US) [david.williams8.civ@mail.mil]
Subject:	SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Attachments:	Meeting Agenda 20170131.pdf; Discussion of the I2MCM ideas and goals.pdf; Potbelly Lunch Order Form.pdf
Location:	O'Neill House Office Building - Washington, D.C.
Start:	1/31/2018 9:00:00 AM
End:	1/31/2018 1:30:00 PM
Show Time As:	Busy
Required Attendees:	Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E]; Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID); Merlin, Toby (CDC/OID/NCEZID); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC); Mair, Michael (FDA/OC); Bryant, Paula (NIH/NIAID) [E]; Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E]; Hepburn, Matthew; Hann, Ronald K Jr SES DTRA (US); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US); Paragas, Jason Jared; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil'; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH); bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto); Patel, Jean (CDC/OID/NCEZID); McDonald, Clifford (CDC/OID/NCEZID); Kadlec, Robert (OS/ASPR/IO); Stephan, Briana (OS/ASPR/IO); Ford-Barnes, Arwenthia (HHS/ASPR/IO)
Optional Attendees:	Williams, David (Dave) CIV USARMY DOD JPEOCBD (US)

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If you plan on attending, please "accept" the calendar invite so that we have a headcount.

We will have light refreshments (coffee, cookies, etc.) during the meeting. Lunch will be for 45 minutes (11:40-12:25), so in order to maximize participants' time to collaborate, we are offering the option to order/bring in Potbelly sandwiches (order form attached). If you are interested in this option, please let Natalie Avilés (Natalie.aviles@hhs.gov) know by Tuesday morning (Jan. 30); exact change is greatly appreciated. Otherwise, you are welcome to also leave the building to get lunch at the various nearby restaurants.

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ASPR Strategic Innovation

Interactome-Informed Medical Countermeasures (I2MCM)

Dr. George Korch, Senior Science Advisor, ASPR

There are two major commonalities between novel **naturally-occurring pandemic pathogens and the potential for newly engineered biological threats**. First, whatever the genetic or metabolic structure of the pathogen might possess, it must phenotypically perform within a set of biological patterns that create the disease outcome, i.e. they must behave like other human pathogen to cause disease, otherwise, they are non-pathogenic. Secondly, the immune system will eventually act against the threat to attempt to restore homeostasis, but the adaptive arm of the immune system needs time to achieve its greatest effect. How can we use these two fundamental truths to craft wide-ranging therapies across multiple and diverse pathogens?

The fundamental problem we are seeking to address is how to empower and harness information that increasingly reveals the presence of **deeply-rooted common patterns that span across large and diverse groups of pathogens, and even across diverse disease states**. The hypothesis that there should be common patterns makes biological and evolutionary sense. The host can be viewed by the pathogen as a system of integrated physiological processes from which it must gain energy for survival and reproduction while avoid being defeated by defense mechanisms. While there is a large array of gene interactions, gene products and modification of products post-translation to create the integrity and function of the host system, these are not infinite in combination, and are for the most part highly conserved. They form very well ordered systems that we are beginning to understand through the rapid advances in sequencing, transcriptomics, proteomics, metabolomics and systems integration through bioinformatics. Once a pathogen unlocks the key to accessing the riches to be gained from the host's energetic stockpiles, either by convergent evolution or other information sharing means, the pathogen is poised to be successful until it is either eliminated by the immune system or finds a way to avoid the immune system's influence.

Evidence for the interaction of diverse pathogens to interrupt the host at key nodes and "subroutines" in the takeover of this machinery by the pathogen are becoming better annotated[1,2,3,4] and there is accumulating information about similarities between non-infectious disease states and pathways that pathogens use to stimulate similar disease such as between epilepsy, cancer, neurodegeneration and Toxoplasma which modulate similar systems in the brain as one example.[5] Bioinformatics tools have suggested for instance that there are distinct patterns to how a group of viruses interacts with the type 1 interferon system when one looks at flaviviruses, herpesviruses, papillomaviruses and retroviruses, but that there are nodes that are highly targeted in this "subroutine" for interferon 1.[2] The literature on this will keep expanding

as similar approaches and big data sets accumulate along with new tools to delve more deeply into these putative relationships and underlying patterns.

There are programs across the USG that appear to address part of this need, or that fund such efforts, but to date, it appears that no single organization in government or academia has established a specific approach of this sort and thus is in a defined leadership position to help orchestrate a bigger fusion of this type of information against the purposed envisioned here to look for overarching patterns that can be then mined for therapeutic or even prophylactic approaches against a diverse or even unknown set of pathogens.

The other major pillar of the I2MCM is that it seeks **to approach pathogen control from a combinatorial approach**. That is, we cannot seek to tackle multiple potential pathogens, that may use different but well defined pattern sets, with a limited set of therapeutic molecules or approaches. An example of this approach is used for the long term control of chronic HIV infection via Highly Active Antiretroviral Therapy (HAART), which combines two nucleoside reverse transcriptase inhibitors along with one non-nucleoside reverse transcriptase inhibitor, protease inhibitor (PI) or Integrase inhibitors. These are all antiviral targets, but the principle of creating so many "pain points" for the virus that it becomes overwhelmed is the approach that should also be considered for host-based targeting. By identifying a list of important nodes spanning a wide range of pathogens, and by looking at druggability, toxicity and interaction effects, it is theoretically possible to provide a large coverage against known and therefore unknown pathogens that would be relying on similar infection and disease producing outcomes.

Developing this capability in ASPR will require investment in a systems biology capability tied directly into a product minded outcome. While this could be argued to be the domain of basic research, it is actually a dedicated and focused effort to derive a very comprehensive set of integrated medical countermeasures. It will need a system that is more aligned with the way that a pharmaceutical company would employ their research assets rather than an approach that looks to expand general knowledge via individual investigator solicited research proposals. In essence, this would be a pre-clinical program that would align or partner directly with BARDA to inform later investment decisions that are driven by metrics and deliverables. Unlike the previous attempts within DoD to achieve such an outcome in the now defunct Translational Medical Technologies Initiative (TMTI), it will not be seeking a set of current products that are kluged together to try to approximate the interactome-informed model, but will be driven initially by deep understanding of the common patterns that will emerge from investment in comparative pathogen-host interaction data sets.

In addition to accumulating basic information on host-pathogen pattern recognition, the I2MCM dimensions can also encompass other pragmatic issues such as novel delivery mechanisms and should include diagnostics to rapidly understand the pathogenesis signals (biomarkers) or specific pathogen markers that would inform therapeutic approach.

Key parameters still need to be discussed, and we are approaching the opportunities through a series of individual and group discussions, with government partners and thought leaders in academia and industry. We will be conducting a meeting of government program managers first to hone our thinking and learn about current capabilities and then will propose to assemble 20-25 subject matter experts (science leaders in the field) at a meeting to be held by the ASPR. The concepts to be further refined will include target areas to help unify the efforts.

Assuming that there is acceptance of the key approaches and concepts, there will be a range of important discussions that will also be needed identify how this type of effort is then organized across agencies or in some other construct.

The following areas could form the basis for discussion as a starting point.

1. **Identify key areas for host-pathogen pattern disruption (some examples include):**
    a. Immune modulation
    b. Sepsis
    c. Exosomal signaling
    d. Control of apoptosis
    e. MAPK cascades
    f. Protein kinase activities
    g. Cell proliferation
    h. Epigenetics – host response/disease exposure/risk profile generation
    i. Others

2. **Key potential pathogen and other target areas for investment / incorporation**
    a. All respiratory transmitted viral pathogens (RRIP)
    b. Multiple approaches to control bacterial pathogens in addition to antibiotics
    c. Control of hemorrhagic fever pathogens
    d. Drug Dispensing Acceleration
    e. Drug-Drug Interaction Module
    f. Mass Casualty Artificial Intelligence Assistance
    g. Impact on commensal organisms / microbiome
    h. One-Health (upstream agricultural approaches to prevent/intervene bacterial MDR generation)
3. **The proposed process to establish a viable program**
    a. Interviews of nationally recognized or identified thinkers in the fields above
    b. Establish cadre of internal experts to initiate process, advise and help course correct
    c. Host a federal roundtable with other potential federal partners to capture ideas
    d. Potential outreach campaign to external subject matter experts and members of BIO or other industry partners for financial and technical leveraging or investment

e. Potential outreach to other key extramural funding agencies as a Public Private enterprise.
f. Validate and finalize approaches on partnerships, business plan and methodologies

4. **Develop most reasonable program management strategy**
to conduct work and look for model systems using Strategic Investor or similar model. Past models of concerted government-directed programs have includes such options as:
    a. Development of FFRDC (Commercial or Academic)
    b. Development of UARC (Academic)
    c. Establish linkage with existing government effort (Fort Detrick Campus)
    d. Consortium of Business approach
    e. Hub and Spoke Model with singular integrator
    f. Other combinations

Literature Cited:

1. Dyer, M., et al. 2010 The landscape of human proteins interacting with viruses and other pathogens. PLoS 4(2):1-14
2. Navratil, V. 2010 System-level comparison of protein-protein interactions between viruses and human type 1 interferon system networks. J. Proteome Res. 9:3527-3536.
3. Segura-Cabrera, A. et al. 2013 A viral-human Interactome based on structural motif-domain interactions captures the human infectome. PLoS 8(8):1-13.
4. Vidal, M., et al. 2011 Interactome Networks and Human Disease. Cell 144(6):986-998
5. Ngo et al. 2017. Toxoplasma modulates signature pathways of human epilepsy, neurodegeneration, and cancer. Nature Scientific Reports. 7:DOI:10.1038/s41598-017-10675-6

NAME:

CIRCLE WHICH OPTIONS YOU WANT

Bread Regular/White Multigrain/Wheat

Perfect Belly ***(sandwich, chips, and cookie)***

$9.00	*Chips*	*Cookie*
Grilled Chicken/Cheddar	Baked Cheetos	Brownie cookie
A Wreck	Baked Lays	Oatmeal/chocolate chip
Turkey Breast	Baked Cheddar/SC	Sugar cookie
Italian	Garden Salsa	
Mediterranean	Hot Peppers Chips	
Mediterranean Chicken	Jalapeño	
Smoked ham	Mesquite BBQ	
Roast Beef	Regular	
Tuna Salad	Salt & Vinegar	
Chicken Salad	Voodoo Heat	
Meatball		
Pizza Sandwich		
Vegetarian		

Basic Belly ***(sandwich & chips)***

$8.00	*Chips*
Turkey Breast	Baked Cheetos
A Wreck	Baked Lays
Italian	Baked Cheddar & Sour Cream
Roast Beef	Garden Salsa
Meatball	Hot Peppers Chips
Chicken Salad	Jalapeño
Smoked ham	Mesquite BBQ
Tuna Salad	Regular
Mediterranean	Salt & Vinegar
Pizza Sandwich	Voodoo Heat
Grilled Chicken	

DRINKS: Coffee and bottled water will be provided at the meeting. There are vending machines and a self-serve café available onsite for those who would like other options.

