DHS SCIENCE AND TECHNOLOGY

Master Question List for COVID-19 (caused by SARS-CoV-2)

Weekly Report

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Homeland Security

Science and Technology

FOREWORD

The Department of Homeland Security (DHS) is paying close attention to the evolving Coronavirus Infectious Disease (COVID-19) situation in order to protect our nation. DHS is working very closely with the Centers for Disease Control and Prevention (CDC), other federal agencies, and public health officials to implement public health control measures related to travelers and materials crossing our borders from the affected regions.

Based on the response to a similar product generated in 2014 in response to the Ebolavirus outbreak in West Africa, the DHS Science and Technology Directorate (DHS S&T) developed the following "master question list" that quickly summarizes what is known, what additional information is needed, and who may be working to address such fundamental questions as, "What is the infectious dose?" and "How long does the virus persist in the environment?" The Master Question List (MQL) is intended to quickly present the current state of available information to government decision makers in the operational response to COVID-19 and allow structured and scientifically guided discussions across the federal government without burdening them with the need to review scientific reports, and to prevent duplication of efforts by highlighting and coordinating research.

The information contained in the following table has been assembled and evaluated by experts from publicly available sources to include reports and articles found in scientific and technical journals, selected sources on the internet, and various media reports. It is intended to serve as a "quick reference" tool and should not be regarded as comprehensive source of information, nor as necessarily representing the official policies, either expressed or implied, of the DHS or the U.S. Government. DHS does not endorse any products or commercial services mentioned in this document. All sources of the information provided are cited so that individual users of this document may independently evaluate the source of that information and its suitability for any particular use. This document is a "living document" that will be updated as needed when new information becomes available.

SARS-CoV-2 (COVID-19)	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
What do we know?	• The human infectious dose of SARS-CoV-2, which causes coronavirus disease 19 (COVID-19) is currently unknown via all exposure routes. Animal data are used as surrogates. • Rhesus macaques are infected with SARS-CoV-2 via the ocular conjunctival and intratracheal route at a dose of 700,000 PFU (10^6 $TCID_{50}$).[51] • A total dose of 700,000 plaque-forming units (PFU) of SARS-CoV-2 infected cynomolgus macaques via a combination intranasal and intratracheal exposure (10^5 $TCID_{50}$ total dose).[109] Macaques did not exhibit clinical symptoms, but shed virus through the nose and throat.[109] • Nonhuman primate infection may not represent human infection. • Initial experiments suggest that SARS-CoV-2 can infect genetically modified mice containing the human ACE2 cell entry receptor. Infection via the intranasal route (dose: 10^5 $TCID_{50}$, approximately 70,000 PFU) causes light infection, however no virus was isolated from infected animals, and polymerase chain reaction (PCR) primers used in the study do not align well with SARS-CoV-2, casting doubt on this study.[14] • The infectious dose for SARS in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route).[49-50] • Genetically modified mice exposed intranasally to doses of MERS virus between 100 and 500,000 PFU show signs of infection. Infection with higher doses result in severe syndromes.[7, 41, 81, 150]	• Pandemic COVID-19 has caused 214,894 infections and 8,732 deaths[72] in at least 173 countries and territories (as of 3/18/2020).[27, 114, 135] • There are 7,769 SARS-CoV-2 cases across 50 US states, with 118 deaths. (as of 3/18/2020)[72]; there is sustained community transmission of COVID-19 in the US.[17] • High-quality estimates of human transmissibility (R_0) range from 2.2 to 3.1[93, 98, 106, 142, 149] Early estimates of the attack rate in China range from 3%-10%, mainly in households.[137] • SARS-CoV-2 is believed to spread through close contact and droplet transmission,[31] with fomite transmission[73], i.e., germs left on surfaces, and close-contact aerosol transmission also plausible.[22] • SARS-CoV-2 replicates in the upper respiratory tract (e.g., throat), and infectious virus is detectable in throat and lung tissue for at least 8 days.[138] • Pre-symptomatic[151] or asymptomatic[12] patients can transmit SARS-CoV-2; between 12%[54] and 23%[90] of infections may be caused by asymptomatic or pre-symptomatic transmission. • SARS-CoV-2 is present in infected patient saliva,[124] lower respiratory sputum,[131] and feces.[86] • Social distancing and behavioral changes are estimated to have reduced COVID-19 spread by 44% in Hong Kong,[47] and a combination of non-pharmaceutical interventions (e.g., school closures, isolation) are likely required to limit transmission.[59] • Up to 86% of early COVID-19 cases in China were undiagnosed, and these infections were the source for 79% of documented cases.[84]	• Early genomic analysis indicates similarity to SARS,[154] with a suggested bat origin.[5,42, 154] • Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.[108] The identity of the intermediate host remains unknown.[85, 87-88] • Positive samples from the South China Seafood Market strongly suggests a wildlife source,[33] though it is possible that the virus was circulating in humans before the disease was associated with the seafood market.[18, 43, 144, 148] • Experiments suggest that SARS-CoV-2 Spike (S) receptor-binding domain binds the human cell receptor (ACE2) stronger than SARS,[141] potentially explaining its high transmissibility; the same work suggests that differences between SARS-CoV-2 and SARS-CoV Spike proteins may limit the therapeutic ability of SARS antibody treatments.[141] • Modeling between SARS-CoV-2 Spike and ACE2 proteins suggests that SARS-CoV-2 can bind and infect human, bat, civet, monkey and swine cells.[129] • There is currently no experimental evidence that SARS-CoV-2 infects domestic animals or livestock, though it is expected that some animal species could be infected.	• The best current estimate of the COVID-19 incubation period is 5.1 days, with 99% of individuals exhibiting symptoms within 14 days of exposure.[79] Fewer than 2.5% of infected individuals show symptoms sooner than 2 days after exposure.[79] • The reported range of incubation periods is wide, with high-end estimates of 24,[60] 11.3,[11] and 18 days.[83] • Individuals can test positive for COVID-19 despite lacking clinical symptoms.[12, 35, 60, 120, 151] • Individuals can be infectious while asymptomatic,[31, 110, 120, 151] and asymptomatic individuals can have similar amounts of virus in their nose and throat as symptomatic individuals.[155] • Infectious period is unknown, but possibly up to 10-14 days [5, 84, 114] • On average, there are approximately 4[54] to 7.5[83] days between symptom onset in successive cases of a single transmission chain. • Most individuals are admitted to the hospital within 8-14 days of symptom onset.[153] • Patients are positive for COVID-19 via PCR for 8-37 days after symptom onset.[153] • Individuals may test positive via PCR for 5-13 days after symptom recovery and hospital discharge.[77] The ability of these individuals to infect others is unknown. • According to the WHO, there is no evidence of re-infection with SARS-CoV-2 after recovery.[78] • Experimentally infected macaques were not capable of being reinfected after their primary infection resolved.[13]

SARS-CoV-2 (COVID-19)	**Infectious dose – how much agent will make a normal individual ill?**	**Transmissibility – How does it spread from one host to another? How easily is it spread?**	**Host range – how many species does it infect? Can it transfer from species to species?**	**Incubation period – how long after infection do symptoms appear? Are people infectious during this time?**
What do we need to know?	• Human infectious dose by aerosol route • Human infectious dose by surface contact (fomite) • Human infectious dose by fecal-oral route	• Capability of SARS-CoV-2 to be transmitted by contact with fomites (doorknobs, surfaces, clothing, etc.) – see also Experimental Stability • Superspreading capacity needs to be refined • Updated person to person transmission rates (e.g., R_0) as control measures take effect • What is the underreporting rate?[71] • Can individuals become re-infected with SARS-CoV-2? • What is the difference in transmissibility among countries? • Is the R0 estimate higher in healthcare or long-term care facilities?	• What is the intermediate host(s)? • What are the mutations in SARS-CoV-2 that allowed human infection and transmission? • What animals can SARS-CoV-2 infect (e.g., pet dogs, potential wildlife reservoirs)?	• What is the average infectious period during which individuals can transmit the disease? • Are individuals infectious after hospital discharge and clinical recovery, or are positive PCR tests only detecting non-infectious virus? • Can individuals become re-infected after recovery? If so, how long after?
Who is doing experiments/has capabilities in this area?	*Capable of performing work* - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Christian Althaus (Bern) - Neil Ferguson (MRC) - Gabriel Leung, Joseph Wu (University of Hong Kong) - Sara Del Valle (Los Alamos) - Maimuna Majumder (Boston Children's Hospital) - Trevor Bedford (Fred Hutchinson Cancer Center) - Sang Woo Park (Princeton)	*Capable of performing work:* - Vincent Munster (Rocky Mountain National Laboratory) - Matthew Frieman (University of Maryland Baltimore) - Ralph Baric (University of North Carolina) - Stanley Perlman (University of Iowa) - Susan Baker (Loyola University Chicago) - Mark Denison (Vanderbilt University) - Vineet Menachery (University of Texas Medical Branch) - Jason McLellan, Daniel Wrapp, Nianshuang Wang (University of Texas) - David O'Conner (U. Wisconsin, Madison)	*Performing work:* - Chaolin Huang (Jin Yin-tan Hospital, Wuhan, China) - The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

SARS-CoV-2 (COVID-19)	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
What do we know?	• The majority of COVID-19 cases are mild (81%, N = 44,000 cases)[120] • Initial COVID-19 symptoms include fever (87.9% overall, but only 43.8% present with fever initially[60]), cough (67.7%[60]), fatigue, shortness of breath, headache, reduction in lymphocyte count.[32, 38, 68] Headache[37] and diarrhea are uncommon[68, 82] • Complications include acute respiratory distress (ARDS observed in 17-29% of hospitalized patients,[40, 67] which leads to death in 4-15% of cases[40, 68, 130]), pneumonia,[96] cardiac injury, secondary infection, kidney failure, arrhythmia, sepsis, and shock.[60,68,130, 153] • Approximately 15% of hospitalized patients were classified as severe,[60, 120] and approximately 5% of patients were admitted to the ICU.[60, 120] • Most deaths are caused by respiratory failure or respiratory failure combined with myocardial (heart) damage.[111] • The case fatality rate (CFR) depends on comorbidities; cardiovascular disease, hypertension, diabetes, and respiratory conditions all increase the CFR.[120, 153] • The CFR increases with age; individuals older than 60 are at higher risk of death,[120, 153] and >60% of confirmed fatalities have been male.[120] • Children of all ages are susceptible to COVID-19,[53] though generally present with milder symptoms.[39] Severe symptoms in children, however, are possible.[89] • In the US, 34% of hospitalizations have been individuals less than 44 years old.[4] Based on one patient, a productive immune response is generated and sustained for at least 7 days.[123]	• PCR protocols and primers have been widely shared among international researchers[26, 45, 83, 116, 132, 136] though PCR-based diagnostic assays do not differentiate between active and inactive virus. • A combination of pharyngeal (throat) RT-PCR and chest tomography are the most effective diagnostic criteria (correctly diagnosing 91.9% of infections).[104] Single throat swabs alone detect 78.2% of true infections, while duplicate tests identify 86.2% of infections.[104] • Nasal and pharyngeal swabs may be less effective as diagnostic specimens than sputum and bronchoalveolar lavage fluid.[131] • RT-PCR tests are able to identify asymptomatic cases; SARS-CoV-2 infection was identified in 2/114 individuals previously cleared by clinical assessment.[66] • The FDA released an Emergency Use Authorization enabling laboratories to develop and use tests in-house for patient diagnosis.[58] • Updated tests from the US CDC are available to states.[26, 31] • US CDC has expanded patient testing criteria to include symptomatic patients at clinician discretion.[16] • Several rapid or real-time test kits have been produced by universities and industry, including the Wuhan Institute of Virology,[48] BGI,[19] and Cepheid.[128] • The US CDC is developing serological tests to determine what proportion of the population has been exposed to SARS-CoV-2.[74] • Machine learning tools are being developed to predict severe and fatal COVID-19 cases based on CT scans.[117]	• Treatment for COVID-19 is primarily supportive care, including mechanical ventilation and antibiotics to prevent secondary infection as appropriate.[60] • Preliminary reports from two clinical trials in China suggest that favipiravir improves lung function and reduces recovery time in COVID-19 patients.[126] • Early results suggest that tocilizumab may be effective at treating severe COVID-19 cases.[145] • Press reports of a small clinical trial suggest that chloroquine is effective at reducing symptom duration.[1] • Combination lopinavir and ritonavir with standard care was no more effective than standard care alone.[24] • Corticosteroids are commonly given to COVID-19 patients[153] at risk of ARDS,[146] but their use is not recommended by the US CDC.[79] • Multiple entities are working to produce a SARS-CoV-2 vaccine,[9] including NIH/NIAID,[63, 80] Moderna Therapeutics and Gilead Sciences,[2-3, 94] and Sanofi with HHS.[21] Moderna has begun phase 1 clinical vaccine trials in humans in WA state.[107] • Regeneron Pharmaceuticals has developed potential SARS-CoV-2 antibody therapies.[99] • The development of a coronavirus fusion inhibitor in the lab suggests efficacy across multiple human coronaviruses.[143] • Takeda Pharma (Japan) is working to create antibody treatments based on infected patient plasma.[62]	*SARS-CoV-2 Data* • SARS-CoV-2 can persist on plastic and stainless steel surfaces for up to 3 days (at 21-23°C, 40% RH), with a half-life of 13-16 hours.[125] • SARS-CoV-2 has an aerosol half-life of 2.7 hours (particles <5 µm, tested at 21-23°C and 65% RH).[125] *Surrogate Coronavirus data*: • Studies suggest that other coronaviruses can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV)[25, 36], and porous surfaces for up to 3-5 days (SARS-CoV)[56] in air conditioned environments (20-25°C, 40-50% RH) • Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),[25, 36, 102, 127] though infectious virus can persist on surfaces for several days in typical office or hospital conditions[127] • SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C) on surfaces.[25] • Beta-coronaviruses (e.g., SARS-CoV) may be more stable than alpha-coronaviruses (HCoV-229E).[102] • No strong evidence for reduction in transmission with seasonal increase in temperature and humidity.[92] • One hour after aerosolization approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)[100] • The aerosol survival of related human coronavirus (229E) was relatively high, (half-life of ~67 hours at 20°C and 50% RH), indicating ~20% of infectious virus remained after 6 days.[70] Both higher and lower RH reduced HCoV-229E survival; lower temperatures improved survival.[70]

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What do we need to know?	• How long does it take for infected individuals to recover outside of a healthcare setting? • Is the reduction in CFR through time an indication of better treatment, less overcrowding, or both?	• False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease) in an individual	• Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?[115] • Is the GLS-5000 MERS vaccine[147] cross-reactive against SARS-CoV-2? • Efficacy of antibody treatments developed for SARS[46, 119] and MERS[34] • What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics? • Are viral replicase inhibitors such as beta-D-N4-hydroxycytidine effective against SARS-CoV-2?[15]	• Stability of SARS-CoV-2 in aerosol, droplets, and other matrices (mucus/sputum, feces) • Particle size distribution (e.g., droplet, large droplet and true aerosol distribution) • Duration of SARS-CoV-2 infectivity via fomites and surface (contact hazard)? • Stability of SARS-CoV-2 on PPE (e.g., Tyvek, nitrile, etc.)
Who is doing experiments/has capabilities in this area?	- Jin Yin-tan Hospital, Wuhan, China - China-Japan Friendship Hospital, Beijing, China - Peking Union Medical College, Beijing, China - Capital Medical University, Beijing, China - Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China - Huazhong University of Science and Technology, Wuhan, China - The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China - Tsinghua University School of Medicine, Beijing, China - Zhongnan Hospital of Wuhan University, Wuhan, China - Peking University First Hospital, Beijing, China - Peking University People's Hospital, Beijing, China - Tsinghua University-Peking University Joint Center for Life Sciences, Beijing, China - The Fifth Medical Center of PLA General Hospital, Beijing, China	*Performing work:* - CDC - Wuhan Institute of Virology - Public Health Agency of Canada - Doherty Institute of Australia - Cepheid - BGI - Fudan University	*Performing work:* - Peter Doherty Institute for Infection and Immunity - Academy of Military Medical Sciences, Beijing, China - Tim Sheahan (University of North Carolina) - Takeda Pharma. (Japan) - Regeneron Pharmaceuticals - CureVac (Germany) *Capable of performing work:* - Ralph Baric (University of North Carolina) - Matthew Frieman (University of Maryland Baltimore) - Sanofi, with BARDA - Janssen Pharma and BARDA[64] *Funded work:* CEPI ($24 million to seven groups): NIAID/NIH: - Moderna and Kaiser Permanente for mRNA vaccine Phase I trial.[3] - University of Nebraska Medical Center Trial (multiple therapeutics including Gilead's Remdesivir).[2]	*Capable of performing work*: - Mark Sobsey (University of North Carolina) - DHS National Biodefense Analysis and Countermeasures Center (NBACC) - Defence Science and Technology Laboratory (Dstl) - Public Health Agency of Canada - CDC - EPA - NIH

SARS-CoV-2 (COVID-19)	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
What do we know?	*SARS-CoV-2* • Twice-daily cleaning with sodium dichloroisocyanurate decontaminated surfaces in COVID-19 patient hospital rooms.[95] • Alcohol-based hand rubs are effective at inactivating SARS-CoV-2 in liquid.[75] • EPA has released a list of SARS-CoV-2 disinfectants, but solutions were not tested on live virus.[6] *Other Coronaviruses* • Chlorine-based[134] and ethanol-based[44] solutions recommended. • Heat treatment at 56°C is sufficient to kill coronaviruses,[102, 152] though effectiveness depends in part on amount of protein in contaminated media[102] • 70% ethanol, 50% isopropanol, sodium hypochlorite [bleach, 200 ppm], and UV radiation are effective at inactivating several coronaviruses (MHV and CCV)[112] • Ethanol-based biocides are effective disinfectants against coronaviruses dried on surfaces, including ethanol containing gels similar to hand sanitizer.[69, 139] • Surface spray disinfectants such as Mikrobac, Dismozon, and Korsolex are effective at reducing infectivity of the closely related SARS-CoV after 30 minutes of contact.[101] • Coronaviruses may be resistant to thermal inactivation for up to 7 days when stabilized in stool.[122-123] • Additionally, coronaviruses are more stable in matrixes such as respiratory sputum.[55] • Hydrogen peroxide vapor is expected to be effective at repeated decontamination of N95 respirators based on other pathogens.[105]	• PPE effectiveness for SARS-CoV-2 is currently unknown; SARS is used as a surrogate. • Healthcare worker illnesses (over 1,000[120]) demonstrates human-to-human transmission despite isolation, PPE, and infection control.[113] • US CDC does not recommend the use of facemasks for healthy people. Facemasks should be used by people showing symptoms to reduce the risk of others getting infected. The use of facemasks is crucial for health workers and people in close contact with infected patients (at home or in a health care facility).[28] • "Healthcare personnel entering the room [of SARS-CoV-2 patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield)"[30] • WHO indicates healthcare workers should wear clean, non-sterile, long-sleeve gowns as well as gloves.[133] • Respirators (NIOSH-certified N95, EUFFP2 or equivalent) are recommended for those dealing with possible aerosols[134] • Additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation)[23] • SARS-CoV-2 transmission has occurred in hospitals inside[130] and outside of China,[61] including the US.[20] • Porous hospital materials, including paper and cotton cloth, maintain infectious SARS-CoV for a shorter time than non-porous material.[76] • Despite extensive environmental contamination, air sampling in patient rooms did not detect SARS-CoV-2.[95]	• Genomic analysis places SARS-CoV-2 into the beta-coronavirus clade, with close relationship to bat viruses. The SARS-CoV-2 virus is distinct from SARS and MERS viruses.[52] • Genomic analysis suggest that SARS-CoV-2 is a natural variant, and is therefore unlikely to be human-derived or otherwise created by "recombination" with other circulating strains of coronavirus.[9, 154] • Some genomic evidence indicates a close relationship with pangolin coronaviruses[140]; data suggests that pangolins may be a natural host for beta-coronaviruses [87-88]. Additional research is needed. • Genomic data support at least two plausible origins of SARS-CoV-2: "(i) natural selection in a non-human animal host prior to zoonotic transfer, and (ii) natural selection in humans following zoonotic transfer."[9] Either scenario is consistent the observed genetic changes found in all known SARS-CoV-2 isolates. • Additionally, "[…] SARS-CoV-2 is not derived from any previously used virus backbone," reducing the likelihood of laboratory origination,[9] and "[…] genomic evidence does not support the idea that SARS-CoV-2 is a laboratory construct, [though] it is currently impossible to prove or disprove the other theories of its origin."[9]	• There have been no documented cases of SARS-CoV-2 prior to December 2019 • Preliminary genomic analyses, however, suggest that the first human cases of SARS-CoV-2 emerged between 10/19/2019 – 12/17/2019.[10, 18, 103] • The mutation rate of SARS-CoV-2 is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be 1.04×10^{-3} substitutions per site per year (N = 116 genomes).[65] • Preliminary phylogenetic analysis identified a very close genetic similarity between SARS-CoV-2 and a Bat coronavirus (RaTG13) isolated from Yunnan Province, China; suggesting that SARS-CoV-2 originated from bats.[97] • Pangolin coronaviruses are closely related to both SARS-CoV-2 and the closely related Bat coronavirus (RaTG13); phylogenetic analysis suggested that SARS-CoV-2 is of bat origin, but is closely related to pangolin coronavirus.[87-88] • The Spike protein of SARS-CoV-2, which mediates entry into host cells and is the major determinant of host range, is very similar to the Spike protein of SARS-CoV.[91] The rest of the genome is more closely related to two separate bat [91] and pangolin[88] coronavirus. • Analysis of SARS-CoV-2 sequences from Singapore has identified a large nucleotide (382 bp) deletion in ORF-8 that may result in an attenuated (less virulent) phenotype.[138]

SARS-CoV-2 (COVID-19)	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
What do we need to know?	• What is the minimal contact time for disinfectants? • Does contamination with human fluids/waste alter disinfectant efficacy profiles? • How effective is air filtration at reducing transmission in healthcare, airplanes and public spaces?	• Mode of aerosol transmission? Effective distance of spread via droplet or aerosol? • How effective are barriers such as N95 respirators or surgical masks? • What is the appropriate PPE for first responders? Airport screeners? • Proper procedures for reducing spread in medical facilities / transmission rate in medical settings	• What tests for attribution exist for coronavirus emergence? • What is the identity of the intermediate species? • Are there closely related circulating coronaviruses in bats or other animals with the novel PRRA cleavage site found in SARS-CoV-2?	• Are there similar genomic differences in the progression of coronavirus strains from bat to intermediate species to human? • Are there different strains or clades of circulating virus? If so, do they differ in virulence?
Who is doing experiments/has capabilities in this area?	*Capable of performing work*: - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Generating recommendations:* - WHO - CDC - Pan-American Health Organization	*Performing genomic investigations:* - Kristian Andersen, Andrew Rambaut, Ian Lipkin, Edward Holmes, Robert Garry (Scripps, University of Edinburgh, Columbia University, University of Sydney, Tulane, Zalgen Labs [Germantown, MD]) *Capable of performing work:* - Pacific Northwest National Laboratory - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Trevor Bedford (Fred Hutchinson Cancer Research Center) - Ralph Baric, UNC - National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention - Shandong First Medical University and Shandong Academy of Medical Sciences - Hubei Provincial Center for Disease Control and Prevention - Chinese Academy of Sciences - BGI PathoGenesis Pharmaceutical Technology, Shenzhen, China - People's Liberation Army General Hospital, Wuhan, China - Wenzhou Medical University, Wenzhou, China - University of Sydney, Sydney, NSW, Australia - The First Affiliated Hospital of Shandong First Medical University (Shandong Provincial Qianfoshan Hospital), Jinan, China

Table 1. Definitions of commonly-used acronyms

Acronym/Term	Definition	Description
Attack Rate	Proportion of "at-risk" individuals who develop infection	Defined in terms of "at-risk" population such as schools or households, defines the proportion of individuals in those populations who become infected after contact with an infectious individual
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	Official name for the virus previously known as 2019-nCoV.
COVID-19	Coronavirus disease 19	Official name for the disease caused by the SARS-CoV-2 virus.
CFR	Case Fatality Rate	Number of deaths divided by confirmed patients
PFU	Plaque forming unit	Measurement of the number of infectious virus particles as determined by plaque forming assay. A measurement of sample infectivity.
$TCID_{50}$	50% Tissue Culture Infectious Dose	The number of infectious units which will infect 50% of tissue culture monolayers. A measurement of sample infectivity.
HCW	Healthcare worker	Doctors, nurses, technicians dealing with patients or samples
SARS	Severe Acute Respiratory Syndrome	Coronavirus with over 8,000 cases in global 2002-2003 outbreak
MERS	Middle-East Respiratory Syndrome	Coronavirus with over 2,000 cases in regional outbreak since 2012
CoV	Coronavirus	Virus typified by crown-like structures when viewed under electron microscope
R_0	Basic reproduction number	A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.
MHV	Mouse hepatitis virus	Coronavirus surrogate

CCV	Canine coronavirus	Canine coronavirus
Fomite	Inanimate vector of disease	Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.
Droplet transmission	Sneezing, coughing	Transmission via droplets requires relatively close contact (e.g., within 6 feet)
Airborne transmission	Aerosolization of infectious particles	Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)
Transgenic	Genetically modified	In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection
Intranasal	Agent deposited into external nares of subject	Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.
Incubation period	Time between infection and symptom onset	Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible
Infectious period	Length of time an individual can transmit infection to others	Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods
Serial interval	Length of time between symptom onset of successive cases in a transmission chain	The serial interval can be used to estimate R_0, and is useful for estimating the rate of outbreak spread
Superspreading	One individual responsible for an abnormally large number of secondary infections	Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections
Nosocomial	Healthcare- or hospital-associated infections	Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures

ACE2	Angiotensin-converting enzyme 2	Acts as a receptor for SARS-CoV, allowing entry into human cells
ARDS	Acute respiratory distress syndrome	Leakage of fluid into the lungs which inhibits respiration and leads to death
PPE	Personal protective equipment	Gowns, masks, gloves, and any other measures used to prevent spread between individuals
PCR	Polymerase chain reaction	PCR (or real-time [RT] or quantitative [Q] PCR) is a method of increasing the amount of genetic material in a sample, which is then used for diagnostic testing to confirm the presence of SARS-CoV-2

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SARS-CoV-2 (COVID-19)	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
What do we know?	• The human infectious dose for novel Wuhan coronavirus (SARS-CoV-2), which causes coronavirus disease 19 (COVID-19) is currently unknown via all exposure routes. Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) coronaviruses (CoV) are used as surrogates. • The infectious dose for SARS in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route).[50-51] • Genetically modified mice exposed intranasally to doses of MERS virus between 100 and 500,000 PFU show signs of infection. Infection with higher doses result in severe syndromes.[5, 41, 73, 129] • Initial experiments suggest that SARS-CoV-2 can infect genetically modified mice containing the human ACE2 cell entry receptor. Infection via the intranasal route (dose: 10^5 $TCID_{50}$) causes light infection, however no virus was isolated from infected animals, and PCR primers used in the study do not align well with SARS-CoV-2, casting doubt on this study.[11]	• The WHO has declared SARS-CoV-2 a Public Health Emergency of International Concern[116] with 95,124 cases and 3,254 deaths[68] in 75 countries (as of 3/4/2020).[22, 96, 114] • High-quality estimates of human transmissibility (R_0) range from 2.2 to 3.1[80, 86, 91, 120, 128] • Large outbreaks are occurring in Japan, Italy, Iran, South Korea, Germany France, and Spain.[119] • There are 153 SARS-CoV-2 cases across 15 US states, with 11 deaths. (as of 3/4/2020).[68] • Sustained transmission may have been occurring in the US (Seattle) for up to 5 or 6 weeks.[14] • SARS-CoV-2 transmission has occurred in hospitals inside[108] and outside of China,[58] including the US.[17] • Pre-symptomatic[130] or asymptomatic[10] patients in China can transmit SARS-CoV-2; the degree of asymptomatic transmission is still unknown. • SARS-CoV-2 is believed to spread through close contact and droplet transmission.[30] • Viable SARS-CoV-2 has been isolated from human feces; fecal-oral transmission is possible.[81, 124, 127] • Transmission via fomites has not been confirmed for SARS-CoV-2, but occurred in prior SARS[40, 121] and MERS[70] outbreaks • SARS-CoV-2 is consistently present in infected patient saliva[104] • Infants have been diagnosed with COVID-19, but no evidence exists for vertical transmission via intrauterine infection or through breastmilk.[38, 109] • China reports no evidence of super-spreading events (SSEs) within hospital patients or staff.[101]	• Early genomic analysis indicates similarity to SARS,[132] with a suggested bat origin.[5,42, 132] • Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.[92] Although the identity of the intermediate species remains unconfirmed, pangolins may be a natural host of related viruses possibly including SARS-CoV-2.[76-77] • Positive samples from the South China Seafood Market strongly suggests a wildlife source,[32] though it is possible that the virus was circulating in humans before the disease was associated with the seafood market.[15, 43, 122, 126] • Experiments suggest that SARS-CoV-2 Spike (S) receptor-binding domain binds the human cell receptor (ACE2) stronger than SARS,[119] potentially explaining its high transmissibility; the same work suggests that differences between SARS-CoV-2 and SARS-CoV Spike proteins may limit the therapeutic ability of SARS antibody treatments.[119] • Modeling between SARS-CoV-2 Spike and ACE2 proteins suggests that SARS-CoV-2 can bind and infect human, bat, civet, monkey and swine cells.[107]	• A study of 1,099 COVID-19 patients found a median incubation period of 3 days, with a range from 0 to 24 days.[57] • Earlier estimates of the incubation period from confirmed cases were higher; 5.8 days with a range from 1.3 to 11.3 days,[9] and 5.2 days with an upper bound of 9.2-18 days.[75] • CDC estimates that the incubation period is between 2 and 14 days [27, 31] • Asymptomatic infection has been documented, where individuals do not present with clinical symptoms but are found positive via diagnostic assay.[10, 34, 57, 101, 130] • Individuals can be infectious while asymptomatic,[30, 93, 101, 130] and asymptomatic individuals have about the same amount of virus in their nose and throat as symptomatic individuals.[133] • Infectious period is unknown, but possibly up to 10-14 days [4, 96] • On average, there are 7.5 days between symptom onset in successive cases of a single transmission chain (i.e., the serial interval).[75] • The average time for individuals to first seek medical care decreased from 5.8 days after symptom onset to 4.6 days before and after January 1st, 2020, respectively, indicating an increase in seeking care behavior.[75] • China recommends 14 quarantine for *recovered* patients due to positive genetic tests days after leaving the hospital, raising the possibility of continued transmission after symptoms subside.[64]

SARS-CoV-2 (COVID-19)	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
What do we need to know?	• Human infectious dose by aerosol route • Human infectious dose by surface contact (fomite) • Human infectious dose by fecal-oral route • Where does SARS-CoV-2 replicate in the respiratory tract?	• Capability of SARS-CoV-2 to be transmitted by contact with fomites (doorknobs, surfaces, clothing, etc.) – see also Experimental Stability • Superspreading capacity needs to be refined • Updated person to person transmission rates (e.g., R_0) as control measures take effect • Tendency for ill individuals to seek medical care due to symptoms • What is the underreporting rate?[67] • Can individuals become re-infected with SARS-CoV-2? • What is the difference in transmissibility among countries? • Is the R0 estimate higher in healthcare or long-term care facilities? • How effective are social distancing measures at reducing spread?	• What is the intermediate host(s)? • What are the mutations in SARS-CoV-2 that allowed human infection and transmission? • What animals can SARS-CoV-2 infect (e.g., pet dogs, potential wildlife reservoirs)?	• How early does asymptomatic transmission begin? • What is the average infectious period during which individuals can transmit the disease? • How long do patients continue to shed infectious virus after physical recovery? • Can individuals become re-infected after recovery? If so, how long after?
Who is doing experiments/has capabilities in this area?	*Capable of performing work* - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Christian Althaus (Bern) - Neil Ferguson (MRC) - Gabriel Leung, Joseph Wu (University of Hong Kong) - Sara Del Valle (Los Alamos) - Maimuna Majumder (Boston Children's Hospital) - Trevor Bedford (Fred Hutchinson Cancer Center) - Sang Woo Park (Princeton)	*Capable of performing work:* - Vincent Munster (Rocky Mountain National Laboratory) - Matthew Frieman (University of Maryland Baltimore) - Ralph Baric (University of North Carolina) - Stanley Perlman (University of Iowa) - Susan Baker (Loyola University Chicago) - Mark Denison (Vanderbilt University) - Vineet Menachery (University of Texas Medical Branch) - Jason McLellan, Daniel Wrapp, Nianshuang Wang (University of Texas) - David O'Conner (U. Wisconsin, Madison)	*Performing work:* - Chaolin Huang (Jin Yin-tan Hospital, Wuhan, China) - The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

SARS-CoV-2 (COVID-19)	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
What do we know?	• The majority of COVID-19 cases are mild (81%, N = 44,000 cases)[101] • Initial COVID-19 symptoms include fever (87.9% overall, but only 43.8% present with fever initially[57]), cough (67.7%[57]), fatigue, shortness of breath, headache, reduction in lymphocyte count.[31, 37, 63] Headache[36] and diarrhea are uncommon[63, 74] • Complications include acute respiratory distress (ARDS) observed in 17-29% of hospitalized patients,[39, 63] which leads to death in 4-15% of cases.[39, 63, 108] • Other complications include pneumonia (characteristic ground glass opacities[84]), acute cardiac injury, secondary infection, kidney failure, arrhythmia, and shock.[57,63,108] • Approximately 15% of hospitalized patients were classified as severe,[57, 101] and severe cases were older and more likely to have underlying disorders[57, 108]; approximately 5% of patients were admitted to the ICU.[57, 101] • Between 23-32% of cases that include pneumonia required intensive respiratory support.[63, 108] • Overactive immune cells may contribute to symptom severity.[123] • Approximately 1% of hospitalizations occur in children < 19 years old.[57, 101] • The case fatality rate (CFR) depends on patient comorbidities; no comorbidities = 0.9%, cardiovascular disease = 10.5%, diabetes = 7.3%, chronic respiratory disease = 6.3%, hypertension = 6.0%, cancer = 5.6%.[101] • The CFR is age-dependent; ≥80 years old = 14.8%, 70-79 = 8.0%, 60-69 = 3.6%, 50-59 = 1.3%, 40-49 = 0.4%, 10-39 = 0.2%, 0-9 = 0%.[101] • 63.8% of confirmed fatalities have been male.[101]	• Updated tests from the US CDC are available to states.[21, 30] • The FDA released an Emergency Use Authorization describing an accelerated policy enabling laboratories to develop and use tests in-house for patient diagnosis.[56] • The US has relaxed criteria for testing patients, no longer requires travel history or close contact with known case.[13] • US CDC has expanded patient testing criteria to include symptomatic patients at Clinician discretion.[13] CDC recommends that testing decisions should be based on local transmission, travel history, patient clinical course, close contact with infected patients, and occupational risk (e.g., Health Care Workers).[24] • SARS-CoV-2 is consistently present in infected patient saliva, suggesting that saliva may be an effective diagnostic specimen.[104] • Several RT-PCR assays have been developed to detect SARS-CoV-2 in humans.[1, 46, 113, 115] • PCR protocols and primers have been widely shared among international researchers.[21, 47, 75, 99, 111, 115] • Several rapid or real-time test kits have been produced by universities and industry, including the Wuhan Institute of Virology,[49] BGI,[16] and Cepheid.[106] • RT-PCR tests are able to identify asymptomatic cases; SARS-CoV-2 infection was identified in 2/114 individuals previously cleared by clinical assessment.[61]	• Treatment for COVID-19 is primarily supportive care including oxygen and mechanical ventilation,[29] though China has released a treatment plan[8]; over 80 clinical trials are set to run on various treatments in China.[82] • Efficacy antivirals (lopinavir, ritonavir, ribavirin, oseltamivir) is unknown[8]; however several therapeutics [Remdesivir[98] and chloroquine] inhibit SARS-CoV-2 infection in human cells *in vitro*[38] and are undergoing clinical trials in China[49] and the US.[2-3, 83] • Multiple entities are working to produce a SARS-CoV-2 vaccine, including NIH/NIAID,[59, 72] Moderna Therapeutics and Gilead Sciences,[2-3, 83] and Sanofi with HHS.[18] • The hospitalized case-fatality rate in China has decreased from 14.4% to 0.8% as of between December, 2019 and February, 2020,[101] suggesting improved treatment or increased capacity • Approximately 38% of COVID-19 patients in China received oxygen therapy, 6.1% received mechanical ventilation, 57.5% received IV antibiotics, and 35.8% received the antiviral oseltamivir.[57] • A clinical report (one patient) suggested that corticosteroids should be considered for severe patients to prevent ARDS.[123] However, US CDC recommends avoiding steroid use due to an increase in viral replication in MERS patients.[45] • Similarity in the spike proteins of SARS-CoV-2 and SARS-CoV might offer target for therapeutics,[44, 52, 71, 119, 132] as vaccines derived from spike proteins are effective at inhibiting MERS symptoms in mice.[41]	• No information yet exists regarding the environmental stability of SARS-CoV-2; SARS and MERS coronaviruses are used as surrogates instead. • Studies suggest that coronavirus can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV)[20, 35], and porous surfaces for up to 3-5 days (SARS-CoV)[54] in air conditioned environments (20-25°C, 40-50% RH) • Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),[20, 35, 89, 105] though infectious virus can persist on surfaces for several days in typical office or hospital conditions[105] • SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C) on surfaces.[20] • Beta-coronaviruses (e.g., SARS-CoV) may be more stable than alpha-coronaviruses (HCoV-229E).[89] • No strong evidence for reduction in transmission with seasonal increase in temperature and humidity.[79] • Survival of SARS-CoV-2 specifically is unknown, and surrogate coronavirus data need to be used at this time. • One hour after aerosolization approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)[87] • The aerosol survival of related human coronavirus (229E) was relatively high, (half-life of ~67 hours at 20°C and 50% RH), indicating ~20% of infectious virus remained after 6 days.[66] Both higher and lower RH reduced HCoV-229E survival; lower temperatures improved survival.[66]

SARS-CoV-2 (COVID-19)	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
What do we need to know?	• How long does it take for infected individuals to recover outside of a healthcare setting? • How does the CFR vary between countries? • Is the reduction in CFR through time an indication of better treatment, less overcrowding, or both?	• False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease) in an individual	• Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?[97] • Is the GLS-5000 MERS vaccine[125] cross-reactive against SARS-CoV-2? • Efficacy of antibody treatments developed for SARS[48, 100] and MERS[33] • What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics? • Are viral replicase inhibitors such as beta-D-N4-hydroxycytidine effective against SARS-CoV-2?[12]	• Stability of SARS-CoV-2 in aerosol, droplets, and other matrices (mucus/sputum, feces) • "Hang time' of the virus in air (Aerosol decay rate) • Particle size distribution (e.g., droplet, large droplet and true aerosol distribution) • Duration of SARS-CoV-2 infectivity via fomites and surface (contact hazard)? • Stability of SARS-CoV-2 on PPE (e.g., Tyvek, nitrile, etc.)
Who is doing experiments/has capabilities in this area?	- Jin Yin-tan Hospital, Wuhan, China - China-Japan Friendship Hospital, Beijing, China - Peking Union Medical College, Beijing, China - Capital Medical University, Beijing, China - Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China - Huazhong University of Science and Technology, Wuhan, China - The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China - Tsinghua University School of Medicine, Beijing, China - Zhongnan Hospital of Wuhan University, Wuhan, China - Peking University First Hospital, Beijing, China - Peking University People's Hospital, Beijing, China - Tsinghua University-Peking University Joint Center for Life Sciences, Beijing, China - The Fifth Medical Center of PLA General Hospital, Beijing, China	*Performing work:* - CDC - Wuhan Institute of Virology - Public Health Agency of Canada - Doherty Institute of Australia - Cepheid - BGI	*Performing work:* - Peter Doherty Institute for Infection and Immunity - Academy of Military Medical Sciences, Beijing, China - Tim Sheahan (University of North Carolina) *Capable of performing work:* - Ralph Baric (University of North Carolina) - Matthew Frieman (University of Maryland Baltimore) - Sanofi, with BARDA - Janssen Pharma and BARDA[60] *Funded work:* CEPI ($12 million to three groups): - Moderna and NIAID for mRNA platform vaccine - Inovio preparing DNA vaccine (for MERS) - University of Queensland, Australia NIAID/NIH: - Moderna and Kaiser Permanente for mRNA vaccine Phase I trial.[3] - University of Nebraska Medical Center Trial (multiple therapeutics including Gilead's Remdesivir).[2]	*Capable of performing work*: - Mark Sobsey (University of North Carolina) - DHS National Biodefense Analysis and Countermeasures Center (NBACC) - Defence Science and Technology Laboratory (Dstl) - Public Health Agency of Canada - CDC - EPA - NIH

SARS-CoV-2 (COVID-19)	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
What do we know?	• No decontamination data for SARS-CoV-2 have been identified. SARS-CoV provides a plausible surrogate, as it is a close genetic relative of SARS-CoV-2 in the beta-coronavirus clade. • Chlorine-based[113] and ethanol-based[45] solutions recommended, and the European CDC has released disinfectant guidelines for non-healthcare facilities.[55] • "The virus [SARS-CoV-2] has relatively weak viability *in vitro* and can be inactivated at 56 ° C for 30 minutes. Chlorine-containing disinfectants and 75% ethanol can effectively inactivate the virus."[131] • Heat treatment at 56°C is sufficient to kill coronaviruses,[89, 131] though effectiveness depends in part on amount of protein in contaminated media[89] • 70% ethanol, 50% isopropanol, sodium hypochlorite [bleach, 200 ppm], and UV radiation are effective at inactivating several coronaviruses (MHV and CCV)[94] • Ethanol-based biocides (including ethanol-containing gels) are effective disinfectants against coronaviruses dried on surfaces, including ethanol containing gels similar to hand sanitizer.[65, 117] • Surface spray disinfectants such as Mikrobac, Dismozon, and Korsolex are effective at reducing infectivity of the closely related SARS-CoV after 30 minutes of contact.[88] • Coronaviruses may be resistant to thermal inactivation for up to 7 days when stabilized in stool.[102-103] • Additionally, coronaviruses are more stable in matrixes such as respiratory sputum.[53]	• PPE effectiveness for SARS-CoV-2 is currently unknown; SARS is used as a surrogate. • US CDC does not recommend the use of face masks for healthy people. Face masks should be used by people showing symptoms to reduce the risk of others getting infected. The use of face masks is crucial for health workers and people in close contact with infected patients (at home or in a health care facility).[73] • "Healthcare personnel entering the room [of SARS-CoV-2 patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield)"[28] • WHO indicates healthcare workers should wear clean, non-sterile, long-sleeve gowns as well as gloves.[112] • Respirators (NIOSH-certified N95, EUFFP2 or equivalent) are recommended for those dealing with possible aerosols[113] • Additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation)[19] • Healthcare worker illnesses (over 1,000[101]) demonstrates human-to-human transmission despite isolation, PPE, and infection control.[55] • Porous hospital materials, including paper and cotton cloth, maintain infectious SARS-CoV for a shorter time than non-porous material.[69] • CDC recommends face masks for individuals attempting to prevent spread of SARS-CoV-2 in the home.[26]	• Genomic analysis places SARS-CoV-2 into the beta-coronavirus clade, with close relationship to bat viruses. The SARS-CoV-2 virus is distinct from SARS and MERS viruses.[52] • Genomic analysis suggest that SARS-CoV-2 is a natural variant, and is therefore unlikely to be human-derived or otherwise created by "recombination" with other circulating strains of coronavirus.[6, 132] • Some genomic evidence indicates a close relationship with pangolin coronaviruses[118]; data suggests that pangolins may be a natural host for beta-coronaviruses [76-77]. Additional research is needed. • Genomic data support at least two plausible origins of SARS-CoV-2: "(i) natural selection in a non-human animal host prior to zoonotic transfer, and (ii) natural selection in humans following zoonotic transfer."[6] Either scenario is consistent the observed genetic changes found in all known SARS-CoV-2 isolates. • Additionally, "[…] SARS-CoV-2 is not derived from any previously used virus backbone," reducing the likelihood of laboratory origination,[6] and "[…] genomic evidence does not support the idea that SARS-CoV-2 is a laboratory construct, [though] it is currently impossible to prove or disprove the other theories of its origin."[6]	• There have been no documented cases of SARS-CoV-2 prior to December 2019 • Preliminary genomic analyses, however, suggest that the first human cases of SARS-CoV-2 emerged between 10/19/2019 – 12/17/2019.[7, 15, 90] • The mutation rate of SARS-CoV-2 is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be between $3.29 \times 10^{-4} – 2.03 \times 10^{-3}$ substitutions per site per year (median 1.07×10^{-3}),[7] though this estimate may change as more genomes are sequenced. • Preliminary phylogenetic analysis identified a very close genetic similarity between SARS-CoV-2 and a Bat coronavirus (RaTG13) isolated from Yunnan Province, China; suggesting that SARS-CoV-2 originated from bats.[85] • Pangolin coronaviruses are closely related to both SARS-CoV-2 and the closely related Bat coronavirus (RaTG13); phylogenetic analysis suggested that SARS-CoV-2 is of bat origin, but is closely related to pangolin coronavirus.[76-77] • The Spike protein of SARS-CoV-2, which mediates entry into host cells and is the major determinant of host range, is very similar to the Spike protein of SARS-CoV.[78] The rest of the genome is more closely related to two separate bat [78] and pangolin[77] coronavirus. • Protein modeling and preliminary laboratory studies suggest that SARS-CoV-2 binds to the human ACE2 receptor,[107, 119] the same cellular entry receptor used by SARS and other beta-coronaviruses.

SARS-CoV-2 (COVID-19)	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
What do we need to know?	• What is the minimal contact time for disinfectants? • Are antiseptic wipes effective for cleaning hard, non-porous surfaces? • Does contamination with human fluids/waste alter disinfectant efficacy profiles? • How effective is air filtration at reducing transmission in healthcare, airplanes and public spaces?	• Mode of aerosol transmission? Effective distance of spread via droplet or aerosol? • Is virus detectable in aerosol samples from patient rooms? • How effective are barriers such as N95 respirators or surgical masks? • What is the appropriate PPE for first responders? • What are the proper procedures for reducing spread in medical facilities / transmission rate in medical settings?	• What tests for attribution exist for coronavirus emergence? • What is the identity of the intermediate species? • Are there closely related circulating coronaviruses in bats or other animals with the novel PRRA cleavage site found in SARS-CoV-2?	• Are there similar genomic differences in the progression of coronavirus strains from bat to intermediate species to human? • Are there different strains or clades of circulating virus? If so, do they differ in virulence?
Who is doing experiments/has capabilities in this area?	*Capable of performing work*: - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Generating recommendations:* - WHO - CDC - Pan-American Health Organization	*Performing genomic investigations:* - Kristian Andersen, Andrew Rambaut, Ian Lipkin, Edward Holmes, Robert Garry (Scripps, University of Edinburgh, Columbia University, University of Sydney, Tulane, Zalgen Labs [Germantown, MD]) *Capable of performing work:* - Pacific Northwest National Laboratory - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Trevor Bedford (Fred Hutchinson Cancer Research Center) - Ralph Baric, UNC - National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention - Shandong First Medical University and Shandong Academy of Medical Sciences - Hubei Provincial Center for Disease Control and Prevention - Chinese Academy of Sciences - BGI PathoGenesis Pharmaceutical Technology, Shenzhen, China - People's Liberation Army General Hospital, Wuhan, China - Wenzhou Medical University, Wenzhou, China - University of Sydney, Sydney, NSW, Australia - The First Affiliated Hospital of Shandong First Medical University (Shandong Provincial Qianfoshan Hospital), Jinan, China

Table 1. Definitions of commonly-used acronyms

Acronym/Term	Definition	Description
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	Official name for the virus previously known as 2019-nCoV.
COVID-19	Coronavirus disease 19	Official name for the disease caused by the SARS-CoV-2 virus.
CFR	Case Fatality Rate	Number of deaths divided by confirmed patients
PFU	Plaque forming unit	Measurement of the number of infectious virus particles as determined by plaque forming assay. A measurement of sample infectivity.
$TCID_{50}$	50% Tissue Culture Infectious Dose	The number of infectious units which will infect 50% of tissue culture monolayers. A measurement of sample infectivity.
HCW	Healthcare worker	Doctors, nurses, technicians dealing with patients or samples
SARS	Severe Acute Respiratory Syndrome	Coronavirus with over 8,000 cases in global 2002-2003 outbreak
MERS	Middle-East Respiratory Syndrome	Coronavirus with over 2,000 cases in regional outbreak since 2012
CoV	Coronavirus	Virus typified by crown-like structures when viewed under electron microscope
R_0	Basic reproduction number	A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.
MHV	Mouse hepatitis virus	Coronavirus surrogate
CCV	Canine coronavirus	Canine coronavirus
Fomite	Inanimate vector of disease	Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.

Droplet transmission	Sneezing, coughing	Transmission via droplets requires relatively close contact (e.g., within 6 feet)
Airborne transmission	Aerosolization of infectious particles	Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)
Transgenic	Genetically modified	In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection
Intranasal	Agent deposited into external nares of subject	Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.
Incubation period	Time between infection and symptom onset	Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible
Infectious period	Length of time an individual can transmit infection to others	Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods
Serial interval	Length of time between symptom onset of successive cases in a transmission chain	The serial interval can be used to estimate R_0, and is useful for estimating the rate of outbreak spread
Superspreading	One individual responsible for an abnormally large number of secondary infections	Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections
Nosocomial	Healthcare- or hospital-associated infections	Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures
ACE2	Angiotensin-converting enzyme 2	Acts as a receptor for SARS-CoV, allowing entry into human cells

ARDS	Acute respiratory distress syndrome	Leakage of fluid into the lungs which inhibits respiration and leads to death
PPE	Personal protective equipment	Gowns, masks, gloves, and any other measures used to prevent spread between individuals

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DHS SCIENCE AND TECHNOLOGY

Master Question List for COVID-19 (caused by SARS-CoV-2)

Weekly Report

25 March 2020

For comments or questions related to the contents of this document, please contact the DHS S&T Hazard Awareness & Characterization Technology Center at HACTechnologyCenter@hq.dhs.gov.

Homeland Security

Science and Technology

FOREWORD

The Department of Homeland Security (DHS) is paying close attention to the evolving Coronavirus Infectious Disease (COVID-19) situation in order to protect our nation. DHS is working very closely with the Centers for Disease Control and Prevention (CDC), other federal agencies, and public health officials to implement public health control measures related to travelers and materials crossing our borders from the affected regions.

Based on the response to a similar product generated in 2014 in response to the Ebolavirus outbreak in West Africa, the DHS Science and Technology Directorate (DHS S&T) developed the following "master question list" that quickly summarizes what is known, what additional information is needed, and who may be working to address such fundamental questions as, "What is the infectious dose?" and "How long does the virus persist in the environment?" The Master Question List (MQL) is intended to quickly present the current state of available information to government decision makers in the operational response to COVID-19 and allow structured and scientifically guided discussions across the federal government without burdening them with the need to review scientific reports, and to prevent duplication of efforts by highlighting and coordinating research.

The information contained in the following table has been assembled and evaluated by experts from publicly available sources to include reports and articles found in scientific and technical journals, selected sources on the internet, and various media reports. It is intended to serve as a "quick reference" tool and should not be regarded as a comprehensive source of information, nor as necessarily representing the official policies, either expressed or implied, of the DHS or the U.S. Government. DHS does not endorse any products or commercial services mentioned in this document. All sources of the information provided are cited so that individual users of this document may independently evaluate the source of that information and its suitability for any particular use. This document is a "living document" that will be updated as needed when new information becomes available.