From: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]
Sent: 1/13/2018 9:19:42 AM
To: Korch, George (OS/ASPR/IO) [George.Korch@hhs.gov]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew (matthew.hepburn@darpa.mil) [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; 'kimberly.a.lebutt.civ@mail.mil' [kimberly.a.lebutt.civ@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared (paragas1@llnl.gov) [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil) [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; 'robert.g.ulrich.civ@mail.mil' [robert.g.ulrich.civ@mail.mil]; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]

Subject: SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Attachments: Meeting Agenda 20170131.pdf
Location: O'Neill House Office Building - Washington, D.C.

Start: 1/31/2018 9:00:00 AM
End: 1/31/2018 1:30:00 PM
Show Time As: Busy

Required Attendees: Korch, George (OS/ASPR/IO); Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA) (Joseph.Larsen@hhs.gov); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E] (ccoleman@mail.nih.gov); Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID) (iad7@CDC.GOV); Merlin, Toby (CDC/OID/NCEZID) (tfm5@CDC.GOV); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC) (carmen.maher@fda.hhs.gov); Mair, Michael (FDA/OC) (Michael.Mair@fda.hhs.gov); Bryant, Paula (NIH/NIAID) [E] (paula.bryant@nih.gov); Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E] (michael.kurilla@nih.gov); Hepburn, Matthew (matthew.hepburn@darpa.mil); Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil); Paragas, Jason Jared (paragas1@llnl.gov); cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil); jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH)

U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: Mining the Pathogen-Host Interactome

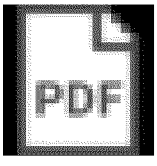
Dear Colleagues:

We would like to invite you to an interagency meeting and discussion regarding the development of an ASPR Innovation Initiative, which will explore current efforts and envision future programs to help develop medical countermeasures against present and future threats. The framework for this discussion will be linked to opportunities that might be realized through recognition and deeper understanding of the pathogenesis patterns that could emerge from the host-pathogen interactome. A short white paper will be provided before the meeting to add further context.

The intent for this meeting is to garner your thoughts on such an approach and to share current areas of investment in this general area from across the interagency. It will be used to inform the ASPR's Innovation Initiative. A draft agenda is attached. **While we have attempted to identify current programs and hope to hear a short (5 minute) synopsis of efforts from the agencies listed, if you wish to include additional programs, *please let us know.***

PLEASE DO NOT FORWARD THIS INVITE—SPACE IS LIMITED. If you know of any other groups who may be doing work that relates to this effort, please let us know so we can consider extending additional invitations.

Materials:
Agenda is attached, and additional materials will be shared as the date approaches. Hard copies will be available onsite.



Address:
O'Neill House Office Building
200 C Street Southwest

Washington, D.C. 20515
Willow Conference Room
Sub-Basement Level

Directions to Building:
If taking the metro to Federal Center SW, make a left at the top of the escalators. The O'Neill building is about a block away on the right at the corner of C & 3rd Street (this is the street the entrance is on). If taking the metro to L'Enfant Plaza station (blue/orange/yellow/green), exit via the Maryland Street exit and proceed right down Maryland Avenue, take a right on 6th Street, and take a left straight down C Street. The O'Neill building will be about 2.5 blocks down on your right. If driving, there are a few parking garages directly on E Street ranging from $16-20 per day and most of these are cash-only. The easiest parking garage is 250 E Street SW; it's $16 and they accept cash and credit.

Meeting Location:
This meeting will be held at the O'Neill House Office Building in Washington, DC. No escort is required. All visitors will proceed through security screening upon entry into the building. After proceeding through security, go straight ahead and to the right towards the elevators. Take the elevator to the "Sub-Basement" level. After exiting the elevator, go down the hallway (stay to the right when it splits); you will find Willow conference room amongst a series of conference rooms. Please allow at least 10 minutes to get through security.

U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: *Mining the pathogen-host interactome*

Tip O'Neill House Office Building
200 C Street Southwest
Washington, D.C. 20515
Sub-Basement Level – Willow Conference Room

January 31, 2018
9:00AM – 1:30PM EST

9:00 – 9:10	Welcome & Introduction
9:10 – 9:20	Overview of Developing an ASPR Innovation Initiative (*George Korch, HHS/ASPR)*
9:20 – 9:50	Current federal efforts *(5 min brief overview from each agency, if applicable) Capturing current or recent federal programs that engage this approach*

- Defense Threat Reduction Agency (DTRA)
- Defense Advanced Research Project Agency (DARPA)
- *Biomedical Advanced Research and Development Authority (BARDA): 1) On-Demand Availability, 2) Non-Clinical Studies, 3) Earlier Indication (Rick Bright)*
- *Department of Energy (DOE): Bioinformatics Investments*
- *National Institutes of Health, NIAID Investments*
- *Other potential contributors (USDA, DOD)*

Facilitated Open Discussion: Joe Hamel (HHS/ASPR)

9:50 – 10:10	Does the hypothetical framework of mining the interactome seem appropriate, and can it be a premise to form coalitions for new approaches in direction?
10:10 – 10:20	BREAK
10:20 – 10:50	Can we identify broad categories or opportunities in host-pathogen interaction that could result in major advances to mitigate entire classes of pathogenic threats? *(e.g., sepsis, control of respiratory transmitted pathogens)*
10:50 – 11:10	What is the potential for short term gains versus longer term gains *(e.g., immediate investments and products versus longer range pattern recognition research).*
11:10 – 11:40	Assuming we identify several major thrusts to energize this approach, using a highly-directed effort, what sort of science management strategy should be employed to achieve the greatest impact?
11:40 – 12:25	LUNCH
12:25 – 12:45	Who would you suggest are the thought leaders outside of government that should be brought in to discuss these concepts and to explore further opportunities?

12:45 – 1:10	What are the logical next steps to create a collaborative program or approach, and what is a reasonable starting level of investment (ROM). What types of funding mechanisms (in addition to the federal budget process) should be considered to help initiate and then to sustain these types of efforts?
1:10 – 1:30	Next Steps & Closing Remarks

From: Aviles, Natalie (OS/ASPR) [Natalie.Aviles@hhs.gov]
Sent: 1/25/2018 4:25:51 PM
To: Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]; Kadlec, Robert P (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=70539a2f88924cc8913781ea74278b12-HHS-Robert.]; Stephan, Briana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86b3179b17604efa9818a549ef7e3fa0-HHS-Briana.]; Ford-Barnes, Arwenthia

(OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=38db99da9c0f4495b790adda00040fe7-HHS-Arwenth]

CC: Williams, David (Dave) CIV USARMY DOD JPEOCBD (US) [david.williams8.civ@mail.mil]

Subject: SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Attachments: Meeting Agenda 20170131.pdf; Discussion of the I2MCM ideas and goals.pdf; Potbelly Lunch Order Form.pdf
Location: O'Neill House Office Building - Washington, D.C.

Start: 1/31/2018 9:00:00 AM
End: 1/31/2018 1:30:00 PM
Show Time As: Tentative

Required Attendees: Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E]; Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID); Merlin, Toby (CDC/OID/NCEZID); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC); Mair, Michael (FDA/OC); Bryant, Paula (NIH/NIAID) [E]; Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E]; Hepburn, Matthew; Hann, Ronald K Jr SES DTRA (US); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US); Paragas, Jason Jared; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil'; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH); bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto); Patel, Jean (CDC/OID/NCEZID); McDonald, Clifford (CDC/OID/NCEZID); Kadlec, Robert (OS/ASPR/IO); Stephan, Briana (OS/ASPR/IO); Ford-Barnes, Arwenthia (HHS/ASPR/IO)

Optional Attendees: Williams, David (Dave) CIV USARMY DOD JPEOCBD (US)

PLEASE DO NOT FORWARD THIS INVITE—SPACE IS LIMITED. If you know of any other groups who may be doing work that relates to this effort, please let us know so we can consider extending additional invitations.

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Assistant Secretary for Preparedness and Response (ASPR)
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If you plan on attending, please "accept" the calendar invite so that we have a headcount.

We will have light refreshments (coffee, cookies, etc.) during the meeting. Lunch will be for 45 minutes (11:40-12:25), so in order to maximize participants' time to collaborate, we are offering the option to order/bring in Potbelly sandwiches

(order form attached). If you are interested in this option, please let Natalie Avilés (Natalie.aviles@hhs.gov) know by Tuesday morning (Jan. 30); exact change is greatly appreciated. Otherwise, you are welcome to also leave the building to get lunch at the various nearby restaurants.

Materials:
Agenda is attached, and additional materials will be shared as the date approaches. Hard copies will be available onsite.

Address:
O'Neill House Office Building
200 C Street Southwest
Washington, D.C. 20515
Willow Conference Room
Sub-Basement Level

Directions to Building:
If taking the metro to Federal Center SW, make a left at the top of the escalators. The O'Neill building is about a block away on the right at the corner of C & 3rd Street (this is the street the entrance is on). If taking the metro to L'Enfant Plaza station (blue/orange/yellow/green), exit via the Maryland Street exit and proceed right down Maryland Avenue, take a right on 6th Street, and take a left straight down C Street. The O'Neill building will be about 2.5 blocks down on your right. If driving, there are a few parking garages directly on E Street ranging from $16-20 per day and most of these are cash-only. The easiest parking garage is 250 E Street SW; it's $16 and they accept cash and credit.

Meeting Location:
This meeting will be held at the O'Neill House Office Building in Washington, DC. No escort is required. All visitors will proceed through security screening upon entry into the building. After proceeding through security, go straight ahead and to the right towards the elevators. Take the elevator to the "Sub-Basement" level. After exiting the elevator, go down the hallway (stay to the right when it splits); you will find Willow conference room amongst a series of conference rooms. Please allow at least 10 minutes to get through security.