SARS-CoV-2 (COVID-19)	Infectious Dose – How much agent will make a healthy individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host Range – How many species does it infect? Can it transfer from species to species?
What do we know?	**The human infectious dose of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unknown by all exposure routes. SARS-CoV-2 is the cause of coronavirus disease 19 (COVID-19).** • A total dose of approximately 700,000 plaque-forming units (PFU) of the novel coronavirus SARS-CoV-2 was sufficient to infect cynomolgus macaques via a combination intranasal and intratracheal exposure (10^6 $TCID_{50}$ total dose).[122] Macaques did not exhibit clinical symptoms, though viral shedding occurred (nose and throat).[122] • Rhesus macaques are effectively infected with SARS-CoV-2 via the ocular conjunctival and intratracheal route at a dose of approximately 700,000 PFU (10^6 $TCID_{50}$).[57] • Initial experiments suggest that SARS-CoV-2 can infect genetically modified mice containing the human ACE2 cell entry receptor. Infection via the intranasal route (dose: 10^5 $TCID_{50}$, approximately 70,000 PFU) causes light infection, however no virus was isolated from infected animals, and PCR primers used in the study do not align well with SARS-CoV-2, casting doubt on this study.[15] • The infectious dose for severe acute respiratory syndrome coronavirus 1 (SARS) in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route).[55-56] • Genetically modified mice exposed intranasally to doses of Middle East respiratory syndrome coronavirus (MERS) virus between 100 and 500,000 PFU show signs of infection. Infection with higher doses result in severe syndromes.[7, 46, 86, 161]	**SARS-CoV-2 is passed easily between humans, likely through close contact with relatively large droplets and possibly through smaller aerosolized particles.** • Pandemic COVID-19 has caused 468,523 infections and 21,192 deaths[77] in at least 173 countries and territories (as of 3/25/2020).[30, 127, 147] • There are 66,132 SARS-CoV-2 cases across 50 US states, with 947 deaths. (as of 3/25/2020)[77]; there is sustained community transmission of COVID-19 in the US.[18] • High-quality estimates of human transmissibility (R_0) range from 2.2 to 3.1[100, 109, 119, 153, 160] • SARS-CoV-2 is believed to spread through close contact and droplet transmission,[34] with fomite transmission[78] and close-contact aerosol transmission also plausible.[23, 67] • SARS-CoV-2 replicates in the upper respiratory tract (e.g., throat), and infectious virus is detectable in throat and lung tissue for at least 8 days.[149] • SARS-CoV-2 is present in infected patient saliva,[137] lower respiratory sputum,[143] and feces.[90] • Aerosolized virus has been detected in COVID-19 patient rooms, with particle sizes within the human respirable range (0.25 – 2.5 µm).[90] **Individuals can transmit SARS-CoV-2 to others before they have symptoms.** • Pre-symptomatic[163] or asymptomatic[13] patients can transmit SARS-CoV-2; between 12%[60] and 23%[95] of infections may be caused by asymptomatic or pre-symptomatic transmission. **Undetected cases play a major role in transmission.** • Models suggest up to 86% of early COVID-19 cases in China were undetected, and these infections were the source for 79% of reported cases.[88] **Behavior changes may limit spread.** • Social distancing and other policies are estimated to have reduced COVID-19 spread by 44% in Hong Kong.[52] Non-pharmaceutical interventions (e.g., school closures, isolation) are likely required to limit transmission.[64]	**SARS-CoV-2 is closely related to other coronaviruses circulating in bats in Southeast Asia. Previous coronaviruses have passed through an intermediate mammal host before infecting humans; the identity of the SARS-CoV-2 intermediate host is unknown.** • Early genomic analysis indicates similarity to SARS,[166] with a suggested bat origin.[5,47, 166] • Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.[121] The identity of the intermediate host remains unknown.[89, 92-93] • Positive samples from the South China Seafood Market strongly suggests a wildlife source,[36] though it is possible that the virus was circulating in humans before the disease was associated with the seafood market.[19, 48, 155, 159] **SARS-CoV-2 uses the same receptor for cell entry as the SARS coronavirus that circulated in 2002/2003.** • Experiments suggest that SARS-CoV-2 Spike (S) receptor-binding domain binds the human cell receptor (ACE2) stronger than SARS,[152] potentially explaining its high transmissibility; the same work suggests that differences between SARS-CoV-2 and SARS-CoV Spike proteins may limit the therapeutic ability of SARS antibody treatments.[152] • Modeling between SARS-CoV-2 Spike and ACE2 proteins suggests that SARS-CoV-2 can bind and infect human, bat, civet, monkey and swine cells.[141] • There is currently no evidence that SARS-CoV-2 infects domestic animals or livestock.

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What do we need to know?	**Identifying the infectious dose for humans by any exposure route will facilitate model development; animal studies are a plausible surrogate.** • Human infectious dose by aerosol route • Human infectious dose by surface contact (fomite) • Human infectious dose by fecal-oral route	**Identifying the contribution of asymptomatic or pre-symptomatic transmission is important for implementing control measures. Additionally, the relative contribution of different infection sources – fomites, droplets, aerosols, and potentially feces – are unknown.** • Capability of SARS-CoV-2 to be transmitted by contact with fomites (phones, doorknobs, surfaces, clothing, etc.) – see also Experimental Stability • Superspreading capacity needs to be refined • Updated person to person transmission rates (e.g., R_0) as control measures take effect • What is the underreporting rate?[76] • Can individuals become re-infected with SARS-CoV-2? • What is the difference in transmissibility among countries? • Is the R_0 estimate higher in healthcare or long-term care facilities? • How effective are social distancing measures? • When will infections peak in various cities and countries?	**Little is known about SARS-CoV-2 in non-human hosts.** • What is the intermediate host(s)? • What are the mutations in SARS-CoV-2 that allowed human infection and transmission? • What animals can SARS-CoV-2 infect (e.g., pet dogs, potential wildlife reservoirs)?

SARS-CoV-2 (COVID-19)	Incubation Period – How long after infection do symptoms appear? Are people infectious during this time?	Clinical Presentation – What are the signs and symptoms of an infected person?	Clinical Diagnosis – Are there tools to diagnose infected individuals? When during infection are they effective?
What do we know?	**The majority of individuals develop symptoms within 14 days of exposure. For most people, it takes at least 2 days to develop symptoms, and on average symptoms develop 5 days after exposure. Some individuals never develop symptoms, but can still transmit disease.** • The best current estimate of the COVID-19 incubation period is 5.1 days, with 99% of individuals exhibiting symptoms within 14 days of exposure.[84] Fewer than 2.5% of infected individuals show symptoms sooner than 2 days after exposure.[84] • The reported range of incubation periods is wide, with high-end estimates of 24,[68] 11.3,[12] and 18 days.[87] • Individuals can test positive for COVID-19 despite lacking clinical symptoms.[13, 38, 68, 133, 163] • Individuals can be infectious while asymptomatic,[34, 123, 133, 163] and asymptomatic individuals can have similar amounts of virus in their nose and throat as symptomatic individuals.[167] • Infectious period is unknown, but possibly up to 10-14 days [5, 88, 127] • On average, there are approximately 4[60] to 7.5[87] days between symptom onset in successive cases of a single transmission chain. • Most individuals are admitted to the hospital within 8-14 days of symptom onset.[165] **Currently, there is no evidence that recovered patients can be reinfected with SARS-CoV-2.** • Experimentally infected macaques were not capable of being reinfected after their primary infection resolved.[14] • According to the WHO, there is no evidence of re-infection with SARS-CoV-2 after recovery.[83] • Patients are positive for COVID-19 via PCR for 8-37 days after symptom onset.[165] • Individuals may test positive via PCR for 5-13 days after symptom recovery and hospital discharge.[82] The ability of these individuals to infect others is unknown. • According to the WHO, there is no evidence of re-infection with SARS-CoV-2 after recovery.[83]	**Most COVID-19 cases are mild, but severe disease can be found in any age group. Older individuals and those with underlying medical conditions are at higher risk of serious illness and death.** • The majority of COVID-19 cases are mild (81%, N = 44,000 cases)[133] • Initial COVID-19 symptoms include fever (87.9% overall, but only 44% - 52% present with fever initially[11, 68]), cough (67.7%[68]), fatigue, shortness of breath, headache, reduction in lymphocyte count.[35, 41, 73] Headache[40] and diarrhea are uncommon,[73, 87] though lack of appetite may be an early symptom.[107] • Complications include acute respiratory distress (ARDS observed in 17-29% of hospitalized patients,[44, 73] which leads to death in 4-15% of cases[44, 73, 142]), pneumonia,[106] cardiac injury, secondary infection, kidney failure, arrhythmia, sepsis, and shock.[68,73,142,165] • Approximately 15% of hospitalized patients were classified as severe,[68, 133] and approximately 5% of patients were admitted to the ICU.[68, 133] • Most deaths are caused by respiratory failure or respiratory failure combined with myocardial (heart) damage.[124] • The case fatality rate (CFR) depends on comorbidities; cardiovascular disease, hypertension, diabetes, and respiratory conditions all increase the CFR.[133, 165] • The CFR increases with age; individuals older than 60 are at higher risk of death,[133, 165] and >60% of confirmed fatalities have been male.[133] • Children of all ages are susceptible to COVID-19,[59] though generally present with milder symptoms[42, 98] or no symptoms at all.[98] Severe symptoms in children, however, are possible.[94] • In the US, 34% of hospitalizations have been individuals less than 44 years old.[4] • Variation in the CFR among countries may be due to demographics, testing criteria, and how COVID-19 related deaths are defined.[104] • Based on one patient, a productive immune response is generated and sustained for at least 7 days.[134]	**Diagnosis relies on identifying the genetic signature of the virus in patient nose, throat, or sputum samples. These tests are relatively accurate, but testing rates in the US are low compared to other countries. As a result, confirmed cases are underreported.** • PCR protocols and primers have been widely shared among international researchers.[29, 50, 87, 129, 144, 148] PCR-based diagnostic assays are unable to differentiate between active and inactive virus. • A combination of pharyngeal (throat) RT-PCR and chest tomography are the most effective diagnostic criteria (correctly diagnosing 91.9% of infections).[116] Single throat swabs alone detect 78.2% of true infections, while duplicate tests identify 86.2% of infections.[116] • Nasal and pharyngeal swabs may be less effective as diagnostic specimens than sputum and bronchoalveolar lavage fluid.[143] • RT-PCR tests are able to identify asymptomatic cases; SARS-CoV-2 infection was identified in 2/114 individuals previously cleared by clinical assessment.[72] • Combination RT-PCR and serology (antibody) testing may increase the ability to diagnose patients with mild symptoms, or identify patients at higher risk of severe disease.[162] • The FDA released an Emergency Use Authorization enabling laboratories to develop and use tests in-house for patient diagnosis.[63] • Updated tests from the US CDC are available to states.[29, 34] • US CDC has expanded patient testing criteria to include symptomatic patients at clinician discretion.[17] • Several rapid or real-time test kits have been produced by universities and industry, including the Wuhan Institute of Virology,[53] BGI,[21] and Cepheid.[140] • The US CDC is developing serological tests to determine what proportion of the population has been exposed to SARS-CoV-2.[79] • Machine learning tools are being developed to predict severe and fatal COVID-19 cases based on CT scans.[130]

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What do we need to know?	**While the incubation period is well-characterized, less is known about how long individuals are infectious before, during, and after symptoms. Additionally, the possibility of reinfection warrants more research.** • What is the average infectious period during which individuals can transmit the disease? • Are individuals infectious after hospital discharge and clinical recovery, or are positive PCR tests only detecting non-infectious virus? • Can individuals become re-infected after recovery? If so, how long after?	**The true case fatality rate is unknown, as the exact number of cases is uncertain. Testing priorities and case definitions vary by location.** • How long does it take for infected individuals to recover outside of a healthcare setting? • Are reductions in CFR through time (e.g., China) an indication of better treatment, less overcrowding, or both? • Are pregnant women at greater risk of complications during labor?[91]	**In general, PCR tests appear to be sensitive and specific, though robust estimates of false positive/negative rates are still lacking.** • False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease) in an individual • With limited testing in many locations, how accurate are clinical diagnoses compared to genetic tests?

SARS-CoV-2 (COVID-19)	Medical Treatment – Are there effective treatments? Vaccines?	Environmental Stability – How long does the agent live in the environment?	Decontamination – What are effective methods to kill the agent in the environment?
What do we know?	**Treatment for COVID-19 is primarily supportive care including ventilation if necessary.[68, 101] A number of therapeutic trials are ongoing, but results are preliminary.[20]** • Preliminary reports from several clinical trials in China suggest that favipiravir improves lung function and reduces recovery time in COVID-19 patients.[43] • Early results suggest that tocilizumab may be effective at treating severe COVID-19 cases.[156] • Some evidence suggests that chloroquine is effective at reducing symptom duration.[1, 65] Hydroxychloroquine in combination with azithromycin may reduce viral load in patients compared to controls.[66] • Combination lopinavir and ritonavir with standard care was no more effective than standard care alone.[25] • JHU is pursuing an Investigational New Drug (IND) approval to provide passive antibody therapy (convalescent serum) to patients,[47] and Takeda Pharma (Japan) is working to create treatments based on patient plasma.[69] • Intravenous immunoglobulin (IVIg) may be effective at inhibiting deterioration when given at the appropriate time in severe cases.[86] • Corticosteroids are commonly given to COVID-19 patients[165] at risk of ARDS,[157] but their use is not recommended by the US CDC.[32] • Regeneron Pharmaceuticals has developed potential SARS-CoV-2 antibody therapies.[110] • The development of a coronavirus fusion inhibitor in the lab suggests efficacy across multiple human coronaviruses.[154] **Work is ongoing to develop a SARS-CoV-2 vaccine in human and animal trials. No preliminary results are available.** • Multiple entities are working to produce a SARS-CoV-2 vaccine,[8] including NIH/NIAID,[70, 85] Moderna Therapeutics and Gilead Sciences,[2-3, 103] and Sanofi with HHS.[22] Moderna has begun phase 1 clinical vaccine trials in humans in WA state.[120] • CEPI has partnered with multiple entities to develop vaccines including University of Oxford, Novavax Hong Kong University, and the Institut Pasteur.	**SARS-CoV-2 can persist on surfaces for at least 3 days depending on conditions. If aerosolized, SARS-CoV-2 is stable for at least several hours. The seasonality of COVID-19 transmission is unknown.** *SARS-CoV-2 Data* • SARS-CoV-2 can persist on plastic and stainless steel surfaces for up to 3 days (at 21-23°C, 40% RH), with a half-life of 13-16 hours.[138] • SARS-CoV-2 has an aerosol half-life of 2.7 hours (particles <5 µm, tested at 21-23°C and 65% RH).[138] • SARS-CoV-2 genetic material (RNA) was detected in symptomatic and asymptomatic cruise ship passenger rooms up to 17 days after cabins were vacated; the infectiousness of this material is not known.[102] *Surrogate Coronavirus data*: • Studies suggest that other coronaviruses can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV)[28, 39], and porous surfaces for up to 3-5 days (SARS-CoV)[62] in air conditioned environments (20-25°C, 40-50% RH). • Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),[28, 39, 113, 139] though infectious virus can persist on surfaces for several days in typical office or hospital conditions[139] • SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C) on surfaces.[28] • No strong evidence exists showing reduction in transmission with seasonal increase in temperature and humidity.[99] • One hour after aerosolization approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)[111] • The aerosol survival of related human coronavirus (229E) was relatively high, (half-life of ~67 hours at 20°C and 50% RH), indicating ~20% of infectious virus remained after 6 days.[75] • Porous hospital materials, including paper and cotton cloth, maintain infectious SARS-CoV for a shorter time than non-porous material.[81]	**Soap and water, as well as common alcohol and chlorine-based cleaners, hand sanitizers, and disinfectants are effective at inactivating SARS-CoV-2 on hands and surfaces.** *SARS-CoV-2* • Twice-daily cleaning with sodium dichloroisocyanurate decontaminated surfaces in COVID-19 patient hospital rooms.[105] • Alcohol-based hand rubs are effective at inactivating SARS-CoV-2.[80] • EPA has released a list of SARS-CoV-2 disinfectants, but solutions were not tested on live virus.[6] *Other Coronaviruses* • Chlorine-based[146] and ethanol-based[49] solutions are recommended. • Heat treatment at 56°C is sufficient to kill coronaviruses,[113, 164] though effectiveness depends in part on amount of protein in contaminated media.[113] • 70% ethanol, 50% isopropanol, sodium hypochlorite [bleach, 200 ppm], and UV radiation are effective at inactivating several coronaviruses (MHV and CCV).[125] • Ethanol-based biocides are effective disinfectants against coronaviruses dried on surfaces, including ethanol containing gels similar to hand sanitizer.[74, 150] • Surface spray disinfectants such as Mikrobac, Dismozon, and Korsolex are effective at reducing infectivity of the closely related SARS-CoV after 30 minutes of contact.[112] • Coronaviruses may be resistant to thermal inactivation for up to 7 days when stabilized in stool.[135-136] • Additionally, coronaviruses are more stable in matrixes such as respiratory sputum.[61] • Hydrogen peroxide vapor was found to be effective with repeated decontamination of N95 respirators.[118]

SARS-CoV-2 (COVID-19)	Medical Treatment – Are there effective treatments? Vaccines?	Environmental Stability – How long does the agent live in the environment?	Decontamination – What are effective methods to kill the agent in the environment?
What do we need to know?	**In general, the efficacy of various therapeutic options for COVID-19 is unknown, though clinical trial results are beginning to be released.** • Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?[128] • Is the GLS-5000 MERS vaccine[158] cross-reactive against SARS-CoV-2? • Efficacy of antibody treatments developed for SARS[51, 132] and MERS[37] • What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics? • Are viral replicase inhibitors such as beta-D-N4-hydroxycytidine effective against SARS-CoV-2?[16]	**Additional testing on SARS-CoV-2, not surrogate viruses, is needed to support initial estimates of stability.** • Stability of SARS-CoV-2 in aerosol, droplets, and other matrices (mucus/sputum, feces) • Particle size distribution (e.g., droplet, large droplet and true aerosol distribution) • Duration of SARS-CoV-2 infectivity via fomites and surface (contact hazard)? • Stability of SARS-CoV-2 on PPE (e.g., Tyvek, nitrile, etc.)	**Additional decontamination studies, particularly with regard to PPE and other items in short supply, are needed.** • What is the minimal contact time for disinfectants? • Does contamination with human fluids/waste alter disinfectant efficacy profiles? • How effective is air filtration at reducing transmission in healthcare, airplanes and public spaces? • Are landfills and wastewater treatment plant processes effective at inactivating SARS-CoV-2?

SARS-CoV-2 (COVID-19)	PPE – What PPE is effective, and who should be using it?	Forensics – Natural vs intentional use? Tests to be used for attribution.	Genomics – How does the disease agent compare to previous strains?
What do we know?	**The effectiveness of PPE for SARS-CoV-2 is currently unknown, and data from other related coronaviruses are used for guidance. Healthcare workers are at high risk of acquiring COVID-19, even with recommended PPE.** • Healthcare worker illnesses (over 1,000[133]) demonstrates human-to-human transmission despite isolation, PPE, and infection control.[126] • Risk of transmission to healthcare workers appears high, with up to 20% of healthcare workers in Lombardy, Italy becoming infected.[115] • US CDC does not recommend the use of facemasks for healthy people. Facemasks should be used by people showing symptoms to reduce the risk of others getting infected. The use of facemasks is crucial for health workers and people in close contact with infected patients (at home or in a health care facility).[31] • "Healthcare personnel entering the room [of SARS-CoV-2 patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield)"[33] • WHO indicates healthcare workers should wear clean long-sleeve gowns as well as gloves.[145] • Respirators (NIOSH-certified N95, EUFFP2 or equivalent) are recommended for those dealing with possible aerosols[146] • Additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation)[24] • Particular attention should be paid to the possibility of transmission via exhaled air during supportive respiratory procedures.[87] • Despite extensive environmental contamination, air sampling in patient rooms did not detect SARS-CoV-2 RNA[105] (but detected RNA in other rooms [36]) • The efficacy of "homemade" PPE, made with T-shirts, bandanas, similar materials, is less than standard PPE, but may be used if no other options are available.[43, 51, 147]	**All current evidence supports the natural emergence of SARS-CoV-2 via a bat and possible intermediate mammal species.** • Genomic analysis places SARS-CoV-2 into the beta-coronavirus clade, with close relationship to bat viruses. The SARS-CoV-2 virus is distinct from SARS and MERS viruses.[58] • Genomic analysis suggest that SARS-CoV-2 is a natural variant, and is therefore unlikely to be human-derived or otherwise created by "recombination" with other circulating strains of coronavirus.[9, 166] • Some genomic evidence indicates a close relationship with pangolin coronaviruses[151]; data suggests that pangolins may be a natural host for beta-coronaviruses [92-93]. Additional research is needed. • Genomic data support at least two plausible origins of SARS-CoV-2: "(i) natural selection in a non-human animal host prior to zoonotic transfer, and (ii) natural selection in humans following zoonotic transfer."[9] Either scenario is consistent the observed genetic changes found in all known SARS-CoV-2 isolates. • Additionally, "[…] SARS-CoV-2 is not derived from any previously used virus backbone," reducing the likelihood of laboratory origination,[9] and "[…] genomic evidence does not support the idea that SARS-CoV-2 is a laboratory construct, [though] it is currently impossible to prove or disprove the other theories of its origin."[9]	**Current evidence suggests that SARS-CoV-2 accumulates mutations at a similar rate as other coronaviruses. Mutations and deletions in specific portions of the SARS-CoV-2 genome have not been linked to any changes in transmission or disease severity.** • There have been no documented cases of SARS-CoV-2 prior to December 2019 • Preliminary genomic analyses, however, suggest that the first human cases of SARS-CoV-2 emerged between 10/19/2019 – 12/17/2019.[10, 19, 114] • The mutation rate of SARS-CoV-2 is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be 1.04×10^{-3} substitutions per site per year (N = 116 genomes).[71] • Preliminary phylogenetic analysis identified a very close genetic similarity between SARS-CoV-2 and a Bat coronavirus (RaTG13) isolated from Yunnan Province, China; suggesting that SARS-CoV-2 originated from bats.[108] • Pangolin coronaviruses are closely related to both SARS-CoV-2 and the closely related Bat coronavirus (RaTG13); phylogenetic analysis suggested that SARS-CoV-2 is of bat origin, but is closely related to pangolin coronavirus.[92-93] • The Spike protein of SARS-CoV-2, which mediates entry into host cells and is the major determinant of host range, is very similar to the Spike protein of SARS-CoV.[97] The rest of the genome is more closely related to two separate bat [97] and pangolin[93] coronavirus. • Analysis of SARS-CoV-2 sequences from Singapore has identified a large nucleotide (382 bp) deletion in ORF-8 that may result in an attenuated (less virulent) phenotype.[131]

SARS-CoV-2 (COVID-19)	PPE – What PPE is effective, and who should be using it?	Forensics – Natural vs intentional use? Tests to be used for attribution.	Genomics – How does the disease agent compare to previous strains?
What do we need to know?	**Most PPE recommendations have not been made on SARS-CoV-2 data, and comparative efficacy of different PPE for different tasks (e.g., intubation) is unknown. Identification of efficacious PPE for healthcare worker is critical due to their high rates of infection.** • What is the importance of aerosol transmission? What is the effective distance of spread via droplet or aerosol? • How effective are barriers such as N95 respirators or surgical masks? • What is the appropriate PPE for first responders? Airport screeners? • What are proper procedures for reducing spread in medical facilities / transmission rate in medical settings? • How effective are homemade masks at reducing transmission?	**Identifying the intermediate species between bats and humans would aid in reducing potential spillover from a natural source.** • What tests for attribution exist for coronavirus emergence? • What is the identity of the intermediate species? • Are there closely related circulating coronaviruses in bats or other animals with the novel PRRA cleavage site found in SARS-CoV-2?	**Research linking genetic changes to differences in phenotype (e.g., transmissibility, virulence, progression in patients) is needed.** • Are there similar genomic differences in the progression of coronavirus strains from bat to intermediate species to human? • Are there different strains or clades of circulating virus? If so, do they differ in virulence?

Table 1. Definitions of commonly-used acronyms

Acronym/Term	Definition	Description
Attack rate	Proportion of "at-risk" individuals who develop infection	Defined in terms of "at-risk" population such as schools or households, defines the proportion of individuals in those populations who become infected after contact with an infectious individual
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	Official name for the virus previously known as 2019-nCoV.
COVID-19	Coronavirus disease 19	Official name for the disease caused by the SARS-CoV-2 virus.
CFR	Case Fatality Rate	Number of deaths divided by confirmed patients
PFU	Plaque forming unit	Measurement of the number of infectious virus particles as determined by plaque forming assay. A measurement of sample infectivity.
$TCID_{50}$	50% Tissue Culture Infectious Dose	The number of infectious units which will infect 50% of tissue culture monolayers. A measurement of sample infectivity.
HCW	Healthcare worker	Doctors, nurses, technicians dealing with patients or samples
SARS	Severe Acute Respiratory Syndrome	Coronavirus with over 8,000 cases in global 2002-2003 outbreak
MERS	Middle-East Respiratory Syndrome	Coronavirus with over 2,000 cases in regional outbreak since 2012
CoV	Coronavirus	Virus typified by crown-like structures when viewed under electron microscope
R_0	Basic reproduction number	A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.
MHV	Mouse hepatitis virus	Coronavirus surrogate

CCV	Canine coronavirus	Canine coronavirus
Fomite	Inanimate vector of disease	Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.
Droplet transmission	Sneezing, coughing	Transmission via droplets requires relatively close contact (e.g., within 6 feet)
Airborne transmission	Aerosolization of infectious particles	Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)
Transgenic	Genetically modified	In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection
Intranasal	Agent deposited into external nares of subject	Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.
Incubation period	Time between infection and symptom onset	Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible
Infectious period	Length of time an individual can transmit infection to others	Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods
Serial interval	Length of time between symptom onset of successive cases in a transmission chain	The serial interval can be used to estimate R_0, and is useful for estimating the rate of outbreak spread
Superspreading	One individual responsible for an abnormally large number of secondary infections	Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections
Nosocomial	Healthcare- or hospital-associated infections	Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures

ACE2	Angiotensin-converting enzyme 2	Acts as a receptor for SARS-CoV, allowing entry into human cells
ARDS	Acute respiratory distress syndrome	Leakage of fluid into the lungs which inhibits respiration and leads to death
PPE	Personal protective equipment	Gowns, masks, gloves, and any other measures used to prevent spread between individuals
PCR	Polymerase chain reaction	PCR (or real-time [RT] or quantitative [Q] PCR) is a method of increasing the amount of genetic material in a sample, which is then used for diagnostic testing to confirm the presence of SARS-CoV-2

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2019-nCoV	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?

What do we know?	• The human infectious dose for novel Wuhan coronavirus (2019-nCoV) is currently unknown via all exposure routes. SARS and MERS coronaviruses are used as surrogates.
	• The infectious dose for SARS in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route)[33-34]
	• Transgenic mice exposed intranasally to doses of MERS virus between 100 and 500,000 PFU show signs of infection, with higher doses exhibiting more severe syndromes.[3, 27, 49, 85]
		• 2019-nCoV has been declared a Public Health Emergency of International Concern by the World Health Organization (WHO).[80]
		• 2019-nCoV is spreading rapidly in major Chinese cities.[47] Human transmissibility estimates range from seasonal influenza (R_0 ~1.4) to that of SARS (R_0 ~2.9):
		  • WHO: 1.4 – 2.5[79]
		  • Majumder: 2.0-3.1[53]
		  • Leung: 2.13 (1.92-2.31)[47]
		  • Althaus: 2.2 (1.4 – 3.8)[59]
		  • Ferguson: 2.6 (1.5 – 3.5)[40]
		  • Liu: 2.92 (2.28 – 3.67)[51]
		  • Read: 3.11 (2.39 – 4.13)[58]
		  • Zhao: 3.3 (2.73 – 3.96)[86]
		• 2019-nCoV is believed to spread between humans via the respiratory route, including droplet transmission[17]. SARS is capable of droplet and airborne transmission,[9, 84] though this has not been confirmed for 2019-nCoV
		• Transmission via fomites (contaminated surfaces) has not been confirmed for 2019-nCoV, but contributed to the large number of nosocomial cases in prior SARS[25, 82] and MERS[44] outbreaks
		• 2019-nCoV-infected travelers from China have been found in 18 countries.[12, 64, 78]
		• Human-to-human transmission via direct contact has occurred outside of China (Germany, Japan, Taiwan, Vietnam, US)[24,63]
		• The likelihood of 2019-nCoV super-spreading events is uncertain, but appears lower than that of SARS and MERS[8, 67,59]
		This information will change as the situation progresses
			• Early genomic analysis indicates similarity to SARS,[88] with a suggested bat origin[5,88]
			• Analysis of 2019-nCoV genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.[60] The identity of the intermediate species is currently unknown.
			• Preliminary studies suggest that nCoV-2019 utilizes the same receptor as SARS, but further research is required[35,45]
			• Positive samples from the South China Seafood Market strongly suggests a wildlife source,[19] though it is possible that the virus was circulating in humans before the disease was associated with the seafood market[7, 28]
			This information will change as the situation progresses
				• Based on 34 travel-related cases, the incubation time for 2019-nCoV is estimated to be 5.8 days (95% CI 4.6-7.9 days), with a range from 1.3 to 11.3 days[5]
				• Using data from 10 confirmed cases, researchers found the mean incubation period to be 5.2 days (95% CI 4.1 – 7.0 days) with an upper bound of 9.2-18 days.[50]
				• Data from several individual case reports suggest incubation times for 2019-nCoV range from ~5-8 days[43, 64]
				• CDC estimates that the incubation period is between 2 and 14 days [13, 18]
				• Asymptomatic infection has been documented, where individuals do not present with clinical symptoms but are found positive via diagnostic assay.[21]
				• It has been reported that individuals are infectious before they begin to show symptoms[64, 72], but this has not been confirmed by the CDC
				• Infectious period is unknown, but possibly up to 10-14 days [2, 64]
				• On average, there are 7.5 days (95% CI, 5.3 – 19 days) between symptom onset in successive cases of a single transmission chain (i.e., the serial interval).[50]
				• The time for individuals to first seek medical care decreased from 5.8 days after symptom onset (95% CI, 4.3 - 7.5 days) to 4.6 days (95% CI, 4.1 - 5.1 days) before and after January 1st, 2020, respectively, indicating an increase in seeking care behavior.[50] On average, it takes 12.5 days (95% CI, 10.3 – 14.8 days) between symptom onset and hospitalization[50] (as of January 11th, 2020)

2019-nCoV	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
What do we need to know?	• Human infectious dose by aerosol route • Route of respiratory transmission (e.g., aerosol or droplet contact transmission) • Human infectious dose by other routes	• Capability of 2019-nCoV to be transmitted by contact with fomites (doorknobs, surfaces, clothing, etc.) – see also Experimental Stability • Superspreading capacity needs to be refined • Updated person to person transmission rates (e.g., R_0) as control measures take effect • Tendency for ill individuals to seek medical care due to symptoms (reporting rate) • Transmission rate with specific regard to healthcare workers (HCW) or in a hospital setting • What is the underreporting rate? [41] • Proper procedures for reducing spread in medical facilities / transmission rate in medical settings • How many infections have occurred in the hospital? • How many confirmed cases are severe? Mild to moderate?	• What is the intermediate host(s)? • Ability of 2019-nCoV to bind to human ACE2 receptor (initial reporting mixed) • Mutations in 2019-nCoV required for human infection and transmission.	• How early does asymptomatic transmission begin? • Are afebrile patients infectious? • What is the average infectious period during which individuals can transmit the disease? • Can recovered or convalescent individuals transmit 2019-nCoV?
Who is doing experiments/has capabilities in this area?	*Capable of performing work* - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Christian Althaus (Bern) - Neil Ferguson (MRC) - Gabriel Leung, Joseph Wu (University of Hong Kong)	*Capable of performing work:* - Vincent Munster (Rocky Mountain National Laboratory) - Matthew Frieman (University of Maryland Baltimore) - Ralph Baric (University of North Carolina) - Stanley Perlman (University of Iowa) - Susan Baker (Loyola University Chicago) - Mark Denison (Vanderbilt University) - Vineet Menachery (University of Texas Medical Branch) *Starting animal work soon:* - David O'Conner (U. Wisconsin, Madison)	*Performing work:* - Chaolin Huang (Jin Yin-tan Hospital, Wuhan, China)

AGENT (DISEASE)	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?

What do we know?	• Initial symptoms:[18, 23, 38]
	  • Fever
	  • Cough
	  • Fatigue
	  • Shortness of Breath
	  • Pneumonia
	  • Dyspnea
	  • Reduction in leukocyte count
	  • Reduction in lymphocyte count
	• Complications include:[38]
	  • Acute respiratory distress (ARDS)
	  • RNAaemia (presence of viral RNA in the blood)
	  • Acute cardiac injury
	  • Secondary infection
	  • Kidney failure
	• "Compared to non-ICU patients, ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNFα."[38]
	• Headache and diarrhea are uncommon,[38] though some patients present with gastrointestinal symptoms[50]
	• The reported mortality rate is relatively low; as of 1/30/2020, 213 individuals out of a reported 9,692 cases (~2.2%).[42] This rate is highly sensitive to the rate of underreporting of both cases and deaths
	• The hospitalized case fatality rate is estimated to be 14% (95% CI from 3.9% - 32%).[81]
	• There is a long delay between time of hospitalization and time of death in fatal cases,[81] indicating a potential lag in the reporting of 2019-nCoV deaths
	• There is currently a delay in reported recoveries,[42] which could indicate an increase in reported fatalities in the near future.
		• In US, diagnostic testing can currently only be performed at CDC[14]
		• CDC has developed a rapid test kit and plans to release to domestic and international partners via their International Reagent Resource[17]
		• WHO interim guidelines suggest PCR,[77] and several RT-PCR assays have been developed to detect 2019-nCoV in humans[1, 30, 77]
		• Real-Time PCR diagnostic protocol and reaction details are published.[74]
		• PAHO advises that molecular diagnosis take place in a BSL-2 laboratory.[54]
		• Wuhan Institute of Virology has reportedly developed a test strip for 2019-nCoV diagnosis[32]
			• Treatment for 2019-nCoV infection is primarily supportive care, no specific treatment regimens exist[16]
			• WHO guidance indicates oxygen therapy for patients with severe acute respiratory infection (SARI), and antimicrobials if sepsis is identified[73]
			• Supportive care such as intubation may lead to increased nosocomial transmission[69]
			• Reports that remdesivir (GS-5734), chloroquine, and ritonavir are undergoing clinical trials.[32]
			• A recent paper indicated that remdesivir was broadly effective at treating coronavirus infections in mice, sometimes in combination with interferon β;[66] efficacy against 2019-nCoV infection has not yet been demonstrated
			• NIH/NIAID is reportedly developing vaccine for 2019-nCoV,[37, 48] and CEPI has funded vaccine work through three different awards
			• Researchers in Australia have successfully cultured 2019-nCoV from isolates of an infected patient;[6] this live virus can be used to develop therapeutics
			• Similarity in the spike proteins of 2019-nCoV and SARS-CoV[35, 46, 88] might offer target for therapeutics.[29] Vaccines derived from spike proteins are effective at inhibiting MERS symptoms in mice[27]
			
			It is anticipated that this information will change as the situation progresses
				• No information yet exists regarding the environmental stability of 2019-nCoV; SARS and MERS coronaviruses are used as surrogates instead.
				
				On surfaces:
				• SARS remains infectious for up to 3 days on hard, nonporous surfaces like plastic [36] and stainless steel,[75] but survives for less time (24-36 hours) on porous surfaces like cloth, wood, and plaster walls[75]
				• Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),[11, 22, 56, 70] though infectious virus can persist on surfaces for several days in typical office or hospital conditions[70]
				
				In the air:
				• One hour after aerosolization (via Collison nebulizer), approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)
				• The aerosol survival of another human coronavirus (229E) was relatively high, with a half-life of ~67 hours at 20°C and 50% RH, indicating ~20% infectious virus at 6 days.[39] Both higher and lower RH reduced viral survival, while lower temperatures improved survival.[39]
				
				SMEs don't anticipate specific 2019-nCoV guidance to be published in the near-term due to the focus on epidemiology, therapies, and host determining factor research. SARS and MERS data are likely the best near-term surrogates for environmental stability.

AGENT (DISEASE)	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
What do we need to know?	• Differences in symptoms as infection progresses • Variability in symptoms among subpopulations (elderly, children, immunocompromised); clinical outcomes in SARS patients were worse for those over 60 yo[26] • How long do patients remain hospitalized? • How long does it take for infected individuals to recover outside of a healthcare setting?	• False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease)	• Is GS-5734 (remdesivir) effective (already used in clinical trials under Emergency Use Authorization)?[65] • Is the GLS-5000 MERS vaccine[83] cross-reactive against 2019-nCoV? • Efficacy of antibody treatments developed for SARS[31, 68] and MERS[20] • What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics?	• Stability of 2019-nCoV in aerosol, droplets, and other matrices (mucus/sputum, feces) • "Hang time' of the virus in air (Aerosol decay rate) • Particle size distribution (e.g., droplet, large droplet and true aerosol distribution) • Duration of infectivity via fomites and surface (contact hazard)? • Stability of 2019-nCoV on PPE (e.g., tyvec, nitrile, etc.)
Who is doing experiments/has capabilities in this area?	- Jin Yin-tan Hospital, Wuhan, China - China-Japan Friendship Hospital, Beijing, China - Peking Union Medical College, Beijing, China - Capital Medical University, Beijing, China - Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China - Huazhong University of Science and Technology, Wuhan, China - The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China - Tsinghua University School of Medicine, Beijing, China - Zhongnan Hospital of Wuhan University, Wuhan, China - Peking University First Hospital, Beijing, China - Peking University People's Hospital, Beijing, China - Tsinghua University-Peking University Joint Center for Life Sciences, Beijing, China	*Performing work:* - CDC - Wuhan Institute of Virology - Public Health Agency of Canada - Doherty Institute of Australia	*Performing work:* - Peter Doherty Institute for Infection and Immunity - Academy of Military Medical Sciences, Beijing, China *Capable of performing work:* - Ralph Baric (University of North Carolina) - Matthew Frieman (University of Maryland Baltimore) *Funded work:* CEPI ($12 million to three groups): - Moderna and NIAID for mRNA platform vaccine - Inovio preparing DNA vaccine - University of Queensland, Australia, producing viral protein from cell culture	*Capable of performing work*: - DHS National Biodefense Analysis and Countermeasures Center (NBACC) - Defence Science and Technology Laboratory (Dstl) - Public Health Agency of Canada

AGENT (DISEASE)	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
What do we know?	• Chlorine-based solutions recommended [77] • "The virus [2019-nCoV] has relatively weak viability in vitro, and can be inactivated at 56 ° C for 30 minutes. Chlorine-containing disinfectants and 75% ethanol can effectively inactivate the virus."[87] • Heat treatment at 56°C is sufficient to kill coronaviruses,[56, 87] though effectiveness depends in part on amount of protein in contaminated media[56] • 70% ethanol, 50% isopropanol, sodium hypochlorite [bleach, 200 ppm], and UV radiation are effective at inactivating several coronaviruses (MHV and CCV)[61]	• "Healthcare personnel entering the room [of 2019-nCoV patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield)"[15] • WHO indicates healthcare workers should wear clean, non-sterile, long-sleeve gowns as well as gloves.[76] • Nosocomial infections with SARS-CoV were more likely during intratracheal intubation, manipulation of oxygen masks, suction before intubation, and non-invasive ventilation[69] • Respirators (NIOSH-certified N95, EUFFP2 or equivalent) are recommended for those dealing with possible aerosols[77] • Additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation)[10] • Healthcare worker illnesses indicate potential for human-to-human transmission despite isolation, PPE, and infection control[62]	• Genomic analysis places 2019-nCoV into the beta-coronavirus clade, with close relationship to bat viruses. The 2019-nCoV virus is distinct from SARS and MERS viruses.[35] • Genomic analysis suggest that 2019-nCoV is a natural variant, and is therefore unlikely to be human-derived or otherwise created by "recombination" with other circulating strains of coronavirus.[88]	• There have been no known outbreaks of 2019-nCoV prior to December 2019 • Preliminary genomic analyses, however, suggest that the first human cases of 2019-nCoV emerged between 10/19/2019 – 12/17/2019.[4, 7, 57] • The mutation rate of 2019-nCoV is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be between $3.29 \times 10^{-4} – 2.03 \times 10^{-3}$ substitutions per site per year (median 1.07×10^{-3}),[4] though this estimate may change as more genomes are sequenced. • Preliminary phylogenetic analysis identified a very close genetic similarity between 2019-nCoV and a Bat coronavirus (RaTG13) isolated from Yunnan Province, China; highly suggesting that 2019-nCoV originated from bats.[55] • The Spike protein of 2019-nCoV, which mediates entry into host cells and is the major determinant of host range, is very similar to the Spike protein of SARS-CoV.[52] The rest of the genome is more closely related to two separate bat coronaviruses.[52] • Genetic evidence and preliminary laboratory studies[45] suggest that 2019-nCoV binds to the human ACE2 receptor[71], the same cellular entry receptor used by SARS.
What do we need to know?	• Are hand sanitizing solutions effective? What is the minimal contact time? • Are antiseptic wipes effective for cleaning hard, non-porous surfaces? • What antiseptic/disinfection methods are effective? • Does contamination with human fluids/waste alter disinfectant efficacy profiles?	• Evidence of spread among patients within hospitals, like SARS? • Mode of aerosol transmission? • Is virus detectable in aerosol samples from patient rooms? • How effective are barriers such as N95 respirators as well as surgical masks?	• What tests for attribution exist for coronavirus emergence?	• Are there similar genomic differences in the progression of coronavirus strains from bat to intermediate species to human?

Who is doing experiments/has capabilities in this area?	*Capable of performing work*: - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Generating recommendations:* - WHO - CDC - Pan-American Health Organization	*Capable of performing work:* - Pacific Northwest National Laboratory - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Trevor Bedford (Fred Hutchinson Cancer Research Center) - National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention - Shandong First Medical University and Shandong Academy of Medical Sciences - Hubei Provincial Center for Disease Control and Prevention - Chinese Academy of Sciences - BGI PathoGenesis Pharmaceutical Technology, Shenzhen, China - People's Liberation Army General Hospital, Wuhan, China - Wenzhou Medical University, Wenzhou, China - University of Sydney, Sydney, NSW, Australia - The First Affiliated Hospital of Shandong First Medical University (Shandong Provincial Qianfoshan Hospital), Jinan, China

Table 1. Definitions of commonly-used acronyms

Acronym/Term	Definition	Description
PFU	Plaque forming unit	Infectious virus particle
HCW	Healthcare worker	Doctors, nurses, technicians dealing with patients or samples
SARS	Severe Acute Respiratory Syndrome	Coronavirus with over 8,000 cases in global 2002-2003 outbreak
MERS	Middle-East Respiratory Syndrome	Coronavirus with over 2,000 cases in regional outbreak since 2012
CoV	Coronavirus	Virus typified by crown-like structures when viewed under electron microscope
R_0	Basic reproduction number	A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.
MHV	Mouse hepatitis virus	Coronavirus surrogate
CCV	Canine coronavirus	Canine coronavirus
Fomite	Inanimate vector of disease	Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.
Droplet transmission	Sneezing, coughing	Transmission via droplets requires relatively close contact (e.g., within 6 feet)
Airborne transmission	Aerosolization of infectious particles	Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)
Transgenic	Genetically modified	In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection
Intranasal	Agent deposited into external nares of subject	Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.

Incubation period	Time between infection and symptom onset	Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible
Infectious period	Length of time an individual can transmit infection to others	Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods
Serial interval	Length of time between symptom onset of successive cases in a transmission chain	The serial interval can be used to estimate R_0, and is useful for estimating the rate of outbreak spread
Superspreading	One individual responsible for an abnormally large number of secondary infections	Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections
Nosocomial	Healthcare- or hospital-associated infections	Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures
ACE2	Angiotensin-converting enzyme 2	Acts as a receptor for SARS-CoV, allowing entry into human cells
ARDS	Acute respiratory distress syndrome	Leakage of fluid into the lungs which inhibits respiration and leads to death

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SARS-CoV-2	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
What do we know?	• The human infectious dose for novel Wuhan coronavirus (SARS-CoV-2) is currently unknown via all exposure routes. Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome coronaviruses are used as surrogates. • The infectious dose for SARS in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route)[39-40] • Transgenic mice exposed intranasally to doses of MERS virus between 100 and 500,000 PFU show signs of infection, with higher doses exhibiting more severe syndromes.[3, 31, 60, 113] • An initial report suggests that SARS-CoV-2 is able to infect transgenic mice modified to contain the human ACE2 cell entry receptor via the intranasal route at a dose of 10^5 $TCID_{50}$;[8] however no virus was isolated from infected animals, and PCR primers used in the study do not align well with SARS-CoV-2, casting doubt on this study.	• SARS-CoV-2 has been declared a Public Health Emergency of International Concern by the WHO[102] with 75,280 cases and 2,014 deaths[53] in 27 countries.[16, 82, 100] • SARS-CoV-2 is spreading rapidly in major Chinese cities,[58] with localized outbreaks outside of China.[80] • Human transmissibility (R_0) estimates were critically assessed; high-confidence estimates range from 2.2 to 3.1[65, 70, 76, 106, 112] • Reports of asymptomatic transmission from Germany were erroneous[78,54]; the degree of asymptomatic transmission is still unknown. • SARS-CoV-2 is believed to spread between humans via the respiratory route, including droplet transmission.[21] • Additionally, SARS-CoV-2 has been shed in feces, raising the possibility of fecal-oral transmission[66] • Transmission via fomites has not been confirmed for SARS-CoV-2, but contributed to the large number of nosocomial cases in prior SARS[30, 107] and MERS[56] outbreaks • SARS-CoV-2 is consistently present in infected patient saliva.[89] • Infants have been diagnosed with COVID-19, but no evidence exists for vertical transmission via intrauterine infection or through breastmilk.[29, 95] • SARS-CoV-2 transmission has occurred in hospitals both inside[94] and outside of China.[46] • China reports no evidence of super-spreading events (SSEs) within hospital patients or staff.[86]	• Early genomic analysis indicates similarity to SARS,[115] with a suggested bat origin.[5,32, 115] • Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.[77] The identity of the intermediate species remains unconfirmed. • Positive samples from the South China Seafood Market strongly suggests a wildlife source,[23] though it is possible that the virus was circulating in humans before the disease was associated with the seafood market[10, 33, 108] • Preliminary studies suggest that nCoV-2019 utilizes the same receptor as SARS, but further research is required.[41,57, 109] • Biophysical binding and structural evaluation of the SARS-CoV-2 Spike (S) receptor-binding domain suggest a higher affinity for human cell receptor ACE2 than SARS[105]; the same work suggests low cross-reactivity between anti-SARS antibodies and SARS-CoV-2, potentially limiting the therapeutic ability of SARS antibody treatments.[105]	• A recent study of 1,099 COVID-19 patients found a median incubation period of 3 days, with a range from 0 to 24 days.[45] • Earlier estimates of the incubation period from confirmed cases were higher; 5.8 days (95% CI 4.6-7.9 days), with a range from 1.3 to 11.3 days[7] and 5.2 days (95% CI 4.1 – 7.0 days) with an upper bound of 9.2-18 days.[62] • CDC estimates that the incubation period is between 2 and 14 days [18, 22] • Individuals may be infectious while asymptomatic,[21, 78] though this needs to be confirmed • Asymptomatic infection has been documented, where individuals do not present with clinical symptoms but are found positive via diagnostic assay.[25, 45, 86] • Infectious period is unknown, but possibly up to 10-14 days [2, 82] • On average, there are 7.5 days (95% CI, 5.3 – 19 days) between symptom onset in successive cases of a single transmission chain (i.e., the serial interval).[62] • The time for individuals to first seek medical care decreased from 5.8 days after symptom onset (95% CI, 4.3 - 7.5 days) to 4.6 days (95% CI, 4.1 - 5.1 days) before and after January 1st, 2020, respectively, indicating an increase in seeking care behavior.[62] On average, it takes 12.5 days (95% CI, 10.3 – 14.8 days) between symptom onset and hospitalization[62] (as of January 11th, 2020)

SARS-CoV-2	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
What do we need to know?	• Human infectious dose by aerosol route • Human infectious dose by surface contact (fomite) • Human infectious dose by fecal-oral route • Where does SARS-CoV-2 replicate in the respiratory tract?	• Capability of SARS-CoV-2 to be transmitted by contact with fomites (doorknobs, surfaces, clothing, etc.) – see also Experimental Stability • Superspreading capacity needs to be refined • Updated person to person transmission rates (e.g., R_0) as control measures take effect • Tendency for ill individuals to seek medical care due to symptoms • What is the underreporting rate?[52] • Proper procedures for reducing spread in medical facilities / transmission rate in medical settings • Can individuals become reinfected with SARS-CoV-2?	• What is the intermediate host(s)? • Ability of SARS-CoV-2 to bind to human ACE2 receptor (need live virus confirmation in addition to genetic similarity) • What are the mutations in SARS-CoV-2 that allowed human infection and transmission?	• How early does asymptomatic transmission begin? • What is the average infectious period during which individuals can transmit the disease? • Can recovered or convalescent individuals transmit SARS-CoV-2? • How long do patients continue to shed infectious virus after physical recovery?
Who is doing experiments/has capabilities in this area?	*Capable of performing work* - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Christian Althaus (Bern) - Neil Ferguson (MRC) - Gabriel Leung, Joseph Wu (University of Hong Kong) - Sara Del Valle (Los Alamos) - Maimuna Majumder (Boston Children's Hospital) - Trevor Bedford (Fred Hutchinson Cancer Center) - Sang Woo Park (Princeton)	*Capable of performing work:* - Vincent Munster (Rocky Mountain National Laboratory) - Matthew Frieman (University of Maryland Baltimore) - Ralph Baric (University of North Carolina) - Stanley Perlman (University of Iowa) - Susan Baker (Loyola University Chicago) - Mark Denison (Vanderbilt University) - Vineet Menachery (University of Texas Medical Branch) - Jason McLellan, Daniel Wrapp, Nianshuang Wang (University of Texas) *Starting animal work soon:* - David O'Conner (U. Wisconsin, Madison)	*Performing work:* - Chaolin Huang (Jin Yin-tan Hospital, Wuhan, China) - The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

SARS-CoV-2	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
What do we know?	• The majority of COVID-19 cases are mild (81%, N = 44,000 cases)[86] • Initial COVID-19 symptoms include fever (87.9% of patients develop during hospitalization, but only 43.8% present with fever initially[45]), cough (67.7%[45]), fatigue, shortness of breath, headache, reduction in lymphocyte count.[22, 28, 49] Headache[27] and diarrhea are uncommon[49, 61] • Complications include acute respiratory distress (ARDS), pneumonia (characteristic ground glass opacities[68]), acute cardiac injury, secondary infection, kidney failure, arrhythmia, and shock.[45,49,94] • Pathological evidence from a single patient indicates severe immune injury instigated by overactive T cells, specifically an increase of Th17 cells and high cytotoxicity of CD8 T cells.[110] • Approximately 15% of hospitalized patients were classified as severe,[45, 86] and severe cases were older and more likely to have underlying disorders[45, 94]; approximately 5% of patients were admitted to the ICU.[45, 86] • Approximately 1% of hospitalizations occur in children < 19 years old.[45, 86] • The case fatality rate (CFR) depends on patient comorbidities; no comorbidities = 0.9%, cardiovascular disease = 10.5%, diabetes = 7.3%, chronic respiratory disease = 6.3%, hypertension = 6.0%, cancer = 5.6%.[86] • The CFR is age-dependent; ≥80 years old = 14.8%, 70-79 = 8.0%, 60-69 = 3.6%, 50-59 = 1.3%, 40-49 = 0.4%, 10-39 = 0.2%, 0-9 = 0%.[86] • 63.8% of confirmed fatalities have been male.[86] • Patients (N = 21) were hospitalized for a mean of 17 days (range = 11 – 26).[68]	• CDC has developed a rapid test kit and is shipping to domestic and international partners via their International Reagent Resource;[15, 21] issues with inconclusive results have been reported using the CDC test kit.[44] • WHO interim guidelines suggest PCR,[99] and several RT-PCR assays have been developed to detect SARS-CoV-2 in humans[1, 35, 99, 101] • Real-Time PCR diagnostic protocol and reaction details are published.[97] • PAHO advises that molecular diagnosis take place in a BSL-2 laboratory.[67] • Wuhan Institute of Virology has reportedly developed a test strip for SARS-CoV-2 diagnosis[38] • Multiple institutions (Hong Kong University, China CDC, U.S. CDC, National Institute of Infectious Disease Japan, the Ministry of Public Health Thailand, Charité) have developed and shared PCR protocols and primers with international researchers.[15, 36, 62, 101] • BGI has developed real-time detection kits: fluorescent RT-PCR and metagenomic sequencing detection kit (probe-anchor synthesis sequencing methods).[11] • Cepheid developing automated molecular test for use in its GeneXpert System.[92] • SARS-CoV-2 is consistently present in infected patient saliva, suggesting that saliva may be an effective diagnostic specimen.[89] • RT-PCR tests positively identified SARS-CoV-2 in 2/114 individuals who had been cleared by clinical assessment.[48]	• Treatment for SARS-CoV-2 infection is primarily supportive care,[20] though China has released a treatment plan[6] • WHO guidance indicates oxygen therapy for patients with severe acute respiratory infection (SARI), and antimicrobials if sepsis is identified[96] • Efficacy for other treatments being administered to patients in China (lopinavir, ritonavir, chloroquine, ribavirin, oseltamivir) is unknown.[6] • The hospitalized case-fatality rate has decreased from 14.4% to 0.8% as of between December, 2019 and February, 2020[86] • Of 1,099 hospitalized COVID-19 patients in China, 38% received oxygen therapy, 6.1% received mechanical ventilation (more prevalent in severe cases), 57.5% received IV antibiotics, and 35.8% received the antiviral oseltamivir.[45] • Presence of pulmonary edema and hyaline membrane formation suggests early use of corticosteroids and mechanical ventilation in severe ARDS patients.[110] • Remdesivir (GS-5734)[84] and chloroquine inhibit SARS-CoV-2 infection in human cells *in vitro*[29] and are undergoing clinical trials.[38] • NIH/NIAID is developing a vaccine for SARS-CoV-2,[47, 59] CEPI has funded vaccine work through an award to Moderna, and Sanofi will work with HHS to develop coronavirus vaccine.[12] • Increased access to live virus should facilitate therapeutic testing.[75] • Similarity in the spike proteins of SARS-CoV-2 and SARS-CoV might offer target for therapeutics.[34, 41, 57, 105, 115] Vaccines derived from spike proteins are effective at inhibiting MERS symptoms in mice[31]	• No information yet exists regarding the environmental stability of SARS-CoV-2; SARS and MERS coronaviruses are used as surrogates instead. • Studies suggest that coronavirus can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV)[14, 26], and porous surfaces for up to 3-5 days (SARS-CoV)[43] in air conditioned environments (20-25°C, 40-50% RH) • Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),[14, 26, 73, 91] though infectious virus can persist on surfaces for several days in typical office or hospital conditions[91] • SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C)[14] • Beta-coronaviruses (e.g., SARS-CoV) may be more stable than alpha-coronaviruses (HCoV-229E).[73] • No strong evidence for reduction in transmission with seasonal increase in temperature and humidity.[64] • Survival of SARS-CoV-2 specifically is unknown, and surrogate coronavirus data need to be used at this time. • One hour after aerosolization (via Collison nebulizer), approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)[71] • The aerosol survival of another human coronavirus (229E) was relatively high, with a half-life of ~67 hours at 20°C and 50% RH, indicating ~20% infectious virus at 6 days.[51] Both higher and lower RH reduced viral survival, while lower temperatures improved survival.[51]

SARS-CoV-2	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
What do we need to know?	• How long does it take for infected individuals to recover outside of a healthcare setting?	• False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease) in an individual	• Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?[83] • Is the GLS-5000 MERS vaccine[111] cross-reactive against SARS-CoV-2? • Efficacy of antibody treatments developed for SARS[37, 85] and MERS[24] • What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics? • Are viral replicase inhibitors such as beta-D-N4-hydroxycytidine effective against SARS-CoV-2?[9]	• Stability of SARS-CoV-2 in aerosol, droplets, and other matrices (mucus/sputum, feces) • "Hang time' of the virus in air (Aerosol decay rate) • Particle size distribution (e.g., droplet, large droplet and true aerosol distribution) • Duration of SARS-CoV-2 infectivity via fomites and surface (contact hazard)? • Stability of SARS-CoV-2 on PPE (e.g., Tyvek, nitrile, etc.)
Who is doing experiments/has capabilities in this area?	- Jin Yin-tan Hospital, Wuhan, China - China-Japan Friendship Hospital, Beijing, China - Peking Union Medical College, Beijing, China - Capital Medical University, Beijing, China - Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China - Huazhong University of Science and Technology, Wuhan, China - The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China - Tsinghua University School of Medicine, Beijing, China - Zhongnan Hospital of Wuhan University, Wuhan, China - Peking University First Hospital, Beijing, China - Peking University People's Hospital, Beijing, China - Tsinghua University-Peking University Joint Center for Life Sciences, Beijing, China - The Fifth Medical Center of PLA General Hospital, Beijing, China	*Performing work:* - CDC - Wuhan Institute of Virology - Public Health Agency of Canada - Doherty Institute of Australia - Cepheid - BGI	*Performing work:* - Peter Doherty Institute for Infection and Immunity - Academy of Military Medical Sciences, Beijing, China - Tim Sheahan (University of North Carolina) *Capable of performing work:* - Ralph Baric (University of North Carolina) - Matthew Frieman (University of Maryland Baltimore) - Sanofi, with BARDA (using their recombinant DNA platform) *Funded work:* CEPI ($12 million to three groups): - Moderna and NIAID for mRNA platform vaccine - Inovio preparing DNA vaccine (for MERS) - University of Queensland, Australia, producing viral protein from cell culture	*Capable of performing work*: - Mark Sobsey (University of North Carolina) - DHS National Biodefense Analysis and Countermeasures Center (NBACC) - Defence Science and Technology Laboratory (Dstl) - Public Health Agency of Canada - CDC - EPA - NIH

SARS-CoV-2	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
What do we know?	• No decontamination data for SARS-CoV-2 have been identified. SARS-CoV provides a plausible surrogate, as it is a close genetic relative of SARS-CoV-2 in the beta-coronavirus clade. • Chlorine-based solutions recommended [99] • "The virus [SARS-CoV-2] has relatively weak viability *in vitro* and can be inactivated at 56 ° C for 30 minutes. Chlorine-containing disinfectants and 75% ethanol can effectively inactivate the virus."[114] • Heat treatment at 56°C is sufficient to kill coronaviruses,[73, 114] though effectiveness depends in part on amount of protein in contaminated media[73] • 70% ethanol, 50% isopropanol, sodium hypochlorite [bleach, 200 ppm], and UV radiation are effective at inactivating several coronaviruses (MHV and CCV)[79] • Ethanol-based biocides (including ethanol-containing gels) are effective disinfectants against coronaviruses dried on surfaces, including ethanol containing gels similar to hand sanitizer.[50, 103] • Surface spray disinfectants such as Mikrobac, Dismozon, and Korsolex are effective at reducing infectivity of the closely related SARS-CoV after 30 minutes of contact.[72] • Coronaviruses may be resistant to thermal inactivation for up to 7 days when stabilized in stool.[87-88] Additionally, coronaviruses are more stable in matrixes such as respiratory sputum.[42]	• PPE effectiveness for SARS-CoV-2 is currently unknown; SARS is used as a surrogate • "Healthcare personnel entering the room [of SARS-CoV-2 patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield)"[19] • WHO indicates healthcare workers should wear clean, non-sterile, long-sleeve gowns as well as gloves.[98] • Nosocomial infections with SARS-CoV were more likely during intratracheal intubation, manipulation of oxygen masks, suction before intubation, and non-invasive ventilation[90] • Respirators (NIOSH-certified N95, EUFFP2 or equivalent) are recommended for those dealing with possible aerosols[99] • Additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation)[13] • Healthcare worker illnesses (over 1,000[86]) indicate potential for human-to-human transmission despite isolation, PPE, and infection control[81] • Porous hospital materials, including paper and cotton cloth, maintain infectious SARS-CoV for a shorter time than non-porous material.[55] • CDC recommends facemasks for individuals attempting to prevent spread of SARS-CoV-2 in the home[17]	• Genomic analysis places SARS-CoV-2 into the beta-coronavirus clade, with close relationship to bat viruses. The SARS-CoV-2 virus is distinct from SARS and MERS viruses.[41] • Genomic analysis suggest that SARS-CoV-2 is a natural variant, and is therefore unlikely to be human-derived or otherwise created by "recombination" with other circulating strains of coronavirus.[115] • Some genomic evidence indicates a potential recombination with a pangolin coronavirus[104]; additional research is needed. • Genomic data support at least two plausible origins of SARS-CoV-2: "(i) natural selection in a non-human animal host prior to zoonotic transfer, and (ii) natural selection in humans following zoonotic transfer."[4] Either scenario is consistent with the development of a high-ACE2 receptor binding domain and novel polybasic furin cleavage site found in all known SARS-CoV-2 isolates. • "[…] SARS-CoV-2 is not derived from any previously used virus backbone," reducing the likelihood of laboratory origination.[4]	• There have been no documented cases of SARS-CoV-2 prior to December 2019 • Preliminary genomic analyses, however, suggest that the first human cases of SARS-CoV-2 emerged between 10/19/2019 – 12/17/2019.[5, 10, 74] • The mutation rate of SARS-CoV-2 is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be between $3.29 \times 10^{-4} – 2.03 \times 10^{-3}$ substitutions per site per year (median 1.07×10^{-3}),[5] though this estimate may change as more genomes are sequenced. • Preliminary phylogenetic analysis identified a very close genetic similarity between SARS-CoV-2 and a Bat coronavirus (RaTG13) isolated from Yunnan Province, China; highly suggesting that SARS-CoV-2 originated from bats.[69] • The Spike protein of SARS-CoV-2, which mediates entry into host cells and is the major determinant of host range, is very similar to the Spike protein of SARS-CoV.[63] The rest of the genome is more closely related to two separate bat coronaviruses.[63] • Genetic evidence and preliminary laboratory studies suggest that SARS-CoV-2 binds to the human ACE2 receptor,[93] the same cellular entry receptor used by SARS.
What do we need to know?	• What is the minimal contact time for disinfectants?	• Evidence of spread among patients within hospitals, like SARS?	• What tests for attribution exist for coronavirus emergence?	• Are there similar genomic differences in the progression of coronavirus

	• Are antiseptic wipes effective for cleaning hard, non-porous surfaces? • Does contamination with human fluids/waste alter disinfectant efficacy profiles?	• Mode of aerosol transmission? • Is virus detectable in aerosol samples from patient rooms? • How effective are barriers such as N95 respirators as well as surgical masks?	• What is the identity of the intermediate species? • Are there closely related circulating coronaviruses in bats or other animals with the novel PRRA cleavage site found in SARS-CoV-2?	strains from bat to intermediate species to human?
Who is doing experiments/has capabilities in this area?	*Capable of performing work*: - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Generating recommendations:* - WHO - CDC - Pan-American Health Organization	*Performing genomic investigations:* - Kristian Andersen, Andrew Rambaut, Ian Lipkin, Edward Holmes, Robert Garry (Scripps, University of Edinburgh, Columbia University, University of Sydney, Tulane, Zalgen Labs [Germantown, MD]) *Capable of performing work:* - Pacific Northwest National Laboratory - DHS National Biodefense Analysis and Countermeasures Center (NBACC)	*Performing work:* - Trevor Bedford (Fred Hutchinson Cancer Research Center) - Ralph Baric, UNC - National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention - Shandong First Medical University and Shandong Academy of Medical Sciences - Hubei Provincial Center for Disease Control and Prevention - Chinese Academy of Sciences - BGI PathoGenesis Pharmaceutical Technology, Shenzhen, China - People's Liberation Army General Hospital, Wuhan, China - Wenzhou Medical University, Wenzhou, China - University of Sydney, Sydney, NSW, Australia - The First Affiliated Hospital of Shandong First Medical University (Shandong Provincial Qianfoshan Hospital), Jinan, China

Table 1. Definitions of commonly-used acronyms

Acronym/Term	Definition	Description
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	Official name for the virus previously known as 2019-nCoV.
COVID-19	Coronavirus disease 19	Official name for the disease caused by the SARS-CoV-2 virus.
CFR	Case Fatality Rate	Number of deaths divided by confirmed patients
PFU	Plaque forming unit	Measurement of the number of infectious virus particles as determined by plaque forming assay. A measurement of sample infectivity.
$TCID_{50}$	50% Tissue Culture Infectious Dose	The number of infectious units which will infect 50% of tissue culture monolayers. A measurement of sample infectivity.
HCW	Healthcare worker	Doctors, nurses, technicians dealing with patients or samples
SARS	Severe Acute Respiratory Syndrome	Coronavirus with over 8,000 cases in global 2002-2003 outbreak
MERS	Middle-East Respiratory Syndrome	Coronavirus with over 2,000 cases in regional outbreak since 2012
CoV	Coronavirus	Virus typified by crown-like structures when viewed under electron microscope
R_0	Basic reproduction number	A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.
MHV	Mouse hepatitis virus	Coronavirus surrogate
CCV	Canine coronavirus	Canine coronavirus
Fomite	Inanimate vector of disease	Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.

Droplet transmission	Sneezing, coughing	Transmission via droplets requires relatively close contact (e.g., within 6 feet)
Airborne transmission	Aerosolization of infectious particles	Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)
Transgenic	Genetically modified	In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection
Intranasal	Agent deposited into external nares of subject	Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.
Incubation period	Time between infection and symptom onset	Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible
Infectious period	Length of time an individual can transmit infection to others	Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods
Serial interval	Length of time between symptom onset of successive cases in a transmission chain	The serial interval can be used to estimate R_0, and is useful for estimating the rate of outbreak spread
Superspreading	One individual responsible for an abnormally large number of secondary infections	Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections
Nosocomial	Healthcare- or hospital-associated infections	Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures
ACE2	Angiotensin-converting enzyme 2	Acts as a receptor for SARS-CoV, allowing entry into human cells

ARDS	Acute respiratory distress syndrome	Leakage of fluid into the lungs which inhibits respiration and leads to death
PPE	Personal protective equipment	Gowns, masks, gloves, and any other measures used to prevent spread between individuals

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To:	Birmingham Joe <joseph.birmingham@birminghamtech.com>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Prautzsch Frank <frank.prautzsch@birminghamtech.com>; Walsh, Brian (Intelligence) <Brian_Walsh@ssci.senate.gov>; Hibbeln Brian (b)(6) @comcast.net>; (b)(6) @comcast.net>; (b)(6) gmail.com>; (b)(6) @gmail.com>; Kuiken, Michael (Schumer) <Michael_Kuiken@schumer.senate.gov>
CC:	(b)(6) (b)(6) @state.gov>
Subject:	FW: A bit more or Covid-19 from Chinese researchers
Date:	2020/03/24 11:27:42
Priority:	Normal
Type:	Note

Hung pointed out that my last email failed to include the attachment that (b)(sent

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From (b)(6) (b)(6) @yahoo.com>
Date: Tuesday, 24 March 2020 at 14:28
To: Kirk McConnell <Kirk_McConnell@armed-services.senate.gov>
Subject: A bit more or Covid-19 from Chinese researchers

Sent from my iPad

Sender:	McConnell, Kirk (Armed Services) <Kirk_McConnell@armed-services.senate.gov>
Recipient:	Birmingham Joe <joseph.birmingham@birminghamtech.com>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Prautzsch Frank <frank.prautzsch@birminghamtech.com>; Walsh, Brian (Intelligence) <Brian_Walsh@ssci.senate.gov>; Hibbeln Brian @comcast.net>; (b)(5) @comcast.net>; Johnson, Ken <(b)(6) @gmail.com>; (b)(6) @gmail.com>; Kuiken, Michael (Schumer) <Michael_Kuiken@schumer.senate.gov>; (b)(6) (b)(6) @state.gov>
Sent Date:	2020/03/24 11:27:06
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The possible origins of 2019-nCoV coronavirus

Preprint · February 2020

DOI: 10.13140/RG.2.2.21799.29601

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The possible origins of 2019-nCoV coronavirus

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The 2019-nCoV coronavirus has caused an epidemic of 28,060 laboratory-confirmed infections in human including 564 deaths in China by February 6, 2020. Two descriptions of the virus published on Nature this week indicated that the genome sequences from patients were 96% or 89% identical to the Bat CoV ZC45 coronavirus originally found in *Rhinolophus affinis* [1,2]. It was critical to study where the pathogen came from and how it passed onto human.

An article published on The Lancet reported that 41 people in Wuhan were found to have the acute respiratory syndrome and 27 of them had contact with Huanan Seafood Market [3]. The 2019-nCoV was found in 33 out of 585 samples collected in the market after the outbreak. The market was suspicious to be the origin of the epidemic, and was shut down according to the rule of quarantine the source during an epidemic.

The bats carrying CoV ZC45 were originally found in Yunnan or Zhejiang province, both of which were more than 900 kilometers away from the seafood market. Bats were normally found to live in caves and trees. But the seafood market is in a densely-populated district of Wuhan, a metropolitan of ~15 million people. The probability was very low for the bats to fly to the market. According to municipal reports and the testimonies of 31 residents and 28 visitors, the bat was never a food source in the city, and no bat was traded in the market. There was possible natural recombination or intermediate host of the coronavirus, yet little proof has been reported.

Was there any other possible pathway? We screened the area around the seafood market and identified two laboratories conducting research on bat coronavirus. Within ~280 meters from the market, there was the Wuhan Center for Disease Control & Prevention (WHCDC) (Figure 1, from Baidu and Google maps). WHCDC hosted animals in laboratories for research purpose, one of which was specialized in pathogens collection and identification [4-6]. In one of their studies, 155 bats including *Rhinolophus affinis* were captured in Hubei province, and other 450 bats were captured in Zhejiang province [4]. The expert in collection was noted in the Author Contributions (JHT). Moreover, he was broadcasted for collecting viruses on nation-wide newspapers and websites in 2017 and 2019 [7,8]. He described that he was once by attacked by bats and the blood of a bat shot on his skin. He knew the extreme danger of the infection so he quarantined himself for 14 days [7]. In another accident, he quarantined himself again because bats peed on him. He was once thrilled for capturing a bat carrying a live tick [8].

Surgery was performed on the caged animals and the tissue samples were collected for DNA and RNA extraction and sequencing [4, 5]. The tissue samples and contaminated trashes were source of pathogens. They were only ~280 meters from the seafood market. The WHCDC was also adjacent to the Union Hospital (Figure 1, bottom) where the first group of doctors were infected during this epidemic. It is plausible that the virus leaked around and some of them contaminated the initial patients in this epidemic, though solid proofs are needed in future study.

The second laboratory was ~12 kilometers from the seafood market and belonged to Wuhan Institute of Virology, Chinese Academy of Sciences [1, 9, 10]. This laboratory reported that the Chinese horseshoe bats were natural reservoirs for the severe acute respiratory syndrome coronavirus (SARS-CoV) which caused the 2002-3 pandemic [9]. The principle investigator participated in a project which generated a chimeric virus using

the SARS-CoV reverse genetics system, and reported the potential for human emergence [10]. A direct speculation was that SARS-CoV or its derivative might leak from the laboratory.

In summary, somebody was entangled with the evolution of 2019-nCoV coronavirus. In addition to origins of natural recombination and intermediate host, the killer coronavirus probably originated from a laboratory in Wuhan. Safety level may need to be reinforced in high risk biohazardous laboratories. Regulations may be taken to relocate these laboratories far away from city center and other densely populated places.

Contributors

BX designed the comment and performed literature search. All authors performed data acquisition and analysis, collected documents, draw the figure, and wrote the papers.

Acknowledgements

This work is supported by the National Natural Science Foundation of China (11772133, 11372116).

Declaration of interests

All authors declare no competing interests.

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3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2019. https://doi.org/10.1016/S0140-6736(20)30183-5.
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Figure 1. The Huanan Seafood Market is close to the WHCDC (from Baidu and Google maps).

From:	Evaluation Only. Created with Aspose.HTML. Copyright 2013-2020 Aspose Pty Ltd.gt;
To:	Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>
Subject:	Fwd: Some Russian expert opinions on the "Wuhan virus"
Date:	2020/03/20 00:13:22
Priority:	Normal
Type:	Note

Bob — I'm sure you are swamped but thought there might be tidbits of information interesting for you here. Will send one other next. Kirk McConnell

Sent from my iPhone

Begin forwarded message:

From: (b)(6) "(b)(6) @state.gov>
Date: March 19, 2020 at 9:12:29 AM EDT
To: "McConnell, Kirk (Armed Services)" <Kirk_McConnell@armed-services.senate.gov>, "Walsh, Brian (Intelligence)" <Brian_Walsh@ssci.senate.gov>
Subject: RE: Some Russian expert opinions on the "Wuhan virus"

Thanks Kirk,

This is all very interesting. You should ask your contacts at State's H Bureau for copies of unclassified cables from 2018 [18-Beijing-138 and 18-Wuhan-38]. I tasked folks on my team to draft these cables and they have some good information from 2018 not in any of the general press.

On the artificial creation of the virus, I don't think the virus has to have been artificially created for it have come out of that lab. Simple "natural" recombinatory mixing taking place inside of host cells coupled with more than one novel coronavirus not listed in the literature could account for the difference noted in the virus structure – this is exactly the type of work on bat coronaviruses that was being done at the Wuhan Institute of Virology. It would also explain with there were two strains early on in China's infection cycle. International experts are looking to bebunk the idea that is was a weapons program, which is likely true, but that doesn't mean it wasn't "manmade" due to careless virology research and incompetence.

Best,

(b)(

From: McConnell, Kirk (Armed Services) <Kirk_McConnell@armed-services.senate.gov>
Sent: Thursday, March 19, 2020 12:16 AM
To: (b)(6) (b)(6) @state.gov>; Prautzsch Frank

<frank.prautzsch@birminghamtech.com>; Birmingham Joe
<joseph.birmingham@birminghamtech.com>; Walsh, Brian (Intelligence)
<Brian_Walsh@ssci.senate.gov>
Subject: Fwd: Some Russian expert opinions on the "Wuhan virus"

(b)(6) this material is from a longtime collaborator, an excellent analyst of Russian military-technical literature. He covers everything imaginable that's printed in Russia, in Russian.

Sent from my iPhone

Begin forwarded message:

From: (b)(6) @sprynet.com'(b)(6) @sprynet.com>
To: "McConnell, Kirk (Armed Services)" <Kirk_McConnell@armed-services.senate.gov>, "Peter Verburgt" (b)(6) @verizon.net>
Cc: "Potter, Jason (Armed Services)" <Jason_Potter@armed-services.senate.gov>, "Greene, Creighton (Armed Services)" <Creighton_Greene@armed-services.senate.gov>, "Hung Nguyen" (b)(6) @comcast.net>
Subject: Some Russian expert opinions on the "Wuhan virus"

Kirk,

Normally this subject is not under my purview, but I found the following selections quite intriguing and not generally discussed in the US. Perhaps you or Jason can pass them on to someone else on the SASC staff whose focus is BW and who can either quickly follow up on or debunk these Russian opinions?

1) "Unrecognized Genome: Could the novel coronavirus be artificially created in the lab?" That's the title of an investigative article published in the leading Russian daily Izvestia on February 4. See the following excerpts from the article:

"The large genome of the 'Chinese' coronavirus, its long incubation period, as well as the severe pulmonary edema caused by it, are factors that can be effectively used to create biological weapons, experts in the field of virology told *Izvestia*. Their assumptions are also supported by a 2015 scientific article in the leading edition of *Nature*, which talks about the risky experiments of Chinese scientists who created a hybrid version of bat coronavirus. However, other researchers who analyzed the pathogen genome did not find traces of artificial inclusions and accelerated evolution in it. *Izvestia* sorted out how justified the assumptions about the laboratory origin of 2019-nCoV could be…
"It's very difficult to understand something from the laid out genome," *Izvestia*'s interlocutor confirmed. - Civilian science does not yet have the ability to quickly determine something. Maybe some classified research is going on. Suspicions of misuse of the genome are partially supported by a 2015 scientific article in the journal *Nature*. It discusses a designed bat coronavirus that can infect human cells. The material was published in *Nature Medicine* on November 19, 2015 (see 1st attachment). Moreover, the 15 authors included 13 Americans and two Chinese scientists from the Wuhan Institute of Virology, located in the city from which the

spread of the 2019-nCoV virus began around the world...However, so far no expert has clear indications that the virus was created artificially."

2) The following is a remarkable report on February 17 from the official TV channel of the Russian MOD:

"Two Chinese biologists, Botao Xiao and Lei Xiao, conducted their own investigation into the causes of the spreading coronavirus epidemic. They came to the conclusion that the source of the disease for people was scientific laboratories located in Wuhan near the seafood market. This is stated in a **report** published by biologists .

It was previously believed that the first case of infection occurred on the market itself - from a bat to a person. However, according to Botao Xiao and Lei Xiao, there were no bats in the market at all, and in Wuhan there is no tradition to eat them. So the infection could not have occurred either through direct contact or by eating bats.

At the same time, literally 280 meters from the market there is a laboratory where experiments with bats are carried out - the Wuhan Center for Disease Control and Prevention. According to the biologists, there were two cases of contact with an infected bat - in one, a bat attacked an employee and left its blood on his skin, in the other, an infected animal urinated on him. It is noted that the employee, realizing the danger of the virus, arranged his own quarantine for 14 days. However, according to the biologists, these cases require additional research.

In addition, the report of the scientists noted that in Wuhan, 12 kilometers from the seafood market, there is a laboratory owned by the Wuhan Institute of Virology. It is reported that experiments were conducted there with the SARS-CoV virus, which caused an epidemic of SARS in 2002-2003 - bats are its carriers. According to the biologists, in the course of the experiments a new virus was obtained, based on the SARS-CoV genome and representing a danger to humans. It could break out of the laboratory.

Researchers note that their findings need further confirmation, but now you can make recommendations about the need to move biological laboratories from urban areas to uninhabited territories."

See the following link for the Chinese scientific report:
https://www.scribd.com/document/447056518/Originsof2019-NCoV-XiaoB-Res

3) Further fueling such suspicions is a TASS News Agency report on January 28 from its science section:
"The first analysis of the DNA structure of the new coronavirus, whose outbreak began in China last December, indicated that the causative agent of this disease arose from the so-called recombination of the RaTG13 virus, which infects bats, and some unknown coronavirus. With this, scientists designate a situation when two viruses

simultaneously infect the same organism, which in some cases leads to the exchange of DNA or RNA, as is the case with coronaviruses that encode some parts of their genome. In the case of the 2019-nCoV virus, Chinese geneticists suggested that such exchanges of genetic material gave it the ability to spread from person to person, as well as a number of other unique features.

Molecular biologists from the University of Athens have doubted this hypothesis by comparing the mutation sets in the 2019-nCoV and RaTG13 genomes (see 2nd attachment). On the one hand, this analysis confirmed that the new virus is indeed closely associated with pathogens that infect bats that live in Yunnan, but at the same time it revealed a number of unique features in the structure of the virus RNA that are incompatible with the theory of recent recombination.

In particular, scientists did not find any hints that the 2019-nCoV genome was a mosaic of RNA fragments of different viruses, and also discovered several unique short sections, the structure of which was unlike the genetic material characteristic of other viruses related to a number of relatives of SARS, the causative agent of SARS 2003, and at the same time affecting bats. Scientists do not yet know how these sequences appeared in the 2019-nCoV RNA, but their existence clearly indicates that the virus could not have arisen as a result of recombination."

4) Then, in early March, mainstream Russian media gave a lot of credence to a Chinese scientific paper postulating that there are actually two different strains or subtypes of the "Wuhan coronavirus" (S-type and L-type). The latter is more virulent and prevalent than the first (see 3rd attachment). A report from *Svobodnaya Pressa* asserted that the S-type is "natural," whereas the L-type is "manmade" or "experimental material" that escaped from the lab.

5) Finally, official Russian numbers on coronavirus cases are wide panned as severe underestimations, and Russian oligarch Deripaska (of the Muller report fame) bluntly warned the Putin government that Russia could face a collapse worse than that of the Soviet Union in 1991 if its government doesn't get its act together soon (see link below):

https://www.themoscowtimes.com/2020/03/14/russia-should-quarantine-itself-to-halt-coronavirus-billionaire-deripaska-says-a69623

It's not to be ruled out that Deripaska got access to some privilege info that couldn't make its way to Putin.

Sender:	McConnell, Kirk (Armed Services) <Kirk_McConnell@armed-services.senate.gov>
Recipient:	Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>
Sent Date:	2020/03/20 00:13:13
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From:	Evaluation Only. Created with Aspose.HTML. Copyright 2013-2020 Aspose Pty Ltd.gt;
To:	(b)(6) (b)(6) @state.gov>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Prautzsch Frank <frank.prautzsch@birminghamtech.com>; Birmingham Joe <joseph.birmingham@birminghamtech.com>
Subject:	Fwd: Some Russian expert opinions on the "Wuhan virus"
Date:	2020/03/21 16:48:29
Priority:	Normal
Type:	Note

Sent from my iPhone

Begin forwarded message:

From: (b)(6) @comcast.net
Date: March 21, 2020 at 4:23:38 PM EDT
To: Kirk_McConnell@armed-services.senate.gov, Hung Nguyen (b)(6) @sprynet.com>
Subject: Re: Fw: Some Russian expert opinions on the "Wuhan virus"
Reply-To (b)(6) @comcast.net

Kirk--Thank your for the feedback from (b)(6) at State. Just an update on his statement that " there were two strains early on in China's infection cycle." It appears that the case for the existence of two different strains of the coronavirus (S- and L-types, the latter more virulent than the former?) propagating far beyond Wuhan is getting stronger, with more recent cases. For example, this could best explain the mystery reported by the NYT that "In a few cases, patients again tested positive for the virus after they were no longer ill."
https://www.nytimes.com/2020/02/29/health/coronavirus-reinfection.html
And such cases of double or recurrent infections were reported not only in China and Japan but also in the US:
"Genetic analysis of a man in the US who tested positive on January 21, also showed it is possible to be infected with both types."
https://www.telegraph.co.uk/science/2020/03/04/coronavirus-has-mutated-aggressive-disease-say-scientists/
A US virology expert also acknowledged the possible existence of 2 different strains, but was reluctant to commit to that hypothesis right away:
"Stanley Perlman, a coronavirus expert at the University of Iowa told Global News 'time will tell' if there are two different strains, but that right now it " does seem like there are two variations of the virus. It seems like there's quite a few mutations so you could interpret it as mutations or two separate entries into human populations ," he said. "I think that it's just really early to know."
(https://globalnews.ca/news/6634604/coronavirus-two-strains/) Bottom line, it appears to me the USG needs to take into account the possible existence of 2 different strains of

the coronavirus because of the following practical implications: (1) a vaccine must be developed to be effective against both types , (2) such a hypothesis could well explain the cryptic remark by Mikhail Kovalchuk, president of the Kurchatov Institute, that " the coronavirus represents a completely misunderstood danger " (see my e-mail on the 19th), and (3) the recent conclusion by US geneticists from Scripps that the coronavirus is "natural" in origin could be, at best, premature (see attached) because they may be looking at only the "S-type" of the bat coronaviruses. I'm very interested in (b)(6) (b)(6) reactions to my thoughts here, if you think these make sense.

-----Original Message-----
From: "McConnell, Kirk (Armed Services)"
Sent: Mar 19, 2020 10:10 PM
To: "Nguyen, Hung"
Subject: Fwd: Some Russian expert opinions on the "Wuhan virus"
Sent from my iPhone
Begin forwarded message:
From (b)(6) (b)(6) @state.gov>
Date: March 19, 2020 at 9:12:29 AM EDT
To: "McConnell, Kirk (Armed Services)" <Kirk_McConnell@armed-services.senate.gov>, "Walsh, Brian (Intelligence)" < Brian_Walsh@ssci.senate.gov>
Subject: RE: Some Russian expert opinions on the "Wuhan virus"
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Best,

(b)(6)

Sender:	McConnell, Kirk (Armed Services) <Kirk_McConnell@armed-services.senate.gov>
Recipient:	(b)(6) (b)(6) @state.gov>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Prautzsch Frank <frank.prautzsch@birminghamtech.com>;

	Birmingham Joe <joseph.birmingham@birminghamtech.com>
Sent Date:	2020/03/21 16:48:09
Delivered Date:	2020/03/21 16:48:29

The proximal origin of SARS-CoV-2

To the Editor — Since the first reports of novel pneumonia (COVID-19) in Wuhan, Hubei province, China[1,2], there has been considerable discussion on the origin of the causative virus, SARS-CoV-2[3] (also referred to as HCoV-19)[4]. Infections with SARS-CoV-2 are now widespread, and as of 11 March 2020, 121,564 cases have been confirmed in more than 110 countries, with 4,373 deaths[5].

SARS-CoV-2 is the seventh coronavirus known to infect humans; SARS-CoV, MERS-CoV and SARS-CoV-2 can cause severe disease, whereas HKU1, NL63, OC43 and 229E are associated with mild symptoms[6]. Here we review what can be deduced about the origin of SARS-CoV-2 from comparative analysis of genomic data. We offer a perspective on the notable features of the SARS-CoV-2 genome and discuss scenarios by which they could have arisen. Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus.

Notable features of the SARS-CoV-2 genome

Our comparison of alpha- and betacoronaviruses identifies two notable genomic features of SARS-CoV-2: (i) on the basis of structural studies[7–9] and biochemical experiments[1,9,10], SARS-CoV-2 appears to be optimized for binding to the human receptor ACE2; and (ii) the spike protein of SARS-CoV-2 has a functional polybasic (furin) cleavage site at the S1–S2 boundary through the insertion of 12 nucleotides[8], which additionally led to the predicted acquisition of three O-linked glycans around the site.

1. Mutations in the receptor-binding domain of SARS-CoV-2. The receptor-binding domain (RBD) in the spike protein is the most variable part of the coronavirus genome[1,2]. Six RBD amino acids have been shown to be critical for binding to ACE2 receptors and for determining the host range of SARS-CoV-like viruses[7]. With coordinates based on SARS-CoV, they are Y442, L472, N479, D480, T487 and Y4911, which correspond to L455, F486, Q493, S494, N501 and Y505 in SARS-CoV-2[7]. Five of these six residues differ between SARS-CoV-2 and SARS-CoV (Fig. 1a). On the basis of structural studies[7–9] and biochemical experiments[1,9,10], SARS-CoV-2 seems to have an RBD that binds with high affinity to ACE2 from humans, ferrets, cats and other species with high receptor homology[7].

While the analyses above suggest that SARS-CoV-2 may bind human ACE2 with high affinity, computational analyses predict that the interaction is not ideal[7] and that the RBD sequence is different from those shown in SARS-CoV to be optimal for receptor binding[7,11]. Thus, the high-affinity binding of the SARS-CoV-2 spike protein to human ACE2 is most likely the result of natural selection on a human or human-like ACE2 that permits another optimal binding solution to arise. This is strong evidence that SARS-CoV-2 is not the product of purposeful manipulation.

2. Polybasic furin cleavage site and O-linked glycans. The second notable feature of SARS-CoV-2 is a polybasic cleavage site (RRAR) at the junction of S1 and S2, the two subunits of the spike[8] (Fig. 1b). This allows effective cleavage by furin and other proteases and has a role in determining viral infectivity and host range[12]. In addition, a leading proline is also inserted at this site in SARS-CoV-2; thus, the inserted sequence is PRRA (Fig. 1b). The turn created by the proline is predicted to result in the addition of O-linked glycans to S673, T678 and S686, which flank the cleavage site and are unique to SARS-CoV-2 (Fig. 1b). Polybasic cleavage sites have not been observed in related 'lineage B' betacoronaviruses, although other human betacoronaviruses, including HKU1 (lineage A), have those sites and predicted O-linked glycans[13]. Given the level of genetic variation in the spike, it is likely that SARS-CoV-2-like viruses with partial or full polybasic cleavage sites will be discovered in other species.

The functional consequence of the polybasic cleavage site in SARS-CoV-2 is unknown, and it will be important to determine its impact on transmissibility and pathogenesis in animal models. Experiments with SARS-CoV have shown that insertion of a furin cleavage site at the S1–S2 junction enhances cell–cell fusion without affecting viral entry[14]. In addition, efficient cleavage of the MERS-CoV spike enables MERS-like coronaviruses from bats to infect human cells[15]. In avian influenza viruses, rapid replication and transmission in highly dense chicken populations selects for the acquisition of polybasic cleavage sites in the hemagglutinin (HA) protein[16], which serves a function similar to that of the coronavirus spike protein. Acquisition of polybasic cleavage sites in HA, by insertion or recombination, converts low-pathogenicity avian influenza viruses into highly pathogenic forms[16]. The acquisition of polybasic cleavage sites by HA has also been observed after repeated passage in cell culture or through animals[17].

The function of the predicted O-linked glycans is unclear, but they could create a 'mucin-like domain' that shields epitopes or key residues on the SARS-CoV-2 spike protein[18]. Several viruses utilize mucin-like domains as glycan shields involved immunoevasion[18]. Although prediction of O-linked glycosylation is robust, experimental studies are needed to determine if these sites are used in SARS-CoV-2.

Theories of SARS-CoV-2 origins

It is improbable that SARS-CoV-2 emerged through laboratory manipulation of a related SARS-CoV-like coronavirus. As noted above, the RBD of SARS-CoV-2 is optimized for binding to human ACE2 with an efficient solution different from those previously predicted[7,11]. Furthermore, if genetic manipulation had been performed, one of the several reverse-genetic systems available for betacoronaviruses would probably have been used[19]. However, the genetic data irrefutably show that SARS-CoV-2 is not derived from any previously used virus backbone[20]. Instead, we propose two scenarios that can plausibly explain the origin of SARS-CoV-2: (i) natural selection in an animal host before zoonotic transfer; and (ii) natural selection in humans following zoonotic transfer. We also discuss whether selection during passage could have given rise to SARS-CoV-2.

1. Natural selection in an animal host before zoonotic transfer. As many early cases of COVID-19 were linked to the Huanan market in Wuhan[1,2], it is possible that an animal source was present at this location. Given the similarity of SARS-CoV-2 to bat SARS-CoV-like coronaviruses[2], it is likely that bats serve as reservoir hosts for its progenitor. Although RaTG13, sampled from a *Rhinolophus affinis* bat[1], is ~96% identical overall to SARS-CoV-2, its spike diverges in the RBD, which suggests that it may not bind efficiently to human ACE2[7] (Fig. 1a).

Malayan pangolins (*Manis javanica*) illegally imported into Guangdong province contain coronaviruses similar to SARS-CoV-2[21]. Although the RaTG13 bat virus remains the closest to SARS-CoV-2 across the

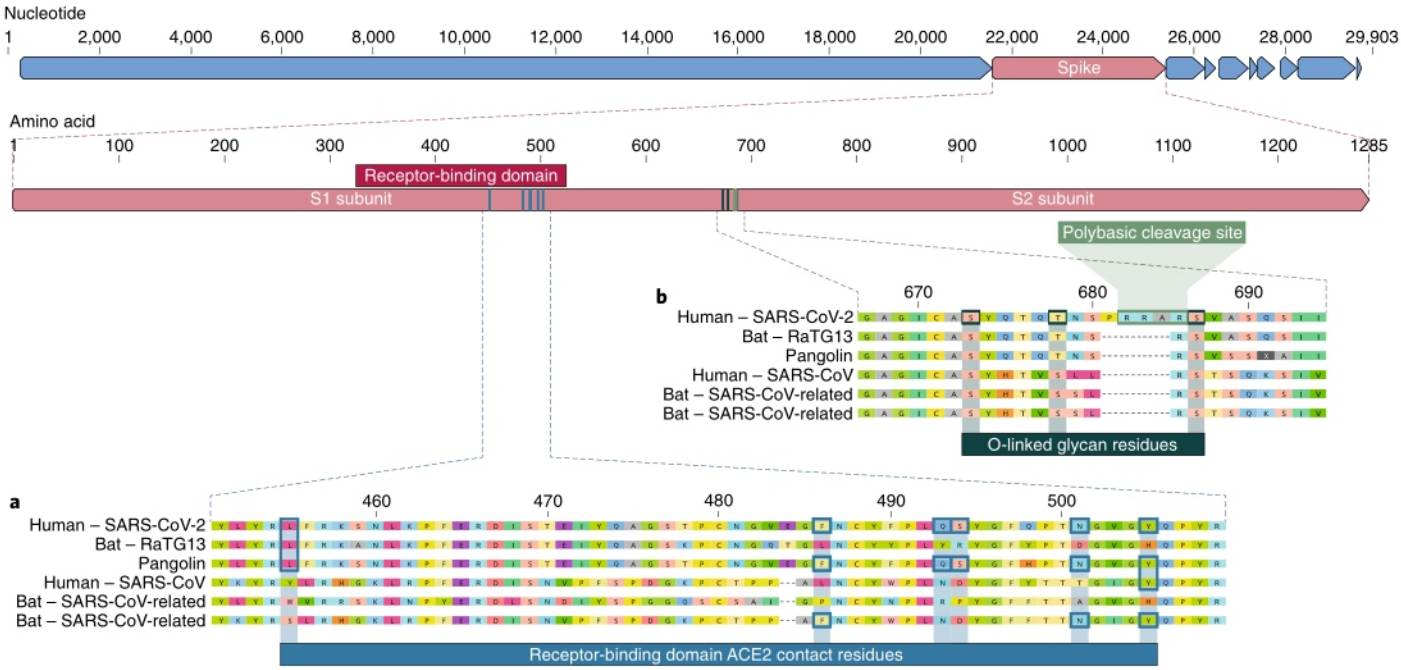

Fig. 1 | Features of the spike protein in human SARS-CoV-2 and related coronaviruses. a, Mutations in contact residues of the SARS-CoV-2 spike protein. The spike protein of SARS-CoV-2 (red bar at top) was aligned against the most closely related SARS-CoV-like coronaviruses and SARS-CoV itself. Key residues in the spike protein that make contact to the ACE2 receptor are marked with blue boxes in both SARS-CoV-2 and related viruses, including SARS-CoV (Urbani strain). **b**, Acquisition of polybasic cleavage site and O-linked glycans. Both the polybasic cleavage site and the three adjacent predicted O-linked glycans are unique to SARS-CoV-2 and were not previously seen in lineage B betacoronaviruses. Sequences shown are from NCBI GenBank, accession codes MN908947, MN996532, AY278741, KY417146 and MK211376. The pangolin coronavirus sequences are a consensus generated from SRR10168377 and SRR10168378 (NCBI BioProject PRJNA573298)[29,30].

genome[1], some pangolin coronaviruses exhibit strong similarity to SARS-CoV-2 in the RBD, including all six key RBD residues[21] (Fig. 1). This clearly shows that the SARS-CoV-2 spike protein optimized for binding to human-like ACE2 is the result of natural selection.

Neither the bat betacoronaviruses nor the pangolin betacoronaviruses sampled thus far have polybasic cleavage sites. Although no animal coronavirus has been identified that is sufficiently similar to have served as the direct progenitor of SARS-CoV-2, the diversity of coronaviruses in bats and other species is massively undersampled. Mutations, insertions and deletions can occur near the S1–S2 junction of coronaviruses[22], which shows that the polybasic cleavage site can arise by a natural evolutionary process. For a precursor virus to acquire both the polybasic cleavage site and mutations in the spike protein suitable for binding to human ACE2, an animal host would probably have to have a high population density (to allow natural selection to proceed efficiently) and an ACE2-encoding gene that is similar to the human ortholog.

2. Natural selection in humans following zoonotic transfer. It is possible that a progenitor of SARS-CoV-2 jumped into humans, acquiring the genomic features described above through adaptation during undetected human-to-human transmission. Once acquired, these adaptations would enable the pandemic to take off and produce a sufficiently large cluster of cases to trigger the surveillance system that detected it[1,2].

All SARS-CoV-2 genomes sequenced so far have the genomic features described above and are thus derived from a common ancestor that had them too. The presence in pangolins of an RBD very similar to that of SARS-CoV-2 means that we can infer this was also probably in the virus that jumped to humans. This leaves the insertion of polybasic cleavage site to occur during human-to-human transmission.

Estimates of the timing of the most recent common ancestor of SARS-CoV-2 made with current sequence data point to emergence of the virus in late November 2019 to early December 2019[23], compatible with the earliest retrospectively confirmed cases[24]. Hence, this scenario presumes a period of unrecognized transmission in humans between the initial zoonotic event and the acquisition of the polybasic cleavage site. Sufficient opportunity could have arisen if there had been many prior zoonotic events that produced short chains of human-to-human transmission over an extended period. This is essentially the situation for MERS-CoV, for which all human cases are the result of repeated jumps of the virus from dromedary camels, producing single infections or short transmission chains that eventually resolve, with no adaptation to sustained transmission[25].

Studies of banked human samples could provide information on whether such cryptic spread has occurred. Retrospective serological studies could also be informative, and a few such studies have been conducted showing low-level exposures to SARS-CoV-like coronaviruses in certain areas of China[26]. Critically, however, these studies could not have distinguished whether exposures were due to prior infections with SARS-CoV, SARS-CoV-2 or other SARS-CoV-like coronaviruses. Further serological studies should be conducted to determine the extent of prior human exposure to SARS-CoV-2.

3. Selection during passage. Basic research involving passage of bat SARS-CoV-like coronaviruses in cell culture and/or animal models has been ongoing for many years in biosafety level 2 laboratories across the world[27], and there are documented instances

of laboratory escapes of SARS-CoV[28]. We must therefore examine the possibility of an inadvertent laboratory release of SARS-CoV-2.

In theory, it is possible that SARS-CoV-2 acquired RBD mutations (Fig. 1a) during adaptation to passage in cell culture, as has been observed in studies of SARS-CoV[11]. The finding of SARS-CoV-like coronaviruses from pangolins with nearly identical RBDs, however, provides a much stronger and more parsimonious explanation of how SARS-CoV-2 acquired these via recombination or mutation[19].

The acquisition of both the polybasic cleavage site and predicted O-linked glycans also argues against culture-based scenarios. New polybasic cleavage sites have been observed only after prolonged passage of low-pathogenicity avian influenza virus in vitro or in vivo[17]. Furthermore, a hypothetical generation of SARS-CoV-2 by cell culture or animal passage would have required prior isolation of a progenitor virus with very high genetic similarity, which has not been described. Subsequent generation of a polybasic cleavage site would have then required repeated passage in cell culture or animals with ACE2 receptors similar to those of humans, but such work has also not previously been described. Finally, the generation of the predicted O-linked glycans is also unlikely to have occurred due to cell-culture passage, as such features suggest the involvement of an immune system[18].

Conclusions

In the midst of the global COVID-19 public-health emergency, it is reasonable to wonder why the origins of the pandemic matter. Detailed understanding of how an animal virus jumped species boundaries to infect humans so productively will help in the prevention of future zoonotic events. For example, if SARS-CoV-2 pre-adapted in another animal species, then there is the risk of future re-emergence events. In contrast, if the adaptive process occurred in humans, then even if repeated zoonotic transfers occur, they are unlikely to take off without the same series of mutations. In addition, identifying the closest viral relatives of SARS-CoV-2 circulating in animals will greatly assist studies of viral function. Indeed, the availability of the RaTG13 bat sequence helped reveal key RBD mutations and the polybasic cleavage site.

The genomic features described here may explain in part the infectiousness and transmissibility of SARS-CoV-2 in humans. Although the evidence shows that SARS-CoV-2 is not a purposefully manipulated virus, it is currently impossible to prove or disprove the other theories of its origin described here. However, since we observed all notable SARS-CoV-2 features, including the optimized RBD and polybasic cleavage site, in related coronaviruses in nature, we do not believe that any type of laboratory-based scenario is plausible.

More scientific data could swing the balance of evidence to favor one hypothesis over another. Obtaining related viral sequences from animal sources would be the most definitive way of revealing viral origins. For example, a future observation of an intermediate or fully formed polybasic cleavage site in a SARS-CoV-2-like virus from animals would lend even further support to the natural-selection hypotheses. It would also be helpful to obtain more genetic and functional data about SARS-CoV-2, including animal studies. The identification of a potential intermediate host of SARS-CoV-2, as well as sequencing of the virus from very early cases, would similarly be highly informative. Irrespective of the exact mechanisms by which SARS-CoV-2 originated via natural selection, the ongoing surveillance of pneumonia in humans and other animals is clearly of utmost importance. ❐

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Competing interests

R.F.G. is co-founder of Zalgen Labs, a biotechnology company that develops countermeasures to emerging viruses.

To:	(FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a02e128c60f4a7195532a1545af9556-Walker, Rob <Robert.Walker@hhs.gov>; Redd, John (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>; Yeskey, Kevin (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6fe6cf13518445fd9c3a1c254e166b3f-Yeskey, Kev <Kevin.Yeskey@hhs.gov>; haszsle; Hamel, Joseph (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=96d2c1602dfa45e5a5e21452a098b96d-Hamel, Jose <Joseph.Hamel@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) (Bryan.Shuy@hhs.gov) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>
Subject:	FW: Remdesivir: URGENT
Date:	2020/04/30 21:20:24
Priority:	Normal
Type:	Note

FYSA cleared use for both severe (invasive mechanical ventilation or eccmo)10 day course a moderate (hospitalized without mecha. Vent or eccmo)

From: Shah, Anand <Anand.Shah@fda.hhs.gov>
Sent: Thursday, April 30, 2020 8:30 PM
To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Woodcock, Janet (FDA/CDER) <Janet.Woodcock@fda.hhs.gov>; Cavazzoni, Patrizia (FDA/CDER) <Patrizia.Cavazzoni@fda.hhs.gov>; Amin, Stacy (FDA/OC) <Stacy.Amin@fda.hhs.gov>; Beers, Donald (FDA/OC) <Donald.Beers@fda.hhs.gov>
Subject: RE: Remdesivir: URGENT

PRE-DECISIONAL, CONFIDENTIAL

Dear Dr Kadlec –

Attached are the memo (draft) and fact sheets.

Thank you

Anand

From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Thursday, April 30, 2020 7:00 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>

Cc: Shah, Anand <Anand.Shah@fda.hhs.gov>; Yeskey, Kevin (OS) <Kevin.Yeskey@hhs.gov>; Redd, John T (OS) <John.Redd@hhs.gov>; Hamel, Joseph (OS) <Joseph.Hamel@hhs.gov>; Adams, Steven A (CDC) <saa1@cdc.gov>; Disbrow, Gary (OS) <Gary.Disbrow@hhs.gov>; Walker, Robert (OS) <Robert.Walker@hhs.gov>; Shuy, Bryan (OS) <Bryan.Shuy@hhs.gov>; Austin, Meredith (OS) <Meredith.Austin@hhs.gov>
Subject: Re: Remdesivir: URGENT

Dr Woodcock for the purposes of your request the ASPR (me) will be the ultimate Allocator. Given that the USG is the ultimate allocator we may suggest altering the formula of allocating to determine pro rata distribution and maintain some Amount as a reserve to allocate drug based on the JHU database on intensity of outbreak.