U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: *Mining the pathogen-host interactome*

Tip O'Neill House Office Building
200 C Street Southwest
Washington, D.C. 20515
Sub-Basement Level – Willow Conference Room

January 31, 2018
9:00AM – 1:30PM EST

9:00 – 9:10	Welcome & Introduction
9:10 – 9:20	Overview of Developing an ASPR Innovation Initiative (*George Korch, HHS/ASPR)*
9:20 – 9:50	Current federal efforts *(5 min brief overview from each agency, if applicable) Capturing current or recent federal programs that engage this approach*

- Defense Threat Reduction Agency (DTRA)
- Defense Advanced Research Project Agency (DARPA)
- *Biomedical Advanced Research and Development Authority (BARDA): 1) On-Demand Availability, 2) Non-Clinical Studies, 3) Earlier Indication (Rick Bright)*
- *Department of Energy (DOE): Bioinformatics Investments*
- *National Institutes of Health, NIAID Investments*
- *Other potential contributors (USDA, DOD)*

Facilitated Open Discussion: Joe Hamel (HHS/ASPR)

9:50 – 10:10	Does the hypothetical framework of mining the interactome seem appropriate, and can it be a premise to form coalitions for new approaches in direction?
10:10 – 10:20	BREAK
10:20 – 10:50	Can we identify broad categories or opportunities in host-pathogen interaction that could result in major advances to mitigate entire classes of pathogenic threats? *(e.g., sepsis, control of respiratory transmitted pathogens)*
10:50 – 11:10	What is the potential for short term gains versus longer term gains *(e.g., immediate investments and products versus longer range pattern recognition research).*
11:10 – 11:40	Assuming we identify several major thrusts to energize this approach, using a highly-directed effort, what sort of science management strategy should be employed to achieve the greatest impact?
11:40 – 12:25	LUNCH
12:25 – 12:45	Who would you suggest are the thought leaders outside of government that should be brought in to discuss these concepts and to explore further opportunities?

12:45 – 1:10	What are the logical next steps to create a collaborative program or approach, and what is a reasonable starting level of investment (ROM). What types of funding mechanisms (in addition to the federal budget process) should be considered to help initiate and then to sustain these types of efforts?
1:10 – 1:30	Next Steps & Closing Remarks

ASPR Strategic Innovation

Interactome-Informed Medical Countermeasures (I2MCM)

Dr. George Korch, Senior Science Advisor, ASPR

There are two major commonalities between novel **naturally-occurring pandemic pathogens and the potential for newly engineered biological threats**. First, whatever the genetic or metabolic structure of the pathogen might possess, it must phenotypically perform within a set of biological patterns that create the disease outcome, i.e. they must behave like other human pathogen to cause disease, otherwise, they are non-pathogenic. Secondly, the immune system will eventually act against the threat to attempt to restore homeostasis, but the adaptive arm of the immune system needs time to achieve its greatest effect. How can we use these two fundamental truths to craft wide-ranging therapies across multiple and diverse pathogens?

The fundamental problem we are seeking to address is how to empower and harness information that increasingly reveals the presence of **deeply-rooted common patterns that span across large and diverse groups of pathogens, and even across diverse disease states**. The hypothesis that there should be common patterns makes biological and evolutionary sense. The host can be viewed by the pathogen as a system of integrated physiological processes from which it must gain energy for survival and reproduction while avoid being defeated by defense mechanisms. While there is a large array of gene interactions, gene products and modification of products post-translation to create the integrity and function of the host system, these are not infinite in combination, and are for the most part highly conserved. They form very well ordered systems that we are beginning to understand through the rapid advances in sequencing, transcriptomics, proteomics, metabolomics and systems integration through bioinformatics. Once a pathogen unlocks the key to accessing the riches to be gained from the host's energetic stockpiles, either by convergent evolution or other information sharing means, the pathogen is poised to be successful until it is either eliminated by the immune system or finds a way to avoid the immune system's influence.

Evidence for the interaction of diverse pathogens to interrupt the host at key nodes and "subroutines" in the takeover of this machinery by the pathogen are becoming better annotated[1,2,3,4] and there is accumulating information about similarities between non-infectious disease states and pathways that pathogens use to stimulate similar disease such as between epilepsy, cancer, neurodegeneration and Toxoplasma which modulate similar systems in the brain as one example.[5] Bioinformatics tools have suggested for instance that there are distinct patterns to how a group of viruses interacts with the type 1 interferon system when one looks at flaviviruses, herpesviruses, papillomaviruses and retroviruses, but that there are nodes that are highly targeted in this "subroutine" for interferon 1.[2] The literature on this will keep expanding

as similar approaches and big data sets accumulate along with new tools to delve more deeply into these putative relationships and underlying patterns.

There are programs across the USG that appear to address part of this need, or that fund such efforts, but to date, it appears that no single organization in government or academia has established a specific approach of this sort and thus is in a defined leadership position to help orchestrate a bigger fusion of this type of information against the purposed envisioned here to look for overarching patterns that can be then mined for therapeutic or even prophylactic approaches against a diverse or even unknown set of pathogens.

The other major pillar of the I2MCM is that it seeks **to approach pathogen control from a combinatorial approach**. That is, we cannot seek to tackle multiple potential pathogens, that may use different but well defined pattern sets, with a limited set of therapeutic molecules or approaches. An example of this approach is used for the long term control of chronic HIV infection via Highly Active Antiretroviral Therapy (HAART), which combines two nucleoside reverse transcriptase inhibitors along with one non-nucleoside reverse transcriptase inhibitor, protease inhibitor (PI) or Integrase inhibitors. These are all antiviral targets, but the principle of creating so many "pain points" for the virus that it becomes overwhelmed is the approach that should also be considered for host-based targeting. By identifying a list of important nodes spanning a wide range of pathogens, and by looking at druggability, toxicity and interaction effects, it is theoretically possible to provide a large coverage against known and therefore unknown pathogens that would be relying on similar infection and disease producing outcomes.

Developing this capability in ASPR will require investment in a systems biology capability tied directly into a product minded outcome. While this could be argued to be the domain of basic research, it is actually a dedicated and focused effort to derive a very comprehensive set of integrated medical countermeasures. It will need a system that is more aligned with the way that a pharmaceutical company would employ their research assets rather than an approach that looks to expand general knowledge via individual investigator solicited research proposals. In essence, this would be a pre-clinical program that would align or partner directly with BARDA to inform later investment decisions that are driven by metrics and deliverables. Unlike the previous attempts within DoD to achieve such an outcome in the now defunct Translational Medical Technologies Initiative (TMTI), it will not be seeking a set of current products that are kluged together to try to approximate the interactome-informed model, but will be driven initially by deep understanding of the common patterns that will emerge from investment in comparative pathogen-host interaction data sets.

In addition to accumulating basic information on host-pathogen pattern recognition, the I2MCM dimensions can also encompass other pragmatic issues such as novel delivery mechanisms and should include diagnostics to rapidly understand the pathogenesis signals (biomarkers) or specific pathogen markers that would inform therapeutic approach.

Key parameters still need to be discussed, and we are approaching the opportunities through a series of individual and group discussions, with government partners and thought leaders in academia and industry. We will be conducting a meeting of government program managers first to hone our thinking and learn about current capabilities and then will propose to assemble 20-25 subject matter experts (science leaders in the field) at a meeting to be held by the ASPR. The concepts to be further refined will include target areas to help unify the efforts.

Assuming that there is acceptance of the key approaches and concepts, there will be a range of important discussions that will also be needed identify how this type of effort is then organized across agencies or in some other construct.

The following areas could form the basis for discussion as a starting point.

1. **Identify key areas for host-pathogen pattern disruption (some examples include):**
    a. Immune modulation
    b. Sepsis
    c. Exosomal signaling
    d. Control of apoptosis
    e. MAPK cascades
    f. Protein kinase activities
    g. Cell proliferation
    h. Epigenetics – host response/disease exposure/risk profile generation
    i. Others

2. **Key potential pathogen and other target areas for investment / incorporation**
    a. All respiratory transmitted viral pathogens (RRIP)
    b. Multiple approaches to control bacterial pathogens in addition to antibiotics
    c. Control of hemorrhagic fever pathogens
    d. Drug Dispensing Acceleration
    e. Drug-Drug Interaction Module
    f. Mass Casualty Artificial Intelligence Assistance
    g. Impact on commensal organisms / microbiome
    h. One-Health (upstream agricultural approaches to prevent/intervene bacterial MDR generation)
3. **The proposed process to establish a viable program**
    a. Interviews of nationally recognized or identified thinkers in the fields above
    b. Establish cadre of internal experts to initiate process, advise and help course correct
    c. Host a federal roundtable with other potential federal partners to capture ideas
    d. Potential outreach campaign to external subject matter experts and members of BIO or other industry partners for financial and technical leveraging or investment

e. Potential outreach to other key extramural funding agencies as a Public Private enterprise.
f. Validate and finalize approaches on partnerships, business plan and methodologies

4. **Develop most reasonable program management strategy**
to conduct work and look for model systems using Strategic Investor or similar model. Past models of concerted government-directed programs have includes such options as:
    a. Development of FFRDC (Commercial or Academic)
    b. Development of UARC (Academic)
    c. Establish linkage with existing government effort (Fort Detrick Campus)
    d. Consortium of Business approach
    e. Hub and Spoke Model with singular integrator
    f. Other combinations

Literature Cited:

1. Dyer, M., et al. 2010 The landscape of human proteins interacting with viruses and other pathogens. PLoS 4(2):1-14
2. Navratil, V. 2010 System-level comparison of protein-protein interactions between viruses and human type 1 interferon system networks. J. Proteome Res. 9:3527-3536.
3. Segura-Cabrera, A. et al. 2013 A viral-human Interactome based on structural motif-domain interactions captures the human infectome. PLoS 8(8):1-13.
4. Vidal, M., et al. 2011 Interactome Networks and Human Disease. Cell 144(6):986-998
5. Ngo et al. 2017. Toxoplasma modulates signature pathways of human epilepsy, neurodegeneration, and cancer. Nature Scientific Reports. 7:DOI:10.1038/s41598-017-10675-6

NAME:

CIRCLE WHICH OPTIONS YOU WANT

Bread Regular/White Multigrain/Wheat

Perfect Belly ***(sandwich, chips, and cookie)***

$9.00	*Chips*	*Cookie*
Grilled Chicken/Cheddar	Baked Cheetos	Brownie cookie
A Wreck	Baked Lays	Oatmeal/chocolate chip
Turkey Breast	Baked Cheddar/SC	Sugar cookie
Italian	Garden Salsa	
Mediterranean	Hot Peppers Chips	
Mediterranean Chicken	Jalapeño	
Smoked ham	Mesquite BBQ	
Roast Beef	Regular	
Tuna Salad	Salt & Vinegar	
Chicken Salad	Voodoo Heat	
Meatball		
Pizza Sandwich		
Vegetarian		

Basic Belly ***(sandwich & chips)***

$8.00	*Chips*
Turkey Breast	Baked Cheetos
A Wreck	Baked Lays
Italian	Baked Cheddar & Sour Cream
Roast Beef	Garden Salsa
Meatball	Hot Peppers Chips
Chicken Salad	Jalapeño
Smoked ham	Mesquite BBQ
Tuna Salad	Regular
Mediterranean	Salt & Vinegar
Pizza Sandwich	Voodoo Heat
Grilled Chicken	

DRINKS: Coffee and bottled water will be provided at the meeting. There are vending machines and a self-serve café available onsite for those who would like other options.