We intend to refine and finalize the process tomorrow.
If you can please share the draft EUA now so we can understand the criteria for potential use that would be extremely helpful. Thank you.
Best. Bob
Sent from my iPhone

On Apr 30, 2020, at 5:36 PM, Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>wrote:

Janet will
Respond with a definitive POC here shortly. Agree I. Principle with the approach outlined. Just want to make sure that what is outlined can be supported operationally.
Best. Bob

Sent from my iPhone

On Apr 30, 2020, at 4:37 PM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>wrote:

Dr. Kadlec, we would like to get the EUA for Gilead's remdesivir done by tomorrow. The final sticking point is the distribution. They have consistently advocated for having the USG oversee the allocation, because they are concerned that there could be a shortage. At the moment, we believe there is adequate supply. They propose that they will distribute most of the drug (ie starting on Saturday) through their distributor Amerisource, but that they will use a formula to allocate to the states based on the Johns Hopkins database of intensity of outbreak, and just allocate proportionately. They further propose that this be broken down to the county level, but I don't believe this is currently necessary because there is enough supply. We need to state who in the USG will "direct" this allocation. I believe it should be ASPR. The government does not need to get immediately involved in distribution since the drug would need to be donated to then accepted by the stockpile etc.

If you agree to be this authority, we need a POC to give to Gilead from USG who would "direct" this allocation. Obviously we can refine this going forward, but we need to agree to language tonight if we are to get it done tomorrow. jw

Gilead proposes the following language relating to distribution in the Conditions of Approval for the EUA. Please coordinate with FDA/ASPR and FEMA to ensure alignment, in particular, Anand Shah, M.D., Deputy Commissioner for Medical and Scientific Affairs (Anand.Shah@fda.hhs.gov).

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Emergency Use Authorization (EUA) for remdesivir, an unapproved product
Center for Drug Evaluation and Research (CDER) Review

Identifying Information

Application Type (EUA or Pre-EUA) If EUA, designate whether pre-event or intra-event EUA request.	EUA
EUA Application Number(s)[1]	46
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Gilead Sciences, Inc. Attention: (b)(6) (b)(6) 333 Lakeside Drive Foster City, CA 94404 (b)(6)
Manufacturer, if different from Sponsor	
Submission Date(s)	April 16, 2020
Receipt Date(s)	April 16, 2020
OND Division / Office	Division of Antivirals (DAV)/Office of Infectious Diseases (OID)
Reviewer Name(s)/Discipline(s)	Kirk Chan-Tack, MD/Clinical Reviewer Adam Sherwat, MD/Clinical Team Leader (TL) Eric Donaldson, PhD/Virology Reviewer Jules O'Rear, PhD/Virology TL Mario Sampson, PharmD/Clinical Pharmacology (C/P) Reviewer Vikram Arya, PhD, FCP/C/P TL John Dubinion, PhD/Pharmacology/Toxicology (P/T) Reviewer Hanan Ghantous, PhD, DABT/P/T TL Erika Englund, PhD/CMC TL Daniel Rubin, PhD/Statistics Reviewer Thamban Valappil, PhD/Statistics TL Jeff Murray, MD, MPH/Deputry Director Debra Birnkrant, MD/Director John Farley, MD, MPH/Director (Acting)/OID
Integrated Review Completion Date	N/A
Proprietary Name	N/A
Established Name/Other names used during development	Remdesivir (RDV)
Dosage Forms/Strengths	Lyophilized formulation for injection, 100 mg Solution formulation for injection, 5 mg/mL

[1] If a Pre-EUA is in existence at the time of the EUA request submission and has been assigned an EUA number, the EUA request should use the same EUA number and electronic archive file.

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From:	Puesan, Cesar (HHS/OS/IOS) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=1704B662180D4631B7B64CB17DE301CD-PUESAN JUAR <Cesar.Puesan@hhs.gov>
To:	(b)(6) (OS/IOS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c145629cc8ac4858bf1f0ce5dd0461dc-(b)(6) (b)(6) @HHS.GOV>
CC:	Harrison, Brian (HHS/IOS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d145efc9c35c4865aca6e9d47786b204-Harrison, B <Brian.Harrison@hhs.gov>; Mango, Paul (HHS/IOS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1d8863b643654b1aad9a38c952af613e-Mango, Paul <Paul.Mango@hhs.gov>; Stecker, Judy (OS/IOS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0280b227911b40b6b30a81b8574ede6b-Stecker, Ju <Judy.Stecker@hhs.gov>; Bird, Catherine (OS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bb9d9180497c49c4a06a0dd1f6043dc7-Bird, Cathe <Catherine.Bird@hhs.gov>
Subject:	E-book Materials for Monday May 4
Date:	2020/05/01 18:20:15
Priority:	Normal
Type:	Note

Sir,

Attached are:

1. Table of Contents
2. TAB A Monday's Agenda
3. TAB B: Meeting with Jared Kushner on Healthcare Legislative Update
4. TAB C: Reoccurring Meeting with NIH Director, Dr. Francis Collins
5. TAB D: NextGen Briefing
6. TAB E: ASPR COVID-19 Top Highlights
7. TAB F: FEMA Senior Leadership Brief
8. TAB G: White House Task Force Materials (*Forthcoming*)
9. TAB H: *INFO ONLY:* ASPR COVID-19 Materials
10. TAB I: *INFO ONLY:* COVID-19 Talking Points
11. TAB J: *INFO ONLY:* Secretary's Regulation Report
12. TAB K: *INFO ONLY:* Correspondence Report
13. TAB L: *INFO ONLY:* ORR/ UAC Dashboard

Please note the following:

- All the attached materials will be printed in a binder and in your limo tomorrow morning.

Cesar Puesan
Briefing Book Coordinator
Immediate Office of the Secretary
U.S. Department of Health & Human Services
Mobile: (b)(6)

Sender:	Puesan, Cesar (HHS/OS/IOS) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=1704B662180D4631B7B64CB17DE301CD-PUESAN JUAR <Cesar.Puesan@hhs.gov>
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Sent Date:	2020/05/01 18:20:07
Delivered Date:	2020/05/01 18:20:15

Monday, May 5, 2020

TAB A	**Schedule for Monday**
TAB B	**Meeting with Jared Kushner on Healthcare Legislative Update**
TAB C	**Reoccurring Meeting with NIH Director, Dr. Francis Collins**
TAB D	**NextGen Briefing**
TAB E	**ASPR COVID-19 Top Highlights**
TAB F	**FEMA Senior Leadership Brief**
TAB G	**White House Task Force Materials (*Materials Forthcoming*)**
TAB H	**INFO ONLY: COVID-19 Materials** **From: ASPR**
TAB I	**COVID-19 Talking Points** **From: ASPA**
TAB J	**INFO ONLY: Secretary's Regulatory Report** **From: Exec Sec**
TAB K	**INFO ONLY: Correspondence Report** **From: ODRM**
TAB L	**INFO ONLY: ORR / UAC Dashboard** **From: ORR**

Monday, May 4, 2020

Weather Forecast:
Washington, D.C.: Cloudy HIGH 57°F LOW 44°F

7:30 A.M.	Pick up by OIG Protective Detail **Depart to Humphrey Building**
8:15 A.M.	**Arrive at Humphrey Building**
8:15 A.M. -8:45 A.M.	Daily Meeting with CoS and DCoS Location: 615-F
8:45 A.M. -9:00 A.M.	Meeting with Jim Parker Location: 615-F
9:00 A.M. -9:30 A.M.	Pre Brief for Kushner Healthcare Legislative Update Meeting Call: (b)(6) Location: 615-F
9:30 A.M.	**Depart to The White House**
10:00 A.M.	**Arrive at The White House**
10:00 A.M. -10:45 A.M.	Meeting with Jared Kushner on Healthcare Legislative Update Location: WHSR – Executive Room
10:45 A.M. -11:15 A.M.	HOLD
11:15 A.M. -11:45 A.M.	Call with NIH Director, Dr. Francis Collins Call: (b)(6) Location: TBC
11:45 A.M. -12:15 P.M.	HOLD
12:15 P.M. -12:45 P.M.	Policy Time Location: TBC
1:00 P.M. -1:30 P.M.	NextGen Briefing Location: WW 120
1:30 P.M. -2:30 P.M.	**LUNCH TIME** Location:: EEOB – TBC
2:30 P.M. -3:00 P.M.	HOLD
3:00 P.M. -4:00 P.M.	WH Task Force Meeting Location: Situation Room

DATE: May 1, 2020

TO: The Secretary

THROUGH: Paul Mango, Deputy Chief of Staff

FROM: Jared Kushner's Office

SUBJECT: Meeting with Jared Kushner –BRIEFING MEMO

Details:
Date: Monday, May 4, 2020
Location: Jared's Office White House
Call: Yes/No

Legislative Proposals for Consideration:

Increase Market Competition & Reduce Development of Monopolies That Drive Up Costs & Healthcare Provider Consolidation

Require Full Price Transparency:
Codify the CMS requirement that hospitals and insurance companies provide consumers with clear and accessible information about the price of all services making it easier to compare prices and quality across the health care system as well as mitigating surprise or balance billing.

Eliminate Surprise or Balance Billing for Patients:
American families deserve to be protected against the burden of costly, surprise bills when their loved ones receive medical care, especially those suffering from the effects of the COVID-19 pandemic. Require health care providers, before scheduling care, to provide patients with information about services that will be delivered by out of network providers and what related costs that may bring.

Level the Playing Field Among Providers In Different Sites of Care:
Medicare payments and policies should encourage competition and a diversity of choices for patients to access care and should not provide higher payments to providers for the same service. Codify CMS proposals to put providers on a level payment playing field.

- Remove the existing law that "grandfathers" certain hospital-owned off-campus outpatient departments that allows them to be paid more by Medicare than physician offices for services (such as clinic visits) that are performed in both settings.
- Equalize payments, to the extent possible, for surgeries performed in hospital outpatient departments and ambulatory surgical centers.
- Remove the limitations placed on Physician Owned Hospitals (POHs) preventing these providers from increasing their capacity to see more patients.

- Ensure taxpayers are not paying extra for discounted drugs. If a hospital gets the federal 340b drug discount, they should not be reimbursed for drugs at the traditional Medicare rate. Any savings from this change should be directed to safety net hospitals with demonstrated services to the uninsured.

Pay Providers for Quality and Value

Hospital Value-Based Care:

- Require that hospitals that do not have at least 50% of their total Medicare revenue in risk based arrangements or participation in value based models (Next-Gen/Direct Contracting, etc) and maintain quality outcomes, such as infection control, within the next three years to return 20% of statutorily mandated coronavirus relief. Recognizing the unique situation and role that rural hospitals play in these circumstances, these provisions would not apply to rural hospitals.
- Consolidate existing quality programs to one quality program for hospitals with no more than 5 key metrics, including infection control and integrating the measurement of patient value via a Net Promoter Score.

Driving Savings and Value in Medicare

- Make permanent all flexibilities given to Medicare Advantage (MA) plans as part of the MA Value-Based Insurance Design (VBID) Model.
- Simplify Medicare Advantage risk adjustment to reduce plan burden and improve accuracy of patient health status.
- Redesign Stars measures so that they align and reflect hospital quality.
- Modify the Part D benefit to require plans to manage risk in the catastrophic phase, and create a true out-of-pocket cap for Medicare Part D beneficiaries.
- Allow ambulance suppliers to transport patients to alternative destinations and provide treatment in place as outlined in the CMMI ET3 model and currently allowed per the Public Health Emergency regulations.
- After a multi-year test of the Direct Contracting model (as announced in December 2019), require the program to be provided on a nationwide basis if the test indicated cost savings and no impact on quality of care or cost neutrality and a demonstrable improvement in quality of care.
- Increase the number of regions for Primary Care First model so that at least 50 percent of the country is paid under this value based arrangement that incentives and rewards high quality primary care.

Improving Kidney Care in the United States:

- Require that by 2026, nephrologists and/or dialysis providers to take full-risk Medicare payments for total annual medical costs for patients with chronic kidney disease in order to ensure that those patients have access to high quality, coordinated care.
- Require CMS to create nationwide payment incentives to encourage the use of in-home dialysis and to encourage kidney transplantation by 2025.
- To improve kidney care, ensure appropriate incentives for in-home r dialysis.

- Waive requirements to allow dialysis facilities to provide service to its patients in the nursing home or skilled nursing facility.

Modernize Government Programs to Meet Evolving Needs of Patients and Providers

Enhance Telehealth Capability and Reach:

New technologies are emerging that have strong promise to address access to care issues, particularly in rural communities. CMS is modernizing the Medicare program so that beneficiaries can take advantage of the latest technology and treatments. Continue changes to telehealth CMS made during emergency declaration in a budget neutral manner and reduce or remove barriers on Medicare payment for telehealth services, including:

- Removing the limitations on which practitioners can be paid for furnishing services via telehealth;
- Removing the geographic restrictions on the originating site of care, allowing patients to receive telehealth services from their homes;
  Remove barriers to telehealth services in rural parts of the country including new authority for Rural Health Clinics (RHCs), Federally Qualified Health Centers (FQHCs) to provide telehealth benefits in Medicare Fee-for-Service, and;
- Reduce restrictions for hospitals and Critical Access Hospitals (CAHs), and requirements for face to face visits.

Modernize the Medicaid Program:

- Require every state to develop a plan and participate in a model to deliver value based care to beneficiaries dually eligible for Medicare and Medicaid by 2022.
- Give states greater flexibility to establish value-driven reimbursement for services provided by RHCs and FQHCs, including allowing states to reimburse for telehealth services outside of the prospective payment system (PPS) and alternative payment methodology (APM) framework.
- Modernize the stated objectives of the Medicaid program to include providing health coverage, improving health and wellness, encouraging financial independence and ensuring fiscal sustainability.

Transform Delivery Systems in Rural America:

- Approximately 60 million Americans or roughly 1 in 5 live in rural areas, with nearly every state having a rural county. Rural areas face workforce shortage issues and since 2010, over 120 rural hospitals have closed, including 18 in 2019, and nearly 46% of rural hospitals are operating with negative margins in 2019.Allow licensed freestanding emergency departments (EDs) to participate in Medicare and Medicaid to help address

the urgent need to increase hospital capacity to provide care to patients by codifying additional flexibilities to allow CAHs to become Medicare-participating, free-standing emergency rooms and making parallel changes in Medicaid.
- Allow rural hospitals to opt into value based payments that includes automatic waivers of the CAH 96-Hour certification rule, telehealth expansions, care management home visits, chronic disease management programs and other waivers from conditions of participation and other requirements.
- Codify the FY 2020 CMS Inpatient Prospective Payment System (IPPS) rural wage index used to adjust hospital payment for local labor costs to better reflect the cost of delivering care in rural hospitals around the country.

Ease Scope of Practice and Licensing Restrictions for a 21st Century Health Care Workforce:

Remove scope of practice hurdles in government programs to allow for a greater range of providers to reach patients and ease licensing restrictions that prevent health care workers from reaching patients in need across the country.

- Make permanent CMS actions temporarily waiving requirements that out-of-state practitioners be licensed in the state where they are providing services when they are licensed in another state.
- Require state grant money be tied to permanently reforming scope of practice laws and joining the Interstate Medical Licensure Compact. This will encourage local reforms to modernize our health care workforce.

Patients over Paperwork:

By removing unnecessary red tape from its programs CMS has saved the healthcare system at least $6.6 billion through 2021 and eliminated at least 42 million hours of burden through 2021 giving that time back to providers and suppliers to spend with their patients and not on needless paperwork. Making additional burden reduction actions permanent would save more money and allow health care professionals greater flexibility to serve their patients. Waive requirements, in a budget neutral manner, for a patient to have a 3-day hospital inpatient stay in order to qualify for Medicare coverage of a skilled nursing facility (SNF) stay and other CMS waivers such as:

- Modernize Evaluation and Management Codes: Codify CMS regulations to ensure appropriate Medicare reimbursement for time spent with patients by both primary and specialist healthcare providers practicing in all types of health professions.
- Institutional Budgets: Certain Conditions of Participation (COPs) contain detailed requirements related to the preparation and review of institutional budgets, based on statutory requirements. Congress should eliminate such requirements as conditions for coverage or requirements of participation.
- Consolidate Provider Enrollment Screening: Require providers receiving federal funding and enrolling in Medicaid or CHIP to undergo centralized CMS Medicare provider

screening and credentialing. State Medicaid and CHIP agencies will retain flexibility to apply additional screening requirements but not to duplicate CMS screening.

Eliminate Waste Fraud and Abuse in Medicare:

Expand the Secretary's authority to use prior authorization and utilization management for Medicare FFS as appropriate to address high risk Medicare FFS coverage, payment, and coding requirements. In addition to expanding the Secretary's authority, and to reduce provider burden and make the process more efficient, appropriate funding should be provided for the development and adoption of standards for electronic prior authorizations processes.

Unleashing Innovation at the FDA:

- *LDT Exclusion from Medical Device Definition.* Exclude lab developed tests (LDTs) from the definition of medical device under the Food, Drug and Cosmetic Act.
- *FDA presumption.* Legislatively create a presumption of approval for drugs and biologics that have been approved by such countries that are determined by the Secretary to be appropriate.

Medical liability reform:

During the current COVID-19 pandemic, the requests of health care providers and others for liability protection and coverage under the PREP Act have demonstrated the concerns over our broken medical liability system. We would propose legislation, consistent with past proposals, to reform the medical liability system. Such reforms would save HHS programs alone $26.9 billion over 10 years, while reducing unnecessary services, curbing the practice of defensive medicine, and decreasing provider burden.

Improving How Government Serves Taxpayers and Patients:

- *Sunset regulations after a set period of time.* A review of HHS's regulations conducted through the use of artificial intelligence (AI) established that 40% of HHS's regulations had not been revised since the early 1990s and some dated back even further, with various references to archaic technology. It is likely that other departments and agencies also have outdated regulations. We would propose legislation that would terminate regulations after a set period of time, unless the relevant agency repromulgated them through appropriate Administrative Procedure Act notice and comment rulemaking.
- *Sunset statutorily required FACAs after a set period of time.* Federal statutes require HHS and other agencies to operate a large number of federal advisory committees. Often the statutes do no specify a termination date, so the agency is required to continue to operate the advisory committee, even after the committee becomes outdated and no longer performs a useful function. HHS and other agencies spend significant sums every year in administering these federal advisory committees, often having to scrounge funds from programmatic activities because Congress often fails to appropriate funds to operate the

committees. We would propose legislation to sunset all statutorily required federal advisory committees within a set period of set after their establishment.

- *Continue COVID-19 Flexibilities.* During the current COVID-19 pandemic, CMS, FDA, and other regulatory agencies have issued nonenforcement notices, provided regulated entities a number of flexibilities with respect to regulatory requirements, etc. We would propose legislation that would continue all such flexibilities that FDA and CMS and other regulatory agencies have provided during this public health emergency, unless proven otherwise.
- *Eliminate unnecessary and outdated reports to Congress*. Federal statutes require HHS and other agencies to produce numerous annual reports to Congress on a wide variety of issues, many with limited utility or on outdated subjects. HHS and other federal agencies expend significant resources and staff time in preparing, reviewing, and issuing these reports to Congress. We would propose legislation that would eliminate such unnecessary and outdated reports to Congress, perhaps by sunsetting any requirement to provide a report to Congress within a set period of time after the enactment of the requirement.
- *Hire Top Experts By Waiving EIGA Requirements*. It is very difficult for HHS to hire, for temporary service, expert scientists with significant experience in manufacturing drugs and biologics, including vaccines, during a public health emergency because of the array of ethics laws. These scientists invariably have significant stock and bond holdings in the healthcare sector. To give "orders" to federal employees, the scientists must become federal employees which subjects to them the full range of conflict laws. To comply with those laws, these scientists would have to sell their stock and other securities, untangle complex investments—frequently which cannot be easily or quickly done—and avoid getting involved in matters involving an entity that employed the individual within the past year. These laws are found primarily at 18 U.S.C. §§ 207, 208, and the Ethics in Government Act of 1978 (EIGA), as amended, 5 U.S.C. App., and its implementing regulations, *e.g.*, 5 C.F.R. pt. 2635, and 5 U.S.C. §§ 7301, 7351, 7353. The solution is to authorize the Secretary during a PHE to waive EIGA requirements and after consulting with the AG to waive specific ethics requirements in title 18.

DATE: May 1, 2020

TO: The Secretary

THROUGH: Laura Pence, Acting Senior Advisor

FROM: Francis S. Collins, M.D., Ph.D., Director, NIH

SUBJECT: Meeting with Dr. Francis Collins—BRIEFING MEMO

Details:
Date: Monday, May 4, 2020
Location: 615-F
Call: Y
HHS Staff: Dr. Francis, Laura Pence, Paul Mango
Press: No

Who requested this briefing? Standing Meeting with the Secretary

Topic: Please see agenda below

Secretary's Role: Standing Meeting with NIH Director Dr. Francis Collins and NIH Principal Deputy Director Dr. Lawrence Tabak

Objective: Discussion and update on NIH significant topics

List of Participants:
HHS Attendees:
Alex M. Azar II, Secretary
Laura Pence, Counselor to the Secretary
Brian Harrison, Chief of Staff

NIH Attendees:
Francis S. Collins, M.D., Ph.D., Director
Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director

Agenda:
I. Ongoing NIH responses to COVID-19
- NIH staff screening and in-house lab testing for COVID-19
- Status of NIH Clinical Center
- Return to work guidance

II. Status of Public-Private Partnership on Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
    - Leadership team meeting, April 22 (Attachment 1)
III. Report on Hever COVID-19 meeting, April 24 (Attachment 2)
IV. New initiative on next generation COVID-19 diagnostics
V. Coordination of COVID-19 activities across HHS

Background: Please see meeting agenda and attachments.

Attachments:

1. Attachment 1 – ACTIV leadership meeting summary
2. Attachment 2 – Hever COVID-19 meeting agenda

Accelerating COVID-19 Therapeutic Interventions and Vaccines

ACTIV Partnership Leadership Group Meeting

April 22, 2020, 10:00 – 11:00 am ET

April 22, 2020

This meeting summary was prepared by Lucas Smalldon, MA, Rose Li and Associates, Inc., under contract to the Foundation for the National Institutes of Health (FNIH).
The views expressed in this document reflect both individual and collective opinions of the meeting participants and not necessarily those of FNIH.

High-Level Meeting Summary

The Leadership Group overseeing the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Partnership convened to review progress made since program launch on April 3, 2020. Dr. Francis Collins, Director of the National Institutes of Health, opened the meeting by reviewing ACTIV's overall aims and current status. Following Dr. Collins' review, the Leadership Group received updates from Co-Chairs of all four ACTIV Working Groups (WGs), which cover the following focus areas: (1) Therapeutics-Preclinical; (2) Therapeutics-Clinical; (3) Clinical Trial Capacity; and (4) Vaccines. The Group discussed significant progress toward identification and prioritization of preclinical and clinical compounds, development of a master protocol and inventory of potential networks for ACTIV trials, and planning for broad data sharing to facilitate vaccine development.

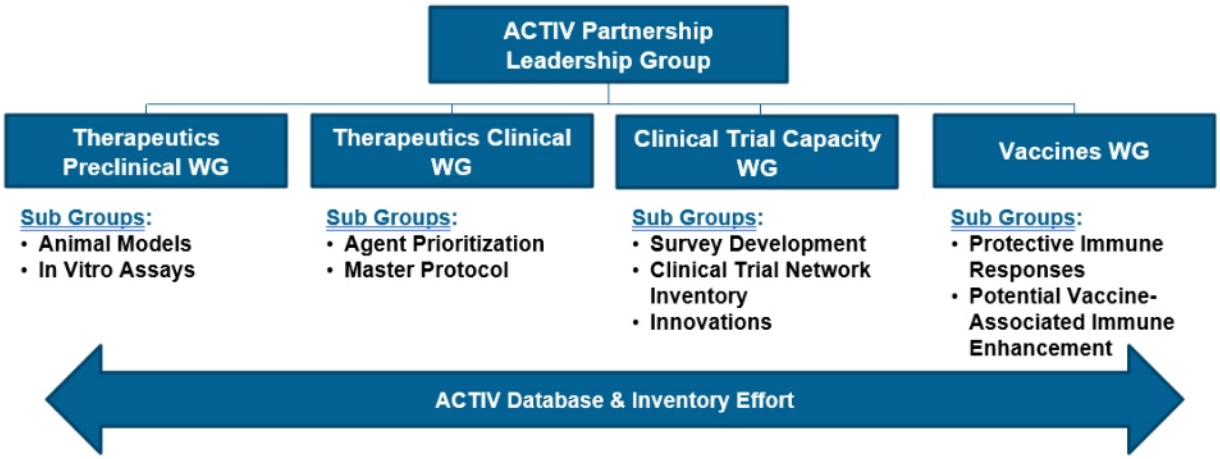
ACTIV's Overall Aims and Current Status

Francis Collins, MD, PhD, Director, NIH

On April 3, in response to the emergence and rapid spread of the SARS-CoV-2 virus and of the Coronavirus Disease 2019 (COVID-19), leaders from NIH, the biopharmaceutical industry, the U.S. Food and Drug Administration (FDA), and the European Medicines Agency (EMA), as well as academic researchers, launched the ACTIV public-private partnership. ACTIV aims to respond rapidly to the COVID-19 crisis by developing a coordinated biomedical research and development strategy to address the pandemic, creating a framework for prioritizing vaccine and drug candidates most likely to succeed in preventing and treating COVID-19, establishing a streamlined infrastructure for conducting clinical trials of promising therapeutic agents and vaccines, and coordinating regulatory processes while leveraging available assets, expertise, and financial resources among all partners.

Based on these aims, the Leadership Group decided during its April 3 meeting to establish four rapid action Working Groups (WGs) in each of the following focus areas: (1) Preclinical Therapeutics, (2) Clinical Therapeutics, (3) Clinical Trial Capacity, and (4) Vaccines. Since that initial meeting, these WGs have moved quickly to launch activities in their respective focus areas, including establishing Subgroups to pursue more specific goals within each area. The WGs will provide updates to the ACTIV Partnership Leadership Group every 2 weeks.

The graphic below captures ACTIV's current structure. ACTIV Database and Inventory Efforts referenced in the figure include projects across the WGs to compile inventories of relevant data, such as available compounds, studies underway, available *in vitro* assays and animal models, Biosafety Level-3 and -4 (BSL3/4) facilities, and clinical trial network capacity.



ACTIV is also coordinating with various other COVID-19 response efforts, including the ACCORD project in the UK, the Bill and Melinda Gates Foundation's COVID-19 Therapeutics Accelerator, and the COVID-19 R&D Leaders Consortium, as well as with federal agencies such as CDC and the Biomedical Advanced Research and Development Authority (BARDA).

Therapeutics-Preclinical WG

Christine Colvis, PhD, National Center for Advancing Translational Sciences (NCATS); John Young, PhD, Roche

The Therapeutics-Preclinical (TX-Preclinical) WG will create an integrated preclinical framework to evaluate drugs and drug candidates that have been in human trials for potential repurposing. The WG has established Animal Models and Screening Assays Subgroups to inventory these resources and has created a preliminary list of BSL 3/4 facilities (documenting each facility's capacity). The WG is also working with the Therapeutics-Clinical (TX-Clinical) WG to develop criteria for rapidly prioritizing preclinical compounds.

The WG has identified several challenges in conducting rapid COVID-19 therapeutic and vaccine research, including limited availability of some testing resources (e.g., supplies of Nonhuman Primates [NHPs], hACE2 mice, and BSL 3/4 facilities); limited data sharing; lack of a framework to compare and validate results across assays; and limited regulatory guidance on animal models for investigational new drug (IND)-enabling studies for COVID-19 therapeutics.

To address these challenges, the TX-Preclinical WG is focusing on defining a national strategy for agent testing (e.g., among National Primate Research Centers); establishing a repository of essential reagents, materials, and protocols to make available to the field; creating a preclinical development roadmap to include criteria for advancing compounds to clinical trials; harmonizing preclinical guidelines with FDA guidelines for IND-enabling studies; generating guidelines for animal testing in the short term; and developing a public data-sharing platform for preclinical small animal model experiments. Although some of these activities will require input from external stakeholders, the TX-Preclinical WG anticipates completing most of them

during May, and completing the repository of agents, materials, and protocols by mid-June, potentially by leveraging NIAID's BEI Resources Repository to help enable reagent sharing.

Discussion

Dr. William Pao noted that, given the large number of antibodies now entering clinical trials, it could be beneficial to establish a repository to share features of antibodies currently being tested (e.g., epitope and antibody format) to inform development of antibodies for future testing waves.

Therapeutics-Clinical WG

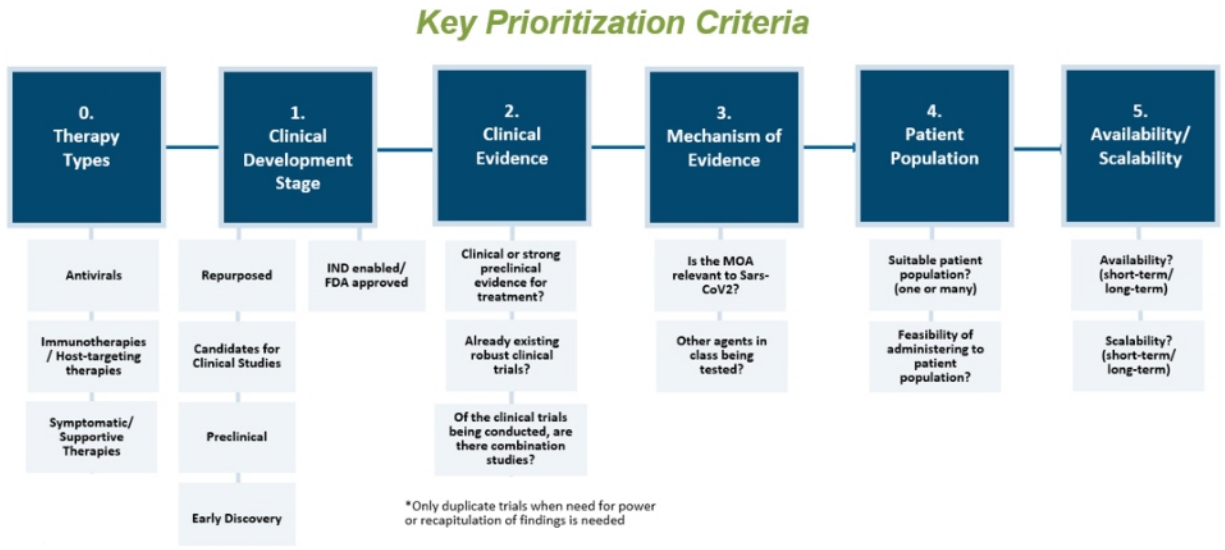
Eric Hughes, MD, PhD, Novartis; Sarah Read, MD, National Institute of Allergy and Infectious Diseases (NIAID)

The TX-Clinical WG has decided to prioritize therapeutics for target patient groups in the following order: (1) hospitalized/moderately ill (non-ICU) and critically ill/ventilated (ICU); (2) outpatient/ambulatory ill; and (3) unaffected (prophylaxis). The WG established two Subgroups to move therapeutics toward clinical trials: Agent Prioritization and Master Protocol development.

Agent Prioritization Subgroup

The Agent Prioritization Subgroup decided to consider compounds in three primary classes: (1) antivirals; (2) immunotherapies; and (3) symptomatic/supportive therapies. The Subgroup has defined prioritization criteria for all agent classes, which will inform development of a Master Protocol to test them.

The TX-Clinical WG is now collecting data needed to evaluate agents against the prioritization criteria; it has also collected several existing inventories of compounds with potential applicability to COVID-19. The WG will prioritize all potential agents in waves: (1) FDA-approved or IND-enabled agents; (2) clinically ready agents; (3) current preclinical agents or agents targeting prophylaxis. During each wave, the WG will classify agents by mechanism of action (MOA) and will eliminate those agents or mechanisms already being adequately tested in other clinical trials. A shortlist of agents will then be submitted to a small Expert Panel that will use the WG's Agent Prioritization Criteria (shown in the diagram below) to select agents for clinical trials under a master protocol in suitable patient populations.



Master Protocol Subgroup

The agent prioritization criteria shown above align with the Master Protocol Subgroup's 'hybrid' master protocol approach, which will involve two parallel processes: (1) amending the existing NIAID-sponsored Adaptive COVID-19 Treatment Trial 2 (ACTT2) protocol (i.e., producing an "ACTT3" protocol) to allow rapid testing of repurposed drugs at existing ACTT2 sites with established standard operating procedures, and (2) designing a *De Novo* ('Gold Standard') Master Protocol to address ACTIV's more comprehensive goal of continuously testing promising therapeutics under a single protocol for all three patient populations of interest.

The *De Novo* master protocol will enable adaptive trials with a shared standard of care (SOC) arm, which could be adapted to new evidence; harmonize endpoints with existing COVID-19 master protocols; support the addition of new agents as they become available; streamline data collection to reduce site burden; operate under a central Institutional Review Board and Data Safety Monitoring Committee; and function under a single IND held by a neutral third party.

Discussion

Deprioritized agents will be continuously reassessed for testing during subsequent prioritization waves as more data become available. The TX-Clinical and TX-Preclinical WGs will coordinate to ensure that data generated from preclinical testing are funneled into prioritization discussions.

Clinical Trial Capacity WG

Elizabeth Desrosiers, MS, PMP, Merck; Michael Kurilla, MD, PhD, NCATS

The Clinical Trial Capacity WG aims to maximize capacity and optimize efficiency of clinical trials in order to expedite testing of prioritized candidate therapeutics for COVID-19. To achieve these goals, the WG has established three Subgroups: (1) Clinical Trial Network Inventory; (2) Survey Development; (3) Innovations.

Clinical Trial Network Inventory Subgroup

The Clinical Trial Network Inventory Subgroup has created a preliminary inventory of 38 existing clinical trial networks along with their known capabilities and capacities. It has divided networks into three tiers according to how quickly they may feasibly begin conducting ACTIV clinical trials (Tier 1: fully functional in 6 weeks or less; Tier 2: fully functional in 6 to 12 weeks; Tier 3: fully functional in more than 12 weeks). Of 38 networks inventoried, 25 are grouped under Tier 1.

Survey Development Subgroup

The Survey Development Subgroup has worked with the TX-Clinical WG to determine the capabilities and capacities required for networks and sites to conduct successful clinical trials under ACTIV's *De Novo* master protocol. It has begun adapting these capabilities and capacities into survey questions to circulate among the networks and sites identified by the Inventory Subgroup. Survey responses, which will ultimately be recorded in a database, will help the Clinical Trial Capacity WG determine the most suitable networks and sites to conduct ACTIV clinical trials and ideally match candidate compounds to specific sites or networks. The survey will also identify what SARS-CoV-2 trials are currently underway at the various sites of interest. The Subgroup plans to begin circulating the survey to networks and sites on April 24.

Innovations Subgroup

The Innovations Subgroup is working to assess current COVID-19 studies to learn from failures and successes, and to apply those lessons learned to future ACTIV studies. Although inpatients remain ACTIV's top priority, this Subgroup is also assessing current studies of other patient populations in multiple care settings (e.g., ambulatory, prophylaxis, home care) to identify innovative ways to improve study design (e.g., remote monitoring).

Discussion

The WG Co-Chairs clarified that they are focused mainly on US-based networks right now, although some of those networks include international sites.

Vaccines WG

Kathrin Jansen, PhD, Pfizer; Douglas Lowy, MD, National Cancer Institute (NCI)

The Vaccines WG aims to coordinate vaccine development programs and to develop a regulatory pathway that will reduce the standard registration timeline by several months. Several vaccines have already entered clinical trials in the US and elsewhere, and more will enter trials soon. Whereas typical vaccine development involves years of studying a virus and designing suitable candidates, vaccine development for SARS-CoV-2 must proceed rapidly.

The accelerated timeline to develop a SARS-CoV-2 vaccine imposes several challenges. Vaccine development programs must continuously make key decisions amid constantly changing evidence and without some relevant information (e.g., protective titers). This process makes it difficult to balance the benefits of rapid development of effective vaccines with unacceptable risks to patient safety. To address these challenges, the Vaccines WG will aggregate and share

information and resources across vaccine development efforts, housing them in a centralized repository so that key decisions benefit from up-to-date, thorough, and accurate information.

The Vaccines WG has established two subgroups focused on ongoing efforts related to (1) protective immune responses and (2) potential vaccine-associated immune enhancement. Each subgroup is now aggregating key information to help inform decisions by efforts in each of these areas.

Subgroup 1 is identifying information sources as well as sharing platforms and processes to help aggregate and circulate the following information:

- Natural history data on COVID-19 to potentially identify a protective immune response
- Assay methods (e.g., to distinguish among vaccine responses for SARS-CoV-2 and other coronaviruses to help characterize protective immune response)
- Animal models to inform whether vaccine-induced responses are adequate

Subgroup 2 is aggregating existing bodies of evidence from animal models and human testing of other viruses including coronaviruses, synthesizing present understandings of potential vaccine-associated immune enhancement, and identifying approaches to monitor for potential immune enhancement in studies.

Discussion

Participants noted the possibility of learning from plasma therapy trials to define correlates of SARS-CoV-2 protection. For example, identifying levels of neutralizing antibody titers that have a therapeutic effect against SARS-CoV-2 could help investigators to characterize what vaccine-induced responses need to be achieved in clinical settings. In addition, vaccine development efforts should aim to target components of SARS-CoV-2 that exhibit limited variability to maximize effectiveness against as many virus strains as possible. Minimizing target variability is particularly important because SARS-CoV-2 is an RNA virus that mutates rapidly. Moreover, it is critical for research groups to share sequences from virus strains detected around the globe as soon as possible to inform vaccine development efforts.

Regulatory Input

Dr. Janet Woodcock emphasized the need to conduct adaptive Bayesian trials with seamless Phase II to III transitions for COVID-19 patients and affirmed FDA's willingness to coordinate with ACTIV to support those efforts.

Next Steps

Lists below capture next steps for each WG, with anticipated completion dates for each action.

TX-Preclinical WG

- Define the prioritization approach for animal use, assay selection, and staging of testing by April 29.
- Finalize the inventory of animal models, assays, and BSL 3/4 facilities by May 8.

TX-Clinical WG

- Gather necessary resources to develop Drug Repurposing master protocol and begin drafting protocol on April 24.
- Decide on a design for the *De Novo* master protocol, gather resources, and begin drafting by April 30.
- Finalize prioritization criteria by April 24 and prioritize potential agents by April 30**.**

Clinical Trial Capacity WG

- Deploy network survey on April 24.
- Finalize inventory of Tier 1 networks by April 22.
- Finalize inventory of Tier 2 and 3 networks by May 13. Deploy survey by May 14.
- Finalize innovations for the Drug Repurposing master protocol amendment by May 8.

Vaccines WG

- Define specific activities for protective immune responses and potential vaccine-associated immune enhancement by April 27.
- Establish knowledge sharing platforms for vaccine developers by May 1.

Appendix A: Participants List

Francis Collins, MD, PhD, *Director, National Institutes of Health (NIH) (Session Leader)*

Christopher P. Austin, MD, *Director, NCATS, NIH*

Marco Cavaleri, *Head of Office, Anti-infectives and Vaccines, EMA*

Christine Colvis, PhD, *Director for Drug Development Partnership Programs, National Center for Advancing Translational Sciences (NCATS), NIH*

Larry Corey, MD, *President and Director Emeritus, Fred Hutchison Cancer Research Center*

Elizabeth Desrosiers, MS, PMP, *Executive Director, Clinical Sciences and Study Management, Merck*

Mikael Dolsten, MD, PhD, *CSO and President, Worldwide R & D, Pfizer*

Emily Erbelding, MD, MPH, *Director, Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases (NIAID), NIH*

Maria Freire, PhD, *President and Executive Director, FNIH*

Jordan Gladman, PhD, *Health Program Specialist, NIH*

Thomas J. Hudson, MD, *Vice President of Oncology Discovery and Early Development, AbbVie*

Eric Hughes, MD, PhD, *Global Development Unit Head, Immunology, Hepatology & Dermatology and China Region Development Head, Novartis*

Kathrin Jansen, PhD, *Senior Vice President, Head of Vaccine Research and Development, Pfizer*

Michael Kurilla, MD, PhD, *Director, Division of Clinical Innovation, NCATS, NIH*

Douglas Lowy, MD, *Principal Deputy Director, National Cancer Institute (NCI)*

Mathai Mammen, MD, PhD, *Global Head, Research & Development, Johnson & Johnson*

John Mascola, MD, *Director, Vaccine Research Center, NIAID, NIH*

David Meeker, MD, *KSQ Therapeutics (formerly Genzyme)*

Hitesh Pandya, MD, *Respiratory Physician, AstraZeneca*

Ashley Parker, PhD, *Health Science Policy Analyst, NIH*

Steven Paul, MD, *Chief Executive Officer and Chairman of the Board, Karuna Pharmaceuticals*

Roger M. Perlmutter, MD, PhD, *EVP and President, Merck Research Laboratories*

Guido Rasi, *Executive Director, European Medicines Agency (EMA)*

Sarah Read, MD, *Deputy Director, Division of AIDS, NIAID, NIH*

Doris J. Rouse, PhD, *VP, Global Health Technologies, RTI International*

Daniel M. Skovronsky, MD, PhD, *Senior Vice President and Chief Scientific Officer, Eli Lilly and Co.*

Lawrence Tabak, DDS, PhD, *Principal Deputy Director, NIH*

Julie Tierney, JD, *Chief of Staff, Center for Biologics Evaluation and Research, FDA*

John Tsai, MD, *Head, Global Drug Development and CMO, Novartis*

William Pao, PhD, MD, *Head, Pharma Research & Early Development, Roche/Genentech*

Andrew S. Plump, MD, PhD, *President, Research and Development, Takeda*

John C. Reed, MD, PhD, *EVP, Global Head: Research, Sanofi*

Herbert (Skip) Virgin, MD, PhD, *EVP Research and CSO, Vir Biotechnology*

Janet Woodcock, MD, *Director, Center for Drug Evaluation and Research (CDER), FDA*

John Young, PhD, *Global Head, Infectious Diseases, Roche*

Stacey Adam, PhD, *Science Program Manager, Foundation for the NIH (FNIH)*
Stephanie James, PhD, *Senior VP of Science, FNIH*
Joseph P. Menetski, PhD, *Associate VP of Research Partnerships, FNIH*
Michael Santos, PhD, *Associate VP of Science, FNIH*
Karen Tountas, PhD, *Scientific Program Manager, FNIH*
David Wholley, MPhil, *Senior VP of Research Partnerships, FNIH*

Margaret Anderson, *Managing Director, Deloitte*
Nina Gonzalez, *Senior Manager, Deloitte*
Elizabeth Kim, *Senior Consultant, Deloitte*
Rosa Marie Alvarez, *Consultant, Deloitte*
Benjamin Stratton, *Senior Consultant, Deloitte*
Brett Tolman, MA, *Strategy Manager, Deloitte*
Jonathan Wachtel, *Manager, Deloitte*

HEVER Teleconference Meeting, April 24 2020

How can HEVER help connecting key global COVID-19 initiatives, to help further accelerate the development of life saving solutions?

Agenda

• Setting the Stage (Mikael Dolsten)	5 min
• COVID R&D Consortium Update (Andy Plump)	5 min
• ACTIV Initiative Update (Francis Collins)	10 min
• FDA Update(Stephen Hahn) *COVID-19 Diagnostic and Serology Testing, CTAP and Focus for vaccines*	5 min
• Discussion (All) – How can we further align COVID-19 initiatives?	30 min
• Conclusions & wrap up (Mikael and Trevor)	5 min

How can HEVER help connecting key global COVID-19 initiatives aimed at therapeutics and vaccine development?

CONTEXT

- Various organizations have been mapping and connecting activities underway to reduce duplication to come to live saving solutions more quickly.

- Globally navigating all activities underway is challenging

  *-FNIH / NIH ACTIV** and the *COVID-19 R&D Consortium*** seek to coordinate and align many of the major players for therapeutics and vaccine development

  -BMGF ReSPONSE / Therapeutics Accelerator

  -IMI CALL (incl. IMI-CARE proposal led by J&J) launched for May-July start

  -WHO coordination of COVID-19 Vaccine development (Andrew Witty)

  BARDA, CEPI, Wellcome Trust, international trade orgs, foundations, governments and others incl. exEU/exUS efforts

**FC and **AP to Highlight*

KEY QUESTIONS For Discussion

- How do we align the current important Covid-19 initiatives so each cover distinct needs and avoid duplication at a time where we need to move with lightning speed and quality execution?
- Can one Covid-19 initiative serve as the over-arching gathering of key stakeholders?
- Should/can we merge some master protocols to more efficiently test therapies across the spectrum of COVID-19 disease?

DATE: May 1, 2020

TO: The Secretary

FROM: Paul Mango, Deputy Chief of Staff

SUBJECT: NextGen SNS Briefing Drafts- BRIEFING MEMO

Details:
Date: Monday May 4, 2020
Location: WH – WW 120
Call: No
HHS Staff: Paul Mango

Who requested this briefing?: N/A

Topic: Creating a NextGen Strategic National Stockpile

Secretary's Role: Familiarize yourself with the attached materials and suggest any edits

Objective: These materials represent the next step in the process initiated by Jared Kushner. At his request in our last session, we have assembled a potential briefing document on the changes we would make to create a more robust, more capable, less vulnerable SNS. His office subsequently asked us to draft potential POTUS Talking points as well. As of now, he believes POTUS will want to make this public next week

Background: We have had discussions with Jared and Adam several times over the last few weeks. We have developed a plan to now restructure the SNS and it has been syndicated with ASPR, DoD, and the Supply Chain Task Force team. The next step is to obtain final approval from the WH.

Attachments:
1. Restructuring our Strategic National Stockpile (SNS) power point
2. Draft of POTUS Talking Points

Restructuring our Strategic National Stockpile (SNS)

A Strategy to Enhance Preparedness and Response

APRIL 29TH 2020

During the initial response to COVID-19, we encountered several SNS challenges which have now created an imperative to restructure

Challenges

We lacked both the **depth** (<1 month's reserve) and **breadth** (only 28% of the items necessary) required for an effective COVID response

We lacked the ability to **determine was needed**

We lacked the ability to target the distribution of PPE and other critical products to hotspots

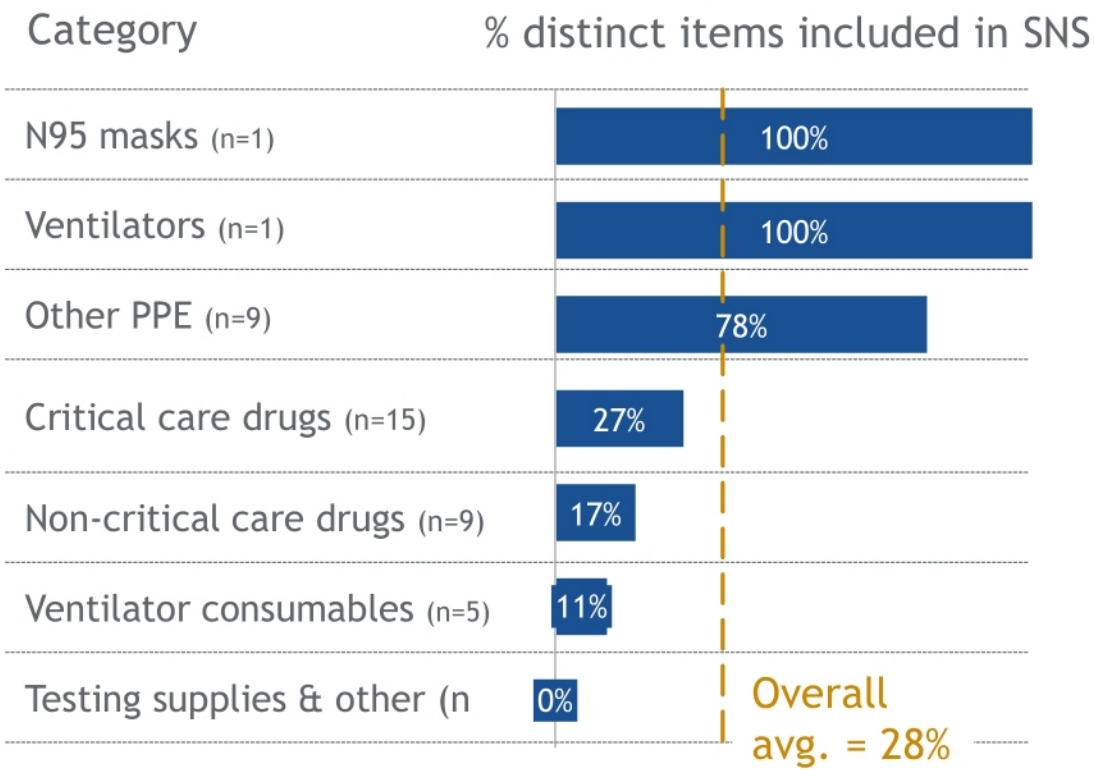
Our supply chain was **extremely vulnerable** to foreign production interruptions (<50% of PPE manufactured in North America)

Future State

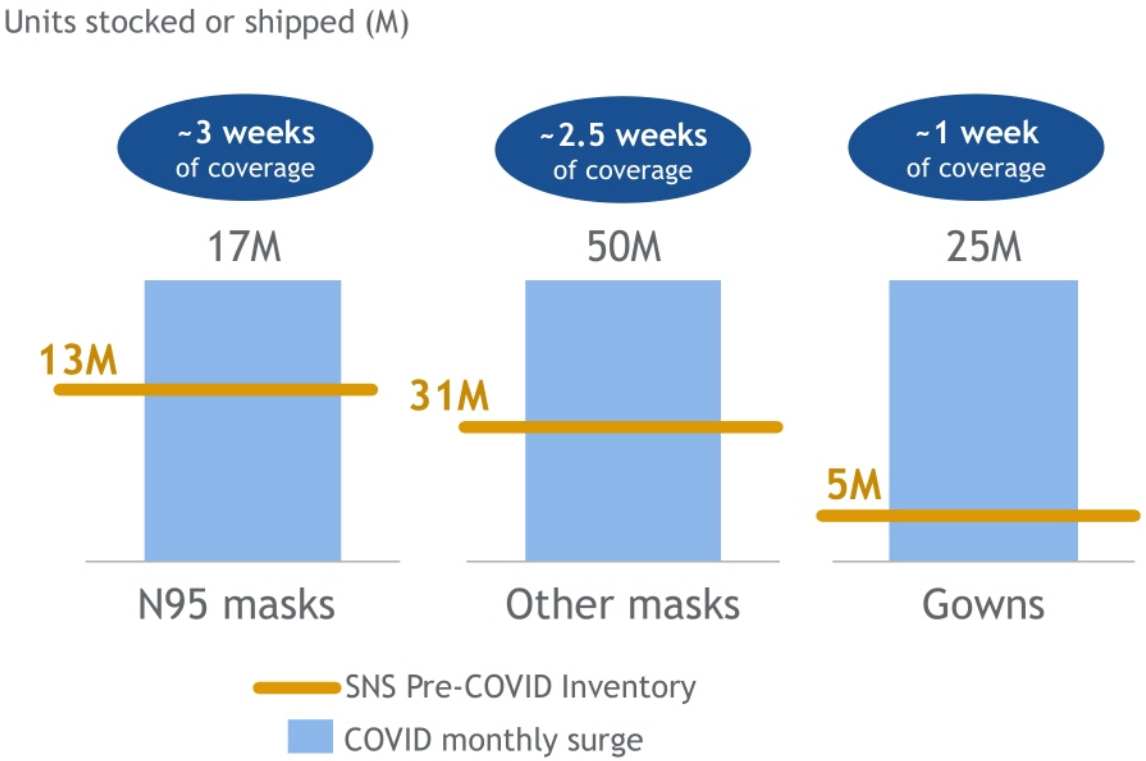
- **More coverage**: Ensure ~90 days' reserve of 100% of major items associated with COVID-like pandemics
- **More insights:** Utilize predictive analytics to forecast requirements
- **More capability:** Utilize "vendor managed inventory" and fully develop supply chain IT system providing real-time insights into supply and demand
- **Less vulnerability**: Draw almost entirely upon North American manufacturing for all items

SNS inventories lacked breadth & depth to respond to pandemic demand

Breadth: 28% of needed items were stocked



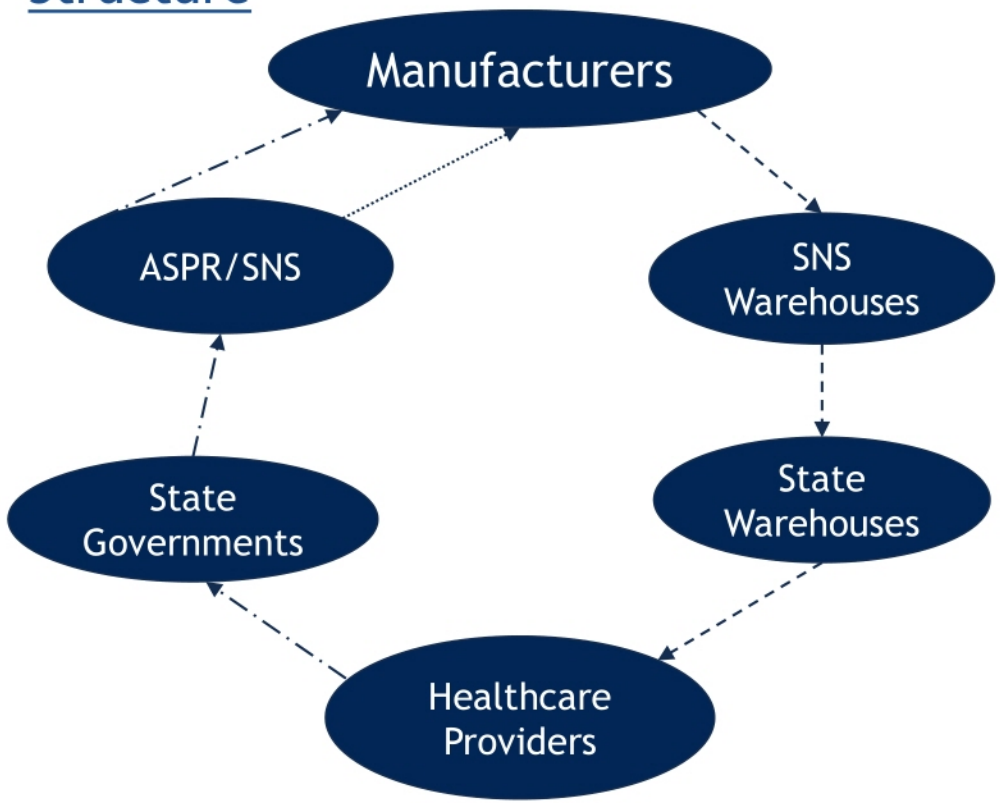
Depth: SNS had <1 month's reserve of key items



Source: SNS as of 4/22/20; data provided by major U.S. medical-surgical distributors (response to an RFI dated 3/30/20). Units in "eaches." Does not include product distributed outside of included distributors; analysis is intended to be directional; some extrapolations have been made.