From: Valdez, Mary Lou [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=80D9C6B02DB946618F69AA301D484A7C-MARYLOU.VAL]
Sent: 4/20/2018 8:10:20 AM
To: Blair, Joan W. (CBER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8cc3d088be164491a76b9ce048d71a02-BLAIR]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Hinton, Denise [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=85feca0be0694803be6030e97c7b4adb-HINTOND]
Subject: FW: MCB Cables for HHS U.S 19Apr18
Attachments: China Virus Institute Welcomes More U.S. Cooperation onGlobal Health Security; Guinea: Inactivation and Destruction of 18,000 Ebola Samples

Thought both of these cables would be of general interest to you. Thanks, Lou

Lou Valdez
Associate Commissioner for International Programs
Office of International Programs
U.S. Food and Drug Administration
Office: 301 794 8400
Direct:
Mobile: (b)(6)

From: OS Secretarys Operations Center [mailto:hhs.soc@hhs.gov]
Sent: Thursday, April 19, 2018 11:59 PM
To: MCB Cables for HHS U.S <MCBCablesforHHSU.S@ees.hhs.gov>
Cc: OS Secretarys Operations Center <hhs.soc@hhs.gov>
Subject: MCB Cables for HHS U.S 19Apr18

China Virus Institute Welcomes More U.S. Cooperation on Global Health Security

(SBU) Summary with Comment: China's Wuhan Institute of Virology, a global leader in virus research, is a key partner for the United States in protecting global health security. Its role as operator of the just-launched Biosafety Level 4 (or "P4") lab -- the first such lab in China -- opens up even more opportunities for expert exchange, especially in light of the lab's shortage of trained staff (Ref A). Given the legacy of SARS and the likelihood that the next global pandemic will originate in China, the United States should prioritize expanding our already significant cooperation with this institute. This should include partnering with the institute on basic science research and the Global Virome Project (Ref B), and possibly trilateral U.S.-China-EU projects, building on the institute's strong ties with France.

Guinea: Inactivation and Destruction of 18,000 Ebola Samples
SBU) Summary: The 2014 Ebola outbreak resulted in the accumulation of tens of thousands of infectious Ebola samples in laboratories across West Africa, many of which were stored in unsafe or unsecure conditions. In 2016, the USG decided to persuade the GOG to retain no live Ebola samples in the country, and that the USG should help Guinea to facilitate the inventory and inactivation or destruction of Guinean Ebola samples. Inactivating Ebola samples would render them unable to cause disease while retaining

some of their research potential. Based on this review and per a November 2016 request for assistance from Guineas Minister of Health, a U.S.
interagency team of biosecurity experts traveled to Guinea to evaluate Guineas Ebola laboratories.

Very respectfully,

Harold F. Frizzar, Jr.
Operations Officer
U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Office of Emergency Management (OEM)
Operations Mission Coordination Branch
200 Independence Ave S.W.
Washington D.C. 20201
Office: (202) (b)(6)
Fax: (202) 619-8602
Email: hhs.soc@hhs.gov

From: (b)(6)
Sent: 4/19/2018 7:43:31 AM
CC: International Cables (HHS/OS) [Personnel@hhs.gov]
Subject: China Virus Institute Welcomes More U.S. Cooperation onGlobal Health Security

RAAUZYUW RUEHBJW8609 1090553-UUUU--RUHNHHS.
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RHMCSII/HQ EPA WASHINGTON DC
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E.O. 13526: N/A
TAGS: SHLH, PGOV, CN, PREL, TBIO, KGHI, CDC, EAID, KHIV, IN, JP, TW, TSPL, PINS, SENV
SUBJECT: China Virus Institute Welcomes More U.S. Cooperation on Global Health Security

REF: 18 BEIJING 138
17 BEIJING 2458
11 MUMBAI 630
17 TOKYO 716
13 SEOUL 790

1. (SBU) Summary with Comment: China's Wuhan Institute of Virology, a global leader in virus research, is a key partner for the United States in protecting global health security. Its role as operator of the just-launched Biosafety Level 4 (or "P4") lab -- the first such lab in China -- opens up even more opportunities for expert exchange, especially in light of the lab's shortage of trained staff (Ref A). Given the legacy of SARS and the likelihood that the next global pandemic will originate in China, the United States should prioritize expanding our already significant cooperation with this institute. This should include partnering with the institute on basic science research and the Global Virome Project (Ref B), and possibly trilateral U.S.-China-EU projects, building on the institute's strong ties with France. End Summary with Comment.

2. (U) Wuhan Institute of Virology researchers and staff gave an overview of the lab and current cooperation with the United States to visiting Environment, Science, Technology and Health Counsellor Rick Switzer and Consulate Wuhan Consul General Jamie Fouss in late March. In the last year, the institute has also hosted visits from the National Institutes of Health (NIH), National Science Foundation, and experts from the University of Texas Medical Branch in Galveston. The institute reports to the Chinese Academy of Sciences in Beijing.

P4 Lab is Open and Transparent, Officials Emphasize

(b)(4)

4. (U) Officials described the lab as a "regional node" in the global biosafety system and said it would play an emergency response role in an epidemic or pandemic. The lab's English brochure highlighted a national security role, saying that it "is an effective measure to improve China's availability in safeguarding national bio-safety if [a] possible biological warfare or terrorist attack happens."

(b)(4)

6. (U) In addition to French assistance, experts from the NIH-supported P4 lab at the University of Texas Medical Branch in Galveston have trained Wuhan lab technicians in lab management and maintenance, institute officials said. The Wuhan institute plans to invite scientists from the Galveston lab to do research in Wuhan's lab. One Wuhan Institute of Virology researcher trained for two years at the Galveston lab, and the institute also sent one scientist to U.S. CDC headquarters in Atlanta for six months' work on influenza.

NIH-Supported Research Revises SARS Origin Story

7. (U) NIH was a major funder, along with the Natural Science Foundation of China (NSFC), of SARS research by the Wuhan Institute of Virology's Shi Zhengli and Cui Jie. The researchers spent five

years of investigation and genome sequencing to show that a population of bats in a cave in Yunnan Province harbored a virus with all the "building blocks" of SARS. This lends weight to the theory that SARS originated in bat populations before jumping first to civet cats (likely via bat feces) and then to humans, after people transported the civet cats from Yunnan to Guangdong Province animal markets. The results were published late last year in HYPERLINK "https://www.nature.com/articles/d41586-017-07766-9"Nature and other publications. Shi said that U.S. scientist Peter Daszak, a leading expert on emerging diseases and president of the New York-based EcoHealth Alliance, was a "strong partner." Daszak's team has provided support in statistical modeling to assess the risk of more coronaviruses like SARS crossing over to human populations.

Ready to Help with the Global Virome Project

8. (U) Institute officials expressed strong interest in the Global Virome Project (GVP), and said Chinese funding for the project would likely come from Chinese Academy of Sciences funding already earmarked for One Belt, One Road-related initiatives. The HYPERLINK "http://science.sciencemag.org/content/359/6378/872.full"GVP aims to launch this year as an international collaborative effort to identify within ten years virtually all of the planet's viruses that have pandemic or epidemic potential and the ability to jump to humans. "We hope China will be one of the leading countries to initiate the Global Virome Project," one Wuhan Institute of Virology official said. China attended a GVP unveiling meeting in January in Thailand and is waiting for more details on the initiative. The officials said that the Chinese government funds projects similar to GVP to investigate the background of viruses and bacteria. This essentially constituted China's own Virome Project, officials said, but they noted the program currently has no official name.

9. (SBU) The Wuhan Institute of Virology's Shi Zhengli is the China Country Coordinator for the USAID-funded PREDICT project, which is designed to show "proof of concept" and be a forerunner to the Global Virome Project. Li Hongying, with the EcoHealth Alliance (a New York City-based NGO that is working with the University of California, Davis to manage the PREDICT project), recently planned to visit Wuhan to meet with Shi. Li noted that China has expressed interest in building the GVP database, which would put China in a leadership position. Other countries have confidence in Chinas ability to build such a database, but are skeptical on whether China could remain transparent as a "gatekeeper" for this information, she said. Li expressed frustration with the slow progress so far in launching GVP, noting that the effort lacked funding sources, needed to hire a CEO, and would have to boost its profile at G7, G20 and other high-level international meetings.

U.S.-China Workshop Explores Research Partnerships

10. (U) The Institute also has ongoing collaboration with the U.S. National Science Foundation, including a just-concluded workshop in Shenzhen, involving about 40 scientists from the United States and China, on the topic of the "Ecology and Evolution of Infectious Diseases." Co-sponsored by the Natural Science Foundation of China (NSFC), the Chinese lead for this workshop was the Wuhan Institute of Virology's Hu Zhihong, and the U.S. co-chair was the University of Oklahoma's Xiao Xiangming. The workshop explored opportunities for U.S.-China research cooperation in areas like using "big data" to predict emerging infectious diseases, climate changes effect on vector-borne diseases, and pathogen transmission between wildlife, domestic animals and humans.

11. (SBU) Some workshop participants also expressed skepticism about

the Global Virome Project's (GVP) approach, saying that gaining a predictive understanding of viruses with pandemic potential would require going beyond the GVPs strategy of sample collection, to take an "ecological" approach that considers the virome beyond vertebrate systems to identify mechanisms driving pathogen evolution. A follow-on workshop will be held in June at the University of Berkeley. NSF and NSFC hope to jointly announce a funding call for collaborative projects later this year.
FOUSS
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NNNN

From: (b)(6)
Sent: 4/19/2018 12:24:49 PM
CC: International Cables (HHS/OS) [Personnel@hhs.gov]
Subject: Guinea: Inactivation and Destruction of 18,000 Ebola Samples

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SENSITIVE

E.O. 13526: N/A
TAGS: PARM, PREL, SHLH, PGOV, TBIO, KGHI, GN
SUBJECT: Guinea: Inactivation and Destruction of 18,000 Ebola Samples

1. (SBU) Summary: The 2014 Ebola outbreak resulted in the accumulation of tens of thousands of infectious Ebola samples in laboratories across West Africa, many of which were stored in unsafe or unsecure conditions. In 2016, the USG decided to persuade the GOG to retain no live Ebola samples in the country, and that the USG should help Guinea to facilitate the inventory and inactivation or destruction of Guinean Ebola samples. Inactivating Ebola samples would render them unable to cause disease while retaining some of their research potential. Based on this review and per a November 2016 request for assistance from Guineas Minister of Health, a U.S. interagency team of biosecurity experts traveled to Guinea to evaluate Guineas Ebola laboratories. In March 2017, Ambassador Hankins signed a Memorandum of Understanding (MOU) with Guineas Minister of Health to permit U.S. scientists to safely inventory Guineas Ebola samples, inactivate all positive samples, and destroy the remaining negative, damaged, or unknown samples. In November 2017, Guineas Ebola samples were inactivated and/or destroyed, thereby averting any potential accidental or intentional misuse of these dangerous materials. Live samples retained in-country by a French research institute remain a source of concern. At the request of Embassy Conakry, the Bureau of International Security and Nonproliferations Office of Cooperative Threat Reduction (ISN/CTR) prepared this cable. End summary.

2. (SBU) Ebola Sample Inventory: To determine the disposition of the Ebola samples, ISN/CTR collaborated with the Department of Energys Sandia National Laboratories (DOE/SNL) and Centers for Disease Control and Prevention (CDC)-Conakry to train Guinean laboratory technicians to safely and securely handle, package, and decontaminate material that comes in contact with especially dangerous pathogens, such as Ebola. Guinean partners used this training to inventory, re-package, and secure the nearly 18,000 Ebola samples stored at the Viral Hemorrhagic Fever (VHF) laboratory in Conakry under supervision from DOE/SNL experts. The sample inventory

allowed CDC and Guinean partners to match the samples that were positive (nearly 1,400) or negative (over 16,000) for the Ebola virus, and make accurate and informed decisions on the samples selected for inactivation or destruction. Importantly, the training and inventory methods are relevant across a spectrum of diseases, and their transfer to Guineans practitioners will contribute to Guineas ability to safely handle and manage numerous pathogens that routinely afflict its people.

3. (SBU) Ebola Sample Destruction and Transport to the CDC in Atlanta: Per the terms of the MOU, the Ebola-positive samples were transferred to CDC-Atlanta for inactivation, and the negative samples were destroyed by incineration in Guinea. In September 2017, DOE/SNL trained Guinean laboratory technicians on the International Air Transport Association (IATA) protocols for safe and secure handling, packaging, and shipping of infectious substances. The IATA-certified Guineans worked with the DOE/SNL experts to safely and securely package the positive samples for transport out of Guinea. They also packaged and destroyed over 16,000 negative, damaged, and unknown samples by incineration on the VHF laboratory grounds, after receiving approval from the VHF Laboratory Director. ISN/CTR collaborated closely with Embassy Conakry and CDC-Conakry to ensure the safe and secure ground transport of the 1,400 positive Ebola samples from the VHF lab to the Conakry airport for transport to CDC-Atlanta using a specially outfitted airplane in collaboration with MED. The samples were escorted to the United States by ISN/CTR, DOE/SNL, States Office of Medical Services (MED), CDC, and a Guinean Ministry of Health official.

4. (SBU) Return of Inactivated Samples to Guinea: In October 2017, the CDC in Atlanta finished inactivating the approximately 1,400 Ebola-positive samples using gamma irradiation. This process eliminated the possibility that the samples could cause disease in the future while maintaining some of their research value. In November 2017, ISN/CTR escorted the inactivated samples back to the VHF lab in Guinea, and met with Guinean Ministry of Health officials to report on successful completion of the U.S.-Guinea collaboration and discuss all phases of activity.

5. (SBU) Comment: A separate collection of live Ebola samples that remain in country under French authority is a cause for concern; we remain in contact with ISN/CTR on addressing the concerned institutions. This collaborative effort involving ISN/CTR, MED, DOE/SNL, the CDC in Guinea and Atlanta, and Embassy Conakry is an example of science diplomacy, biorisk mitigation, and health capacity building at its best. The unsecure and unsafe conditions in which these dangerous Ebola samples were stored greatly increased the risk of their being accidentally or intentionally misused, and the collective effort to neutralize them was a significant contribution to global threat reduction. End comment.
Hankins
BT
#9160

NNNN

From: Hinton, Denise [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=85FECA0BE0694803BE6030E97C7B4ADB-HINTOND]
Sent: 4/20/2018 10:02:36 AM
To: Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Valdez, Mary Lou [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=80d9c6b02db946618f69aa301d484a7c-MaryLou.Val]; Blair, Joan W. (CBER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8cc3d088be164491a76b9ce048d71a02-BLAIR]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]
Subject: RE: MCB Cables for HHS U.S 19Apr18

Thanks, Lou.

Denise

From: Marks, Peter
Sent: Friday, April 20, 2018 8:25 AM
To: Valdez, Mary Lou <MaryLou.Valdez@fda.hhs.gov>; Blair, Joan W. (CBER) <Joan.Blair@fda.hhs.gov>; Mair, Michael <Michael.Mair@fda.hhs.gov>; Hinton, Denise <Denise.Hinton@fda.hhs.gov>
Subject: RE: MCB Cables for HHS U.S 19Apr18

Dear Lou,

Thanks so much for forwarding.

Best Regards,
Peter

From: Valdez, Mary Lou
Sent: Friday, April 20, 2018 8:10 AM
To: Blair, Joan W. (CBER) <Joan.Blair@fda.hhs.gov>; Mair, Michael <Michael.Mair@fda.hhs.gov>; Marks, Peter <Peter.Marks@fda.hhs.gov>; Hinton, Denise <Denise.Hinton@fda.hhs.gov>
Subject: FW: MCB Cables for HHS U.S 19Apr18

Thought both of these cables would be of general interest to you. Thanks, Lou

Lou Valdez
Associate Commissioner for International Programs
Office of International Programs
U.S. Food and Drug Administration
Office: 301 794 8400
Direct:
Mobile: (b)(6)

From: OS Secretarys Operations Center [mailto:hhs.soc@hhs.gov]
Sent: Thursday, April 19, 2018 11:59 PM

To: MCB Cables for HHS U.S <MCBCablesforHHSU.S@ees.hhs.gov>
Cc: OS Secretarys Operations Center <hhs.soc@hhs.gov>
Subject: MCB Cables for HHS U.S 19Apr18

China Virus Institute Welcomes More U.S. Cooperation on Global Health Security

(SBU) Summary with Comment: China's Wuhan Institute of Virology, a global leader in virus research, is a key partner for the United States in protecting global health security. Its role as operator of the just-launched Biosafety Level 4 (or "P4") lab -- the first such lab in China -- opens up even more opportunities for expert exchange, especially in light of the lab's shortage of trained staff (Ref A). Given the legacy of SARS and the likelihood that the next global pandemic will originate in China, the United States should prioritize expanding our already significant cooperation with this institute. This should include partnering with the institute on basic science research and the Global Virome Project (Ref B), and possibly trilateral U.S.-China-EU projects, building on the institute's strong ties with France.

Guinea: Inactivation and Destruction of 18,000 Ebola Samples
SBU) Summary: The 2014 Ebola outbreak resulted in the accumulation of tens of thousands of infectious Ebola samples in laboratories across West Africa, many of which were stored in unsafe or unsecure conditions. In 2016, the USG decided to persuade the GOG to retain no live Ebola samples in the country, and that the USG should help Guinea to facilitate the inventory and inactivation or destruction of Guinean Ebola samples. Inactivating Ebola samples would render them unable to cause disease while retaining some of their research potential. Based on this review and per a November 2016 request for assistance from Guineas Minister of Health, a U.S.
interagency team of biosecurity experts traveled to Guinea to evaluate Guineas Ebola laboratories.

Very respectfully,

Harold F. Frizzar, Jr.
Operations Officer
U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Office of Emergency Management (OEM)
Operations Mission Coordination Branch
200 Independence Ave S.W.
Washington D.C. 20201
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Fax: (202) 619-8602
Email: hhs.soc@hhs.gov

From: Mair, Michael [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=F4511BDAD7564D7FAC7EADC7961467AB-MICHAEL.MAI]
Sent: 4/20/2018 12:35:23 PM
To: Valdez, Mary Lou [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=80d9c6b02db946618f69aa301d484a7c-MaryLou.Val]; Blair, Joan W. (CBER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8cc3d088be164491a76b9ce048d71a02-BLAIR]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Hinton, Denise [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=85feca0be0694803be6030e97c7b4adb-HINTOND]
Subject: RE: MCB Cables for HHS U.S 19Apr18

Lou – Hi and thx for sending. Do you happen to have 'Ref A' referred to in the cable on China Virus Institute? We (in collaboration w/other partners) offer a course every year in achieving data quality and integrity in BSL 4 labs e (this year's course runs next week). **(b)(5)**

(b)(5)

From: Valdez, Mary Lou
Sent: Friday, April 20, 2018 8:10 AM
To: Blair, Joan W. (CBER) <Joan.Blair@fda.hhs.gov>; Mair, Michael <Michael.Mair@fda.hhs.gov>; Marks, Peter <Peter.Marks@fda.hhs.gov>; Hinton, Denise <Denise.Hinton@fda.hhs.gov>
Subject: FW: MCB Cables for HHS U.S 19Apr18

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Associate Commissioner for International Programs
Office of International Programs
U.S. Food and Drug Administration
Office: 301 794 8400
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From: OS Secretarys Operations Center [mailto:hhs.soc@hhs.gov]
Sent: Thursday, April 19, 2018 11:59 PM
To: MCB Cables for HHS U.S <MCBCablesforHHSU.S@ees.hhs.gov>
Cc: OS Secretarys Operations Center <hhs.soc@hhs.gov>
Subject: MCB Cables for HHS U.S 19Apr18

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Operations Officer
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Office of Emergency Management (OEM)
Operations Mission Coordination Branch
200 Independence Ave S.W.
Washington D.C. 20201
Office: (202) (b)(6)
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Email: hhs.soc@hhs.gov

From: Aviles, Natalie (OS/ASPR) [Natalie.Aviles@hhs.gov]
Sent: 1/30/2018 4:04:13 PM
To: Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]; Kadlec, Robert P (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=70539a2f88924cc8913781ea74278b12-HHS-Robert.]; Stephan, Briana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86b3179b17604efa9818a549ef7e3fa0-HHS-Briana.]; Ford-Barnes, Arwenthia