The legacy distribution through the States did not give us the nimbleness to target product to specific "hotspots" quickly

Current Structure

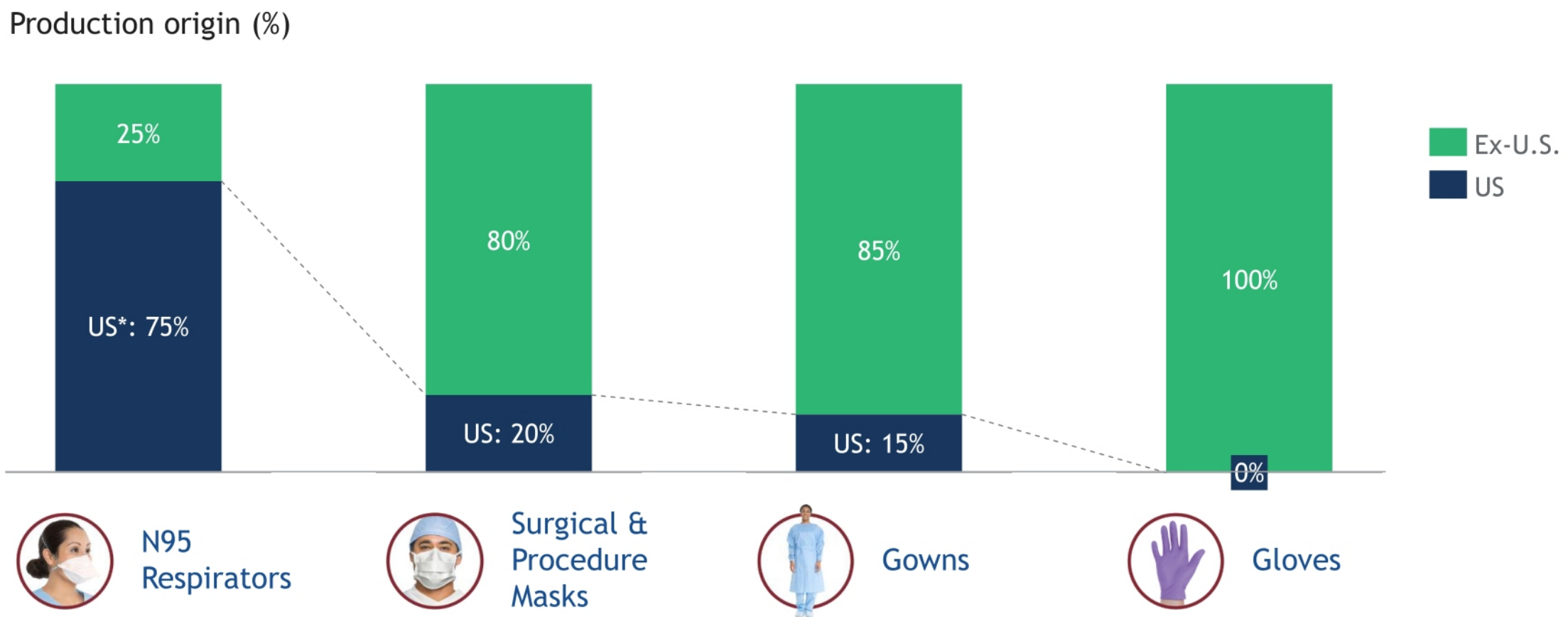


Key: = order; = payment; =shipment

Deficiencies

- Did not permit us to target specific hot spots
- Precluded us from a contracting perspective from rapidly replenishing stocks
- Did not allow us to track where the product actually went and got used
- Gave us very little insight into actual supply and demand patterns

Our COVID response also revealed a vulnerable dependence on foreign sources of supply (PPE example)



Source: GHX, information & interviews provided by several PPE distributors & manufacturers, analysis
* Includes some production in UK

In the restructured model, DoD and private sector partners will complement HHS capabilities to respond to surge in demand

DoD

Enhancing N. America manufacturing capacity

Procurement on behalf of HHS

Manufacturers

Reserved capacity

Commercial Distributors

Inventory management

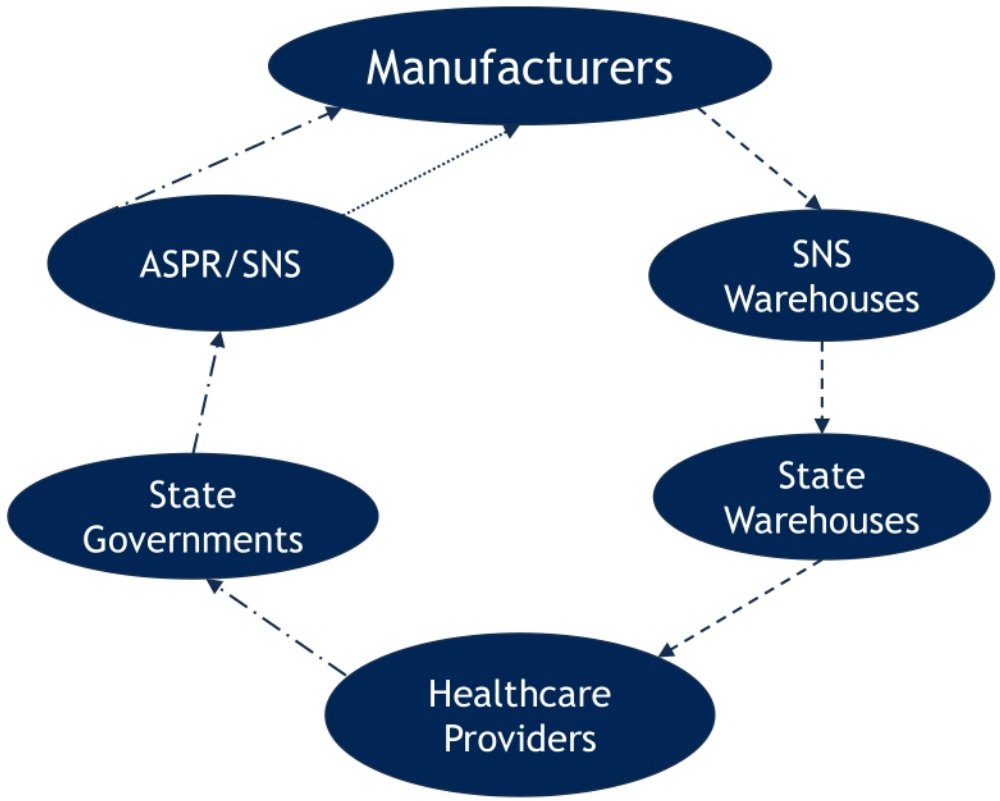
Logistics

Point of care

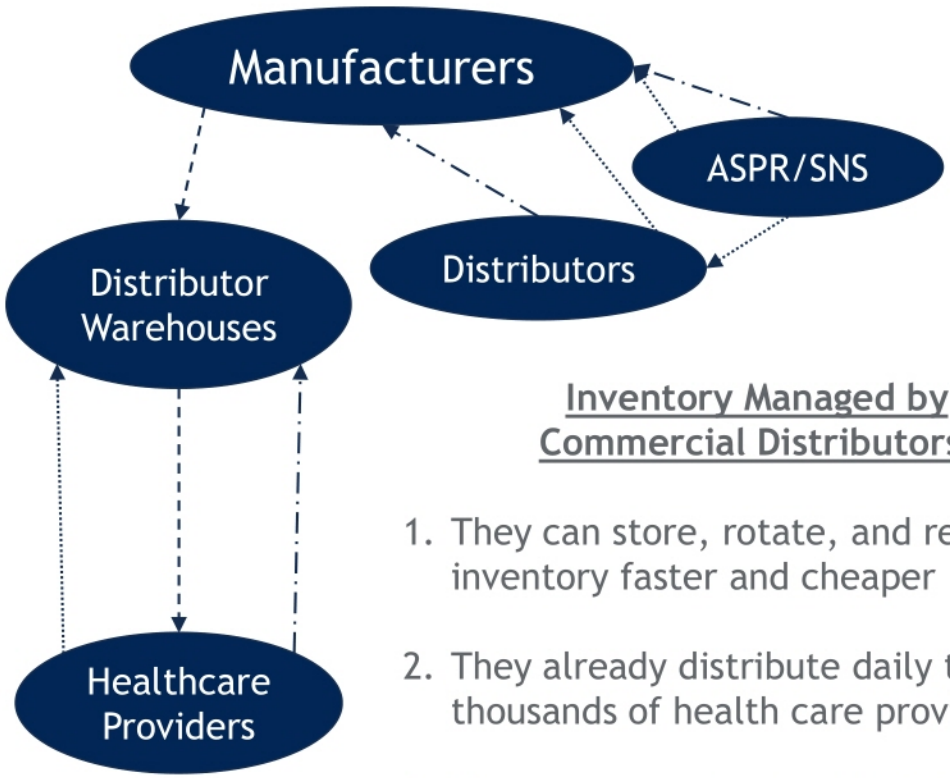
Additional safety stock

Our proposed future state enables better inventory management, targeted delivery, and insights into supply & demand patterns

TODAY



FUTURE



Inventory Managed by Commercial Distributors:

1. They can store, rotate, and replenish inventory faster and cheaper
2. They already distribute daily to thousands of health care providers
3. They can provide valuable insights into changing supply and demand patterns

Key: —·—·—▸ = order; ·····▸ = payment; - - - - -▸ =shipment

Our newly designed supply chain IT system will enable end-to-end visibility for informed decision-making in a crisis

Create visibility

- End-to-end inventory levels
- Manufacturer capacity
- Distribution flows
- Point-of-care consumption

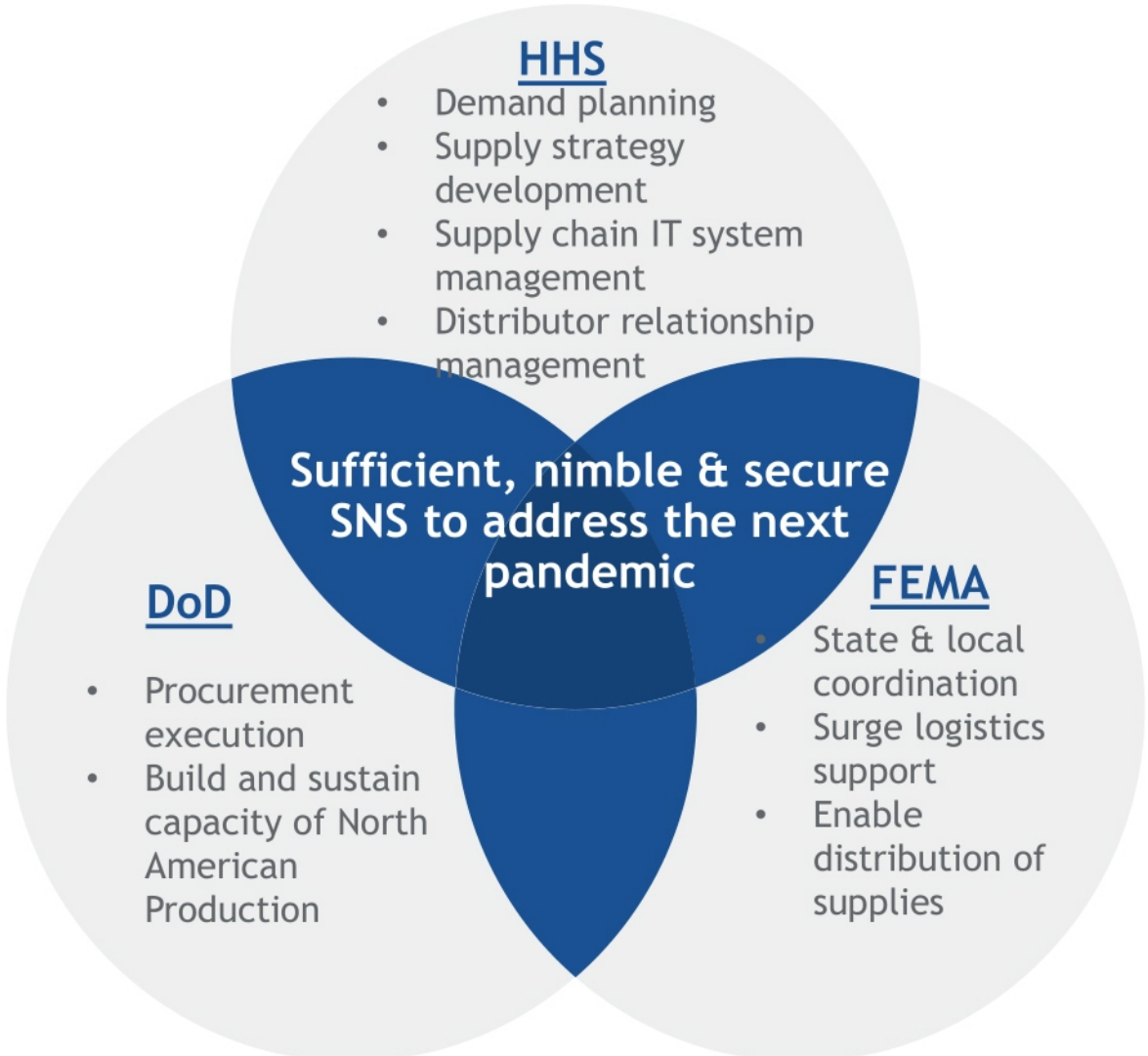
Provide insights

- Demand forecasting
- Gap prioritization
- Scenario modeling

Orchestrate response

- Capacity planning & acquisition strategy
- Targeted distribution
- Strategy & policy refinement

The restructured SNS will have a clear delineation of roles and responsibilities



This effort will require coordination across a broad set of stakeholders

US Federal Government

HHS · DoD · DHS · FEMA

State Governments

New York · Louisiana · Washington

Supply Chain Partners

3M · Cardinal Health · Concordance Healthcare Solutions · Premier · McKesson · Henry Schein · HealthTrust · GE · Owens & Minor · Medline · Morris & Dickson Co. LLC · Vizient

Providers

American Hospital Association · AHCA American Health Care Association

The way ahead: SNS restructuring key implementation steps

Short-term (next 30-60 days)

- Complete stockpile replenishment
  - Procurements already underway for several items, including vents & N95s
- Finish developing functionality of supply chain IT system
- Complete RFI, RFP, and engage in contracts with commercial partners
- Convey HHS requirements and authorities to DoD

Long-term (balance of 2020 and beyond)

- Collaborate with DoD to ensure North American manufacturing capacity
- Extend strategy beyond COVID-19
  - Actively & continuously identify new threats
  - Ensure stockpile is prepared for evolving set of threats
  - Invite participation of States and other Government entities

Restructuring the Strategic National Stockpile (SNS)

Suggested POTUS talking points

1. The SNS the previous Administration left me proved to be completely inadequate in our response to COVID 19: we did not have the depth or breadth of supplies needed, we did not have an effective means of distributing products quickly to COVID "hotspots", and we learned we were dependent on China for many vital supplies
2. It was only through the heroic efforts of FEMA's air bridge flying thousands of tons of medical supplies from Asia, the Supply Chain Task Force's efforts led by ADM Polowczyk, and Peter Navarro's work converting domestic manufacturing capacity that prevented us from stocking out
3. I therefore directed HHS and Secretary Azar to restructure the SNS to be much better prepared for the next pandemic
4. I am pleased to announce that the restructuring is well underway, and will be complete prior to this fall, should COVID or any pandemic return. Indeed, today we are issuing a Request for Information (RFI) to the industry which will provide detail for much of the strategy we are pursuing
5. Specifically, the restructured SNS will change what existed in the following ways:
    a. Rather than having less than 1 month reserve supply for key items such as face masks, it will have much more depth covering ~90 days' worth
    b. Rather than carrying less than 30% of the items consumed by COVID patients and their care providers, we will increase the breadth of the inventory to cover 100% of these items

(e.g., for instance testing supplies and pharmaceuticals required by patients on Ventilators)

c. We will establish partnerships with medical product and pharmaceutical distributors permitting us to get supplies quickly to the right hospital or nursing home at the right time
d. We are investing in an information technology system giving us real time insight into the supplies being produced, those in the warehouses, and those being shipped to hospitals and nursing homes at any given time. We will have a full "end-to-end" understanding of the entire medical product supply chain
e. We will draw upon the procurement capabilities of the DoD and Peter Navarro's team to work with the SNS to bring production of critical medical supplies and pharmaceuticals back to North America

6. With all of this restructuring we will have a *much better stocked, much more capable, and much less vulnerable* Strategic National Stockpile all for the benefit of the American people.

HHS S1 High Level Briefing

May 01, 2020

US CASE COUNTS & OUTBREAK UPDATES

- Total cases: 1,057,435 *[+30,144]* (1,054,179 confirmed, 3,256 probable)
- Total deaths: 62,189 *[+2,188]* (56,440 confirmed, 5,749 probable)
- 26,566 U.S. healthcare workers COVID positive and 89 deaths
  **new numbers are received each day from CDC at 0730ET*
- **Domestic outbreaks, widespread***:*
  - 50 states + DC, Guam, PR, USVI, and CNMI have cases
  - 7 states have over 10,000 cases and 13 states have over 20,000. New York has 299,106 cases (including 162,212 in NYC (54% of the state total))
- **International outbreaks, widespread:**
  - There were over 71,800 new cases and over 9,700 new deaths in the last 24 hours. The PAHO region accounted for 46%. Europe accounted for 39% of the reported cases.

TESTING

- Together, the State/Local Public Health Laboratories, Commercial Laboratories, VA, Hospital Laboratories, and Abbott ID NOW have tested 6,482,602 samples.
  - Public Health Labs: Reported results for 15,056; total tests performed 561,120.
  - Commercial (ACLA) Lab: Reported results for 126,580; total tests performed 3,388,605.
  - To date, the CDC has tested 5,840 samples.
  - To date, the VA has tested 4,314 samples (veterans and employees).
  - To date, Academic/Hospital testing laboratories have tested 1,504,199 samples.
  - Abbott ID NOW point of care instruments have performed 1,018,524 tests.
- Community Based Testing:
  - 14 sites are live, 0 in progress, 7 closed, and 20 transitioned to the state
  - Sample collection/testing throughput:
    Beginning with data for 27Apr, numbers being screened no longer will be collected, and the number 'tested' will be reported as 'samples collected'
    - Yesterday: 3,641 samples were collected
    - Overall: 144,343 samples collected
  - Tests processed: 137,796 tests processed; 23,055 positive results (16.7%)

PURCHASES

- SNS Procurements:
  - Contracted with Cepheid US to purchase ~2.3M in Cepheid Test Kits for point of care testing and rapid testing

MISC SIGNIFICANT NEWS

- Gilead Sciences announced its ability to produce several million rounds of remdesivir next year to assist in the battle against COVID-19

Senior Leadership Brief COVID-19

May 1, 2020 12:00 p.m. ET

For the most up to date COVID-19 data (account required): https://geohealth.hhs.gov/arcgis/home/

Current Situation: FEMA, HHS, and our federal partners are working with state, local, tribal and territorial (SLTT) governments to execute a Whole-of-America response to the COVID-19 pandemic. The President released *Guidelines for Opening America Up Again* and the Federal Government is continuing to work with SLTT leaders across the country to ensure they have the equipment, supplies, and testing resources they need to reopen safely and responsibly. The HHS Secretary issued a renewal of the January 31 COVID-19 Public Health Emergency Declaration; the renewal becomes effective April 26 and extends the Declaration for 90 days. **CDC Update:** CDC confirmed, probable, and presumptive U.S. cases of COVID-19: 1,057,435 (+30,144) (across 50 states and D.C., Guam, PR, CNMI, and USVI; Deaths: 62,189 (+2,188); Combined CDC and WHO reported global cases: 3,090,445 (+71,839); global deaths: 217,769 (+9,797); Countries and areas with cases: 213 *(HHS Update, May 1, 2020, 7:58 a.m. ET)*

Testing: 6,482,602 (+406,899) cumulative as of May 1 (includes samples tested by State/Local Public Health Laboratories, Commercial Laboratories, Hospital Laboratories, CDC, VA, and Abbott ID NOW instruments).

Health and Medical Lifeline

Public Health

Federal Assistance

- USACE has awarded 34 contracts for ACS with a projected bed capacity of 14,779; 1,495 USACE staff supporting *(ESF-3 Update, May 1, 2020, 8:43 a.m. ET)*

Mitigation

- The President announced the formation of Coronavirus Commission for Safety and Quality in Nursing Homes to review their response and recommend improvements; will include nursing home operators, resident advocates, and public officials *(CISA Update, May 1, 2020, 3:36 a.m. ET)*

Testing

- VA: Division of Consolidated Laboratory Services, in coordination with VA Hospital and Healthcare Association and VA Department of Health, allocated two Abbott ID Now Test devices to Bath Community Hospital and Buchanan General Hospital; both hospitals are in rural areas and lack testing options *(FEMA Region III Update, April 30, 2020, 2:08 p.m. ET)*
- PR: Puerto Rico Core Advisory Groups are working with the Department of Health to facilitate testing in homes for people with disabilities and others with access and functional needs *(FEMA Region II Update, April 30, 2020, 1:38 p.m. ET)*

Personal Protective Equipment

- MI: Delivering 1,320 gallons of hand sanitizer to MI Tribes to slow spread of virus through communities *(FEMA Region V Update, April 30, 2020, 2:12 p.m. ET)*

Medical Care

Hospital Capacity

- NYC: Javits Center: 8 (-23)/202 beds filled; 0 (-1)/48 ICU beds filled; 1,095 total patients seen; 8 (-23) COVID+ patients being treated; 6 deceased; patients will be discharged by May 1; all DoD personnel and equipment withdrawn by May 5 *(DoD Update, May 1, 2020, 7:59 a.m. ET)*
- NYC: USNS Comfort departed for its home base in Norfolk, VA on April 30 *(DHS NOC Update, April 30, 2020, 7:51 p.m. ET)*
- CA: USNS Mercy: 9/250 total beds filled; 0/142 beds w/vents filled; 5 (-1)/40 ICU beds filled; 77 (+1) total patients seen; 0 COVID+ patients being treated; 3 deceased; will cease accepting patients by order of state; State requested small teams of 4-5 personnel to augment local medical facilities *(DoD Update, May 1, 2020, 7:59 a.m. ET)*
- CA: USNS Mercy medical personnel augmenting Fairfield Development Center as of April 22; Status: 4 (+1)/100 beds filled; 5 (+1) total patients seen *(DoD Update, May 1, 2020, 7:59 a.m. ET)*
- DE: Beebe Healthcare Hospital is working at 99% capacity; Sussex County hospitals nearing capacity; may need decompression or additional staff to manage higher number of hospitalizations; potential to activate 17 additional staff *(FEMA Region III Update, April 30, 2020, 2:08 p.m. ET)*
- CA: Emergency Medical Services Authority continues to coordinate the approval of out-of-state medical professionals to practice in California for the duration of COVID-19 emergency; as of April 29, 7,735 medical professionals have been approved *(FEMA Region IX Update, April 30, 2020, 10:30 p.m. ET)*

Cases	New Cases
1,057,435	30,144
	Percent Change in Cases
	3.1%
Deaths	**New Deaths**
62,189	2,188
	Percent Change in Deaths
	3.9%

Key Updates/Actions

FEMA HQ: National Watch Center Steady State; NRCC Level I; Level 1: Region I, IX; Level 2: Regions II, III, IV, V, VI, VII, VIII, X; COVID-19 Major Declarations: 56 *(FEMA Update, April 25, 2020, 2:51 a.m. ET)*
Department of Homeland Security: 3,152 (-5) FEMA employees deployed to support COVID-19 Response; IMAT-A teams deployed to 27 states, territories, and DC; LNOs deployed to 37 states and territories *(FEMA Update, May 1, 2020, 9:56 a.m. ET)*
Department of Health and Human Services: 591 HHS personnel deployed to support COVID-19 response; Health and Medical Task Force (HMTF): 155 personnel deployed to 8 sites; Rapid Deployment Force (RDF): 201 deployed to 5 sites; Disaster Mortuary Operational Response Team (DMORT): 49 personnel deployed to 10 sites; IMT/Logistics: 56 personnel deployed to 6 sites; RECs/LNOs: 130 personnel deployed *(HHS Update, April 29, 2020, 1:40 p.m. ET)*

Other Domestic Lifelines

Safety & Security

- DHS Cybersecurity and Infrastructure Security Agency is providing a Protective Security Advisor to the Delmarva Poultry Production Task Force to assist with coordinating and addressing MD, DE, and VA poultry production issues *(DHS NOC Update, May 1, 2020, 9:29 a.m. ET)*
- CA: 911 calls between April 20 and April 26 were down 14.32% compared to the same period in 2019 *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*
- RI Governor announced large events such as concerts, parades, festivals, and weddings are not allowed this summer due to COVID-19 (Region I Update, April 30, 2020, 5:00 p.m. ET)
- AZ: Growing concern over legal/illegal border crossing with COVID-19 due to Mexico having sustained community transmission and rapid rise in infections; 15,529 confirmed cases and 1,434 reported casualties in Mexico *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*
- VA Governor announced that hospitals and dentists will be allowed to resume non-emergency procedures as of midnight 4/30; requesting Individual Assistance Declaration for crisis counseling *(Region III Update, April 30, 2020, 5:00 p.m. ET)*

Food, Water, & Shelter

- CA: Department of Education Superintendent received the USDA approval of the Pandemic Electronic Benefit Transfer (P-EBT) program for students who were receiving free/reduced-price school meals on April 29; P-EBT will provide approx. $1.4 billion toward the feeding of school children throughout State *(FEMA Region IX Update, April 30, 2020, 10:30 p.m. ET)*
- AZ: National Guard focused on food distribution (food bank support), COVID-19 medical education (selection/proper wear of PPE), and logistical throughput distribution (rapid distribution of supplies to point of need) *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*
- CA: Shelter (at-risk population): 12,647 (+44) hotel/motel rooms acquired; 1,274 trailers deployed to Santa Clara, LA, and Sacramento counties; total of 13,921 (+44) units secured to shelter at-risk individuals; total rooms occupied: 5,725 (+48); total units required: 15,000 *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*
- Navajo Nation (NN): ACS facilities under evaluation as initial non-congregate shelters; currently processing four non-congregate shelter agreements; Winslow, AZ Residential Hall approved by NN as an isolation site, assessing funding *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*

Comms

- AZ: Communications company in NE AZ experienced equipment failure on April 29 due to power spike; five 911 centers affected and changed to backup centers; communication services and 911 centers have resumed normal operations *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*

Trans

- CA: Federal Motor Carrier Administration delivered 100,000 cloth face masks to CA Highway Patrol to be distributed to truckers at strategic locations around the state *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*
- HI: Per U.S. Maritime Administration's April 29 Weekly Report, the "no sail" order by CDC has been extended until July 18 *(FEMA Region IX Update, April 30, 2020 9:00 p.m. PT)*

Senior Leadership Brief COVID-19

May 1, 2020 12:00 p.m. ET

For the most up to date COVID-19 data (account required): https://geohealth.hhs.gov/arcgis/home/

Operational Task Forces	
Medical Counter-Measure (MCM) Development	• Emergency Use Authorizations granted by FDA: 44 (+2) molecular diagnostic tests, 23 laboratory-developed tests, 9 (+1) antibody tests, and 2 repurposed treatments (chloroquine, hydroxychloroquine) *(MCM TF Update, May 1, 2020, 9:38 a.m. ET)* • 2638 (+25) market research submissions and 256 (+3) CoronaWatch meetings held *(MCM TF Update, May 1, 2020, 9:38 a.m. ET)* • Accelerating vaccine manufacturing efforts to ensure rapid delivery of vaccines once a vaccine is shown to be safe and effective *(MCM TF Update, May 1, 2020, 9:38 a.m. ET)*
Health Care Resilience (HCR)	• Supply Preservation Strategy: continued focus on implementation and messaging to stakeholders to increase preservation of supplies, including PPE; working with NRCC and SCTF to increase utilization of deployed decontamination systems; found NYC decontamination unit to be underutilized due to the declining number of cases in the area and a recent re-supply of N-95's *(HCR TF Update, April 30, 2020, 10:22 a.m. ET)* • Webinar on the Medical Operations Coordination Cell (MOCC) concept is available on ASPR TRACIE; MOCC Toolkit, 1st edition, in final review; developing a COVID-19 lessons learned webinar, featuring speakers from hospitals in NYC, NJ, New Orleans, and Detroit to focus on promising practices for addressing hospital space, staff, and supply challenges *(HCR TF Update, April 30, 2020, 10:22 a.m. ET)* • Cloth Face Coverings: UCG leadership prioritized nursing homes and dialysis facilities for provision of cloth face coverings *(HCR TF Update, April 30, 2020, 10:22 a.m. ET)* • Nursing Home (NH) Support: Pilot moving forward with 9 centers contracted in the four states in the pilot; task order has been submitted for testing of ~300 residents and staff in one facility in TN *(HCR TF Update, April 30, 2020, 10:22 a.m. ET)*
Lab Diagnostics	• Public Health Lab International Reagent Resource (IRR) Supply/Demand Dashboard pending approval by HHS leadership; dashboard will be available on GeoHEALTH *(LDTF Update, May 1, 2020 9:22 a.m. ET)* • Working with IHS, FEMA, and HHS to develop guidance for tribes to request federal support for COVID-19 response *(LDTF Update, May 1, 2020 9:22 a.m. ET)* • Held weekly call with Association of Public Health Laboratories (APHL) to discuss federal support to public health labs and planning for APHL-sponsored webinar on Abbott ID NOW tentatively planned for next week *(LDTF Update, May 1, 2020 9:22 a.m. ET)* • Continuing to work the contracting for the serology pilots in New York City and Detroit; targeting testing to begin early next week *(LDTF Update, May 1, 2020 9:22 a.m. ET)* • Continuing to work with the White House Testing at Scale Task Force to ensure testing supplies are sent to states the first week of May *(LDTF Update, May 1, 2020 9:22 a.m. ET)*
Community Based Testing Sites (CBTS)	• 144,343 (+3,641) samples collected at CBTS locations since March 20 *(CBTS TF Update, May 1, 2020, 9:51 a.m. ET)* • 137,796 (+4,300) tests processed and received by call center since March 20; 23,055 (+492) positive, 1,434 (+60) indeterminate, and 113,307 (+3,746) negative *(CBTS TF Update, May 1, 2020, 9:51 a.m. ET)* • 102,341 (+12,466) tests processed from Private-Partnership Testing Sites since April 5; 11,133 (+1,120) positive, 330 (+134) indeterminate, and 90,878 (+11,250) negative *(CBTS TF Update, May 1, 2020, 9:51 a.m. ET)* • Developing guidance for State Emergency Management Agencies and FEMA Regional Administrators for full implementation of COVIDResponder for data collection *(CBTS TF Update, May 1, 2020, 9:51 a.m. ET)*
Supply Chain Stabilization	• April 30 Airbridge Activity: 5 flights; Chicago (2); Los Angeles (2); New York City (1); 104/135 flights complete; 31 flights scheduled *(SC TF Update, May 1, 2020, 10:19 a.m. ET)* • On April 30, Airbridge flight #100 and #101 arrived in Los Angeles;; Airbridge flight #102 arrived in New York City; Airbridge flight #103 and #104 arrived in Chicago;; Cargo for all flights is being assessed *(SC TF Update, May 1, 2020, 10:19 a.m. ET)* • Four flights carrying 4.5M FEMA procured N-95 masks arrived April 30 in New York City, Chicago, Baltimore, and Washington, D.C.; including these flights, total 3M masks received 31.5M/55M currently scheduled for shipment *(SC TF Update, May 1, 2020, 10:19 a.m. ET)*
Community Mitigation Measures	• In collaboration with academic partners, developing questions for next iteration of survey on public compliance and support for mitigation strategies (*CMM TF Update, May 1, 2020, 10:13 a.m. ET)*
Continuity of Operations (COOP)	• Over the past 24 hours 1 Wireless Emergency Alert (WEA) messages related to COVID-19 sent by local authorities; 1 stay at home/curfew reminder (*COOP TF Update, May 1, 2020, 8:25 a.m. ET)* • Developing webinar products supporting reconstitution in both Federal and "whole community" versions; Fact Sheet entitled "Planning Considerations for Organizations in Reconstituting Operations" approved and distributed via GovDelivery to continuity stakeholders (*COOP TF Update, May 1, 2020, 8:25 a.m. ET)* • Additional reconstitution briefing materials and exercise starter kit beginning approval process (*COOP TF Update, May 1, 2020, 8:25 a.m. ET)*
Data and Analysis	• Briefed the Community Mitigation Task Force on the varying impacts of mitigation strategies across states and territories to inform policy and guidance on April 30 *(DA TF Update, May 1, 2020, 10:35 a.m. ET)* • Completed training for CDC and Laboratory Diagnostics Task Force on the International Reagent Resource (IRR) Allocation Tool configured to support decision-making and testing supply allocation; training delivered on April 30 *(DA TF Update, May 1, 2020, 10:35 a.m. ET)* • Completed preliminary Gate Indicators dashboard visualizing key data points reflecting community trends and ability to meet criteria for scaling back community mitigation measures; dashboard posted to the COP on April 30 *(DA TF Update, May 1, 2020, 10:35 a.m. ET)*

FEMA

Senior Leadership Brief COVID-19

May 1, 2020 12:00 p.m. ET

For the most up to date COVID-19 data (account required): https://geohealth.hhs.gov/arcgis/home/

Region	State/Location	EMAC	Federally Supported		Total Federal Vents (SNS + DoD)	SNS Status
			SNS	DoD		
1	CT		350		350	Delivered
1	MA		400		400	Delivered
1	RI		100		100	Delivered
2	NY	100	2,140		2,140	Delivered
2	NYC		2,400		2,400	Delivered
2	NJ	100	1,050	500	1,550	Delivered
3	MD	50	470		470	Delivered
3	DE	50	50		50	Delivered
3	DC	50	200		200	Delivered
4	FL		200		200	Delivered
4	GA		150		150	Delivered
5	IL	100	310		310	300 – Delivered 10 – En Route
5	Chicago		310		310	300 – Delivered 10 – En Route
5	MI		700		700	Delivered
5	IN		110		110	100 – Delivered 10 – En Route
6	LA		350		350	Delivered
6	BOP		20		20	Delivered
6	Navajo Nation		50		50	Delivered
6	Cherokee Nation (OK)		10		10	En Route
8	CO		100		100	Delivered
9	CA		0		0	N/A
9	LA County		170		170	Delivered
9	GU		55		55	30 – Delivered 25 – En Route
9	NV	50	150		150	Delivered
9	AZ		100		100	Delivered
9	CNMI		25		25	En Route
9	Federated States of Micronesia		30		30	En Route
9	Palau		10		10	En Route
9	Republic of the Marshal Islands		10		10	En Route
10	AK		60		60	Delivered
10	OR		0		0	Transferred to 140 NY
10	WA		73		73	WA returned 427 vents to the SNS
Total		**500**	**10,153**	**500**	**10,653**	

As of 4/29/2020 4:48 p.m.

PPE and Ventilator Quantities by Resource Subcategory and Status

Resource	Resource Subcategory	Obligated [1]	In Transit [2]	Delivered [3]	Total
Personal Protective Equipment (PPE)	Coveralls	1,420	39,000	566,863	607,283
	Face Shields	91,663	14,000	6,512,226	6,617,889
	Gloves	8,458,000	11,293,000	43,802,614	63,553,614
	Goggles	800		5,030	5,830
	K90 Masks			1,622,000	1,622,000
	N95 Respirators	25,822,417	3,355,440	48,009,243	77,187,100
	PAPR	1,200			1,200
	Surgical Gowns	287,058	98,200	4,948,810	5,334,068
	Surgical Masks	3,315,982	1,500,000	31,454,691	36,270,673
	Tychem Suits			43,525	43,525
	Tyvek Suits			6,575	6,575

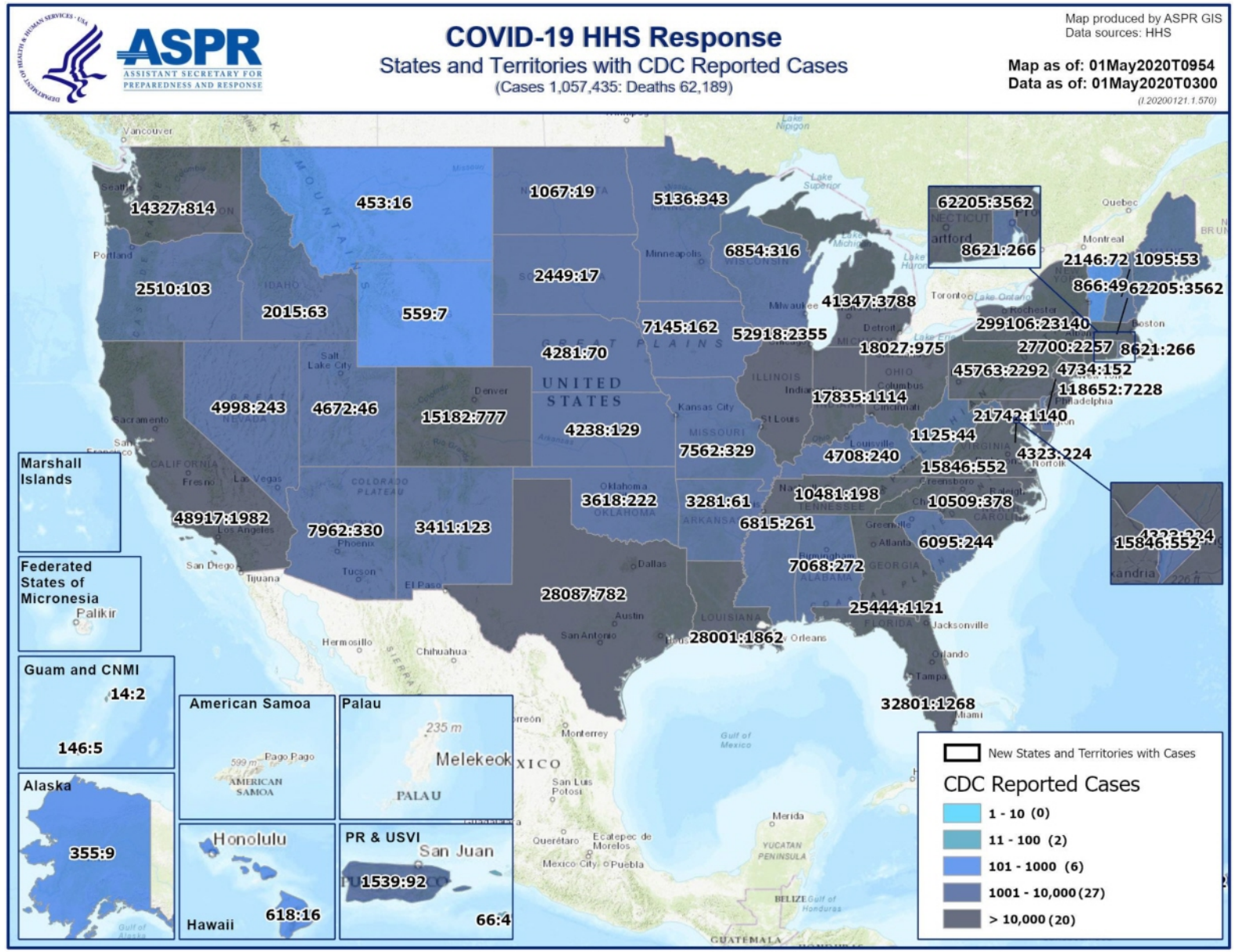
As of 4/30/2020 10:03 a.m.

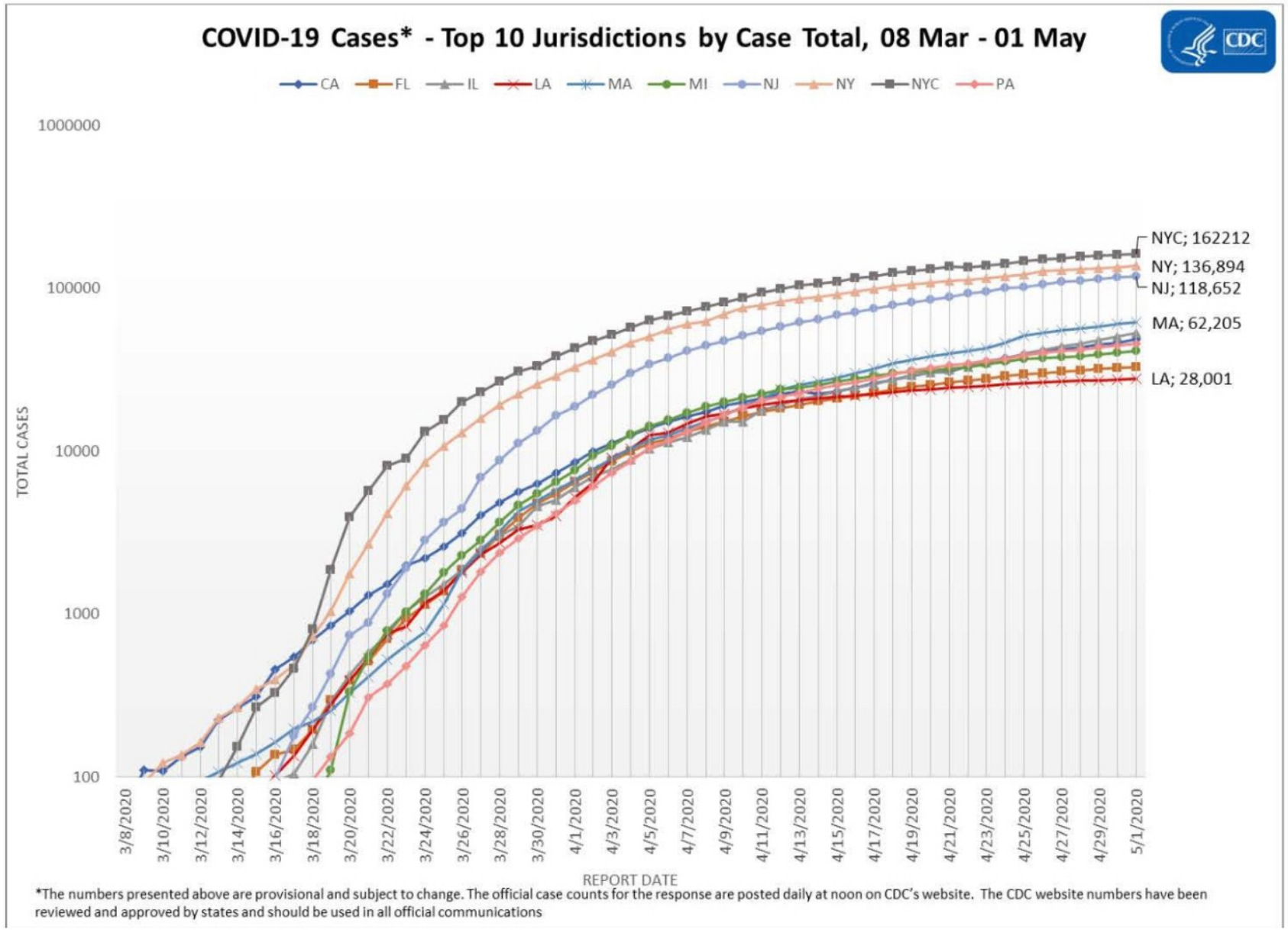
FEMA

Senior Leadership Brief COVID-19

May 1, 2020 12:00 p.m. ET

For the most up to date COVID-19 data (account required): https://geohealth.hhs.gov/arcgis/home/




COVID-19 Cases* - Top 10 Jurisdictions by Case Total, 08 Mar - 01 May
CDC
CA
FL
IL
LA
MA
MI
NJ
NY
NYC
PA
1000000
100000
10000
1000
100
TOTAL CASES
NYC; 162212
NY; 136,894
NJ; 118,652
MA; 62,205
LA; 28,001
3/8/2020
3/10/2020
3/12/2020
3/14/2020
3/16/2020
3/18/2020
3/20/2020
3/22/2020
3/24/2020
3/26/2020
3/28/2020
3/30/2020
4/1/2020
4/3/2020
4/5/2020
4/7/2020
4/9/2020
4/11/2020
4/13/2020
4/15/2020
4/17/2020
4/19/2020
4/21/2020
4/23/2020
4/25/2020
4/27/2020
4/29/2020
5/1/2020
REPORT DATE
*The numbers presented above are provisional and subject to change. The official case counts for the response are posted daily at noon on CDC's website. The CDC website numbers have been reviewed and approved by states and should be used in all official communications

Senior Leadership Brief COVID-19

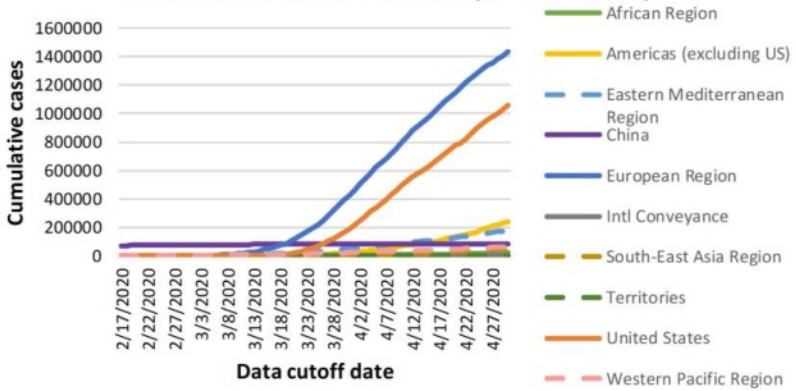
May 1, 2020 12:00 p.m. ET

For the most up to date COVID-19 data (account required): https://geohealth.hhs.gov/arcgis/home/

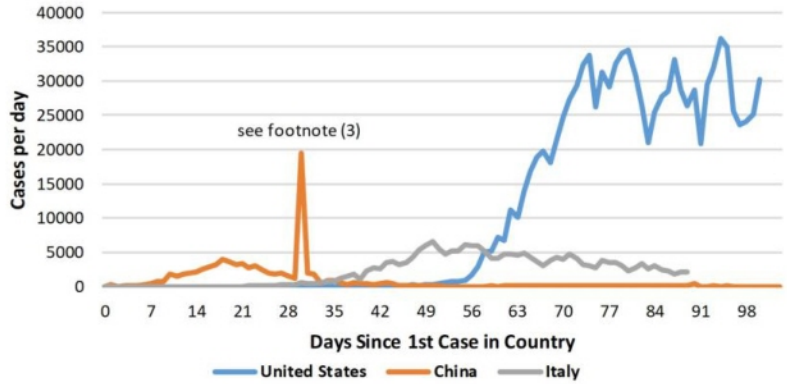
COVID-19 Cases

CDC SITREP data, as of May 1, 2020

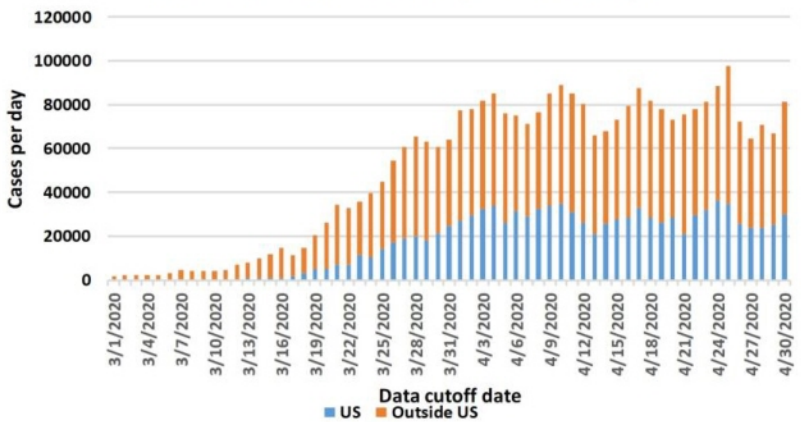
Cumulative COVID-19 cases (n = 3,143,906)



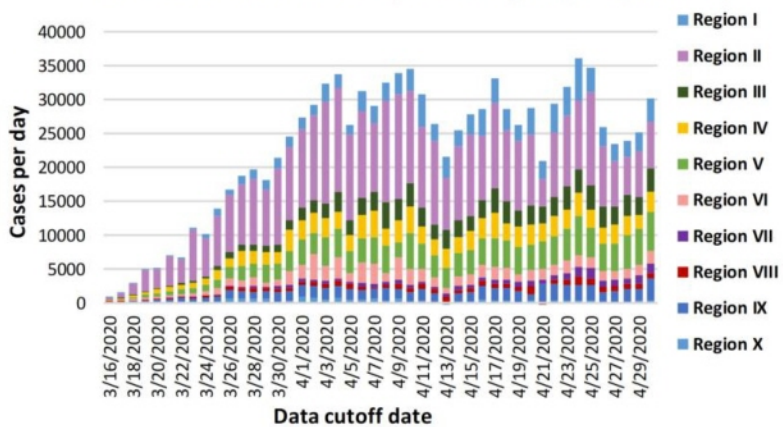
Incident Case Trends: China, Italy, and United States



Incident COVID-19 cases (n = 3,143,906)



Incident COVID-19 cases by FEMA region (n = 1,057,435)



Analyst notes: (1) International Conveyance captures the cruise ship "Diamond Princess," which arrived at Yokohama Port in Japan on 03FEB2020. (2) U.S. cases from "Diamond Princess" are being counted both in international conveyance and U.S. cases. (3) The sharp increase in cases reported for China on 17Feb2020 reflects a change in China's reporting of cases. For 17Feb2020, China reported 19,457 cases. Before this date, only laboratory confirmed cases were reported. Chinese case counts currently combine lab-confirmed and clinically diagnosed. (4) As of 03MAR2020, the case data were reported from the World Health Organization (WHO) SITREPS. Previously the data were obtained from the CDC updates and SITREPS. (5) Cumulative chart displays data since 17FEB2020. China's first case was reported on 19JAN2020 and the first case outside China on 20JAN2020. (6) Region I: CT, ME, MA, NH, RI, VT; Region II: NJ, NY, PR, VI; Region III: DE, DC, MD, PA, VA, WV; Region IV: AL, FL, GA, KY, MS, NC, SC, TN; Region V: IL, IN, MI, MN, OH, WI; Region VI: AR, LA, NM, OK, TX; Region VII: IA, KS, MO, NE; Region VIII: CO, MT, ND, SD, UT, WY; Region IX: AS, AZ, CA, GU, HI, MH, FM, NV, MP, PW; Region X: AK, ID, OR, WA. (7) Titles show cumulative cases through most recent date. (8) FEMA region chart displays data since 16MAR2020. Total cases before 16MAR2020 was 3730. (9) Incident COVID-19 cases graph displays data since 01Mar2020. Total US cases prior to 01Mar is 66. Total cases outside the US prior to 01Mar is 85,135.