	(OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=38db99da9c0f4495b790adda00040fe7-HHS-Arwenth]; Sundaram, Shivshankar [sundaram1@llnl.gov]; Reichert, Erin D CIV (US) (erin.d.reichert.civ@mail.mil) [erin.d.reichert.civ@mail.mil]; david.m.hone2.civ@mail.mil
CC:	Williams, David (Dave) CIV USARMY DOD JPEOCBD (US) [david.williams8.civ@mail.mil]; Shuren, Jeff [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=44335a0c2f834535bc8713dfd643905e-Jeff.Shuren]; Johnson, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9c7eb3a419464ea2917f9d1e3f6e57a4-HHS-Robert.]; Maisel, William [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a1173dcb42794e11805d85993d1f9797-WZM]; Dorsey, Christopher B CIV USARMY DOD JPEOCBD (US) [christopher.b.dorsey2.civ@mail.mil]
Subject:	SAVE THE DATE - Innovation Initiative: Mining the Pathogen-Host Interactome
Attachments:	Discussion of the I2MCM ideas and goals.pdf; Potbelly Lunch Order Form.pdf; Agenda - ASPR Innovation Initiative.pdf
Location:	O'Neill House Office Building - Washington, D.C.
Start:	1/31/2018 9:00:00 AM
End:	1/31/2018 1:30:00 PM
Show Time As:	Tentative
Required Attendees:	Bright, Rick (OS/ASPR/BARDA); Disbrow, Gary (OS/ASPR/BARDA); Schafer, Julie (OS/ASPR/BARDA); Larsen, Joseph (OS/ASPR/BARDA); Hamel, Joseph (OS/ASPR/IO) (CTR); Alton, Jennifer (OS/ASPR/IO) (CTR); Coleman, Norman (NIH/NCI) [E]; Fisher, Robert (OS/ASPR/IO) (Robert.Fisher1@hhs.gov); Damon, Inger K. (CDC/OID/NCEZID); Merlin, Toby (CDC/OID/NCEZID); Cox, Edward M (FDA/CDER); Throckmorton, Douglas C (FDA/CDER); Woodcock, Janet (FDA/CDER); Marks, Peter (FDA/CBER); Maher, Carmen (FDA/OC); Mair, Michael (FDA/OC); Bryant, Paula (NIH/NIAID) [E]; Eakin, Ann (NIH/NIAID) [E]; Kincaid, Randall (NIH/NIAID) [E]; Kurilla, Michael (NIH/NCATS) [E]; Hepburn, Matthew; Hann, Ronald K Jr SES DTRA (US); christian.j.whitchurch.civ@mail.mil; kimberly.a.lebutt.civ@mail.mil; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US); Paragas, Jason Jared; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil'; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; robert.g.ulrich.civ@mail.mil; blake.bextine@darpa.mil; Salvatore.Clementi@dtra.mil; Ashar, Binita S (FDA/CDRH); bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto); Patel, Jean (CDC/OID/NCEZID); McDonald, Clifford (CDC/OID/NCEZID); Kadlec, Robert (OS/ASPR/IO); Stephan, Briana (OS/ASPR/IO); Ford-Barnes, Arwenthia (HHS/ASPR/IO); Sundaram, Shivshankar; Reichert, Erin D CIV (US) (erin.d.reichert.civ@mail.mil); david.m.hone2.civ@mail.mil
Optional Attendees:	Williams, David (Dave) CIV USARMY DOD JPEOCBD (US); Shuren, Jeff (FDA/CDRH); Johnson, Robert (OS/ASPR/BARDA); Maisel, William (FDA/CDRH); Dorsey, Christopher B CIV USARMY DOD JPEOCBD (US)

PLEASE DO NOT FORWARD THIS INVITE—SPACE IS LIMITED. If you know of any other groups who may be doing work that relates to this effort, please let us know so we can consider extending additional invitations.

NEW

*Updated/final agenda attached

*Opportunity to tour the BARDA VizHub added *(details in the agenda)*

*Please respond asap to Natalie.aviles@hhs.gov if you'll be participating in the box lunch *(details below)*

U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: Mining the Pathogen-Host Interactome

Dear Colleagues:

We would like to invite you to an interagency meeting and discussion regarding the development of an ASPR Innovation Initiative, which will explore current efforts and envision future programs to help develop medical countermeasures against present and future threats. The framework for this discussion will be linked to opportunities that might be realized through recognition and deeper understanding of the pathogenesis patterns that could emerge from the host-pathogen interactome. A short white paper is provided to add further context.

The intent for this meeting is to garner your thoughts on such an approach and to share current areas of investment in this general area from across the interagency. It will be used to inform the ASPR's Innovation Initiative. A draft agenda is attached. **While we have attempted to identify current programs and hope to hear a short (5 minute) synopsis of efforts from the agencies listed, if you wish to include additional programs, *please let us know.***

If you plan on attending, please "accept" the calendar invite so that we have a headcount.

We will have light refreshments (coffee, cookies, etc.) during the meeting. Lunch will be for 45 minutes (11:45-12:30), so in order to maximize participants' time to collaborate, we are offering the option to order/bring in Potbelly sandwiches (order form attached). If you are interested in this option, please let Natalie Avilés (Natalie.aviles@hhs.gov) know as soon as possible; exact change is greatly appreciated. Otherwise, you are welcome to also leave the building to get lunch at the various nearby restaurants.

From 12:00-12:20PM during our lunch break, the BARDA VizHub is allowing meeting participants to attend a tour (down the hallway from our meeting). The VizHub is an initiative to advance modeling, visualization and collaboration within the offices of ASPR. The centerpiece is the CAVE2 visualization system, used to promote visualization, application development and collaborative technology to develop solutions to challenging problems. The infrastructure provides hardware, software and methodologies for 2D and 3D modeling to assist HHS leadership to understand the data trends, information, and models that are critical to data-informed decision making. As a result the value to providing insight, a novel perspective, saving time, conveying information, facilitating stakeholder engagement, and generating confidence in decision making is priceless. The facility is an ideal environment for data discovery to support development teams, training, exercises, simulations, workshops and structured collaboration activities unlike any other HHS location for preparedness and response environments.

Materials:
Agenda and white paper are attached. Hard copies of the presentation will be available onsite.

Address:
O'Neill House Office Building
200 C Street Southwest
Washington, D.C. 20515
Willow Conference Room
Sub-Basement Level

Directions to Building:
If taking the metro to Federal Center SW, make a left at the top of the escalators. The O'Neill building is about a block away on the right at the corner of C & 3rd Street (this is the street the entrance is on). If taking the metro to L'Enfant Plaza station (blue/orange/yellow/green), exit via the Maryland Street exit and proceed right down Maryland Avenue, take a right on 6th Street, and take a left straight down C Street. The O'Neill building will be about 2.5 blocks down on your right. If driving, there are a few parking garages directly on E Street ranging from $16-20 per day and most of these are cash-only. The easiest parking garage is 250 E Street SW; it's $16 and they accept cash and credit.

Meeting Location:
This meeting will be held at the O'Neill House Office Building in Washington, DC. No escort is required. All visitors will proceed through security screening upon entry into the building. After proceeding through security, go straight ahead and to the right towards the elevators. Take the elevator to the "Sub-Basement" level. After exiting the elevator, go down the hallway (stay to the right when it splits); you will find Willow conference room amongst a series of conference rooms. Please allow at least 10 minutes to get through security.

ASPR Strategic Innovation

Interactome-Informed Medical Countermeasures (I2MCM)

Dr. George Korch, Senior Science Advisor, ASPR

There are two major commonalities between novel **naturally-occurring pandemic pathogens and the potential for newly engineered biological threats**. First, whatever the genetic or metabolic structure of the pathogen might possess, it must phenotypically perform within a set of biological patterns that create the disease outcome, i.e. they must behave like other human pathogen to cause disease, otherwise, they are non-pathogenic. Secondly, the immune system will eventually act against the threat to attempt to restore homeostasis, but the adaptive arm of the immune system needs time to achieve its greatest effect. How can we use these two fundamental truths to craft wide-ranging therapies across multiple and diverse pathogens?

The fundamental problem we are seeking to address is how to empower and harness information that increasingly reveals the presence of **deeply-rooted common patterns that span across large and diverse groups of pathogens, and even across diverse disease states**. The hypothesis that there should be common patterns makes biological and evolutionary sense. The host can be viewed by the pathogen as a system of integrated physiological processes from which it must gain energy for survival and reproduction while avoid being defeated by defense mechanisms. While there is a large array of gene interactions, gene products and modification of products post-translation to create the integrity and function of the host system, these are not infinite in combination, and are for the most part highly conserved. They form very well ordered systems that we are beginning to understand through the rapid advances in sequencing, transcriptomics, proteomics, metabolomics and systems integration through bioinformatics. Once a pathogen unlocks the key to accessing the riches to be gained from the host's energetic stockpiles, either by convergent evolution or other information sharing means, the pathogen is poised to be successful until it is either eliminated by the immune system or finds a way to avoid the immune system's influence.

Evidence for the interaction of diverse pathogens to interrupt the host at key nodes and "subroutines" in the takeover of this machinery by the pathogen are becoming better annotated[1,2,3,4] and there is accumulating information about similarities between non-infectious disease states and pathways that pathogens use to stimulate similar disease such as between epilepsy, cancer, neurodegeneration and Toxoplasma which modulate similar systems in the brain as one example.[5] Bioinformatics tools have suggested for instance that there are distinct patterns to how a group of viruses interacts with the type 1 interferon system when one looks at flaviviruses, herpesviruses, papillomaviruses and retroviruses, but that there are nodes that are highly targeted in this "subroutine" for interferon 1.[2] The literature on this will keep expanding

as similar approaches and big data sets accumulate along with new tools to delve more deeply into these putative relationships and underlying patterns.

There are programs across the USG that appear to address part of this need, or that fund such efforts, but to date, it appears that no single organization in government or academia has established a specific approach of this sort and thus is in a defined leadership position to help orchestrate a bigger fusion of this type of information against the purposed envisioned here to look for overarching patterns that can be then mined for therapeutic or even prophylactic approaches against a diverse or even unknown set of pathogens.

The other major pillar of the I2MCM is that it seeks **to approach pathogen control from a combinatorial approach**. That is, we cannot seek to tackle multiple potential pathogens, that may use different but well defined pattern sets, with a limited set of therapeutic molecules or approaches. An example of this approach is used for the long term control of chronic HIV infection via Highly Active Antiretroviral Therapy (HAART), which combines two nucleoside reverse transcriptase inhibitors along with one non-nucleoside reverse transcriptase inhibitor, protease inhibitor (PI) or Integrase inhibitors. These are all antiviral targets, but the principle of creating so many "pain points" for the virus that it becomes overwhelmed is the approach that should also be considered for host-based targeting. By identifying a list of important nodes spanning a wide range of pathogens, and by looking at druggability, toxicity and interaction effects, it is theoretically possible to provide a large coverage against known and therefore unknown pathogens that would be relying on similar infection and disease producing outcomes.

Developing this capability in ASPR will require investment in a systems biology capability tied directly into a product minded outcome. While this could be argued to be the domain of basic research, it is actually a dedicated and focused effort to derive a very comprehensive set of integrated medical countermeasures. It will need a system that is more aligned with the way that a pharmaceutical company would employ their research assets rather than an approach that looks to expand general knowledge via individual investigator solicited research proposals. In essence, this would be a pre-clinical program that would align or partner directly with BARDA to inform later investment decisions that are driven by metrics and deliverables. Unlike the previous attempts within DoD to achieve such an outcome in the now defunct Translational Medical Technologies Initiative (TMTI), it will not be seeking a set of current products that are kluged together to try to approximate the interactome-informed model, but will be driven initially by deep understanding of the common patterns that will emerge from investment in comparative pathogen-host interaction data sets.