Created by ODA

Senior Leadership Brief COVID-19

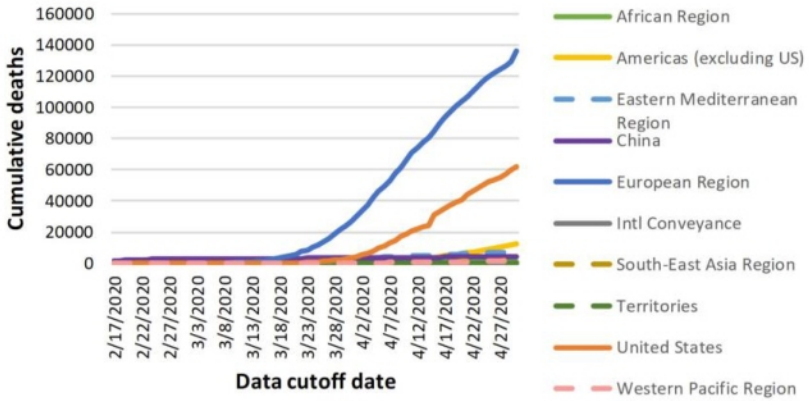
May 1, 2020 12:00 p.m. ET

For the most up to date COVID-19 data (account required): https://geohealth.hhs.gov/arcgis/home/

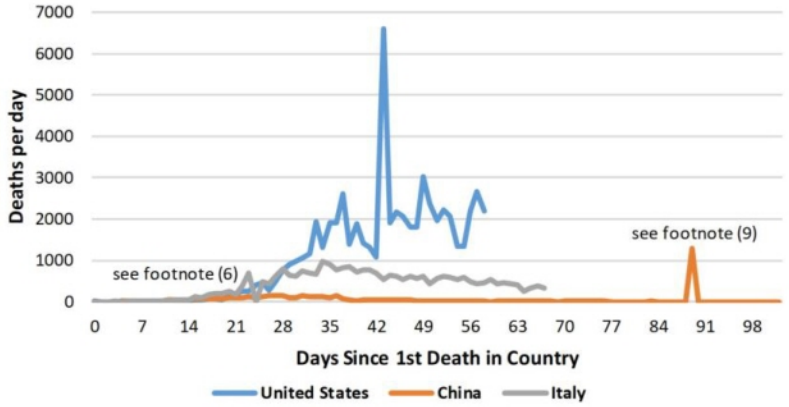
COVID-19 Deaths

CDC SITREP data, as of May 1, 2020

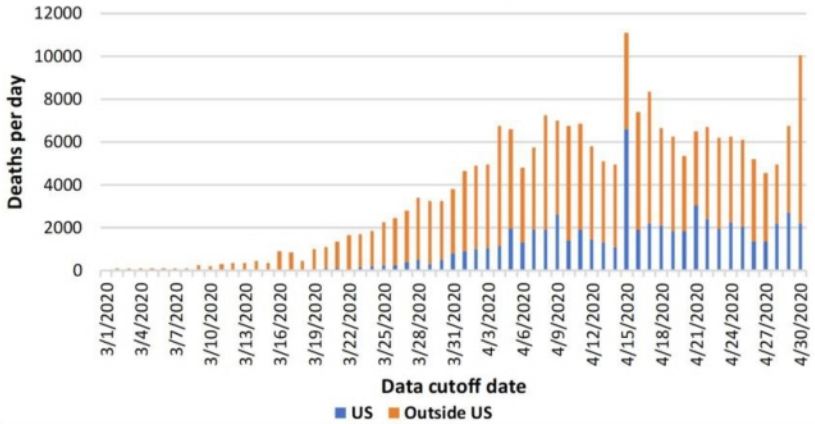
Cumulative COVID-19 deaths (n = 227,530)



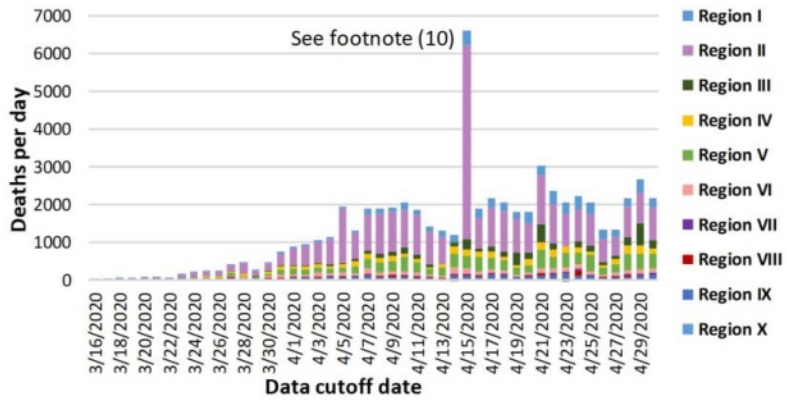
Incident Death Trends: China, Italy, and United States



Incident COVID-19 deaths (n = 227,530)



Incident COVID-19 deaths by FEMA region (n = 62,189)

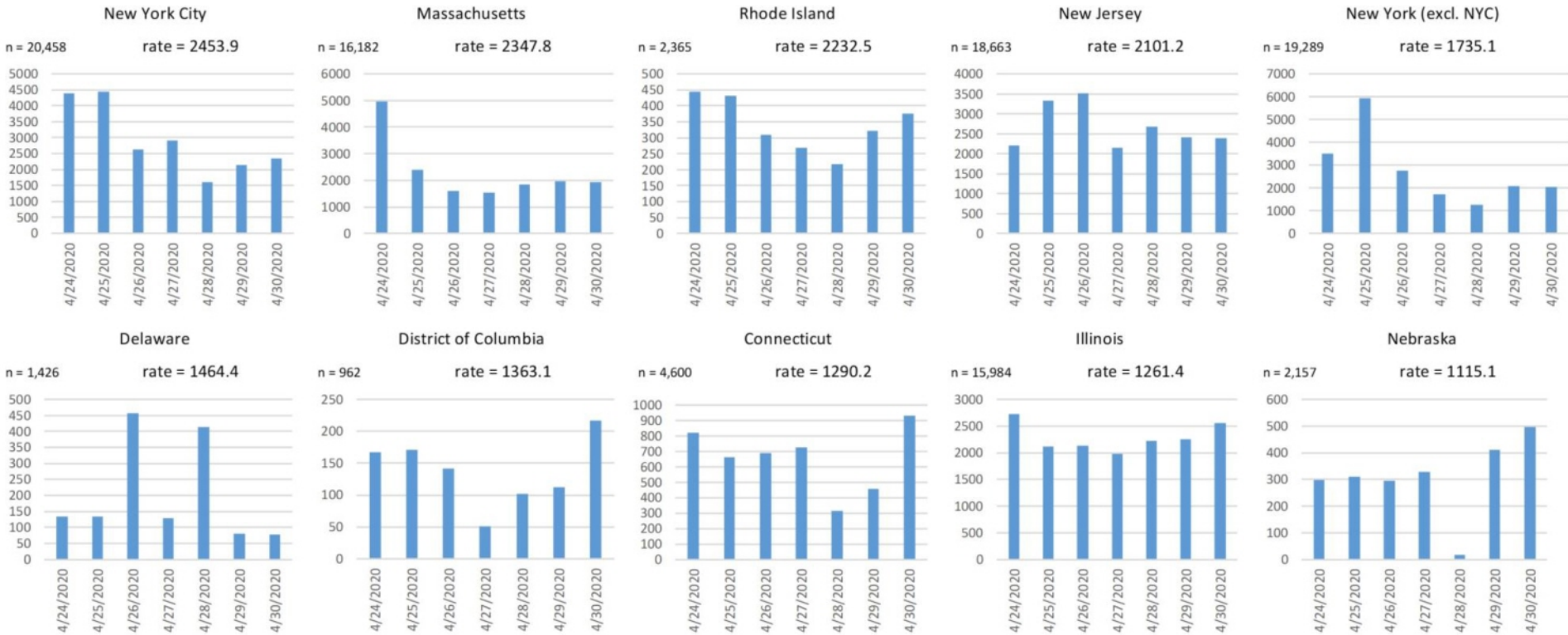


Analyst notes: (1) International Conveyance captures the cruise ship "Diamond Princess," which arrived in Japan on February 3rd. (2) Cumulative chart displays data since 17FEB2020. China's first death was reported on 19JAN2020 and the first death outside China on 02FEB2020. (3) Region I: CT, ME, MA, NH, RI, VT; Region II: NJ, NY, PR, VI; Region III: DE, DC, MD, PA, VA, WV; Region IV: AL, FL, GA, KY, MS, NC, SC, TN; Region V: IL, IN, MI, MN, OH, WI; Region VI: AR, LA, NM, OK, TX; Region VII: IA, KS, MO, NE; Region VIII: CO, MT, ND, SD, UT, WY; Region IX: AS, AZ, CA, GU, HI, MH, FM, NV, MP, PW; Region X: AK, ID, OR, WA. (4) Titles show cumulative deaths through most recent date. (5) As of 03MAR2020, the deaths data were reported from WHO SITREPS. Previously the data were obtained from the CDC updates and SITREPS. (6) The 18MAR2020 WHO SITREP did not have death updates for Italy. (7) FEMA region chart displays data since 16MAR2020. Total deaths before 16MAR2020 was 68. (8) Incident COVID-19 deaths graph displays data since 01Mar2020. Total US deaths prior to 01Mar is 0. Total deaths outside the US prior to 01Mar is 2,922. (9) The spike in deaths in China on 17APR2020 is due to a review of deaths in Wuhan. (10) The large spike in U.S. deaths on 15APR2020 is due to inclusion of deaths of probable cases.

Created by ODA

Number and rate (per 1M persons) of COVID-19 cases, past 7 days among top 10 U.S. locations with highest rates

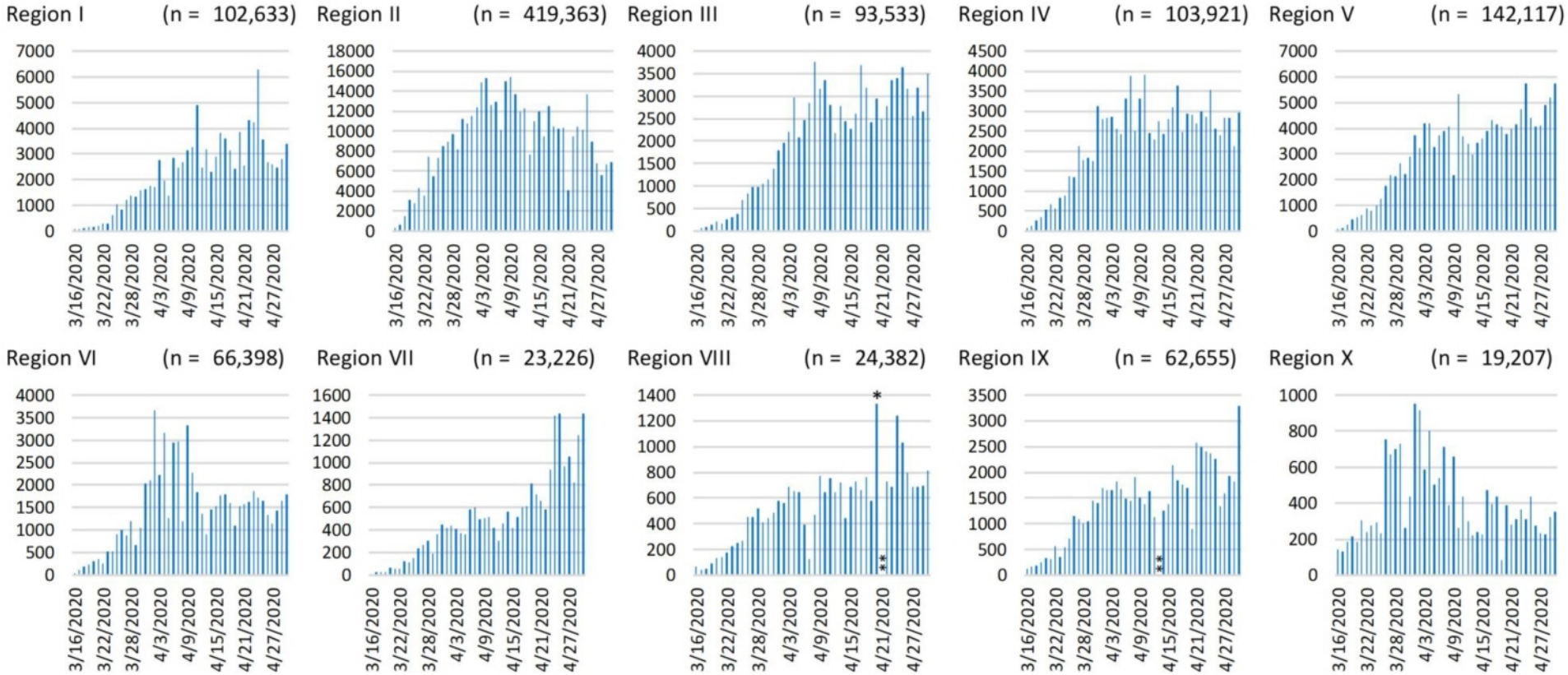
CDC SITREP data, as of May 1, 2020



Notes: (1) Data are from CDC SITREPS. (2) The y-axis of the graphs varies.

Incident COVID-19 cases by FEMA region (cumulative cases in parentheses)

CDC SITREP data, as of May 1, 2020



*Notes: (1) Data are from CDC SITREPS. (2) The y-axis of the graphs varies. (3) The charts display data since 16MAR2020. Total cases in the U.S. before 16MAR2020 was 3,730. *The increase in Region VIII cases on 20Apr is due to the inclusion of probable cases reported in Colorado. **A state in the region updated reported values of new cases, resulting in negative values.*

Coronavirus (COVID-19) Pandemic Whole-of-America Response

Friday, May 1, 2020

"TOGETHER, WE HAVE TURNED A CRITICAL DEMAND FOR PPE FOR OUR SENIORS AND FRONTLINE HEALTH WORKERS INTO A REALITY." - FEMA ADMINISTRATOR PETE GAYNOR

Topline Briefing Points and Messages

- On **April 30**, President Trump announced additional efforts to ensure the safety and well-being of America's seniors during the coronavirus pandemic.
  - FEMA is coordinating two shipments totaling a 14-day supply of personal protective equipment to all 15,400 Medicaid and Medicare-certified nursing homes in America. The first shipments are expected to begin next week. The shipments are meant to supplement existing efforts to provide equipment to nursing homes.
  - The Centers for Medicare & Medicaid Services is providing states with $81 million from the CARES Act to increase their inspections of nursing homes.
  - HHS recently announced nearly $1 billion in grants to assist older adults and people with disabilities, providing services such as home delivered meals and care services in the home.
- On **April 27**, President Trump unveiled the Opening Up America Again Testing Overview and Testing Blueprint designed to facilitate state development and implementation of the robust testing plans and rapid response programs described in the President's Guidelines for Opening Up America Again.
  - The President's Testing Blueprint sets forth the partnership between federal, state, local, and tribal governments, along with the private-sector and professional associations, all of which will play important roles in meeting the Nation's testing needs.
- To support the Administration's Testing Blueprint, FEMA, at the direction of the White House Coronavirus Task Force, is working to source and procure testing material – specifically, testing swabs and transport media.
  - The FEMA-sourced material will be provided to states, territories and tribes for a limited duration to help increase testing capacity in support of their individualized plans.
  - Once sourced and procured, the intent is to have this material shipped directly to a single location within each state, territory or tribe for their ultimate distribution.
  - Each state, territory and tribe will develop its own distribution strategy to align with its testing plan and unique needs.
- As of **April 30**, CDC, state, and local public health labs and other laboratories have tested more than 6 million samples.
  - States should be making full use of the testing resources available to them, to include leveraging the full capacity available through commercial laboratories in addition to the capability provided through state laboratories.
  - HHS and FEMA have expanded items supplied by the International Reagent Resource (IRR) to help public health labs access free diagnostics supplies and reagents.

  - To date, the FDA has issued 50 individual emergency use authorizations for test kit manufacturers and laboratories.

- As of **April 30**, FEMA, HHS, and the private sector combined have coordinated the delivery of or are currently shipping: 78.3 million N95 respirators, 111.8 million surgical masks, 7.3 million face shields, 16.9 million surgical gowns, 888.6 million gloves, 10,653 ventilators and 8,450 federal medical station beds.

Supply Chain Task Force

- FEMA continues to expedite movement of commercially pre-sourced and commercially procured critical supplies from the global market to medical distributors in various locations across the U.S. through Project Airbridge.
- As of April 30, Project Air Bridge has completed 104 flights with an additional 31 scheduled, or in transit, for a total of approximately 135 flights.
  - Five flights landed yesterday, April 30: two in Chicago, two in Los Angeles, and one in New York.
  - Four flights are scheduled to land today, May 1: three in Chicago, and one in Los Angeles.
  - It is important to note that any number of variables can affect international flight schedules, causing unexpected delays, cancellations or variations in final cargo quantities.
- The Air Bridge program delivers PPE to the point of greatest need through prioritized distributor supply chains nine times faster than movement by sea.
- Through Project Air Bridge, the following supplies have been delivered from overseas manufacturers to the U.S. and into private sector supply chains from March 29 through April 30:
  - More than 768,000 N95 respirators
  - 825 million gloves
  - 75.5 million surgical masks
  - 11.6 million surgical gowns
  - More than 2.2 million thermometers
  - More than 648,000 face shields
  - More than 198,000 coveralls
  - 109,000 stethoscopes
- Additionally, five flights of FEMA-procured 3 million masks are scheduled to land today, May 1: two in Washington, D.C. (Dulles), two in New York City (JFK) and one in Chicago. Four flights landed yesterday, April 30: one each in Baltimore, Chicago, New York City and Washington, D.C.
  - Since April 12, 33 flights carrying a total of approximately 30 million FEMA-procured masks and respirators form 3M have landed. Masks are inventoried at a warehouse and then distributed to prioritized areas as determined by FEMA and HHS.
- The strategy to allocate medical supplies and equipment is based on COVID-19 disease activity and its effects, as well as the need to facilitate distribution of limited supplies to areas where resources are needed most urgently.
  - Leveraging quantitative data sets provided by FEMA, HHS, and Centers for Disease Control and Prevention (CDC), FEMA's National Resource Prioritization Cell combines these data streams, analyzes the available COVID-19 disease activity data to determine current and potential future areas that most urgently require resources.

  - The team of experts works through this process every 96 hours to ensure resource prioritization recommendations are driven by the best available or most current data.
- The Defense Logistics Agency awarded a contract to Battelle for 60 N95 Critical Care Decontamination System units for the sanitation and reuse of N95 respirators.
  - Thirty systems have been delivered: three to Texas, two to California and New York and one each to Arkansas, Colorado, Connecticut, Florida, Georgia, Illinois, Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Missouri, Montana, New Jersey, New Mexico, North Dakota, Ohio, Pennsylvania, Rhode Island, Virginia, Washington and the District of Columbia. Additional systems are allocated to Alabama, Arizona, Colorado (second unit), Idaho, Indiana, Nevada, Oregon, Tennessee, and Texas (fourth and fifth units).
  - Additional units are planned for deployment across the U.S. by early May.

By the Numbers

- Forty-two states, four territories and more than 37 tribes have issued stay-at-home orders.
- All 50 states, five territories, and Washington, D.C. have been approved for major disaster declarations to assist with additional needs identified.
- To date, CDC, state, and local public health labs and other laboratories have tested more than 6 million samples.
  - As of **April 30**, 133,496 samples have been tested at Community Based Testing Sites.
- FEMA and HHS combined have obligated $51.1 billion to support COVID-19 response efforts from the first three emergency supplemental appropriations.
- The federal government has approximately 12,014 total ventilators available: 10,932 in the Strategic National Stockpile; 1,082 from the Department of Defense.
- As of **April 30**, FEMA and HHS have provided or are currently shipping 10,653 ventilators from the Strategic National Stockpile and the Defense Department to states, tribes and territories.
- In support of the U.S. Department of Veterans Affairs and our nation's veterans, FEMA has coordinated shipments of more than 4.3 million respirator masks, 1 million surgical masks, 1.5 million gloves, and 14,000 face shields to facilities across the country. An additional 1 million surgical masks and 28,000 gowns are shipping this week.
- FEMA has 3,157 employees supporting COVID-19 pandemic response out of a total 20,605 agency employees ready to respond to other emergencies should they occur.
- As of **April 30**, FEMA has obligated $5.8 billion in support of COVID-19 efforts.
- As of **May 1**, 85 agencies across 28 states, the District of Columbia, one tribe and one U.S. territory have sent 214 alerts with information on COVID-19 via the Wireless Emergency Alert system; 51 alerts to broadcast stations via the Emergency Alert System.
- To date, the President has approved 48 National Guard requests for federal support for the use of National Guard personnel in a Title 32 duty status.
  - Pursuant to this approval, the federal government will fund 100 percent of the cost share for T-32 National Guard orders through May 31.
  - More than 38,000 National Guard troops have activated in T-32 duty status and 1,367 troops have activated in State Active Duty status to help with testing and other response efforts.

- The CDC has 3,977 personnel supporting the outbreak response.
- The U.S. Public Health Service deployed more than 1,500 officers in support of nation-wide efforts to mitigate the virus' potential spread.
- To date, the U.S. Department of Veterans Affairs has made more than 1,400 acute and intensive care hospital beds across the nation available to non-veteran patients, if necessary.
- The U.S. Army Corps of Engineers has awarded 34 contracts for the design and build of alternate care facilities in Alaska, Arizona, California, Colorado, District of Columbia, Florida, Illinois, Maryland, Michigan, Missouri, the Navajo Nation, New Jersey, New Mexico, New York, Oklahoma, Oregon, Tennessee, U.S. Virgin Islands, and Wisconsin.
    - As of **May 1,** 1,354 USACE personnel are activated to support the COVID-19 mission, with more than 15,000 personnel engaged in additional response efforts.

FEMA and HHS Response

- FEMA, HHS, and our federal partners work with state, local, tribal and territorial governments to execute a whole-of-America response to COVID-19 pandemic and protect the health and safety of the American people.
- FEMA, HHS and the Cybersecurity Infrastructure and Security Agency (CISA) along with other federal agencies are distributing cloth face coverings for critical infrastructure workers as part of a multi-prong approach to re-open American economic activity while continuing to limit spread of COVID-19.
    - As of **April 29**, over 50.5 million cloth face coverings are being processed and distributed to state, local, tribal, private sector, and federal entities
    - The federal government will provide additional face coverings in production to states, territories and tribes for distribution, with priority to emergency services, food production and distribution, and other sectors that support community lifelines.
    - FEMA and HHS are also providing face coverings to federal departments and agencies with mission essential functions to promote health and safety in the workplace and in their execution of public-facing missions

FEMA

- On **March 13**, President Trump declared a nationwide emergency pursuant to the Stafford Act.
    - 50 states, the District of Columbia, five territories, and 37 tribes are working directly with FEMA.
    - A tribal government may choose to be a subrecipient under a state that has chosen to be a recipient of FEMA assistance, or choose to be a direct recipient of FEMA.
    - All 10 Regional Response Coordination Centers and emergency operations centers in all states and territories are active and supporting response efforts across the country.
- Requests for assistance, especially for critical supplies, should be routed through the proper channels as soon as possible. The most efficient way to identify critical gaps and get results:
    - Consistent with the principle of locally executed, state managed, and federally supported response, requests for assistance at the local and county levels should first be routed to their respective state.

  - Any needs that cannot be met by the state or tribe should then be sent to the respective FEMA regional office. FEMA regions will direct requests to the FEMA NRCC in Washington, D.C. for fulfillment.

- HHS and FEMA deployment of ventilators from the stockpile have helped ensure that hospitals in states such as New York have not run out of ventilator capacity while working to save lives.
  - The federal government adopted a process to manage allocation of federal ventilator resources to ensure the right number of ventilators are shipped to the right states to sustain life within a 72-hour window.
  - Emergency managers and public health officials submit requests for ventilators to FEMA/HHS, providing detailed data on total medical/ hospital beds; total acute care (ICU) beds; normal occupancy; predicted surge occupancy; and number of ventilators available in the state.
- On **April 25**, FEMA announced that more than $5.1 million dollars in crisis counseling service grants have been made available to five states to support programs providing free, confidential counseling through community-based outreach and educational services.
    - On **April 30**, amendments were made to 31 major disaster declarations, making crisis counseling service grants available to an additional 30 states and the District of Columbia.
- On **April 23**, FEMA announced an additional $100 million in funding for the Assistance to Firefighters Grant Program. This supplemental funding will provide financial assistance directly to eligible fire departments, non-affiliated emergency medical service organizations and State Fire Training Academies for critical PPE and supplies needed to respond to COVID-19. The application period begins April 28.
- On **April 20**, President Trump launched the Dynamic Ventilator Reserve Program, an innovative public-private partnership to access up to 65,000 additional ventilators in hospitals across the country that can be redeployed when not in use.
- On **April 15**, FEMA Administrator Pete Gaynor issued a letter to the nation's emergency managers outlining lessons learned from the first 30 days of FEMA leading the "Whole-of-America" response to the coronavirus (COVID-19) pandemic.
  - This guidance is a follow-on to the Administrator's first letter to emergency managers on March 27, which requested key actions and outlined critical steps for the initial COVID-19 response
- On **April 15**, FEMA's Office of Equal Rights issued a bulletin outlining best practices to assist state, local, tribal and territorial partners in anticipating and attending to civil rights concerns during the COVID-19 response and recovery.
- On **April 13**, The Department of Homeland Security and FEMA announced the funding notice for an additional $100 million in supplemental Emergency Management Performance Grant Program funds.
- On **April 12**, FEMA issued guidance on the framework, policy details and requirements for determining the eligibility for FEMA reimbursement of states purchasing and distributing food to meet the immediate needs of those who do not have access to food as a result of COVID-19 and to protect the public from the spread of the virus.
- On **April 9**, FEMA announced that it is suspending rent for disaster survivors living in FEMA-purchased temporary housing units in California, Florida, North Carolina and Texas. The temporary suspension means residents will not have to pay rent in April, May or June.

- On **March 26**, FEMA issued a request for quotation for vendors who have medical equipment and supplies to sell to the agency. The RFQ can be found on www.sam.gov.

U.S. Department of Health and Human Services Agencies and Offices

- On **April 30**, HHS through the Health Resources and Services Administration, awarded $20 million to increase telehealth access and infrastructure for providers and families to help prevent and respond to COVID-19.
    - The funds will increase capability, capacity and access to telehealth and distant care services for providers, pregnant women, children, adolescents and families. It will assist telehealth providers with cross-state licensure to improve access to health care during the pandemic.
- On **April 29**, the National Institutes of Health announced positive results of a trial using Remdesivir; patients with advanced COVID-19 and lung involvement who received Remdesivir recovered, on average, faster than similar patients who received placebo.
- On **April 29**, the National Institutes of Health announced a new initiative, Rapid Acceleration of Diagnostics; aimed at speeding innovation, development, and commercialization of COVID 19 testing technologies and funded by $1.5 billion from federal stimulus.
- On **April 27**, HHS, through the Health Resources and Services Administration (HRSA), launched a new COVID-19 Uninsured Program Portal, allowing health care providers who have conducted COVID-19 testing or provided treatment for uninsured COVID-19 individuals on or after Feb. 4 to submit claims for reimbursement.
- On **April 24**, the Substance Abuse and Mental Health Services Administration (SAMHSA) announced an additional $250 million in emergency COVID-19 funding for the grants have been to increase access to and to improve the quality of community mental and substance use disorder (SUD) treatment services through the expansion of Certified Community Behavioral Health Clinics (CCBHC).
- As of **April 24**, the Biomedical Advanced Research and Development Authority (BARDA) within the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR) has a COVID-19 Medical Countermeasure Portfolio that includes development of 26 products supported under public-private partnerships.
    - Of these, 15 are diagnostics, seven are treatments, three are vaccines, and one is a rapidly deployable capability to help protect the American people from COVID-19.
    - To date, BARDA has obligated $39.8 million for diagnostics, $334.9 million for treatments, more than $979.3 million for vaccines.
- On **April 23**, HHS, through the through the Health Resources and Services Administration, awarded nearly $5 million to Poison Control Centers across the country to improve their capacity to respond to increased calls due to the COVID-19 pandemic.
    - As more Americans heed cleaning recommendations to combat exposure to COVID-19, the nation's Poison Control Centers are seeing sharp increases in calls related to cleaners and disinfectants.
- On **April 22**, HHS launched Telehealth.hhs.gov. The site is a central source of information on telehealth resources and tools for patients and providers.
- On **April 21**, HHS announced $955 million in grants from the Administration for Community Living to help meet the needs of older adults and people with disabilities. The grants will fund

home-delivered meals, care services in the home, respite care and other support to families and caregivers, and other support services.

- On **April 20**, the Substance Abuse and Mental Health Services Administration under HHS began releasing $110 million in emergency grant funding to strengthen access to treatments for substance use disorders and serious mental illnesses during the COVID-19 pandemic.
- On **April 13**, HHS announced five new contracts for ventilator production rated under the Defense Production Act (DPA), to General Electric, Hill-Rom, Medtronic, ResMed, and Vyaire, as well as two other contracts for ventilator production, to Hamilton and Zoll.
    - Combined with contracts with General Motors, Philips and GE rated under the DPA issued last week, the contracts will provide a total of 187,431 ventilators by the end of 2020.
- Beginning **April 10**, HHS and FEMA are working with states with federal Community-Based Testing Sites to clarify whether sites want to continue as they are now, or transition to full state control.
- On **April 10**, HHS began delivering the initial $30 billion in relief funding to providers in support of the national response to COVID-19, with $26 of the $30 billion expected to be delivered to providers' bank accounts the same day.
- On **April 10**, HHS Secretary Azar sent a follow up letter to hospital administrators, reinforcing the need for data to be provided daily to facilitate planning, monitoring, and resource allocation in response to COVID-19.
- On **April 8**, HHS, through the Health Resources and Services Administration awarded more than $1.3 billion to 1,387 health centers. These centers will help communities across the country detect coronavirus; prevent, diagnose, and treat COVID-19; and maintain or increase health capacity and staffing levels to address this public health emergency.
- On **April 6**, HHS announced it will release $186 million in additional CDC funding to state and local jurisdictions with accelerating or rapidly accelerating COVID-19 cases to support response activities and surveillance capabilities.
- HHS identified $80 million dollars specifically for tribes, tribal organizations, and tribal health service providers.

Centers for Disease Control and Prevention

- The nation's Slow the Spread campaign ended **April 30**. CDC continues to recommend that everyone use a cloth face covering in community settings to help reduce the spread of COVID-19.
- On **April 28**, the Centers for Disease Control and the Environmental Protection Agency issued guidance on for cleaning and disinfecting spaces when reopening America; the guidance offers step by step instructions on how Americans can reduce risk of exposure to COVID 19 and stay safe in public spaces, workplaces, businesses, schools, and homes.
- CDC continues to encourage use of personal protective equipment optimization strategies for healthcare providers to optimize resources, deal with limited resources, and make contingency plans or alternative strategies when supplies are limited.
- On **April 26**, CDC and the Occupational Safety and Health Administration (OSHA) released targeted guidance to help meat and poultry processing facilities implement infection control practices to reduce the risk of transmission and illness from COVID-19 in these facilities.
- On **April 8**, CDC issued additional guidance to help ensure critical infrastructure workers can perform their jobs safely after potential exposure to the virus.

- On **April 3**, CDC launched COVIDView, a weekly report that summarizes and interprets key indicators from a number of existing surveillance systems.

Food and Drug Administration (FDA)

- FDA launched the Coronavirus Treatment Acceleration Program (CTAP) to speed approval of drugs and therapies. 72 therapies are now being tested, including hydroxychloroquine, and another 211 are in active planning for clinical trials.
- FDA published a new blog post on the Coronavirus Treatment Acceleration Program. The program uses every available method to move new treatments to patients as quickly as possible, while at the same time finding out whether the treatments are helpful or harmful.
- FDA has granted more than 71 Emergency Use Authorizations of commercially available diagnostic tests, including 41 molecular diagnostic tests, 21 laboratory-developed tests, seven antibody tests, and two repurposed treatments (chloroquine, hydroxychloroquine).
- FDA has authorized four mask sterilizations systems to disinfect N95 masks, with one system that can decontaminate 4 million N95 masks per day.
- On **April 28**, the FDA issued a new video resource explaining Emergency Use Authorizations (EUAs), one of several tools FDA uses to help make important medical products available quickly during public health emergencies like the COVID-19 pandemic.
    - EUAs provide more timely access to drugs, diagnostic tests and/or other critical medical products that can help diagnose, treat and/or prevent COVID-19.
- On **April 27**, the FDA released two new fact sheets for the food and agriculture sector outlining guidelines on use of disposable facemasks and cloth coverings, as well as summarizing key steps employers and coworkers can take to stay open, continue to slow the spread and support continuity of essential operations.
- During the **April 24** White House Press Briefing, FDA Commissioner Dr. Stephen Hahn announced approval the first COVID-19 home collection test kit.
- On **April 21**, the FDA issued an emergency use authorization for IntelliVue Patient monitors intended to be used by healthcare professionals in the hospital environment for remote monitoring of adult, pediatric and neonate patients having or suspected of having COVID-19 to reduce healthcare provider exposure.
- On **April 16**, the FDA announced an expansion of testing options through use of synthetic swabs – with a design similar to Q-tips – to test patients by collecting a sample from the front of the nose.
- On **April 14**, the FDA issued a consumer update: How You Can Make a Difference During the Coronavirus Pandemic, outlining ways to help such as donating blood or saving PPE for frontline workers.
- On **April 3**, the FDA announced a new national effort to bring blood-related therapies for COVID-19 to market as fast as possible.
    - HHS and the Assistant Secretary for Preparedness and Response's Biomedical Advanced Research and Development Authority (BARDA) will collaborate with American Red Cross and three companies on the development of convalescent plasma and hyperimmune globulin immunotherapies to make safe and effective treatments available.
- The FDA released food shopping information to reassure consumers that there is currently no evidence of human or animal food or food packaging being associated with transmission of the coronavirus that causes COVID-19.

Other Federal Agencies

- American Red Cross and the American Association of Blood Banks (AABB) continue to seek blood and convalescent plasma donations. To find where you can donate blood, visit aabb.org.
- On **April 28**, President Trump signed an executive order to keep meat processing plants open to ensure the continued supply of beef, pork, and poultry to the American people. The order uses the Defense Production Act to classify meat processing as critical infrastructure.
    - The Centers for Disease Control and Prevention and the Occupational Safety and Health Administration have put out guidance for plants to help ensure employee safety.
- On **April 27**, the Small Business Administration relaunched the Paycheck Protection Program after distributing $350 billion in loans to 1.6 million businesses earlier this month. Including last week's funding bill, more than $670 billion is available for the loan program in total.
- As of **April 23**, the USCG has facilitated the safe discharge of over 275,000 passengers from more than 125 cruise ships as a result of the orderly shutdown of the cruise industry. The Coast Guard will continue to work with CDC, state and local authorities to manage cruise ships and commercial vessels in US waters.
- On **April 17**, U.S. Department of Agriculture announced the Coronavirus Food Assistance Program, an immediate relief program that provides $16 billion in direct support to farmers and ranchers as well as $3 billion to purchase and distribute fresh produce, dairy and meat products to food banks, community and faith-based organizations and other non-profits
- On **April 17**, the Cybersecurity and Infrastructure Security Agency released version 3.0 of the Essential Critical Infrastructure Workers guidance to help state and local jurisdictions and the private sector identify and manage their essential workforce while responding to COVID-19.
- On **April 15**, Immigration and Customs Enforcement Homeland Security Investigations launched Operation Stolen Promise to combat COVID-19 related fraud and other criminal activity.
- On **April 9**, the U.S Department of Education announced more than $6 billion from the CARES Act will be distributed to colleges and universities to provide direct emergency cash grants to college students whose lives and educations have been disrupted by the coronavirus outbreak.
    - On **April 21**, the Department of Education is planning to announce an additional $6.28 billion in funding for institutions to cover costs associated with significant changes to the delivery of instruction due to COVID-19.
- On **April 3**, President Trump issued "Memorandum on Allocating Certain Scarce or Threatened Health and Medical Resources to Domestic Use" directing DHS and FEMA, in consultation with the HHS, to use the Defense Production Act to keep scarce medical resources within the United States for domestic use. CBP is assisting FEMA in temporarily detaining export shipments of PPE.
- The U.S. Department of Labor announced availability of up to $100 million for Dislocated Worker Grants to help address the workforce-related impacts related to COVID-19.

Coronavirus (COVID-19) Pandemic: Daily Briefing Points Supplemental

Friday, May 1, 2020

Regional Response

Region II

Metro New York/New Jersey

- Total medical supplies and equipment obligated or provided to New York include 12.5 million N95 respirators, 2.6 million surgical masks, 469,682 face shields, 298,810 surgical gowns, 289,820 coveralls, 2.2 million gloves, and 4,540 ventilators.
    - Governor Cuomo has sent ventilators to Michigan (100), New Jersey (100), Massachusetts (400) and Maryland (50).
- Medical supplies and equipment obligated or provided to the State of New Jersey include 5.9 million N95 respirators, 2 million surgical masks, 307,358 face shields, 184,335 surgical gowns, 133,848 coveralls, 12.1 million gloves, 1,550 ventilators and 1,000 federal medical station beds.
- As of April 30, FEMA has obligated more than $1.09 billion in federal support to the state of New York and $402 million in federal support to the state of New Jersey.
- FEMA issued a Mission Assignment to the U.S. Army Corps of Engineers (USACE) to support design and build out of alternative medical facilities in New York and New Jersey.
    - The Jacob Javits Center is operational with a maximum capacity of 2,148 beds and has cared for more than 1,095 patients. All patients will be transitioned out of Javits Center by May 1.
    - The USACE buildout of three New York state priorities for alternate care facility conversions at State University (SUNY) Stony Brook, SUNY Old Westbury, and the Westchester Community Center have been completed. These sites, including all staffing, equipment and wrap around services, will be managed by the State.
    - Four FMS are being utilized to establish temporary medical facilities at three New Jersey locations: Secaucus, Edison FMS and Atlantic City.
- The USNS Comfort completed its mission in New York City. The hospital ship arrived on March 30 to relieve strain on local hospital systems. The ship cared for 182 patients. The USNS Comfort departed New York City on April 30.
- More than 1,200 Department of Defense (DOD) medical staff, including six Urban Augmentation Medical Task Forces (UAMTF) are supporting New York by:
    - Providing medical support for the Javits Center and USNS Comfort alternate care sites.
    - Supplementing medical staff at 10 hospitals throughout the five boroughs.
- Three UAMTFs made up of 255 medical personnel are supporting five sites in New Jersey: the ACF in Edison, Newark University Hospital, Salem Hospital, JFK Medical Center, and the ACF in Atlantic City.

- New York State medical surge support includes 85,000 surge volunteers, 24,600 mental health workers and more than 200 NY National Guard members.
  - NYSDOH hired an additional 7,000 health care workers.
- New York Governor Cuomo announced that the state would allow elective outpatient treatment in hospitals around the state if they meet specific criteria including the number of available beds and the number of COVID-19 hospitalizations in that facility.
- At New York State's request, FEMA issued a $6 million mission assignment to HHS to provide round the clock medical staff to care for non-critical patients in the state.
- FEMA contracted 525 ambulances and 1,190 emergency personnel from across the country to support New York and New Jersey. They were contracted to supplement the state medical transportation and support capabilities. The units include Advanced Life Support and Basic Life Support ambulances, and medical/support personnel necessary to operate.
  - 350 ambulances and 790 emergency personnel began arriving in New York on March 30, are providing interfacility transfer throughout the most impacted areas. To date, they have responded to more than 10,000 calls to 9-1-1 and transferred more than 4,800 patients to hospitals and alternate care facilities.
  - 175 ambulances and 400 emergency personnel began arriving in New Jersey on April 11 and are providing interfacility transfers in Hudson, Passaic, Bergen, Essex, Union, Middlesex, Ocean and Mercer counties. To date, they have responded to more than 3,900 calls to 9-1-1 and transferred more than 1,400 patients to hospitals and alternate care facilities.
- The city is operating temporary morgue facilities across the New York City. One Disaster Portable Morgue Unit (DPMU) unit is operating out of the Brooklyn Marine Terminal.
- New York National Guard, DoD and HHS have arrived and are supporting mortuary operations.
  - 70 DoD and 43 HHS personnel are supplementing local mortuary capacity.
  - 250 New York National Guard personnel are supporting collection and transport operations.
- Eighty-five refrigerated storage units have arrived and are being pre-staged on Randall's Island. As needed, the units are pushed to location identified by city officials.
- New Jersey is operating two temporary morgue facilities at centralized location.
- FEMA issued a $350 million Mission Assignment to the U.S. Army Corps of Engineers for construction of additional alternate care facilities in New York.

Region III

Washington D.C. Metro Area (Washington, D.C., Maryland and Virginia)

- As of April 30, FEMA has obligated more than $43.5 million in federal support for the state of Maryland, more than $176 million to the state of Virginia and more than $55.6 million to the District of Columbia.
- FEMA delivered a 250-bed Federal Medical Station package to the state of Maryland.
  - Maryland National Guard deployed the FMS package to establish an alternate care site at the Baltimore Convention Center to increase state hospital capacity.
  - An additional 50 bed Federal Medical Station is allocated for the Metro DC area.

- As of April 28, one Battelle N95 decontamination unit is operational in Washington, DC.
- As of April 25, one Battelle N95 decontamination unit is operational in Baltimore.
- Virginia Governor Northam announced that hospitals and dentists may resume non-emergency procedures as of midnight Thursday, April 30.
- On April 8, FEMA obligated $55 million for USACE assessment and construction of medical surge support alternate care facilities for the District of Columbia.
    - USACE awarded a contract for an alternate care facility at Hagerstown Correctional Facility in Hagerstown, MD. The State took over construction operations on April 24.
    - USACE awarded contracts for two alternate care facilities in the District of Columbia at United Medical Center and the Walter Washington Convention Center. The United Medical Center facility completed construction on April 22.

Region V

State of Illinois and the City of Chicago

- Medical supplies and equipment delivered to the State of Illinois from FEMA, HHS, and donations include more than 3.4 million N95 respirators, more than 1.5 million surgical masks, 280,330 face shields, 223,320 million surgical gowns, 7,622 coveralls, and 6.3 million gloves.
- As of April 30, FEMA has obligated $262 million in federal support for the state of Illinois for the response to COVID-19.
- Through a collaborative engagement between FEMA, HHS, USACE, DOD personnel and state & city planners, FEMA has already committed more than $125 million in federal funding for the design and build out of four alternate care sites in the Chicagoland area, to help ensure surge capacity is available for residents to continue to get the best healthcare possible.
    - The 3,000-bed ACS at McCormick Place Convention Center is currently operational.
    - The sites at Sherman Hospital in Elgin (est. 280 bed capacity) and Metro South Hospital in Blue Island (est. 300 bed capacity) were completed and turned over to the state.
    - The Westlake Hospital site in Melrose Park (est. 435 bed capacity) was completed and turned over the state on April 25.
- One Battelle N95 decontamination unit is operational in Waukegan, Illinois.

State of Michigan

- Medical supplies and equipment delivered to the State of Michigan from FEMA, HHS, and donations include 2.1 million N95 respirators, 740,018 million surgical masks, 308,671 face shields, 121,703 surgical gowns, 3,888 coveralls, and 718,930 gloves.
- As of April 30, FEMA has obligated more than $246 million to the state of Michigan.
- As of April 26, FEMA and HHS delivered 700 ventilators and 500 federal medical station beds from the Strategic National Stockpile to Michigan.
- FEMA has committed $31 million in federal funding for the planning, design and build out of two alternate care sites in Michigan:
    - A 1,000-bed ACF at the TCF Convention Center in Detroit is operational.
    - One Battelle N95 decontamination unit has been delivered to the ACF at the TCF Convention Center.

- A second 250-bed ACF at Suburban Collection Showplace in Novi is open.

Region VI

State of Louisiana and the City of New Orleans

- As of April 30, FEMA has obligated $139 million in federal support for the state of Louisiana, including $55.7 million to the state to reimburse costs related to the COVID-19 response.
- Medical supplies and equipment delivered to the State of Louisiana include 1.1 million N95 respirators, 494,800 surgical masks, 88,433 surgical gowns, and 1.2 million gloves.
- 350 ventilators have been provided to the state.

State of Texas

- As of April 30, FEMA has obligated $393 million in federal support for the state of Texas, including $66.6 million to the state to reimburse costs related to the COVID-19 response.
- Medical supplies and equipment delivered to the State of Texas include 955,978 N95 respirators, 1.7 million surgical masks, 286,303 surgical gowns, and 1.6 million gloves.

Region IX

State of California

- Medical supplies and equipment delivered to the State of California include 2.2 million N95 respirators, 3.8 million surgical masks, 504,442 face shields, 416,017 surgical gowns, 7,007 coveralls, and 1.8 million gloves.
- As of April 30, FEMA had obligated more than $995 million in federal support for the state of California, including $619.8 million to the state to reimburse costs related to the COVID-19 response.
- USACE continues assessment of eight state-selected facilities to develop large-scale, supplemental hospital space as the state works to expand existing hospital capacity by up to 50,000 beds.
  - Out of the assessed facilities, USACE completed an alternate care facility at the Porterville Development Center in Porterville, CA.
  - The first of eight Federal Medical Stations initiated operations on March 29.
- Federal and state partners are working to convert the Craneway Pavilion into a 250-bed federal medical station.
- Two Battelle N95 decontamination units have been approved for California. One is operational in Burbank and the second will be set up in Fairfield.
- FEMA approved the state of California's emergency feeding program, Restaurants Deliver: Home Meals for Seniors. The initiative leverages restaurants struggling to maintain business to deliver meals to at-risk seniors over 65 years of age.
- The USNS Mercy hospital ship has seen 77 patients and has 250 staffed hospital beds available to help relieve strains on local hospital systems in Los Angeles.
  - USNS Mercy medical personnel are also providing support for 100 beds in a local facility.

- 170 ventilators from the Strategic National Stockpile were delivered to Los Angeles county.
- Through California's Emergency Management Assistance Compact, the state has loaned 500 ventilators to six states and the District of Columbia.
- The state is working on shelter space for at-risk population by providing over 11,000 hotel/motel rooms and 1,126 trailers deployed to Santa Clara, Los Angeles, and Sacramento counties. There are 12,156 units secured with 4,257 units currently occupied.
- FEMA completed the sale of 105 travel trailers to the state to support a State COVID-19 housing initiative for impacted individuals.
- On April 13, California Governor Newsom, Washington Governor Inslee and Oregon Governor Brown announced a Western States Pact to work on a shared approach for reopening their economies and controlling COVID-19.

State of Nevada

- As of April 30, FEMA has obligated $43.8 million in federal support for the state of Nevada.

Region X

State of Alaska

- Medical supplies and equipment delivered to the State of Alaska include 74,114 N95 masks, 176,063 surgical masks, 68,605 face shields, 41,542 surgical gowns, 1,791 coveralls, 286,252 gloves and 60 ventilators.
- As of April 30, FEMA has obligated $9.8 million in federal support for the state of Alaska.
- USACE completed construction of an alternate care site at Alaska Airlines Center. Activation date is to be determined.
- On April 21, Alaska Governor Dunleavy announced Phase One of the State's approach to reopening segments of the Alaskan economy starting on April 24.

State of Idaho

- Medical supplies and equipment delivered to the State of Idaho include 90,610 N-95 respirator masks, 215,357 surgical masks, 44,887 face shields, 36,842 surgical gowns, 223,974 gloves and 1,823 coveralls.
- As of April 19, the state of Idaho has released 300 FMS beds back to HHS for redeployment to meet other needs. Fifty were redeployed to New Mexico, 250 were redeployed to Colorado.
- As of April 30, FEMA has obligated $907,217 in federal support for the state of Idaho.
- On April 22, a Community Based Testing Site 2.0 began conducting tests at a Rite Aid in Meridian, ID. discussions continue on potential deployment of additional CBTS 2.0.
- One Battelle Critical Care Decontamination System is being prepared for shipment to Idaho National Laboratory in Idaho Falls.
- On April 14, Governor Little announced the four phases of reopening the economy.

State of Oregon

- Medical supplies and equipment delivered to the State of Oregon include 357,920 N95

respirator masks, 319,101 surgical masks, 130,643 face shields, 138,898 surgical gowns, 3,630 coveralls, and 596,724 gloves.