In addition to accumulating basic information on host-pathogen pattern recognition, the I2MCM dimensions can also encompass other pragmatic issues such as novel delivery mechanisms and should include diagnostics to rapidly understand the pathogenesis signals (biomarkers) or specific pathogen markers that would inform therapeutic approach.

Key parameters still need to be discussed, and we are approaching the opportunities through a series of individual and group discussions, with government partners and thought leaders in academia and industry. We will be conducting a meeting of government program managers first to hone our thinking and learn about current capabilities and then will propose to assemble 20-25 subject matter experts (science leaders in the field) at a meeting to be held by the ASPR. The concepts to be further refined will include target areas to help unify the efforts.

Assuming that there is acceptance of the key approaches and concepts, there will be a range of important discussions that will also be needed identify how this type of effort is then organized across agencies or in some other construct.

The following areas could form the basis for discussion as a starting point.

1. **Identify key areas for host-pathogen pattern disruption (some examples include):**
    a. Immune modulation
    b. Sepsis
    c. Exosomal signaling
    d. Control of apoptosis
    e. MAPK cascades
    f. Protein kinase activities
    g. Cell proliferation
    h. Epigenetics – host response/disease exposure/risk profile generation
    i. Others

2. **Key potential pathogen and other target areas for investment / incorporation**
    a. All respiratory transmitted viral pathogens (RRIP)
    b. Multiple approaches to control bacterial pathogens in addition to antibiotics
    c. Control of hemorrhagic fever pathogens
    d. Drug Dispensing Acceleration
    e. Drug-Drug Interaction Module
    f. Mass Casualty Artificial Intelligence Assistance
    g. Impact on commensal organisms / microbiome
    h. One-Health (upstream agricultural approaches to prevent/intervene bacterial MDR generation)
3. **The proposed process to establish a viable program**
    a. Interviews of nationally recognized or identified thinkers in the fields above
    b. Establish cadre of internal experts to initiate process, advise and help course correct
    c. Host a federal roundtable with other potential federal partners to capture ideas
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e. Potential outreach to other key extramural funding agencies as a Public Private enterprise.
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to conduct work and look for model systems using Strategic Investor or similar model. Past models of concerted government-directed programs have includes such options as:
    a. Development of FFRDC (Commercial or Academic)
    b. Development of UARC (Academic)
    c. Establish linkage with existing government effort (Fort Detrick Campus)
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Literature Cited:

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NAME:

CIRCLE WHICH OPTIONS YOU WANT

Bread Regular/White Multigrain/Wheat

Perfect Belly ***(sandwich, chips, and cookie)***

$9.00	*Chips*	*Cookie*
Grilled Chicken/Cheddar	Baked Cheetos	Brownie cookie
A Wreck	Baked Lays	Oatmeal/chocolate chip
Turkey Breast	Baked Cheddar/SC	Sugar cookie
Italian	Garden Salsa	
Mediterranean	Hot Peppers Chips	
Mediterranean Chicken	Jalapeño	
Smoked ham	Mesquite BBQ	
Roast Beef	Regular	
Tuna Salad	Salt & Vinegar	
Chicken Salad	Voodoo Heat	
Meatball		
Pizza Sandwich		
Vegetarian		

Basic Belly ***(sandwich & chips)***

$8.00	*Chips*
Turkey Breast	Baked Cheetos
A Wreck	Baked Lays
Italian	Baked Cheddar & Sour Cream
Roast Beef	Garden Salsa
Meatball	Hot Peppers Chips
Chicken Salad	Jalapeño
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Pizza Sandwich	Voodoo Heat
Grilled Chicken	

DRINKS: Coffee and bottled water will be provided at the meeting. There are vending machines and a self-serve café available onsite for those who would like other options.

U.S. Department of Health and Human Services (HHS)
Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: *Mining the Pathogen-Host Interactome*

Tip O'Neill House Office Building
200 C Street Southwest
Washington, D.C. 20515
Sub-Basement Level – Willow Conference Room

January 31, 2018
9:00AM – 1:30PM EST

9:00 – 9:05	Welcome & Introduction
9:05 – 9:15	Overview of Developing an ASPR Innovation Initiative (*George Korch, HHS/ASPR)*
9:15 – 9:30	ASPR Innovation Framework Introduction *(Joe Hamel, HHS/ASPR)*
9:30 – 10:05	Current federal efforts *(5 min brief overview from each agency, if applicable)* *Capturing current or recent federal programs that engage this approach*

- Defense Threat Reduction Agency (DTRA) - *(Ron Hann)*
- Defense Advanced Research Project Agency (DARPA) - *(Brad Ringeisen)*
- Biomedical Advanced Research and Development Authority (BARDA) - *(Rick Bright)*
- Department of Energy (DOE) - *(Shankar Sundaram)*
- National Institutes of Health (NIH) – *(Randy Kincaid & Ann Eakin)*
- U.S. Department of Agriculture - *(Cyril Gay)*
- Centers for Disease Control and Prevention (CDC) - *(Inger Damon)*

Facilitated Open Discussion: Joe Hamel

10:05 – 10:20	Does the hypothetical framework of mining the interactome seem appropriate, and can it be a premise to form coalitions for new approaches in direction?
10:20 – 10:30	BREAK
10:30 – 10:55	Can we identify broad categories or opportunities in host-pathogen interaction that could result in major advances to mitigate entire classes of pathogenic threats? *(e.g., sepsis, control of respiratory transmitted pathogens)*
10:55 – 11:15	What is the potential for short term gains versus longer term gains *(e.g., immediate investments and products versus longer range pattern recognition research).*
11:15 – 11:45	Assuming we identify several major thrusts to energize this approach, using a highly-directed effort, what sort of science management strategy should be employed to achieve the greatest impact?
11:45 – 12:30	LUNCH **For those who wish to join, the **BARDA Visualization Hub (VizHub)** is offering a tour from 12:00-12:20. We encourage those who wish to participate to join the Potbelly lunch to cut down on time reentering the building (if leaving for lunch).*

12:30 – 12:50	Who would you suggest are the thought leaders outside of government that should be brought in to discuss these concepts and to explore further opportunities?
12:50 – 1:15	What are the logical next steps to create a collaborative program or approach, and what is a reasonable starting level of investment (ROM). What types of funding mechanisms (in addition to the federal budget process) should be considered to help initiate and then to sustain these types of efforts?
1:20 – 1:30	Next Steps & Closing Remarks

From: Aviles, Natalie (OS/ASPR) [Natalie.Aviles@hhs.gov]
Sent: 1/25/2018 2:57:10 PM
To: Bright, Rick (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3bec03ac81843dab3ad88c0dd5013c1-HHS-Rick.Br]; Disbrow, Gary (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0265d217b2344c6bbbaad0cbb2f0c6a-HHS-Gary.Di]; Schafer, Julie (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ad453f0426b24a52bef9d08e1fef7967-HHS-Julie.S]; Larsen, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d01661f2f25e4d6797a6cdaedf2e8bc4-HHS-Joseph.]; Alton, Jennifer (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fd8a0f207f3d44a983078c4999a56e79-HHS-Jennife]; Coleman, Norman N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d3fea4ee87d42008e5385dc48408718-HHS-ccolema]; Coleman, CNorman (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ab50ba656ac84bcd9d04461513bd4ce6-HHS-CNorman]; Damon, Inger K (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=42b35bd733a34c66a5698f43f7026e88-HHS-iad7-cd]; Merlin, Toby L (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a656f0a8465744899dead7e628416d32-HHS-tfm5-cd]; Cox, Edward M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=162e42f507494baca7b6b8299a7bbbbb-COXE]; Throckmorton, Douglas C [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdc411a0b9be442daec5172d411e2fd3-THROCKMORTO]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Marks, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dfbb2b5bd38445cb9c9adca3f72df53a-MarksP]; Maher, Carmen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=036c2d54a02e458aad1c293fb4e5d9b7-Carmen.Mahe]; Mair, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f4511bdad7564d7fac7eadc7961467ab-Michael.Mai]; Bryant, Paula R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3eb42f9318014bbb8c14d39ef311d8f9-HHS-paula.b]; Eakin, Ann E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d126f4c08a514e12ac2e646ae79bbd20-HHS-ann.eak]; Kurilla, Michael (NIH/NIAID) [E] [mkurilla@niaid.nih.gov]; Hepburn, Matthew (matthew.hepburn@darpa.mil) [matthew.hepburn@darpa.mil]; Hann, Ronald K Jr SES DTRA (US) (ronald.k.hann2.civ@mail.mil) [ronald.k.hann2.civ@mail.mil]; christian.j.whitchurch.civ@mail.mil; 'kimberly.a.lebutt.civ@mail.mil' [kimberly.a.lebutt.civ@mail.mil]; Bavari, Sina CIV USARMY MEDCOM USAMRIID (US) <sina.bavari.civ@mail.mil> (sina.bavari.civ@mail.mil) [sina.bavari.civ@mail.mil]; Paragas, Jason Jared (paragas1@llnl.gov) [paragas1@llnl.gov]; cyril.gay@ARS.USDA.GOV; Dimitri.Kusnezov@nnsa.doe.gov; carol.r.kuntz.civ@mail.mil; 'David.C.Hassell4.civ@mail.mil' (David.C.Hassell4.civ@mail.mil) [David.C.Hassell4.civ@mail.mil]; jason.w.roos.civ@mail.mil; eric.vangieson@darpa.mil; 'robert.g.ulrich.civ@mail.mil' [robert.g.ulrich.civ@mail.mil]; blake.bextine@darpa.mil; salvatore.clementi@dtra.mil; Ashar, Binita S [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=163dac785c1641709451a95afbc3edec-BSA]; bradley.ringeisen@darpa.mil; paul.sheehan@darpa.mil; Baumgartner, Bridget (contr-bto) (bridget.baumgartner.ctr@darpa.mil) [bridget.baumgartner.ctr@darpa.mil]; Patel, Jean (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11f69e12385e4509a5fd252939e8b900-HHS-vzp4-cd]; Mcdonald, Lawrence C (CDC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e0539cf8d47a46a5aa1364ae3a0a67d9-HHS-ljm3-cd]; 'david.williams8.civ@mail.mil' [david.williams8.civ@mail.mil]; Kincaid, Randall L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=63cce0a284b74df4bd214b99ca0f5d51-HHS-randall]; david.m.restione.ctr@mail.mil

CC: Kadlec, Robert P (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=70539a2f88924cc8913781ea74278b12-HHS-Robert.]; Korch, George (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8111eaa6fff24228b9d5ce8eb46028c4-HHS-George.]; Fisher, Robert (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3d0e55e26774087982248071a6a05a8-HHS-Robert.]; Hamel, Joseph (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b90f78a9c02426eb8d62bd1ad9117b8-HHS-Joseph.]; Stephan, Briana (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86b3179b17604efa9818a549ef7e3fa0-HHS-Briana.]; Ford-Barnes, Arwenthia (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=38db99da9c0f4495b790adda00040fe7-HHS-Arwenth]
Subject: Innovation Initiative: Mining the Pathogen-Host Interactome - January 31, 2018
Attachments: Discussion of the I2MCM ideas and goals.pdf; Meeting Agenda 20170131.pdf; Potbelly Lunch Order Form.pdf

Importance: High

Dear Colleagues,

Attached is a white paper for the approaching "ASPR Innovation Initiative: Mining the Pathogen-Host Interactome" meeting this Wednesday, January 31 (9AM-1:30PM). **If you plan on attending, please "accept" the calendar invite** so that we have a headcount. If you are unable to attend and would like to send an alternate representative, please let us know and we will extend the calendar invite.