- On April 24, a Community Based Testing Site 2.0 began conducting tests at a Walgreens in Hillsboro, Oregon.
- As of April 30, FEMA has obligated $66 million in federal support for the state of Oregon.
- On April 28, the Oregon Department of Human Services was awarded a FEMA Public Assistance program grant for $1.5 million to purchase and distribute food to 22 food banks throughout the state.
- As of April 17, a 50-bed federal medical site was redeployed to New Mexico
- The 45-bed alternate care site at the VA clinic in Eugene is anticipated to be done May 13.
- On April 14, Governor Brown announced the "Framework for Reopening Oregon."
- On April 13, Governor Brown announced that the state will provide $8 million to the Oregon Food Bank to meet urgent food assistance needs.
- On April 13, Oregon Governor Brown, Washington Governor Inslee and California Governor Newsom announced a Western States Pact to work on a shared approach for reopening their economies and controlling COVID-19.

State of Washington

- Medical supplies and equipment delivered to the State of Washington include 1 million N95 respirator masks, 841,348 surgical masks, 126,201 face shields, 3,772 coveralls, 167,225 gowns, and 500 ventilators.
  - The state has returned 427 ventilators to the SNS to support other states.
- As of April 30, FEMA has obligated $93 million in federal support for the state of Washington.
- Field hospital/alternate medical facility support for the COVID-19 response in Washington includes:
  - As of April 19, a 250-bed federal medical station was redeployed to New Mexico
  - As of April 15, two 50-bed federal medical stations are available for redeployment.
  - As of April 15, USACE has completed 19 alternate care site assessments.
  - On April 15, the CenturyLink Event Center field hospital closed.
  - On April 14, the alternate care site at Astria Regional Medical Center in Yakima closed.
  - On April 3, USACE conducted an assessment for the Makah Tribe; an assessment request is pending from Confederated Tribes of the Colville Reservation.
- On April 22, FEMA awarded $2,194,955 for the Crisis Counseling Immediate Services Program to support state resident's mental health needs due to COVID-19.
- On April 27, Washington Governor Inslee announced Colorado and Nevada will join Washington, Oregon and California in the Western States Pact for COVID-19.
- On April 13, Washington Governor Inslee, Oregon Governor Brown and California Governor Newsom announced a Western States Pact to work on a shared approach for reopening their economies and controlling COVID-19.
- On April 21, Washington Governor Inslee announced the state's COVID-19 Recovery Plan.

COVID-19 By the Numbers

FEMA Region 1

3
Alternate Care Facilities

808
Hospital Beds

Funding

Emergency Protective Measures

Connecticut **$23.0 million**	New Hampshire **$17.5 million**
Maine **$12.6 million**	Rhode Island **$19.3 million**
Massachusetts **$62.6 million**	Vermont **$8.5 million**

4,299

Deployed Personnel

DoD
291

Title 32 National Guard activated
3,762

FEMA
231

HHS
15

Critical Supplies Delivered

787,304	2.5 million	17,753	3.6 million	2.5 million	380,733	850
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

Numbers as of 5/01/2020

FEMA

COVID-19 By the Numbers

FEMA Region 2

13
Alternate Care Facilities

6,993
Hospital Beds

Funding

Emergency protective measures

New Jersey
$402.8 million

New York
$1.0 billion

U.S. Virgin Islands
$12.5 million

Puerto Rico
$31.6 million

6,809

Deployed Personnel

DoD
1,839

Title 32 National Guard activated
4,569

FEMA
287

HHS
114

Critical Supplies Delivered

835,890	4.3 million	426,389	9.2 million	12.8 million	478,525	6,090
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

Numbers as of 5/01/2020

FEMA

COVID-19 By the Numbers

FEMA Region 3

7
Alternate Care Facilities

1,249
Hospital Beds

Funding

Emergency protective measures

Washington D.C.	Virginia
$55.6 million	**$176.3 million**
Maryland	Delaware
$43.5 million	**$4.9 million**
Pennsylvania	West Virginia
$60.3 million	**$8.7 million**

3,500

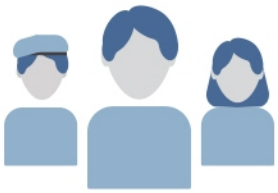
Deployed Personnel

DoD
85

Title 32 National Guard activated
3,044

FEMA
253

HHS
118



Critical Supplies Delivered

630,318	2.8 million	16,275	3.3 million	6.7 million	493,510	720
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

FEMA

Numbers as of 5/01/2020

COVID-19 By the Numbers

FEMA Region 4

3
Alternate Care Facilities

1,101
Hospital Beds

Funding

Emergency protective measures

Alabama **$18.7 million**	Kentucky **$54.0 million**
Florida **$106.4 million**	North Carolina **$29.6 million**
Georgia **$68.5 million**	South Carolina **$70.3 million**
Tennessee **$130.5 million**	Mississippi **$54.4 million**

9,090

Deployed Personnel

DoD
0

Title 32 National Guard activated
8,809

FEMA
201

HHS
80

Critical Supplies Delivered

915,988	4.4 million	21,631	3.8 million	5.7 million	874,201	350
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

FEMA

Numbers as of 5/01/2020

COVID-19 By the Numbers

FEMA Region 5

10
Alternate Care Facilities

7,039
Hospital Beds

Funding

Emergency protective measures

Illinois **$262.5 million**	Ohio **$73.0 million**
Indiana **$36.8 million**	Wisconsin **$61.4 million**
Michigan **$246.0 million**	Minnesota **$353,743**

4,839

Deployed Personnel

DoD
85

Title 32 National Guard activated
4,487

FEMA
177

HHS
90

Critical Supplies Delivered

977,021	4.3 million	19,628	14.9 million	9.4 million	654,119	1,430
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

FEMA

Numbers as of 5/01/2020

COVID-19 By the Numbers

FEMA Region 6

11
Alternate Care Facilities

1,635
Hospital Beds

Funding

Emergency protective measures

Arkansas
$340,664

Texas
$393.7 million

Louisiana
$139.3 million

Oklahoma
$22.9 million

New Mexico
$27.3 million

5,160

Deployed Personnel

DoD
145

Title 32 National Guard activated
4,828

FEMA
166

HHS
21

Critical Supplies Delivered

612,729	3.3 million	15,621	3.9 million	2.5 million	560,451	430
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

Numbers as of 5/01/2020

FEMA

COVID-19 By the Numbers

FEMA Region 7

1
Alternate Care Facilities

118
Hospital Beds

Funding

Emergency protective measures

Iowa
$70.6 million

Missouri
$26.3 million

Kansas
$41.6 million

Nebraska
$17.4 million

2,598

Deployed Personnel

DoD
0

Title 32 National Guard activated
2,452

FEMA
138

HHS
8

Critical Supplies Delivered

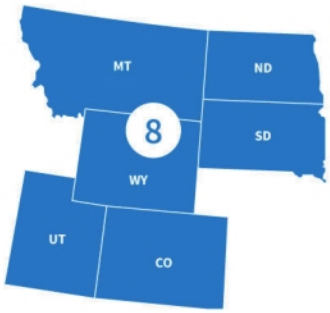
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators
337,961	**1.5 million**	**9,429**	**3.4 million**	**1.6 million**	**248,758**	**0**

FEMA

Numbers as of 5/01/2020

COVID-19 By the Numbers

FEMA Region 8



3
Alternate Care Facilities

1,685
Hospital Beds

Funding

Emergency protective measures

Colorado
$206.5 million

Montana
$13.6 million

North Dakota
$9.2 million

South Dakota
$178,935

Utah
$336,249

Wyoming
$30,500

689

Deployed Personnel

DoD
0

Title 32 National Guard activated
556

FEMA
127

HHS
6

Critical Supplies Delivered

313,760	1.5 million	14,247	1.6 million	1.2 million	280,817	100
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

Numbers as of 5/01/2020

FEMA

COVID-19 By the Numbers

FEMA Region 9

17
Alternate Care Facilities

3,000
Hospital Beds

Funding

Emergency protective measures

Arizona
$21.6 million

California
$995.9 million

Hawaii
$30.2 million

Nevada
$43.8 million

American Somoa
$855,109

CNMI
$4.9 million

Guam
$10.4 million

5,856

Deployed Personnel

DoD
1,027

Title 32 National Guard activated
4,535

FEMA
241

HHS
53

Critical Supplies Delivered

720,919	4.9 million	14,874	2.8 million	3.3 million	593,189	550
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

FEMA

Numbers as of 5/01/2020

COVID-19 By the Numbers

FEMA Region 10

2
Alternate Care Facilities

93
Hospital Beds

Funding

Emergency protective measures

Alaska
$9.8 million

Oregon
$66.9 million

Idaho
$907,217

Washington
$93.0 million

1,169

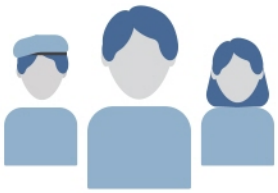
Deployed Personnel

DoD
0

Title 32 National Guard activated
984

FEMA
175

HHS
10



Critical Supplies Delivered

370,336	1.5 million	11,016	2.0 million	1.6 million	384,507	700
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns	ventilators

FEMA

Numbers as of 5/01/2020

COVID-19 By the Numbers

56
Major Disaster Declarations

approved in all
50 states,
5 territories and
Washington DC

$5.8 billion

in emergency protective measures

104

airbridge flight missions

214

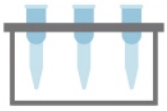
messages
to cell phones via the Wireless Emergency Alert System

51

messages
to broadcast stations via the Emergency Alert System

critical supplies shipped

7.3 million	111.8 million	607,283	888.6 million	78.3 million	16.9 million
face shields	surgical masks	coveralls	gloves	N95 respirators	gowns



6.0 million

samples tested

137,796 samples tested at Community-Based Testing Sites
102,341 private partner site samples

12,014

ventilators available

38,000

National Guard troops activated in a Title 32 duty status

Numbers as of 5/01/2020

FEMA

Secretary's Regulatory Report

As of April 29, 2020

Pre-Development Memos to HHS Clearance - Week of April 27		
Agency	**Subject**	**Submitted**

Regulations Expected to Enter HHS Clearance - Week of May 4		
Agency	Subject	**Expected to OMB (ROCIS)**
CMS	CY 2021 Physician Fee Schedule NPRM (Segment 1)	5/13

Regulations Expected to be Sent to OMB for Clearance - Week of May 4		
Agency	**Subject**	**Expected to Display at OFR***
OGC	HHS/FEMA Hoarding IFR	TBD
ACF	Updating Refugee Resettlement Program Requirements NPRM	6/30

Regulations Expected to Display at OFR - Weeks of April 27 & May 4		
Agency	**Subject**	**Expected to Display at OFR***
CMS	COVID IFC #2	5/1
CMS	FY 2021 IPPS/LTCH PPS NPRM (pending Sec sig)	5/1
ACF	Adoption & Foster Care Analysis & Reporting System (AFCARS) Final Rule	5/8

***Tentative date, subject to change**

Secretary's Regulatory Report

As of April 29, 2020

Major Regulations Under OMB Review		
Agency	**Subject**	**Expected to Display at OFR***
CMS	COVID IFC #2	5/1
CMS	FY 2021 IPPS/LTCH PPS NPRM	5/1
ACF	Adoption & Foster Care Analysis & Reporting System (AFCARS) Final Rule	5/8
ACF	Strengthening Work In TANF NPRM	5/15
OCR	Nondiscrimination in Health and Health Education Programs or Activities Final Rule	5/15
SAMHSA	Mandatory Guidelines for Workplace Drug Testing Programs of Hair NPRM	5/15
SAMHSA	42 CFR Part 2: Confidentiality of Substance Use Disorder Patient Records Final Rule	5/22
FDA	Nutrient Content Claims; Definition of Term: Healthy NPRM	5/29
FDA	Submission of FDA Import Data in the Automated Commercial Environment for Veterinary Devices NPRM	5/29
FDA	Gluten-Free Labeling of Fermented or Hydrolyzed Foods Final Rule	5/29
ACF	Child Support Technical Corrections Final Rule	6/1
CMS	DMEPOS & HCPCS NPRM	6/5
CMS	CY 2021 Outpatient PPS/ASC Payment NPRM (Segment 1)	6/30
FDA	Postmarketing Safety Reports for Approved New Animal Drugs Final Rule	6/30
FDA	Annual Summary Reporting Requirements Under the Right to Try Act NPRM	6/30
CMS	Treatment of Medicare Part C Days NPRM	TBD
CMS	Medicare Coverage of Innovative Technology NPRM	TBD
CMS	Medicaid DUR & Supporting VBP for Drugs NPRM	TBD
CMS	CMMI Specialty Care Models Final Rule	TBD
CMS	Medicaid & CHIP Managed Care Final Rule	TBD
CMS	ESRD Third Party Payments NPRM	TBD
CMS	Accrediting Organization: Conflict of Interest NPRM	TBD
CMS	Most Favored Nations (IPI) Drug Pricing Model NPRM	TBD
OGC	Hoarding IFR	TBD
OGC	Interstate Practice of Certain Health Professionals During COVID-19 IFR	TBD

***Tentative date, subject to change**

DATE: May 1, 2020

TO: The Secretary

THROUGH: Ann C. Agnew, Executive Secretary

FROM: Janice Cotter, Director of ODRM

SUBJECT: Correspondence Report for April 22 – April 28, 2020 INFORMATION

ISSUE

Below for your information is a Correspondence Report summarizing correspondence from April 22 – April 28, 2020.

This memo is for your information only; you do not need to take any action on this.

SUMMARY

- Congress – 44 letters were received from the House and Senate.
    - Senator Bob Casey and 17 Senators write President Trump to urge HHS to withdraw all rules and regulations negatively impacting seniors and people with disabilities and redirect personnel working on these rules to the Coronavirus response efforts. The Senators include details of the rules. Three under the Centers for Medicare & Medicaid Services; four under the Social Security Administration; and four under the United States Department of Agriculture.

- Representative Bill Foster and 34 Representatives write to Secretary Azar and FDA Commissioner Stephan Hahn urging rapid COVID-19 vaccine development. Rapid vaccine development balances risks to human health of voluntary test subjects in clinical trials, the risks of early deployment of a moderately tested vaccine to the general population, and the certainty of human suffering and death from delayed vaccine deployment. The Representatives write to assure HHS that Congress understands that a more risk-tolerant development process is likely appropriate in the case of a COVID-19 vaccine. In the case of accelerated human trials, justifiable risks may be taken by parallel testing of multiple dose levels, advancing more rapidly from phase to phase and potentially by challenge trials that involve deliberately infecting volunteers who have received candidate vaccines or placebos to confirm the efficacy of those vaccines and are at very low risk of serious disease from the infection. This could accelerate the emergency use and eventual licensure of vaccines that have also shown safety in larger groups by many months. The Representatives urge HHS to consider these and other options, provided they proceed with the principle of informed consent of truly voluntary subjects and are backed by the best available science. The situation in this pandemic is analogous to war, in which there is a long tradition of volunteers risking their health and lives on dangerous missions for which they understand the risks and are willing to do so in order to help save the lives of others.
- Senator Steve Daines supports allocations for Montana providers in desperate need urging Secretary Azar to ensure the next distribution of funding under the CARES Act targets the needs of children's hospitals and Montana's extensive network of rural providers.
- Senator Jeff Merkley and 10 Senators write to Secretary Azar, Vice President Pence, and CDC Director Robert Redfield urging the Administration to develop a plan regarding nationwide contact tracing and testing. The Senators ask HHS to craft, release, and implement a plan that includes robust testing for the virus and expanded contact tracing immediately. The Senators also request information from HHS about any current or forthcoming COVID-19 relief strategy that includes testing and contact tracing: (1.) A detailed summary of resources needed to design and execute nationwide testing and contact tracing. (2.) A comprehensive explanation of HHS's strategy and efforts to support states and localities in recruiting, hiring, and training a sufficient number of qualified contact tracers across the country, including efforts to recruit tracers with diverse language capabilities, as well as strategies to accommodate seniors and Americans with disabilities. (3.) A thorough outline of HHS's plan to protect and secure the private data of Americans during all contact tracing efforts**.** A top priority is ensuring the use of personal data is protected in a manner that respects the privacy of our citizens.

- Representative Richard Neal writes to ensure hospitals in Massachusetts receive funds to provide quality care to patients impacted by COVID-19. Massachusetts received $841,425,130 from the disbursement, but unfortunately the basis for distribution short-changes many essential community hospitals that do not have a large Medicare fee-for-service revenue base.
- Representative Frank Pallone, Jr., Representative Anna Eshoo, and Representative Diana DeGette write to Secretary Azar and FEMA Administrator Peter Gaynor concerning the Administration's fulfillment of supplies and disbursement of funds. The Representatives request information regarding the Administration's fulfillment of states' requests for supplies and subsequent disbursements. They specifically request an itemized accounting of supplies such as ventilators, PPE, beds, and various other medical equipment.
- Senator Jack Reed and the Rhode Island delegation urge that CARES funding account for providers with disproportionate Medicare and Medicaid patients. In particular, children's hospitals and other specialty hospitals in Rhode Island were entirely left out of the first distribution of funds because they do not see Medicare patients. In addition, many nursing homes, residential care and senior living facilities, community health centers, and hospitals simply did not receive sufficient funding to compensate for the costs these providers are incurring in response to COVID-19. They ask that the distribution of the remaining funding better account for providers that see a disproportionate number of Medicare Advantage enrollees and Medicaid beneficiaries.
- Representative John Yarmouth supports the University of Louisville's Center for Predictive Medicine and Emerging Infectious Diseases and their applications for funding through the CDC's Broad Agency Announcement – Applied Research to Address the Coronavirus Emerging Public Health Emergency.
- Senator Ed Markey and four Senators write to Secretary Azar and SAMHSA Assistant Secretary Dr. Elinore McCance-Katz seeking to ensure that patients with opioid use disorder can continue to access life-saving medication assisted treatment—in particular, buprenorphine—during the Coronavirus pandemic.
- Representative Andy Barr encourages monies for skilled nursing facilities in next round of CARES Act allotments. The staff and residents in skilled nursing facilities and assisted living communities in the Commonwealth of Kentucky desperately need your immediate and ongoing support. Ensuring that this funding is delivered to these providers promptly is critical to protecting Kentucky's seniors and most vulnerable.
- Senator Kyrsten Sinema and seven Arizona delegation Members write to Secretary Azar and CMS Administrator Seema Verma supporting the state of Arizona's request for a Section 1115 waiver to allow retainer payments be made to essential Medicaid providers. The request was submitted on March 24, 2020, by our state's Medicaid program, known as the Arizona Health Care Cost Containment System.

- Representative A. Donald McEachin and Representative Raul Grijalva write about the need to monitor and address racial disparities in our nation's response to the Coronavirus. The legacy of racism and inequality has made communities of color and low-income communities especially vulnerable to the virus. Without resources and dedicated, publicly available data, the Administration will not be able to effectively respond to the impact of the pandemic. While the Representatives are pleased that several states have begun releasing preliminary data, they write that it is imperative that HHS work with states, localities, and private labs to collect comprehensive data on racial health disparities, and reallocate federal resources necessary to address these disparities. For decades, environmental justice communities–including communities of color, low-income communities, and Tribal and indigenous communities across the U.S. and U.S. territories–have suffered disproportionately from cumulative exposure to multiple pollutants, often without the necessary resources to respond to the impacts nor influence in the political process to promote equitable outcomes. These communities live on the frontlines of our climate crisis and the "fence-line" of industries and transportation corridors, often residing in areas with higher levels of lethal pollution. Consequently, these communities are more likely to suffer from chronic health conditions caused in part by this persistent pollution–such as high blood pressure, heart disease, diabetes, hypertension, obesity, and asthma. As Americans are ordered to shelter in place to combat the pandemic, members of environmental justice communities are experiencing adverse indoor health conditions, including exposure to mold and poor ventilation in low-income housing. Further threatening their health and safety, these same communities often lack access to clean water, a necessity during this public health crisis.
- Representative Doris Matsui and 34 Representatives write to Secretary Azar and CMS Administrator Seema Verma requesting that a portion of the remaining $70 billion in CARES Act funding for provider relief be allocated to community-based health care providers that comprise the public health safety net for mental health and addiction services.
- Senator Martha McSally and Senator Kyrsten Sinema write to secretary Azar and CMS Administrator Seema Verma seeking relief for children's hospitals which cannot benefit from the extensive financial remediation provided to date through Medicare, such as the enhanced payments and sequester extension, making relief from the PHSSEF even more essential. Children's hospitals are not-for-profit, community-benefit organizations and Medicaid, not Medicare, is the payer for more than 50% of all patient volumes. Per congressional intent, children's hospitals must be included in the distribution and all federal relief packages, reflecting their stand with the nation's efforts to support the health of everyone, children and adults, during the pandemic.

- Senator Martha McSally and Representative Matt Gaetz write to the NIH Director Francis Collins to express their deep concerns regarding the NIH's past and current relationship with China's controversial bio-agent laboratory the Wuhan Institute of Virology (WIV) and to ensure no additional U.S. tax dollars are directed to this notorious institution. Taxpayers' money should not be sent to a dangerous Chinese state-run bio-agent laboratory that lacks any meaningful oversight from U.S. authorities and is run by adversaries with a history of lab leaks, including SARS, and deception about the causes and extent of deadly disease outbreaks, including COVID-19. They respectfully request that all active grants, sub-grants and contracts awarded to WIV be canceled immediately and that WIV be stripped of its eligibility to receive taxpayer funds from the NIH in the future. Additionally, they request that details to a number of questions about the NIH's relationship with the WIV are included in the correspondence.
- Senator Kamala Harris and 51 bicameral Members of Congress write to Secretary Azar and Department of Homeland Security Acting Secretary Chad Wolf regarding protecting the health and safety of nearly 2,400 children in the Office of Refugee Resettlement (ORR) within HHS custody, including licensed shelters. According to public health experts, people in confined spaces "are at special risk of infection, given their living situations," and "may also be less able to participate in proactive measures to keep themselves safe, and infection control is challenging in these settings." The Members are especially concerned that most ORR facilities require children to share bedrooms, bathrooms, and dining spaces, which make remaining at least six feet apart difficult to observe. The virus has spread quickly and has now infected at least 40 children in ORR custody and 69 self-reported ORR contractor staff and foster parents. They ask that HHS urgently and safely pursue expedited release of all immigrant children from U.S. custody to the care of sponsors and loved ones and take all reasonable steps to protect children in custody.
- Representative Joaquin Castro and 57 Representatives request access to benefits under the Affordable Care Act for Deferred Action for Childhood Arrivals (DACA) recipients during the pandemic. Access to health coverage for DACA recipients and their U.S. citizen children is absolutely critical during this pandemic in order to ensure that they have access to COVID-19 testing and treatment, particularly for the over 200,000 DACA recipients that the U.S. Department of Homeland Security classifies as "essential critical infrastructure workers," including the 29,000 DACA recipients employed as healthcare practitioners and supporting occupations on the front lines of responding to COVID-19.

- Senator Jeanne Shaheen and the New Hampshire Congressional delegation write to Secretary Azar and CMS Administrator Seema Verma to urge approval of New Hampshire's pending application for a waiver under section 1332 of the Affordable Care Act to help enable the state to establish a reinsurance program within New Hampshire's Health Insurance Marketplace for qualified health plans. If approved and established, this reinsurance program is expected to result in a 15 percent reduction in premiums in New Hampshire's individual health insurance market in 2021. Granite Staters are in dire need of the premium savings that this program could help to provide.
- Representative Mike Waltz and 16 Florida Representatives write to Secretary Azar and CMS Administrator Seema Verma regarding Medicare's Accelerated and Advanced Payment Program. The state of Florida is one of 10 states with the greatest number of confirmed COVID-19 cases. The hospitals, long-term care facilities, nursing homes, and other healthcare facilities have been hit especially hard by this outbreak. The main priority of providers in our communities, and across the entire nation, has been caring for the sick. The expansion of the Medicare Accelerated and Advanced Payment Program will provide critical financial relief to hospitals and providers on the frontlines of this pandemic, however, we must ensure this short-term assistance does not lead to long-term hardships when it comes time to pay back these loans. Given the unprecedented circumstances of the current health crisis and the essential role of healthcare facilities and providers, we believe that accelerated and advanced payments should be interest-free loans with considerable repayment periods conducive to maintaining operations.
- Senator Chuck Grassley writes to Vice President Pence regarding his concern that scam artists are taking advantage of the COVID-19 pandemic and defrauding hospitals and other healthcare providers. Senator Grassley is interested in learning how HHS is approaching this issue, whether it is working with law enforcement agencies, and how it is encouraging providers to report bad behavior to the authorities. The Senator understands the difficulty our nation is facing in procuring legitimate PPE and other medical supplies right now and how the U.S. can identify and mitigate supply-chain vulnerabilities in advance of natural disasters. He urges the Administration take every reasonable effort to ensure the safety and security of our supply-chain so hospitals are not being defrauded or sold fake or faulty PPE. The last thing our hospitals and healthcare professionals need to worry about during this crisis is whether their PPE are safe, reliable, and legitimate.

- Representative Charlie Crist urges HHS to pay Widescope Consulting and Contracting Services Department of Information Services (DISA) contract HHSP 233201850065A payment of approximately $656,000 (including Prompt Payment Penalty) or adequate justification after completing all required contract services for the government. It is a service-disabled veteran-owned small business that performs national defense communications work. It is Representative Crist's understanding that all work under the contract was successfully completed on or before July 2019 and has been verified and/or approved by the appropriate Contracting Officer's Representative and DISA Program Manager. After repeated attempts, Widescope and his staff have received no actionable updates or communication since October. Recently, Appropriations Committee staff were informed by HHS that Widescope received partial payment and that the remaining balance is due to an ongoing discussion with DOD about deliverables, and no longer related to delays at the Program Support Center. Widescope informed the Representative that this is false, and they have received no recent communication or partial payment. Widescope's subcontractors are now threatening legal action, which could put Widescope out of business—solely due to the government's failure to promptly pay.
- Representative Collin Peterson writes to Vice President Pence to coordinate a robust federal response to address the dire situation for pork, other livestock, and poultry producers who have no access to processing which gives them no choice but to depopulate their herds. Eight suggestions to address this dire situation are in the letter.
- Representative Don Beyer and five Representatives write to "Trump Administration Supply Chain Managers" which includes Secretary Azar, Vice President Pence, CDC Director Robert Redfield, FEMA Supply Chain Task Force Rear Admiral John Polowczyk, White House Trade Advisor Peter Navarro, White House Advisor Jared Kushner, and Defense Logistics Agency Director LTG, U.S. Army, Darrell K. Williams, deeply concerned about the supply chain management response. Insight from congressional communication, local hospitals, state, and media reporting describes disorganized, dysfunctional supply chain management from the federal government. The letter included 16 questions.
- Senator Rick Scott asks questions about CARES Act funding as it continues to be administered. The protection of taxpayer dollars is one of the most important roles of the federal government, and we must work to ensure that taxpayer funds are spent responsibly and that assistance is only provided to those in need. And let's not forget, this year's federal budget deficit will be the largest in the history of our nation, in excess of the cumulative deficits for the first 200 years of our country's existence. We will end the year with more than $25 trillion in federal debt. We must ensure taxpayer dollars are going to those that are truly in need during the Coronavirus pandemic.

- Senator Bernard Sanders asks to schedule a call to help fix an issue with the funding Vermont hospitals recently received from HHS. It has come to Senator Sanders' attention that the share of funding sent to Vermont was calculated without including a portion of their Medicare payments. Vermont hospitals are paid through an All-Inclusive Population Based Payment by CMS, which means their Medicare spending appears differently than all other states. In this instance, approximately $225 million in claims were not counted, which led to a shortfall in the state's share of PHSSEF of approximately $13 million. He understands that HHS staff has reached out to CMMI to verify this amount and that they have provided the needed information.
- Senator Rob Portman writes regarding expanding the definition of high impact areas to account for outbreaks occurring after April 10th and for hospitals caring for prisoners affected by this crisis. The sharp cut off for April 10th causes concern for Ohio that has begun to deal with unexpected spikes in cases in just the past few days. The new hotspots revolve around two state prisons in Pickaway County and Marion County that have seen outbreaks that are driving an exponential increase in new cases for the state and account for two of the largest sources of the COVID-19 in the country. The state of Ohio has designated The Ohio State University's Wexner Medical center to care for all inmates in the state, due to the high quality of care that they provide and their capacity and infrastructure to hold these types of patients.
- Senator Tammy Baldwin and two Representatives write to President Trump that Wisconsin needs what has been lacking from the "Whole of America" response to this pandemic–strong leadership from this White House that provides a national, centralized plan to conduct widespread testing.
- Senator Ben Cardin writes to follow up on multiple reports indicating the Trump Administration plans to use funds from the $100 billion Public Health and Social Services Emergency Fund to reimburse hospitals for providing care to uninsured Americans. If HHS plans to use funds this way, it is critical that hospitals and other health providers are not allowed to balance bill patients who seek testing and treatment for COVID-19 and end up having a non-related illness. The Prudent Layperson Standard must apply to those uninsured patients seeking emergency care in order to protect them from high out-of-pocket costs and further economic hardship.
- Senator Chris Van Hollen and seven bicameral Members of the Maryland delegation urging President Trump to exercise authority under the Defense Production Act to order General Motors to reopen its plant in White Marsh, Maryland, for production of much-needed ventilators for hospitals. As numbers continue to rise across the state and region, reopening the White Marsh plant will put high-skilled workers back to work and ensure that ventilators will be available and easily accessible in an area with multiple hotspots.
- Senator Ed Markey and Senator Elizabeth Warren call on HHS to prioritize coronavirus hot spots, providers not adequately covered in initial disbursements, and transparency in future Provider Relief Fund implementation. Six questions are included in the letter.

- Representative Brian Higgins writes to HRSA Administrator Thomas Engels to urge postponing all ongoing and upcoming hospital audits related to the 340B program while our health system is responding to the coronavirus disease pandemic. Given the current realities hospitals are facing, all of their resources must be diverted to treating and containing this pandemic. Representative Higgins urges Administrator Engels to postpone all 340B audits until after this public health crisis has abated.
- Senator Patty Murray and Representative Rosa DeLauro write with great concern regarding reports that the Office of Refugee Resettlement (ORR) is considering implementing aggressive immigration policies that are not in the best interests of the children in its care. The writers call on Secretary Azar to ensure HHS upholds the letter and the spirit of the laws that protect children and that ORR's top priority remains children's wellbeing.
- Representative Steve Cohen writes to Secretary Azar, Department of Transportation Secretary Elaine Chao, FAA Administrator Stephen Dickson, and CDC Director Robert Redfield expressing concern that the CDC guidelines on the use of cloth face coverings to help slow the spread of COVID-19 are not being followed on airplanes, where there is incredible exposure and risk. As the CDC noted on April 3, 2020, "We now know from recent studies that a significant portion of individuals with coronavirus lack symptoms and that even those who eventually develop symptoms can transmit the virus to others before showing symptoms. This means that the virus can spread between people interacting in close proximity—for example, speaking, coughing, or sneezing—even if those people are not exhibiting symptoms." The CDC also recommended that individuals wear cloth face coverings in public settings where other social distancing measures are difficult to maintain. It is quite evident that airplanes fall into this category and that airlines should have extra precautions put into place to protect all crewmembers and passengers. Representative Cohen requests that the FAA, in conjunction with the CDC, update its guidance to airlines to ensure more robust safety protections are put in place for frontline workers and passengers including the requirement of face coverings for all employees of air carriers, their crews and passengers**.**
- Senator Gary Peters and Senator Debbie Stabenow write that Congress just passed an additional $75 billion in much-needed funding to protect the viability of our health system, and it is urgent that HHS take immediate steps to make all the direct support available to health providers as quickly as possible. Health providers cannot wait another month for access to financial relief like they have had to do for $70 billion of the initial $100 billion appropriated through the CARES Act that HHS has yet to distribute. Our health providers desperately need the $175 billion in funding, which will help keep our health system intact only if it reaches providers right away.

- Representative Gwen Moore urges secretary Azar to ensure that the CARES distribution fully considers the disproportionately higher racial and socioeconomic impact of infections and death rates from this disease in determining "hot spots," not just geographical factors or facility caseload. Given what the data is saying about COVID-19's impact by race and socioeconomic status, it is critical that this data play a crucial part in these decisions.
- Senator Roger Wicker writes that HRSA has excluded air medical services from the CARES Act to reimburse providers and suppliers for providing testing and treatment to uninsured COVID-19 patients. Air medical services are a critical asset in connecting individuals in rural America to health care facilities that can provide intensive care. The Senator urges Secretary Azar to direct HRSA to revise its guidance to include air ambulance services explicitly in the program.
- Representative Bennie Thompson writes to Secretary Azar and FEMA Administrator Peter Gaynor concerning numerous inquiries and expressions of concern from constituents who are deeply worried about loved ones facing the unique risks of contracting COVID-19 in long-term care and nursing homes. Like so many aspects of the Administration's approach to acquiring and distributing PPE and other medical supplies and equipment, the specific processes for distributing PPE to long-term care and nursing homes remains "a mystery shrouded in confusion." He requests that FEMA provide a list of documents included in the letter.
- Representative G.K. Butterfield, Jr., and 16 Representatives write to express their deep concern regarding the lack of transparency on how funds from the Provider Relief Fund established in the CARES Act, will be dispersed to rural providers. On April 22, 2020, HHS announced additional allocations of the Provider Relief Fund, including $10 billion for rural providers. However, the announcement failed to provide any information regarding the criteria for eligible entities or how the funds will be distributed. To date, HHS officials have been unable or unwilling to provide clarity on the types of providers that qualify, how HHS is defining "rural," and what methodology HHS plans to use to distribute the funds. In order to distribute these funds in a manner that best serves the needs of all rural providers and the patients they serve, the Representatives strongly urge HHS to thoughtfully develop eligibility criteria and a methodology for the distribution of these funds.

- Senator Mike Rounds writes to Secretary Azar, Department of Labor Secretary Eugene Scalia, and Department of the Treasury Secretary Steven Mnuchin to bring a regulatory challenge to their attention that could further the common healthcare goals if it is appropriately resolved. The issue of concern relates to fixed indemnity policies that pay a cash benefit to the policyholder when a specific medical event occurs. These "excepted benefit" policies are referred to as such because they are excepted by statute from insurance mandates applicable to primary medical insurance under the PPACA and HIPAA. Such policies are also recognized as supplemental coverage and are not intended or sold as primary health coverage. Excepted benefit policies have existed in the marketplace for decades, are regulated by state law, and are an affordable means for consumers to help manage potential financial risks associated with certain medical events. Current federal guidance creates some confusion in the insurance marketplace because of differences related to how the group and individual markets are treated. A proposal on excepted benefit policies submitted to your Departments by the insurance industry would eliminate this confusion by harmonizing the permitted payment triggers in the group market regulations with those in the individual market. This will clarify that benefits can be paid on either a per service basis or a per period basis.
- Representative James Hagedorn understands the initial $30 billion was to expedite distribution of traditional fee-for-service Medicare but this does not accurately represent the reality of funding streams for many rural providers. By excluding Medicare Advantage and Medicaid payments in the formula, many rural providers did not receive adequate funding to help cover their losses. I appreciate that you and your team are working to address these issues in future distributions, and I urge you to do so as quickly as possible. While the first payments from the Provider Relief Fund helped, they account for less than a quarter of lost revenues to date. Because rural healthcare providers operate on very narrow margins, they are less able to sustain such incredible losses compared to larger and more urban providers.
- Representative Joe Wilson is so encouraged to see firsthand the American Spirit of "It Can Be Done" responsibility and recovery during the National Emergency, which he was grateful to recognize in the Congressional Record. It is an honor to represent the people of the Second Congressional District of South Carolina, and Representative Wilson values Secretary Azar's input and his service.
- Representative Warren Davidson and 21 Representatives ask that children's hospitals have access to these funds, so that they can continue to provide lifesaving care to our nation's children during this health crisis. All medical facilities are experiencing financial strain due to required cancelations of elective care, increased costs of personal protective equipment for both patients and providers, and increased use of screening and detection services. Children's hospitals are no exception. Since mid-March, they have seen revenue losses up to 50 percent and operating cost increases of more than 10 percent. Overall, the children's hospital industry is projected to suffer over $10 billion in losses during this crisis. If children's hospitals are unable to remain operational due to these losses, millions of children will lose access to high quality medical care.

- Senator Roger Wicker and 34 Senators write to President Trump thanking him for his bold and consistent efforts to defend the sanctity of all human life, including our youngest and most vulnerable. The Trump Administration's decisive actions to protect human life and human dignity on every front have brought great hope to our nation. In particular, they thank him for last year's decision to stop taxpayer funding in federal laboratories of the horrific practice of using aborted baby body parts for experiments. The decision to stop funding for this research and to redirect funds toward ethical, successful alternatives should be maintained.
- Representative Mike Levin and 15 Representatives write with concern regarding the Administration's testing objectives for COVID-19, and to appeal for an aggressive, detailed testing strategy. Because research has shown that a significant portion of individuals with COVID-19 are asymptomatic, widespread testing will be especially critical to quickly identify and contain small outbreaks as states gradually relax their respective stay-at-home orders.

- Other Government – 10 letters were received from other governments.
    - Indiana Attorney General Curtis T. Hill, Jr, and 18 State Attorneys General write to Secretary Azar, President Trump, Vice President Pence, and NIH Director Francis S. Collins supporting the fetal tissue ban especially during the COVID-19 crisis. The States of Indiana, Alabama, Alaska, Arizona, Arkansas, Florida, Georgia, Idaho, Kentucky, Louisiana, Missouri, Nebraska, Oklahoma, South Carolina, South Dakota, Tennessee, Texas, Utah, and West Virginia write in support of the current ban on federal funding for fetal tissue research that took effect in June 2019. California and several other States (the "California letter") recently entreated this administration to end what they call the "Fetal Tissue Ban" in order to facilitate research on COVID-19. The 19 Attorneys General urge the Administration to deny that request**.** In order to make advances in the ethical treatment of human remains, this nation must reject the false notion that scientists cannot achieve the laudable goal of creating vaccines and treatment for COVID-19 without using unethical means.
    - Texas Governor Greg Abbott writes: "Pursuant to 42 U.S.C. § 247d(e)(1), I hereby designate Donna Sheppard, who is Chief Financial Officer of the Texas Department of State Health Services, to serve as my designee for purposes of submitting the State of Texas's request for reassignment flexibility under 42 U.S.C. § 247d(e)(2)."
    - National Association of Medicaid Directors (NAMD) President Beth Kidder and President-Elect Jami Snyder request engagement to facilitate funds to critical Medicaid providers. NAMD is a bipartisan, nonprofit, professional organization representing leaders of state Medicaid agencies across the country. The members drive major innovations in health care while overseeing Medicaid, which provides a vital health care safety net for more than 72 million Americans. Medicaid is at the forefront of states' COVID-19 response efforts, providing critical coverage to vulnerable populations and fiscal resources to a wide array of providers. Medicaid will also become a source of coverage for many of the 26 million Americans filing for unemployment benefits in recent weeks. Specifically, NAMD requests that HHS work directly with state Medicaid agencies to obtain critical information to ensure the solvency of critical Medicaid providers at risk of imminent closure. Action requests and goals are included in the letter.

- General Public – 111 letters were received from private citizens and businesses.
    - The President and CEO of LeadingAge writes to Secretary Azar and CMS Administrator Seema Verma to express their concern with the recently announced order for nursing homes to report cases of COVID-19 to the CDC. They strongly support accurate and consistent reporting to identify and to address the impact of COVID-19 on the communities. However, complicated, duplicative reporting, as required under the new QSO memo, will lead to inconsistent and contradictory data, and exacerbate public confusion. LeadingAge offers to develop a standardized reporting form for universal reporting to states, localities, the federal government, and the public. They feel that one form will provide consistent, uniform information which can be used to provide necessary services and supports to nursing homes experiencing COVID-19 outbreaks and the transparency everyone deserves.
    - Dr. William W. Stead, Chair of the National Committee on Vital and Health Statistics, presents recommendations for adoption of new pharmacy standard under HIPAA. The letter conveys recommendations to HHS to adopt updated versions of pharmacy standards developed by the National Council for Prescription Drugs Programs. Adoption as a national HIPAA standard would result in greater interoperability for entities exchanging prescription information, improvements in patient care, better data for drug utilization monitoring, and burden reduction for providers.
    - Association of Flight Attendants International President Sara Nelson urges Secretary Azar and Department of Transportation Secretary Elaine Chao to use their authority to mandate masks in aviation for crew, employees and passengers; require personal protective equipment; and end all leisure travel until the virus is contained. While the global system is integral to our modern economy, its essential inter-connectedness also provides a convenient pathway for opportunistic pathogens to hitch rides on unsuspecting crewmembers and travelers to spread all over the world. Three categories which are discussed in the letter are: (1) mandate masks in airports and on airplanes (2) require provision of PPE and resource management (3) protect essential service by air and end leisure travel until the virus is contained.
    - Dorian L. Spence, Director of Special Litigation and Advocacy, on behalf of Lawyers' Committee for Civil Rights Under Law expresses deep concern about the inadequate race and ethnic demographic data related to COVID-19 tests, cases and outcomes released by the CDC. They call on HHS to coordinate with all relevant agencies and provide answers to nine requests in the letter.

- White House Referral Letters – 9 letters from private citizens and businesses addressed to the President were referred to HHS by the White House.
    - An Iowa man writes to President Trump expressing concerns related to wind energy. Over the last year Alliant Energy, which serves much of the state of Iowa has recently constructed a new "wind farm" of roughly 100 new wind turbines in close proximity to his residence. Since they started producing wind energy, he developed symptoms of "wind turbine syndrome and vibroacoustic disease". It is negatively affecting him and his neighbors. He feels that local, state, and other elected officials are working with the companies constructing these so called "wind farms" and falsely representing this as nonsense. He asks the President for advice on informing the public of the serious health concerns these "wind farms" are causing. His first son is due in June and he is very concerned.
    - A Michigan woman writes to President Trump:

      Please help Michigan! We are out of control i am afraid for my safety and my family. With the protest i feel my husband would have to work and i have stage 5 kidney failure and only have 9 % working kidneys on dialysis if this virus is brought home it will kill me. Im a nobody, i dont vote being i feel i dont matter but i hope you can help us here in michigan. Not just for me but all familys that this virus can harm. Hope this was not a waste of time. Thanks.
    - A Pennsylvania Mother writes to President Trump:

      I am 25 years old & a single mother to my 1½ year old daughter, Jordyn who was diagnosed with hypoplastic left heart syndrome in the womb, & has had multiple open heart surgeries, with one being the end of this year. I live with my mother whom is also trying so hard to make ends meet. I can't work due to not wanting to be the reason if my daughter got sick. Cause she will die, with her condition. Please please PLEASE anything would help I'm begging you mr.trump please.
    - A Georgia Mother writes to President Trump:

      I am begging and pleading with you to please stop whatever is happening behind closed doors. Open the schools and the restaurants.and.the stores. My son is 15 and completely blind and severely autistic. He requires routine. Please open the schools. I am begging you as a working mother and no family support to please allow children to go back to school. He is very hard to handle. He attacks me and he is upset. If you have a heart at all... please.....
    - An Indiana man writes to President Trump:

      Mr. President,
      I'm so sorry to come to you with this, for I know you have so much on your plate. I have a problem. I need insulin everyday and I just fell into what they call the donut hole. It means I have to pay for much of the cost of my meds. Right now it would cost me like $365.00 for just one month of lantus insulin. Please tell me what to do to get the insulin I need. Your the best President in my lifetime and I'm very thankful you are President. You have my number. Please help me with this.
      In Christ Jesus,

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SARS-like cluster of circulating bat coronavirus pose threat for human emergence

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Abstract

The emergence of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome (MERS)-CoV underscores the threat of cross-species transmission events leading to outbreaks in humans. In this study, we examine the disease potential for SARS-like CoVs currently circulating in Chinese horseshoe bat populations. Utilizing the SARS-CoV infectious clone, we generated and characterized a chimeric virus expressing the spike of bat coronavirus SHC014 in a mouse adapted SARS-CoV backbone. The results indicate that group 2b viruses encoding the SHC014 spike in a wild type backbone can efficiently utilize multiple ACE2 receptor orthologs, replicate efficiently in primary human airway cells, and achieve *in vitro* titers equivalent to epidemic strains of SARS-CoV. Additionally, *in vivo* experiments demonstrate replication of the chimeric virus in mouse lung with notable pathogenesis. Evaluation of available SARS-based immune-therapeutic and prophylactic modalities revealed poor efficacy; both monoclonal antibody and vaccine approaches failed to neutralize and protect from CoVs utilizing the novel spike protein. Importantly, based on these findings, we synthetically rederived an

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Author Contributions

VDM designed, coordinated, performed experiment, completed analysis, and wrote the manuscript. BLY designed infectious clone and recovered chimeric viruses. SA completed neutralization assays. LEG helped perform mouse experiments, TS and JAP completed mouse experiments and plaque assays. XG performed pseudotyping experiments. KD generated structural figures and predictions. ED generated phylogenetic analysis. RLG completed RNA analysis. SHR provided primary human airway epithelial cultures. AL and WM provided critical monoclonal antibody reagents. ZLS provided SHC014 spike sequences and plasmids. RSB designed experiments and wrote manuscript.

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infectious full length SHC014 recombinant virus and demonstrate robust viral replication both *in vitro* and *in vivo*. Together, the work highlights a continued risk of SARS-CoV reemergence from viruses currently circulating in bat populations.

Introduction

Emergence of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) heralded a new era in the cross-species transmission of severe respiratory illness[1,2]. Since then, several strains, including influenza A H5N1, H1N1, H7N9, and Middle East Respiratory Syndrome (MERS) CoV have emerged from animal populations causing considerable disease and mortality[3]. While public health measures silenced the SARS-CoV outbreak[2], recent metagenomics studies have identified sequences of closely related SARS-like viruses circulating in Chinese bat populations that may pose a future threat[4,5]. However, sequence data alone provides minimal insights to identify and prepare for future pre-pandemic viruses. Therefore, to examine emergence potential of circulating CoVs, we built a chimeric virus that encodes a novel, zoonotic spike protein in the context of a viable CoV backbone. This approach characterized the threat posed by SHC014-CoV spike in primary human airway cells, *in vivo*, as well as the efficacy of available immune therapeutics. Together, the strategy translates metagenomics data to help predict and prepare for future emergent viruses.

Results

SHC014 and WIV1 sequences represent the closest relatives to the epidemic SARS-CoV strains (Fig. 1 a,b), but maintain important differences in the 14 residues that bind human ACE2, including the five critical for host range: Y442, L472, N479, T487, and Y491[6]. In WIV1, three of these residues vary from SARS-CoV Urbani, but were not expected to alter binding (Supplementary Fig. 1a, b, Supplementary Table 1). This fact is confirmed by both pseudotyping experiments (Supplementary Fig. 1d) and *in vitro* replication of WIV1-CoV[5]. In contrast, seven of the 14 ACE2 interaction residues in SHC014 are different than SARS-CoV, including all five critical residues (Supplementary Fig. 1c, Supplementary Table 1). These changes, coupled with failure of pseudotyping (Supplementary Fig. 1d), suggested that SHC014 spike is unable to bind human ACE2. However, similar changes had been reported to convey ACE2 binding in related SARS-CoV strains[6,7] and thus suggested functional testing was required for verification. Therefore, we synthesized the SHC014 spike in the context of the replication competent, mouse-adapted SARS-CoV backbone (SHC014-MA15) (Supplementary Fig. 2a). Despite predictions from both structure-based modeling and pseudotyping experiments, SHC014-MA15 was viable and replicated to high titers in Vero cells (Supplementary Fig. 2b). Similar to SARS, SHC014-MA15 also required a functional ACE2 molecule for entry, but uses human, civet, and bat orthologs (Supplementary Fig. 2c, d). To test the ability of SHC014 spike to mediate infection of the human airway, we examined 2B4 Calu-3 cells, a human epithelial airway cell line[8], and found robust SHC014-MA15 replication comparable to SARS-CoV Urbani (Fig. 1c). To extend these findings, primary human airway epithelial cultures (HAEs) were infected and indicated robust replication of both viruses (Fig. 1d). Together, the data confirm the ability

of SHC014 spike to infect human airway cells and underscore the threat of cross-species transmission.

We next evaluated *in vivo* infection of 10-week old BALB/c mice with 10^4 plaque-forming units (PFU) of either SARS-MA15 or SHC014-MA15 (Fig. 1e–h). Animals infected with SARS-MA15 experienced rapid weight loss and lethality by four days post infection (DPI); in contrast, SHC014-MA15 produced substantial weight loss (10%), but no lethality (Fig. 1e). Examination of viral replication revealed nearly equivalent titers from lungs of mice infected with SARS-MA15 and SHC014-MA15 (Fig. 1f). While SARS-CoV MA15 produced robust staining in both the terminal bronchioles and the lung parenchyma 2 DPI (Fig. 1g), SHC014-MA15 had a deficit in airway antigen staining (Fig. 1h). In contrast, no equivalent deficit was observed in the parenchyma or overall histology scoring, suggesting differential infection following SHC014-MA15 (Supplementary Table 2). Shifting to more susceptible aged animals, SARS-MA15 infected animals rapidly lost weight and succumb to infection (Supplementary Fig. 3 a, b); SHC014-MA15 induced robust and sustained weight loss, but had minimal lethality. Histology and antigen staining trends observed in young mice were conserved in the older animals (Supplementary Table 3). We excluded use of an alterative receptor based on *Ace2*$^{-/-}$ mice infection, which did not produce weight loss or antigen staining following SHC014-MA15 infection (Supplementary Fig. 4a, b; Supplementary Table 2). Together, the data indicate that viruses utilizing SHC014 spike are capable of inducing considerable disease in mice in the context of a virulent CoV backbone.

Given the efficacy of Ebola monoclonal antibody therapies like ZMApp[9], we next sought to determine the efficacy of SARS-CoV monoclonal antibodies against SHC014-MA15. Four broadly neutralizing human monoclonal antibodies had been previously reported and are likely reagents for immunotherapy[10–12]. Examining percent inhibition, wild-type SARS-CoV Urbani was strongly neutralized by all four antibodies at relatively low antibody concentrations (Fig. 2a–d). In contrast, neutralization varied for SHC014-MA15. Fm6, an antibody generated by phage display and escape mutants[10,11], achieved only background levels of inhibition of SHC014-MA15 (Fig. 2a). Similarly, antibodies 230.15 and 227.14, derived from memory B cells of SARS-CoV infected patients[12], also failed to block SHC014-MA15 (Fig. 2b, c). For all three antibodies, differences between SARS and SHC014 spikes corresponded to direct or adjacent residue changes found in escape mutants (fm6 - N479R; 230.15 - L443V; 227.14- K390). Finally, monoclonal antibody 109.8 was able to achieve 50% neutralization of SHC014-MA15, but only at very high concentrations (Fig. 2d). Together, the results demonstrate that despite the development of broadly neutralizing antibodies against SARS-CoV, these reagents may only have marginal efficacy against emergent SARS-like CoV strains like SHC014.

To evaluate existing vaccines against SHC014-MA15, aged mice were vaccinated with double-inactivated whole SARS-CoV (DIV). Previously, DIV had shown neutralization and protection from homologous virus challenge[13], but vaccine failure and augmented immune pathology in aged animals indicated a possibility for harm due to vaccination[14]. In this study, DIV provided no protection from SHC014-MA15 in regards to weight loss or viral titer (Supplementary Fig. 5a, b). Consistent with previous reports[14], serum from DIV-vaccinated aged mice also failed to neutralize SHC014-MA15 (Supplementary Fig. 5c).

Perhaps most importantly, DIV vaccination resulted in robust immune pathology (Supplementary Table 4) and eosinophilia (Supplementary Fig. 5d–f). Together, these results confirm DIV vaccine failure and illustrated augmented disease for the aged vaccinated group.