We will have light refreshments (coffee, cookies, etc.) during the meeting. Lunch will be for 45 minutes (11:40-12:25), so in order to maximize participants' time to collaborate, we are offering the option to order/bring in Potbelly sandwiches (order form attached). If you are interested in this option, please let me know by next Tuesday morning (Jan. 30); exact change is greatly appreciated. Otherwise, you are welcome to also leave the building to get lunch at the various nearby restaurants.

Materials will also be attached in the calendar invite; hard copies will be available at the meeting. Thank you and we look forward to seeing everyone!

Very respectfully,

Natalie Avilés
Program Analyst
U.S. Department of Health & Human Services (HHS)
Assistant Secretary for Preparedness & Response (ASPR)
Immediate Office (I/O)
202 (b)(6) Direct
202 (b)(6) Mobile

ASPR Strategic Innovation

Interactome-Informed Medical Countermeasures (I2MCM)

Dr. George Korch, Senior Science Advisor, ASPR

There are two major commonalities between novel **naturally-occurring pandemic pathogens and the potential for newly engineered biological threats**. First, whatever the genetic or metabolic structure of the pathogen might possess, it must phenotypically perform within a set of biological patterns that create the disease outcome, i.e. they must behave like other human pathogen to cause disease, otherwise, they are non-pathogenic. Secondly, the immune system will eventually act against the threat to attempt to restore homeostasis, but the adaptive arm of the immune system needs time to achieve its greatest effect. How can we use these two fundamental truths to craft wide-ranging therapies across multiple and diverse pathogens?

The fundamental problem we are seeking to address is how to empower and harness information that increasingly reveals the presence of **deeply-rooted common patterns that span across large and diverse groups of pathogens, and even across diverse disease states**. The hypothesis that there should be common patterns makes biological and evolutionary sense. The host can be viewed by the pathogen as a system of integrated physiological processes from which it must gain energy for survival and reproduction while avoid being defeated by defense mechanisms. While there is a large array of gene interactions, gene products and modification of products post-translation to create the integrity and function of the host system, these are not infinite in combination, and are for the most part highly conserved. They form very well ordered systems that we are beginning to understand through the rapid advances in sequencing, transcriptomics, proteomics, metabolomics and systems integration through bioinformatics. Once a pathogen unlocks the key to accessing the riches to be gained from the host's energetic stockpiles, either by convergent evolution or other information sharing means, the pathogen is poised to be successful until it is either eliminated by the immune system or finds a way to avoid the immune system's influence.

Evidence for the interaction of diverse pathogens to interrupt the host at key nodes and "subroutines" in the takeover of this machinery by the pathogen are becoming better annotated[1,2,3,4] and there is accumulating information about similarities between non-infectious disease states and pathways that pathogens use to stimulate similar disease such as between epilepsy, cancer, neurodegeneration and Toxoplasma which modulate similar systems in the brain as one example.[5] Bioinformatics tools have suggested for instance that there are distinct patterns to how a group of viruses interacts with the type 1 interferon system when one looks at flaviviruses, herpesviruses, papillomaviruses and retroviruses, but that there are nodes that are highly targeted in this "subroutine" for interferon 1.[2] The literature on this will keep expanding

as similar approaches and big data sets accumulate along with new tools to delve more deeply into these putative relationships and underlying patterns.

There are programs across the USG that appear to address part of this need, or that fund such efforts, but to date, it appears that no single organization in government or academia has established a specific approach of this sort and thus is in a defined leadership position to help orchestrate a bigger fusion of this type of information against the purposed envisioned here to look for overarching patterns that can be then mined for therapeutic or even prophylactic approaches against a diverse or even unknown set of pathogens.

The other major pillar of the I2MCM is that it seeks **to approach pathogen control from a combinatorial approach**. That is, we cannot seek to tackle multiple potential pathogens, that may use different but well defined pattern sets, with a limited set of therapeutic molecules or approaches. An example of this approach is used for the long term control of chronic HIV infection via Highly Active Antiretroviral Therapy (HAART), which combines two nucleoside reverse transcriptase inhibitors along with one non-nucleoside reverse transcriptase inhibitor, protease inhibitor (PI) or Integrase inhibitors. These are all antiviral targets, but the principle of creating so many "pain points" for the virus that it becomes overwhelmed is the approach that should also be considered for host-based targeting. By identifying a list of important nodes spanning a wide range of pathogens, and by looking at druggability, toxicity and interaction effects, it is theoretically possible to provide a large coverage against known and therefore unknown pathogens that would be relying on similar infection and disease producing outcomes.

Developing this capability in ASPR will require investment in a systems biology capability tied directly into a product minded outcome. While this could be argued to be the domain of basic research, it is actually a dedicated and focused effort to derive a very comprehensive set of integrated medical countermeasures. It will need a system that is more aligned with the way that a pharmaceutical company would employ their research assets rather than an approach that looks to expand general knowledge via individual investigator solicited research proposals. In essence, this would be a pre-clinical program that would align or partner directly with BARDA to inform later investment decisions that are driven by metrics and deliverables. Unlike the previous attempts within DoD to achieve such an outcome in the now defunct Translational Medical Technologies Initiative (TMTI), it will not be seeking a set of current products that are kluged together to try to approximate the interactome-informed model, but will be driven initially by deep understanding of the common patterns that will emerge from investment in comparative pathogen-host interaction data sets.

In addition to accumulating basic information on host-pathogen pattern recognition, the I2MCM dimensions can also encompass other pragmatic issues such as novel delivery mechanisms and should include diagnostics to rapidly understand the pathogenesis signals (biomarkers) or specific pathogen markers that would inform therapeutic approach.

Key parameters still need to be discussed, and we are approaching the opportunities through a series of individual and group discussions, with government partners and thought leaders in academia and industry. We will be conducting a meeting of government program managers first to hone our thinking and learn about current capabilities and then will propose to assemble 20-25 subject matter experts (science leaders in the field) at a meeting to be held by the ASPR. The concepts to be further refined will include target areas to help unify the efforts.

Assuming that there is acceptance of the key approaches and concepts, there will be a range of important discussions that will also be needed identify how this type of effort is then organized across agencies or in some other construct.

The following areas could form the basis for discussion as a starting point.

1. **Identify key areas for host-pathogen pattern disruption (some examples include):**
    a. Immune modulation
    b. Sepsis
    c. Exosomal signaling
    d. Control of apoptosis
    e. MAPK cascades
    f. Protein kinase activities
    g. Cell proliferation
    h. Epigenetics – host response/disease exposure/risk profile generation
    i. Others

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    b. Multiple approaches to control bacterial pathogens in addition to antibiotics
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4. **Develop most reasonable program management strategy**
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    a. Development of FFRDC (Commercial or Academic)
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Assistant Secretary for Preparedness and Response (ASPR)
Innovation Initiative: *Mining the pathogen-host interactome*

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Sub-Basement Level – Willow Conference Room

January 31, 2018
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9:20 – 9:50	Current federal efforts *(5 min brief overview from each agency, if applicable) Capturing current or recent federal programs that engage this approach*

- Defense Threat Reduction Agency (DTRA)
- Defense Advanced Research Project Agency (DARPA)
- *Biomedical Advanced Research and Development Authority (BARDA): 1) On-Demand Availability, 2) Non-Clinical Studies, 3) Earlier Indication (Rick Bright)*
- *Department of Energy (DOE): Bioinformatics Investments*
- *National Institutes of Health, NIAID Investments*
- *Other potential contributors (USDA, DOD)*

Facilitated Open Discussion: Joe Hamel (HHS/ASPR)

9:50 – 10:10	Does the hypothetical framework of mining the interactome seem appropriate, and can it be a premise to form coalitions for new approaches in direction?
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12:45 – 1:10	What are the logical next steps to create a collaborative program or approach, and what is a reasonable starting level of investment (ROM). What types of funding mechanisms (in addition to the federal budget process) should be considered to help initiate and then to sustain these types of efforts?
1:10 – 1:30	Next Steps & Closing Remarks

NAME:

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Turkey Breast	Baked Cheddar/SC	Sugar cookie
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Smoked ham	Mesquite BBQ	
Roast Beef	Regular	
Tuna Salad	Salt & Vinegar	
Chicken Salad	Voodoo Heat	
Meatball		
Pizza Sandwich		
Vegetarian		

Basic Belly ***(sandwich & chips)***

$8.00	*Chips*
Turkey Breast	Baked Cheetos
A Wreck	Baked Lays
Italian	Baked Cheddar & Sour Cream
Roast Beef	Garden Salsa
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Sent: 2/2/2018 4:37:07 PM
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Subject: Thank You - Innovation Initiative - January 31, 2018

Dear Colleagues:

(On behalf of George, Rick, and Joe)

We want to take this opportunity to thank you for your generous commitment of time and wisdom in participating in ASPR Innovation Initiative meeting. My overall impression was that this event provided us all an opportunity to learn from each other's programs and investments in new research and operational efforts to tackle the large challenges our agencies and constituencies all face. It also provided a forum for exploration of new ideas or for conferring on areas of investment moving into the future that would have broad support or appeal in developing and accelerating products to tackle big demand issues, like sepsis or ability to identify pre-clinical markers of clinical disease from pathogens of important public health concern. We also appreciated the frank discussion of what we can learn from past attempts or data from studies that give context to the difficulty and inherent risk of broad-application approaches. But we also heard and learned from the group discussion that there is validity to the overarching need and to the hypothetical framework that we described yesterday. That was evidenced by some of the data that you all presented as well.

We are hoping to provide to you all in the near future a listing of the "bucket" items we identified in the short time we had to capture your ideas, and will ask your help in giving us your relative (rank order) priority of what may be most beneficial items to pursue and what timelines you would estimate on getting a return on the efforts to find and implement solutions (products). Part of this request will also be to capture things we may have not discussed but that you would like to include for consideration. We also hope to ask for your recommendations of thought leaders from outside government with whom we should confer as we move forward on several of these opportunities.

Once again, our deepest gratitude for your participation and continued interest and support.

Very respectfully,

Natalie Avilés
Program Analyst
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