In contrast to DIV, SHC014-MA15 challenge as a vaccine showed promise, but with important caveats. Utilizing a high dose, we infected young mice with SHC014-MA15 and followed over 28-days; the mice were subsequently challenged with SARS-MA15 (Supplementary Fig. 6a). Prior high-dose infection with SHC014-MA15 conferred protection against lethal SARS-MA15 challenge, but only minimal SARS-CoV neutralization response from SHC014-MA15 antisera (Supplementary Fig. 6b, 1/200) implying diminished protection over time. Similar results were observed in aged BALB/C mice in terms of weight loss and viral replication (Supplementary Fig. 6c, d). However, this infection dose induced > 10% weight loss and lethality in some aged animals (Fig. 1 and Supplementary Fig. 3). Using low-dose infection, SHC014-MA15 failed to protect aged animals from lethal SARS-CoV challenge (Supplementary Fig. 6e, f). Together, the data suggest that SHC014-MA15 challenge can confer cross-protection against SARS-CoV through conserved epitopes, but requires a dose that induces pathogenesis.

Having established SHC014 spike as a potential threat, we next synthesized a full-length SHC014-CoV infectious clone based on the approach used for SARS-CoV (Fig. 3a)[15]. Replication in Vero cells revealed no deficit for SHC014-CoV relative to SARS-CoV (Fig. 3b); however, SHC014-CoV was significantly ($p < 0.01$) attenuated in primary human airway epithelial cultures at both 24 and 48 hours post infection (Fig. 3c). *In vivo* infection demonstrated no significant weight loss, but defined reduced viral replication for full length SHC014-CoV infection compared to SARS-CoV Urbani (Fig. 3d, e). Together, the results establish the viability of full length SHC014-CoV, but suggest further adaptation is required to be equivalent to epidemic SARS-CoV replication in human respiratory cells and in mice.

During the SARS-CoV epidemic, links were quickly established between palm civets and coronavirus strains detected in humans[2]. Building upon this finding, the common emergence paradigm argued that epidemic SARS-CoV originated as a bat virus, jumped to civets, and incorporated changes within the RBD to improve binding to civet *Ace2*[16]. Subsequent exposure to humans in live markets permitted infection with the civet strain, which, in turn, adapted to become the epidemic strain (Fig. 4a). However, phylogenetic analysis suggested that early human SARS strains appear more closely related to bat than civet strains[16]. Therefore, a second paradigm argued that direct bat-human transmission initiated SARS-CoV emergence, with palm civets serving as a secondary host and reservoir for continued infection (Fig. 4b,[17]). For both paradigms, spike adaptation in a secondary host is seen as a necessity, with most mutations expected within the RBD and facilitating improved infection. Both theories imply that pools of bat CoVs are limited and host range mutations are both random and rare, reducing the likelihood of future emergence events in humans.

While not invalidating the other emergence routes, the current study argues for a third paradigm in which circulating bat CoV pools maintain “poised” spike proteins capable of infecting humans without mutation or adaptation (Fig. 4c). Illustrated with SHC014 spike in

the SARS-CoV backbone, robust infection occurs in both human airway cultures and *in vivo* without RBD adaptation. Coupled with previous identification of pathogenic CoV backbones[1,18], the results suggest that the starting materials required for SARS-like emergent strains are currently circulating in animal reservoirs. Importantly, while full-length SHC014-CoV likely requires additional backbone adaption to mediate human disease, the documented high frequency recombination events in CoV families underscores the possibility of future emergence and the need for further preparation.

To date, genomics screens of animal populations have primarily been used to identify novel viruses in outbreak settings[19]. The approach in this manuscript extends these datasets to examine questions of emergence and therapeutic efficacy. For the SHC014 spike, we define a threat due to replication in primary human airway cultures, the best available model for human disease. In addition, pathogenesis in mice indicates a capacity to cause disease in mammalian models without RBD adaptation. Notably, differential tropism in the lung and attenuation of full-length SHC014-CoV in HAE cultures suggest factors beyond ACE2 binding may contribute to emergence including spike processivity, receptor bio-availability, or antagonism of the host immune responses. However, further testing in non-human primates is required to translate these finding into pathogenic potential in humans. Importantly, the failure of available therapeutics defines a critical need for further study and treatment development. With this knowledge, surveillance programs, diagnostic reagents, and effective treatments can be produced to protect from emergence of group 2b specific CoVs like SHC014 as well as other CoV branches that maintain similar heterogeneous pools.

While offering preparation against future emerging viruses, this approach must be considered in the context of the US government-mandated pause on gain of function (GOF) studies[20]. Based on previous models of emergence (Fig. 4a, b), the creation of chimeric viruses like SHC014-MA15 was not expected to increase pathogenicity. However, while SHC014-MA15 is attenuated relative to parental mouse adapted, equivalent studies examining the wild-type Urbani spike within the MA15 backbone produced no weight loss and replication attenuation[21]. As such, relative to the Urbani Spike-MA15 CoV, SHC014-MA15 constitutes a gain in pathogenesis (Fig. 1). Based on these findings, review panels may deem similar studies too risky to pursue as increased pathogenicity in mammalian models cannot be excluded. Coupled with restrictions on mouse adapted strains and monoclonal antibodies generated against escape mutants, research into CoV emergence and therapeutic efficacy may be severely limited moving forward. Together, these data and restrictions represent a crossroads of GOF research concerns; the potential to prepare and mitigate future outbreaks must be weighed against the risk of creating more dangerous pathogens. In developing policies moving forward, it is important to consider the value of the data generated by these studies and if they warrant further study or the inherent risks involved.

Overall, our approach has used metagenomics data to identify a threat posed by circulating bat SARS-like CoV SHC014. With the ability to replicate in human airway cultures, produce *in vivo* pathogenesis, and escape current therapeutics, SHC014 chimeric viruses illustrate the need for both surveillance and improved therapeutics against circulating SARS-

like viruses. The approach also unlocks metagenomics data to predict viral emergence with possible applications for preparing to treat future emerging virus infections.

Online Methods

Viruses, Cells, In Vitro Infection, and Plaque Assays. Wild-type SARS-CoV (Urbani), mouse adapted SARS-CoV (MA15) and chimeric SARS-like CoVs were cultured on Vero E6 cells, grown in DMEM (Gibco, CA) and 5% Fetal Clone Serum (Hyclone, South Logan, UT) along with anti/anti (Gibco, Carlsbad, CA). DBT cells expressing ACE2 orthologs have been previously described for both human and civet; bat ACE2 sequence based on *Rhinolophus leschenaulti* and established as described previously[22]. Pseudotyping experiments were based on HIV-based pseudovirus prepared as previously described[23] and examined on HeLa cells expressing ACE2 orthologs grown in Dulbecco's modified Eagle's medium supplemented with 10% fetal calf serum (Gibco) as previously described[24]. Growth curves in Vero, DBT, Calu-3 2B4, and primary human airway epithelial cells were performed as previously described[22, 25]. Vero E6 cells were originally obtained from USAMRIID; Calu3 cells were originally provided by Dr. CT Tseng, Universtiy of Texas Medical Branch; none of the cell line working stocks have not been recently authenticated or tested for mycoplasma, although the original seed stocks used to create the working stocks are free from contamination. Human lungs for HAE cultures were procured under University of North Carolina at Chapel Hill Institutional Review Board-approved protocols and represent highly differentiated human airway epithelium containing ciliated and non-ciliated epithelial cells as well as goblet cells. The cultures are also grown on an air-liquid interface for several weeks prior to use as previously described[26]. Briefly, cells were washed with PBS, and inoculated with virus or mock diluted in PBS for 40 minutes at 37 °C. Following inoculation, cells were washed 3 times, and fresh media added to signify time 0. Three or more biological replicates were harvested at each described time point. No blinding was used in any sample collections nor were samples randomized. All virus cultivation was performed in a BSL3 laboratory with redundant fans in Biosafety Cabinets as described previously by our group. All personnel wore Powdered Air Purifying Respirator (3M breathe easy) with Tyvek suits, aprons, booties and were double-gloved.

Sequence Clustering and Structural Modeling

The full-length genome sequences and S1 domains of spike amino acid sequences of representative CoVs were downloaded from Genbank or PATRIC, aligned with ClustalX, and phylogenetically compared by Maximum Likelihood using 100 bootstraps or with the PhyML package respectively. The tree was generated using Maximum Likelihood with the PhyML package. The scale bar represents nucleotide substitutions. Only nodes with bootstrap support above 70% are labeled. The tree shows that CoVs are divided into three distinct phylogenetic groups defined as α, β, and γ. Classical subgroup clusters are marked as 2a–2d for β CoVs and 1a and 1b for the α CoVs. Structural models were generated using Modeller (Max Planck Institute Bioinformatics Toolkit) to generate homology models for SHC014 and Rs3367 of the SARS RBD in complex with ACE2 based on crystal structure 2AJF (RCSB PBD identifier). Homology models were visualized and manipulated in MacPyMol (version 1.3).

Construction of chimeric SL-Viruses

Both wild-type and chimeric viruses were derived from either SARS-CoV Urbani or corresponding mouse adapted (MA15) infectious clone as previously described[27]. Plasmids containing spike sequences for SHC014 were extracted by restriction digest and ligated into the E and F plasmid of the MA15 infectious clone. The clone was designed and purchased from Bio Basic as six contiguous cDNAs using published sequences flanked by unique class II restriction endonuclease sites (BglI). Thereafter, plasmids containing wild-type, chimeric SARS-CoV and SHC014-CoV genome fragments were amplified, excised, ligated, and purified. In vitro transcription reactions were then preformed to synthesize full-length genomic RNA, which was transfected into Vero E6 cells as previously described[28]. The media from transfected cells were harvested and served as seed stocks for subsequent experiments. Chimeric and full length viruses were confirmed by sequence analysis prior to use in these studies. Synthetic construction of chimeric mutant and full length SHC014-CoV were approved by the University of North Carolina Institutional Biosafety Committee and the Dual Use Research of Concern committee.

Ethics Statement

This study was carried out in accordance with the recommendations for care and use of animals by the Office of Laboratory Animal Welfare (OLAW), National Institutes of Health. The Institutional Animal Care and Use Committee (IACUC) of The University of North Carolina at Chapel Hill (UNC, Permit Number A-3410-01) approved the animal study protocol (IACUC #13-033) followed in this manuscript.

Mice & In Vivo Infection

Female 10 week and 12 month old Balb/cAnNHsD mice were ordered from the Harlan Labs. Mouse infections occurred as previously described[29]. Briefly, animals were brought into a biosafety lab level 3 and allowed to acclimate for 1 week prior to infection. For infection and live-attenuated virus vaccination, mice were anesthetized with a mixture of ketamine and xylazine and infected intranasally when challenged with 50 μl of phosphate-buffered saline (PBS) or diluted virus with three to four mice per time point, per infection group per dose as described in the figure legends. For individual mice, notations for infection including failure to inhale entire dose, bubbling of inoculum from nose, or infection through the mouth may lead to exclusion of mouse data at discretion of the researcher; post-infection, no other pre-established exclusion/inclusion criteria are defined. No blinding was used in any animal experiments and animals were not randomized. For vaccination, young and aged mice were vaccinated by footpad injection with a 20 μl volume of either 0.2 μg of double-inactivated SARS-CoV vaccine with alum or mock PBS; mice were then boosted with the same regimen 22 days later, and challenged 21 days thereafter. For all groups, as per protocol, animals were monitored daily for clinical signs of disease (hunching, ruffled fur, reduced activity) for the duration of the experiment. Weight loss was monitored daily for the first 7 days after which, weight monitoring continued until the animals recovered to their initial starting weight or displayed three continuous days of weight gain. All mice losing greater than 20% of their starting body weight were ground fed and further monitored multiple times per day as long as they were under the 20% cutoff.

Mice losing greater than 30% of their starting body weight were immediately sacrificed as per protocol. Any mouse deemed to be moribund or unlikely to recover were also humanly sacrificed at the discretion of the researcher. Euthanasia was preformed via isoflurane overdose and confirmation of death by cervical dislocation. All mouse studies were performed at the University of North Carolina (Animal Welfare Assurance #A3410-01) using protocols approved by the UNC Institutional Animal Care and Use Committee (IACUC).

Histological Analysis

The left lung was removed and submerged in 10% buffered formalin (Fisher) without inflation for 1 week. Tissues were embedded in paraffin, and 5 μm sections were prepared by the UNC Lineberger Comprehensive Cancer Center histopathology core facility. To determine the extent of antigen staining, sections were stained for viral antigen using a commercially available polyclonal SARS-CoV anti-nucleocapsid antibody (Imgenex) and scored in a blinded manner by for staining of the airway and parenchyma as previously described[29]. Images were captured using an Olympus BX41 microscope with an Olympus DP71 camera.

Virus Neutralization Assays

Plaque reduction neutralization titer assays were performed with previously characterized antibodies against SARS-CoV as previously described[30–32]. Briefly, nAbs or serum were serially diluted 2-fold and incubated with 100 PFU of the different icSARS-CoV strains for 1 h at 37°C. The virus and antibodies were then added to a 6-well plate with 5×10^5 Vero E6 cells/well with $N \geq 2$. After a 1-h incubation at 37°C, cells were overlaid with 3 ml of 0.8% agarose in media. Plates were incubated for two days at 37° C and then stained with neutral red for 3 hours, and plaques were counted. The percentage of plaque reduction was calculated as [1 − (no. of plaques with antibody/no. of plaques without antibody)] × 100.

Statistical Analysis

All experiments were conducted contrasting two experimental groups (either two viruses, or vaccinated and unvaccinated cohorts). Therefore, significant differences in viral titer and histology scoring were determined by a two-tailed student's t test at individual time points. Data was normally distributed in each group being compared and had similar variance.

Biosafety and biosecurity

Reported studies were initiated after the University of North Carolina Institutional Biosafety Committee approved the experimental protocol: Project Title: Generating infectious clones of Bat SARS-like CoVs; Lab Safety Plan ID: 20145741; Schedule G ID: 12279. These studies were initiated prior to the U.S. Government Deliberative Process Research Funding Pause on Selected Gain of Function Research Involving Influenza, MERS, and SARS Viruses (http://www.phe.gov/s3/dualuse/Documents/gain-of-function.pdf), and the current manuscript has been reviewed by the funding agency, the National Institutes of Health (NIH). Continuation of these studies have been requested and approved by NIH.

SARS-CoV is a select agent

All work for these studies was performed with approved standard operating procedures (SOPs) and safety conditions for SARS-CoV, MERs-CoV and other related CoVs. Our institutional CoV BSL3 facilities have been designed to conform to the safety requirements recommended in Biosafety in Microbiological and Biomedical Laboratories (BMBL), the U.S. Department of Health and Human Services, the Public Health Service, the Centers for Disease Control (CDC) and the NIH. Laboratory safety plans have been submitted, and the facility has been approved for use by the UNC Department of Environmental Health and Safety (EHS) and the CDC. Electronic card access is required for entry into the facility. All workers have been trained by EHS to safely use powered air purifying respirators (PAPRs), and appropriate work habits in a BSL3 facility and active medical surveillance plans are in place. Our CoV BSL3 facilities contain redundant fans, emergency power to fans, and biological safety cabinets and freezers and can accommodate SealSafe mouse racks. Materials classified as BSL3 agents will consist of SARS-CoV, bat CoV precursor strains, MERS-CoV, and mutants derived from these pathogens. Within the BSL3 facilities, experimentation with infectious virus will be performed in a certified Class II Biosafety Cabinet (BSC). All staff wear scrubs, PAPRs, tyvek suits and aprons, and shoe covers, and hands are double-gloved. BSL3 users are subject to a medical surveillance plan monitored by the University Employee Occupational Health Clinic (UEOHC), which includes a yearly physical, annual influenza vaccination, and mandatory reporting of any symptoms associated with CoV infection during periods when working in the BSL3. All BSL3 users are trained in exposure management and reporting protocols, are prepared to self-quarantine, and have been trained for safe delivery to a local infectious disease management department in an emergency situation. All potential exposure events are reported and investigated by EHS and UEOHC, with reports filed to both the CDC and the NIH.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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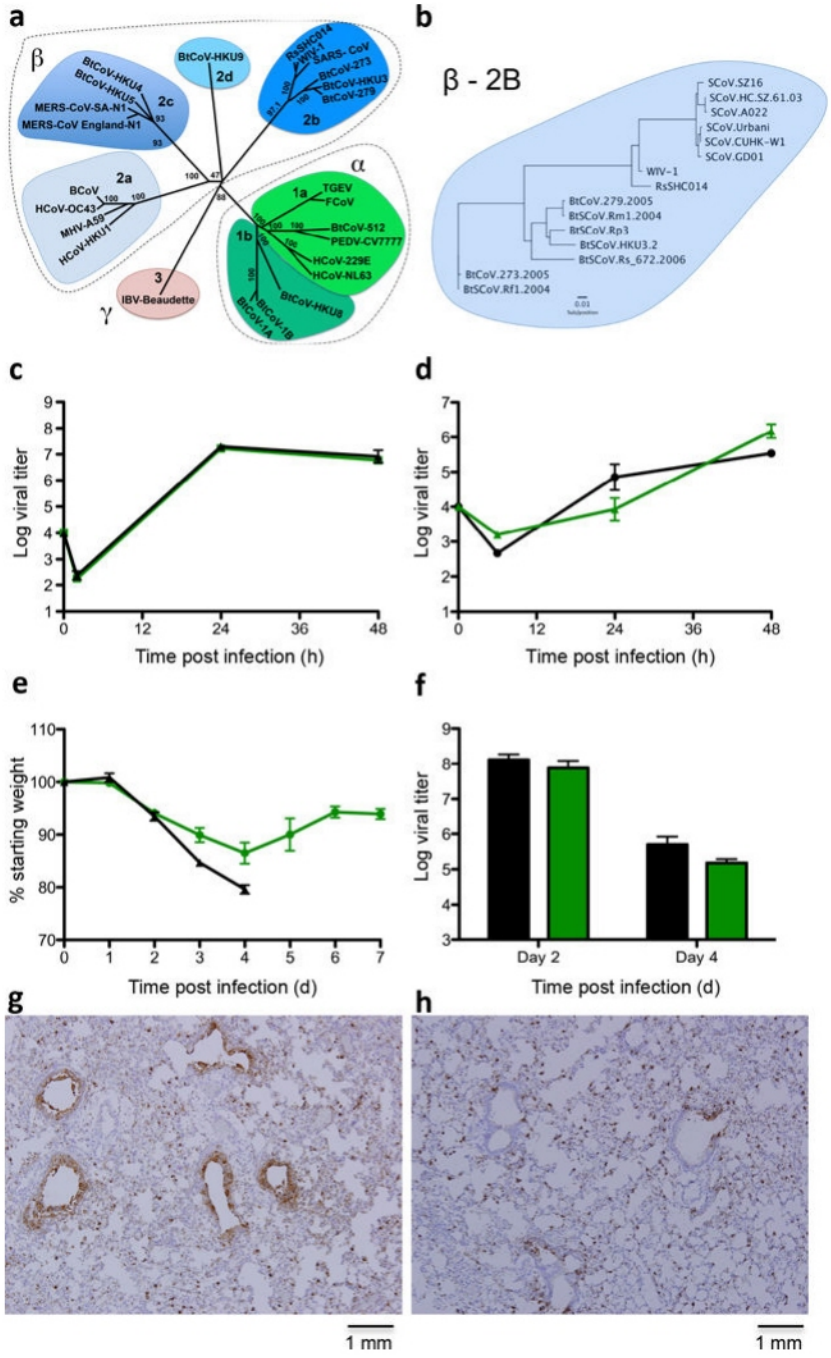

Figure 1. SARS-like viruses replicate in human airway cells and produce *in vivo* pathogenesis

(**a**) The full-length genome sequences of representative CoVs were aligned and phylogenetically mapped as described in the methods. The scale bar represents nucleotide substitutions, with only bootstrap support above 70% labeled. The tree shows CoVs divided into three distinct phylogenetic groups, defined as α,β, and γ. Classical subgroup clusters are marked as 2a–2d for the β CoVs and 1a and 1b for the α CoVs. (**b**) The S1 domains of the spike amino acid sequences of representative β CoVs of the 2b group, including SARSCoV, were aligned and phylogenetically mapped. The scale bar represents amino acid

substitutions. (**c**–**d**) Viral replication of SARS-CoV Urbani (black) and SHC014-MA15 (green) following infection of (**c**) Calu-3 2B4 cells or (**d**) well-differentiated, primary air-liquid interface human airway epithelial cell cultures at an MOI of 0.01. Samples were collected at individual time point with biological replicates (n =3) for both Calu3 experiments and HAE. (**e**–**h**) *In vivo* infection of 10-week-old BALB/c mice infected with 1×10^4 PFU of mouse adapted SARS-CoV MA15 (black) or SHC014-MA15 (green) via the *i.n.* route showing (**e**) weight loss (n =9 for MA15 n =16 for SHC014-MA15) and (**f**) viral replication in the lung (n =3 for MA15, n =4 for SHC014-MA15), and representative anti-SARS-CoV N antigen straining for (**g**) SARS-CoV MA15 and (**h**) SHC014-MA15. For each graphical figure, center value representative of group mean and error bars defined by SEM.

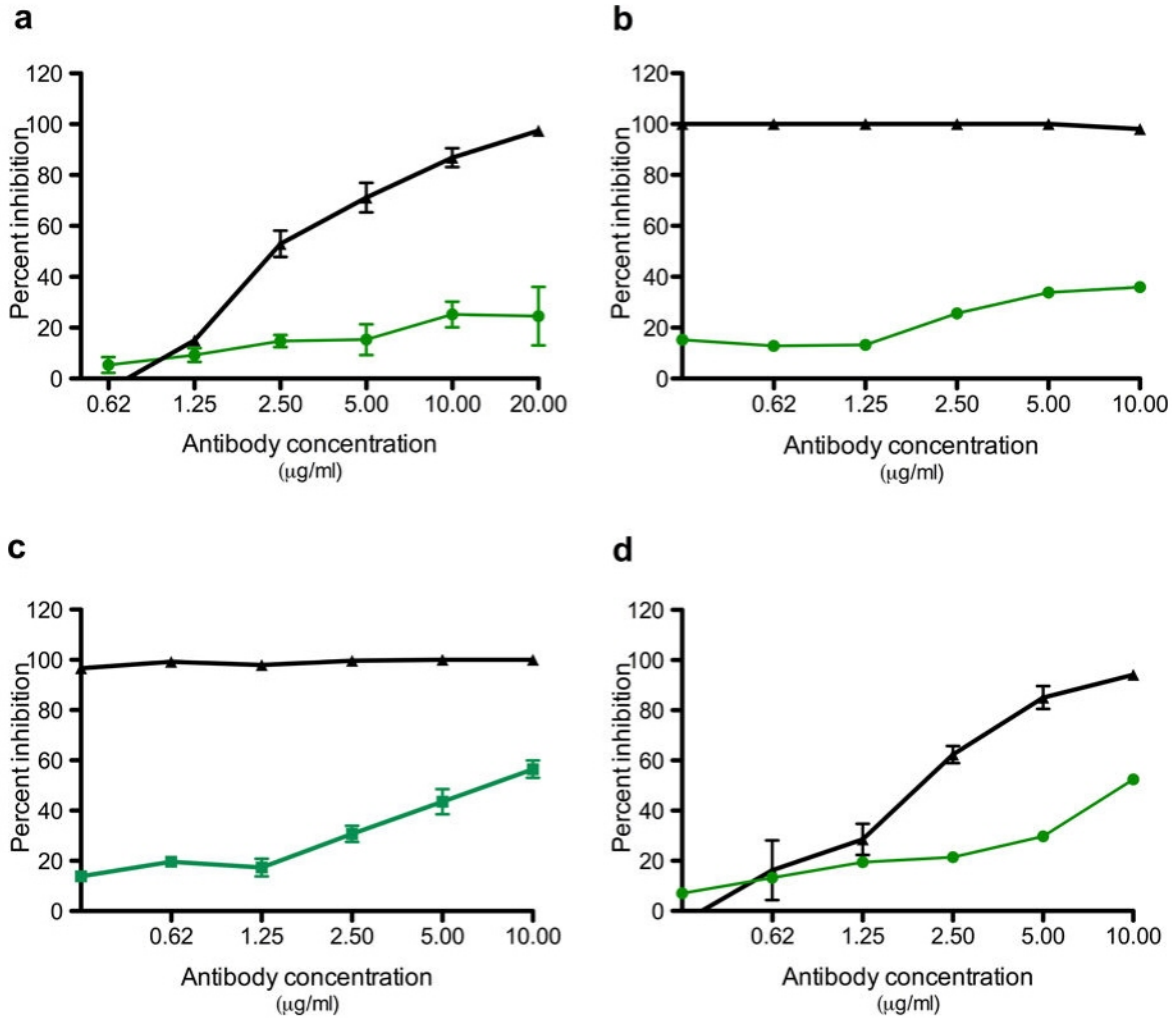

Figure 2. SARS-CoV monoclonal antibodies have marginal efficacy against SARS-like CoVs

Neutralization efficacy was evaluated using percent neutralization assays against SAR-CoV Urbani (black) or SHC014-MA15 with a panel of monoclonal antibodies: (**a**) fm6 (n = 3 for Urbani, n = 5 for SHC014-MA15)[10,11], (**b**) 230.15 (n = 3 for Urbani, n = 2 for SHC014-MA15), (**c**) 227.15 (n = 3 for Urbani, n = 5 for SHC014-MA15) and (**d**) 109.8 (n = 3 for Urbani, n = 2 for SHC014-MA15)[12], were all originally generated against epidemic SARS-CoV. Each data point representative of multiple center value represents group mean and error bars defined by SEM.

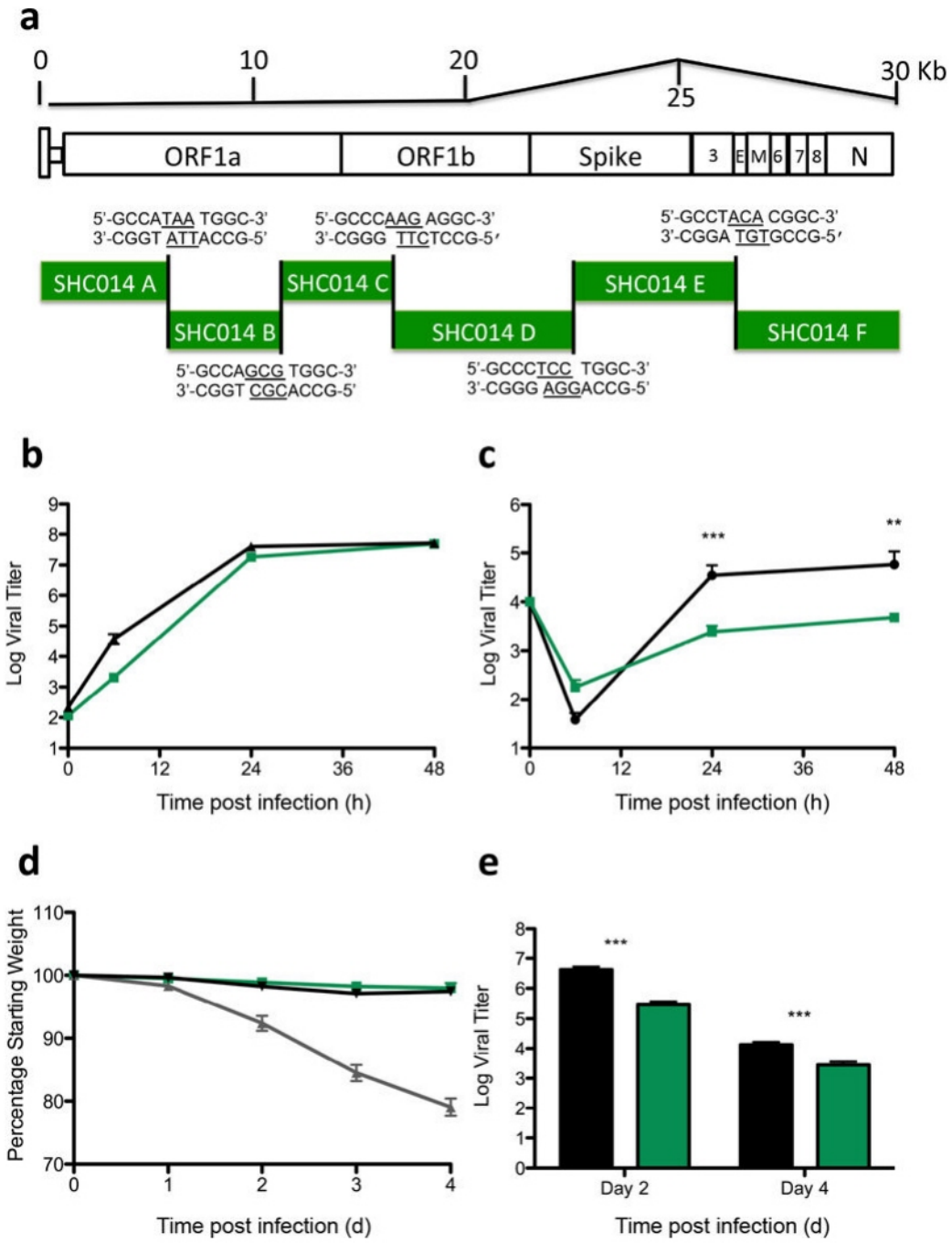

Figure 3. Full-length SHC014-CoV replicates in human airways, but lacks epidemic SARS virulence

(**a**) SHC014-CoV molecular clone was synthesized as six contiguous cDNAs designated A – F flanked by unique BglI sites that allowed for directed assembly of full-length cDNA. (**b–c**) Viral replication of SARS-CoV Urbani (black) and SHC014-CoV (green) following infection of (**b**) Vero cells or (**c**) well differentiated, primary air liquid interface human airway epithelial cell cultures at an MOI of 0.01. Samples were collected at individual time point with biological replicates ($n = 3$) for each group and representative of 1 experiment for

both Vero and HAE. (**d**–**e**) *In vivo* infection of 10-week-old BALB/c mice infected with 1×10^5 PFU of SARS-CoV Urbani (black), SARS-CoV MA15 (gray), or SHC014-CoV (green) via the *i.n.* route showing (**d**) weight loss ($n = 3$ for MA15, $n = 7$ for SHC014-CoV, $n = 6$ for SARS-Urbani) and (**e**) viral replication ($n = 3$ for SARS-Urbani and SHC014-CoV) in the lung. Each data point representative of multiple center value represents group mean and error bars defined by SEM. *P-values* based on 2-tailed Student's T-test of individual time points and are marked as indicated: **<0.01 ***<0.001.

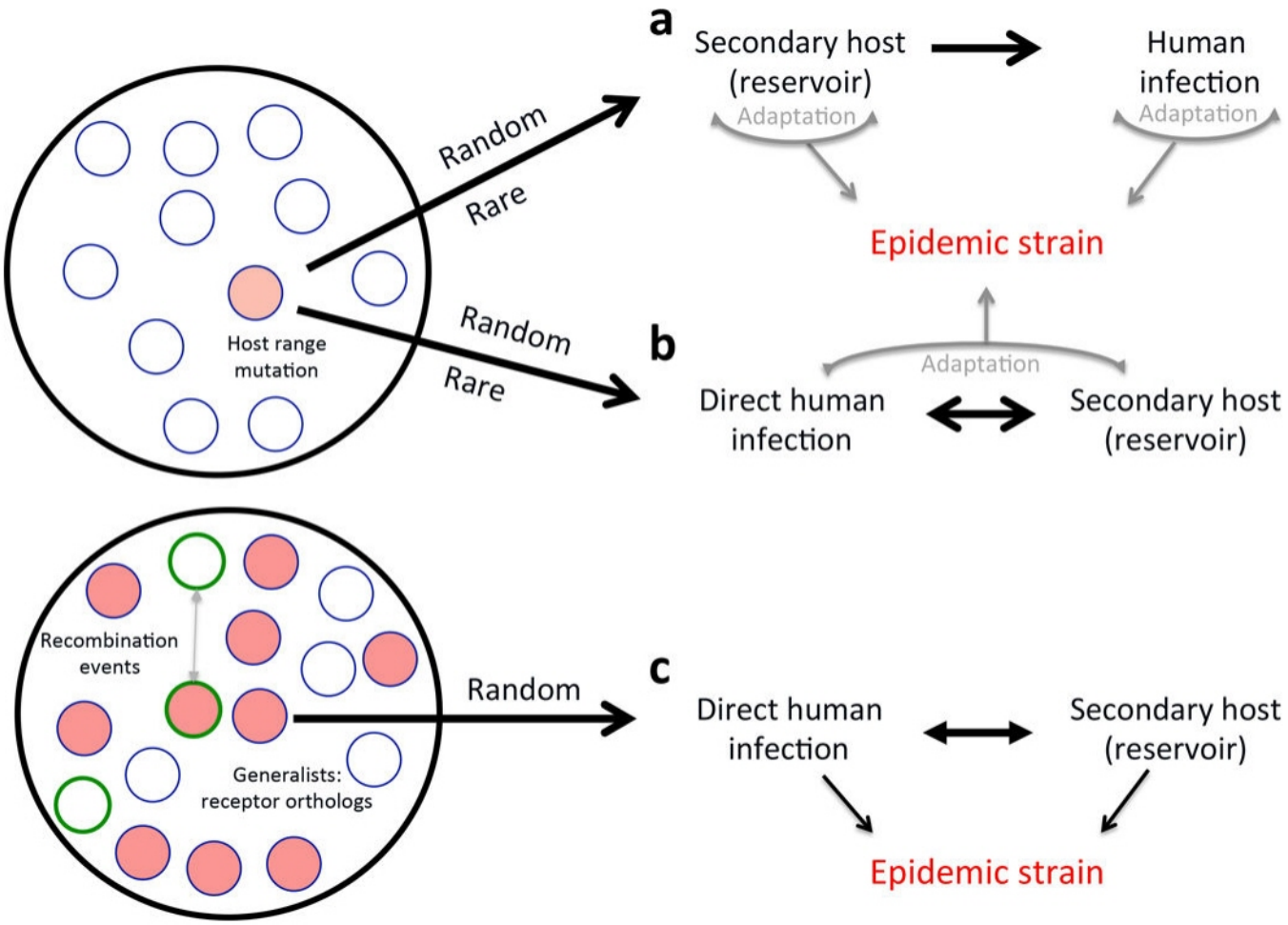

Figure 4. Emergence paradigms for coronaviruses

Coronavirus strains are maintained in quasi-species pools circulating in bat populations. (**a**–**b**) Traditional SARS-CoV emergence theories posit that host range mutants (red-filled circle) represent random and rare occurrences that permit infection of alternative hosts. (**a**) The secondary host paradigm argues that a non-human host is infected by a bat progenitor virus and, through adaptation, facilitates transmission to humans; subsequent replication in humans leads to the epidemic virus. (**b**) The direct paradigm suggests that transmission occurs between bats and humans without an intermediate host required; selection then occurs in the human population with closely related viruses replicating in a secondary host, permitting continued viral persistence and adaptation in both. (**c**) The data from chimeric SARS-like viruses argue that the quasi-species pools maintain multiple viruses capable of infecting human cells without the need for mutations (red-filled circles). While adaptations in secondary or human hosts may be required for epidemic emergence, if combined with virulent CoV backbones (green outlines), epidemic disease may be the result in humans. Existing data supports elements of all three paradigms.

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This was drafted by the US Health Attaché in Beijing. Helpful summary.

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China COVID-19 Vaccine Development Update as of August 2020

This update on COVID-19 vaccine developments in China summarizes information from sources including news/media releases, pharmaceutical company websites, WHO/Chinese/NIH Clinical Trial Registries and peer-reviewed publications. As of August 26, 2020, 7 Chinese candidate vaccines are in human clinical trials and 3 of them in phase III clinical trials.

Table 1: China COVID-19 Candidate Vaccines under Clinical Evaluation as of August 26, 2020

Type of candidate vaccine	Developer	Other partners	Registration No.	Outcome/Status
Inactivated: CoronaVac	Sinovac	Butantan (Brazil)	NCT04456595	Phase II result ; Phase III ongoing in Brazil ,Bangladesh and Indonesia;
Inactivated: BBIBP-CorV	CNBG Beijing; Sinopharm	Tiantan Bio Product Inc; China CDC; Henan CDC; NHC; Chinese Academy of Medical Science	ChiCTR2000034780	Phase I/II result; Phase III ongoing in Abu Dhabi, Peru, Morocco and Argentina
Inactivated	CNBG Wuhan; Sinopharm	Wuhan Institute of Virology; Henan CDC		
Inactivated	IMBCAMS*	West China Second University Hospital; Yun Nan CDC	NCT04412538; NCT04470609;	Phase I/II ongoing
Ad5-nCoV	Cansino; Insitute of Biotechbiology; Military Medical Science; PLA	Beijing Institute of Biotechnology; Canadian Center for Vaccinology	ChiCTR2000030906 ChiCTR2000031781 NCT04398147; NCT04341389	Phase II result; Phase III ongoing in Saudi Arabia
Protein subunit	Anhui Zhifei Longcom	Institute of Microbiology; Chinese Academy of Sciences	NCT04445194; NCT04466085	Phase I/II ongoing
mRNA	Walvax, Suzhou Abogen Pharm; Academy of Military Medicine; PLA	Shulan Hospital (Hangzhou); Yongfu County CDC (Guangxi)	ChiCTR2000034112	Phase I ongoing

* IMBCAMS: Institute of Medical Biology Chinese Academy of Medical Sciences

Domestic Emergency Use:

- On August 22, China NHC Science and Technology Development Center Director Zheng Zhongwei confirmed that China started the COVID vaccine emergency use process on July 22 following the COVID Vaccine Emergency Use Protocol approved by the State Council. The first priority populations are medical workers, epidemic control staff, and customs staff. Based on news released online, several populations are already approved for COVID vaccine emergency use, including international travelers, workers in high risk settings, and the military.
- Zheng Zhongwei also said that to prevent possible epidemic conditions in autumn and winter, they will consider expanding the scope of emergency use to other populations such as medical personnel and basic urban operations personnel (such as market personnel, traffic security personnel, service industry personnel).
- *CanSino Biologics reported* that its Ad5-nCoV vaccine received a one-year designation as a "military-specially-needed drug" from the Central Military Commission, meaning it can be developed through the military system pharmaceutical production for China's armed forces.

On the Horizon:

- CNGB director said in an interview that their vaccine product is expected to be listed on the market at the end of 2020 if the phase III trials and national approval processes go well. The company yearly capacity is said to be 220 million doses.

Table 2: China's International Commitments for COVID-19 Vaccine as of August 26, 2020

Target country (ies)	Commitment*
The World _*click here*	COVID-19 vaccine development and deployment in China, when available, will be made a global public good. China will contribute $2 billion to ensure vaccine accessibility and affordability in developing countries.
GAVI_ *click here*	Chinese government will contribute $20 million to GAVI for the next pledging cycle, encourages Chinese research institutes and vaccine producers to collaborate closely with GAVI, and supports its important role in promoting vaccine coverage.
African countries *click here*	China pledged that once the development and deployment of COVID-19 vaccine is completed in China, African countries will be among the first to benefit.
Latin American and Caribbean Countries *click here*	$1 billion in loans promised for Latin American and Caribbean countries to purchase potential COVID-19 vaccines (Mexico, Argentina, Barbados, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Panama, Peru, Trinidad and Tobago, and Uruguay)
Afghanistan, Pakistan and Nepal *click here*	After China's COVID-19 vaccine research and development is completed and put into use, it will be used as a global public product to increase the availability of vaccines in the three countries and help them to strengthen the construction of their public health systems.
Philippines *click here*	China is willing to give priority to the vaccine request made by Philippines.
Malaysia *click here*	A potential MOU with China to ensure early access to the COVID-19 vaccine when it is safe and effective to use.
Pakistan *click here*	China pledges that Pakistan will get 44 million doses to vaccinate about one-fourth of its population as part of the agreement for collaborating in phase III clinical trial between China and Pakistan.
Indonesia *click here*	Indonesia's state-owned Bio Farma signed an agreement with China's Sinovac Biotech which will import 50 million doses of vaccine from Sinovac from November through March 2021. Sinovac will also give priority to Bio Farma for further supply.
Mekong River countries *click here*	Once developed and deployed in China, COVID-19 vaccines will be provided to Mekong River countries (Cambodia, Laos, Myanmar, Thailand and Vietnam) on a priority basis.

*All monetary values are in US dollars

From:	Radonovich, Lewis (CDC/NIOSH/NPPTL/RB) (b)(@cdc.gov>
To:	Hanfling, Dan <DHanfling@iqt.org>; Carter Mecher <(b)(6) @charter.net>; Hillen, John (CDC/NIOSH/NPPTL) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87b65198eab243cca531742a4ed1a2d5-john.hillen (b)(@cdc.gov>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>
Subject:	Fwd: Page-Fan-Khan 03-06-2020 WSJ.pdf
Date:	2020/03/09 05:45:21
Priority:	Normal
Type:	Note

Here is the piece. You may know Mario - he worked on SARS commission in Canada.
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Sent: Sunday, March 8, 2020 5:52:13 PM
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Subject: Page-Fan-Khan 03-06-2020 WSJ.pdf

In case you missed this.
Parker

Parker A. Small, Jr. M.D.
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Sender:	Radonovich, Lewis (CDC/NIOSH/NPPTL/RB) <mto5@cdc.gov>
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https://www.wsj.com/articles/how-it-all-started-chinas-early-coronavirus-missteps-11583508932

How It All Started: China's Early Coronavirus Missteps

China's errors, dating back to the very first patients, were compounded by political leaders who dragged their feet to inform the public of the risks and to take decisive control measures

By Jeremy Page, Wenxin Fan and Natasha Khan
March 6, 2020 10:36 am ET

WUHAN—It was on Dec. 10 that Wei Guixian, a seafood merchant in this city's Hua'nan market, first started to feel sick. Thinking she was getting a cold, she walked to a small local clinic to get some treatment and then went back to work.

Eight days later, the 57-year-old was barely conscious in a hospital bed, one of the first suspected cases in a coronavirus epidemic that has paralyzed China and gripped the global economy. The virus has spread around the world and sickened more than 100,000.

For almost three weeks, doctors struggled to connect the dots between Ms. Wei and other early cases, many of them Hua'nan vendors. Patient after patient reported similar symptoms, but many, like her, visited small, poorly resourced clinics and hospitals. Some patients balked at paying for chest scans; others, including Ms. Wei, refused to be transferred to bigger facilities that were better-equipped to identify infectious diseases.

When doctors did finally establish the Hua'nan link in late December, they quarantined Ms. Wei and others like her and raised the alarm to their superiors. But they were prevented by Chinese authorities from alerting their peers, let alone the public.

The closed Hua'nan market in Wuhan.

PHOTO: NOEL CELIS/AGENCE FRANCE-PRESSE/GETTY IMAGES

One of the first doctors to alert Chinese authorities was criticized for "spreading rumors" after sharing with a former medical-school classmate a test result showing a patient had a coronavirus. Another doctor had to write a self-criticism letter saying his warnings "had a negative impact."

Even after Chinese President Xi Jinping personally ordered officials to control the outbreak on Jan. 7, authorities kept denying it could spread between humans—something doctors had known was happening since late December—and went ahead with a Chinese Lunar New Year banquet involving tens of thousands of families in Wuhan.

China has rejected any criticism of its epidemic response, saying it bought time for the rest of the world. Mr. Xi told 170,000 officials in a teleconference on Feb. 23 that the country's leadership acted swiftly and cohesively since the beginning.

A Wall Street Journal reconstruction paints a different picture, revealing how a series of early missteps, dating back to the very first patients, were compounded by political leaders who dragged their feet to inform the public of the risks and to take decisive control measures.

Last week, Zhong Nanshan, one of China's most highly regarded epidemiology experts and the leader of the National Health Commission's task force on the epidemic, said officials had identified a coronavirus by Dec. 31 and took too long to publicly confirm human-to-human transmission. If action had been taken earlier, in December or even early January, "the number of sick would have been greatly reduced," he said.

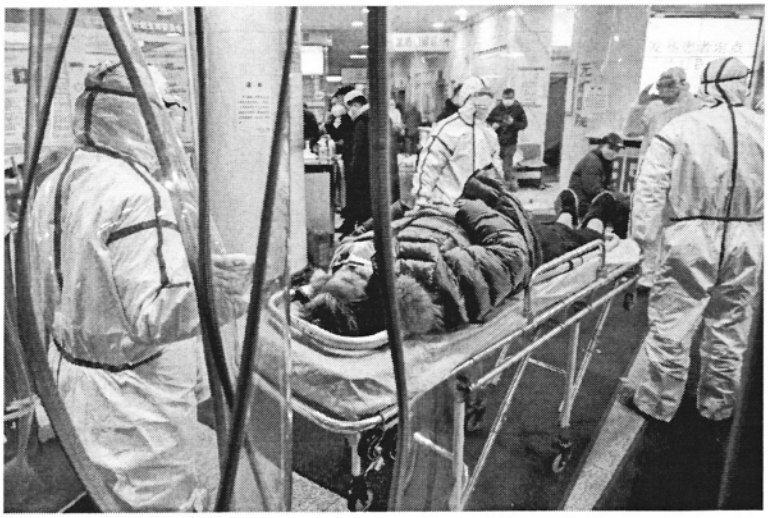
Although doctors worked hard to identify the disease quickly, they were hobbled by a health-care system that, despite huge improvements in the past 15 years, often leaves working-class people like Ms. Wei with insufficient access to general doctors and with crippling hospital bills.

When doctors did learn enough to sound the alarm, their efforts were stymied as the crisis became enmeshed in politics, both at the local and national level.

It now appears that, based on a speech by Mr. Xi published in a Communist Party magazine in February, he was leading the epidemic response when Wuhan went ahead with New Year celebrations despite the risk of wider infections. He was also leading the response when authorities let some five million people leave Wuhan without screening, and when they waited until Jan. 20 to announce the virus was spreading between humans.

As a result, the virus spread much more widely than it might have by the time Beijing locked down Wuhan and three other cities on Jan. 23, in the biggest quarantine in history. Those and other later measures appear to have slowed the spread within China's borders, but the global consequences of the early missteps have been severe.

"A lot fewer people would have died" in China had the government acted sooner, said Ms. Wei, in an interview on Feb. 16. She is now fully recovered and back home in the two-bedroom apartment she has barely left for almost two months. Her daughter, infected in mid-January, was still in a field hospital, she said.



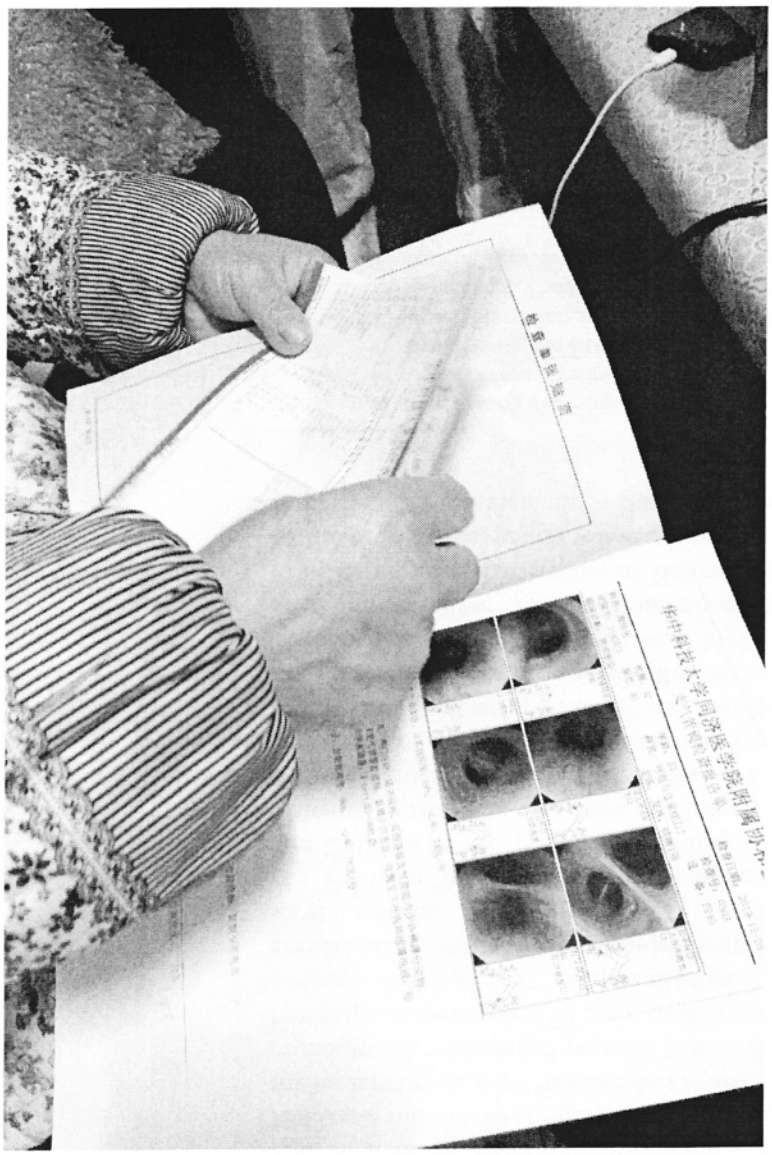
Medical staff and patients at the Wuhan Red Cross Hospital on Jan. 25.

PHOTO: HECTOR RETAMAL/AGENCE FRANCE-PRESSE/GETTY IMAGES

China's government information office, its National Health Commission and local authorities in Wuhan and the surrounding province of Hubei didn't respond to requests for comment.

Precisely how and when the epidemic began remains a mystery, as does the identity of the first person infected—Patient Zero. The dominant theory is that the virus originated in a bat and jumped to humans via other live, or dead, wild animals, probably sold in the Hua'nan market.

Epidemiologists who have studied the case data say the virus could have first jumped from an animal to a human as early as October or November, and then spread among individuals who either never got noticeably sick or didn't seek medical care.



Wei Guixian, who worked at the Hua'nan market and contracted the coronavirus, looked over her medical records.

PHOTO: THE WALL STREET JOURNAL

What is clear is that by the second week of December, several Hua'nan workers were falling sick with similar symptoms, including fever, coughing, fatigue and aching limbs. Even at that initial stage, there were indications that it was spreading to people with no market exposure—a signal of human-to-human transmission.

Wuhan's government announced last month that the first confirmed case was a person surnamed Chen who fell sick on Dec. 8 but had fully recovered and been discharged from the hospital. The person denied going to the Hua'nan market, it said.

Wu Wenjuan, a doctor at Wuhan's Jinyintan Hospital, which specializes in infectious diseases and handled many of the early cases, confirmed in a phone interview that among the earliest cases were four people in the same family, including a 49-year-old Hua'nan market vendor and his father-in-law. The vendor got sick on Dec. 12, while the father-in-law, who had no exposure

to the market, fell ill seven days later, according to a study by Chinese disease control researchers.

Ms. Wei, the market vendor who fell sick on Dec. 10, first sought help at a small private clinic across the street from her home.

For two consecutive days, she went there to take antibiotics through an intravenous drip, a treatment popular among Hua'nan workers because it was cheap and relatively quick. "It's pretty effective for ordinary colds," she said. "There's always a line inside."

By Dec. 12, however, her condition didn't improve. She rushed to the midsize Wuhan Red Cross Hospital, also near the market.

There, she recalls, a middle-aged doctor informed her that her symptoms were compatible with bronchitis. She was sent home with medicine and told not to worry. After that, she went back to the private clinic for more antibiotics. None had any effect.

She took a turn for the worse. On Dec. 16, unable to work and barely able to speak, she showed up at the emergency room of Xiehe Hospital but was sent home, and got a bed in a respiratory ward there only two days later, after one of her daughters helped make an appointment with a specialist.

She recalls seeing her daughters in tears before she lost consciousness. The older one "would touch me every so often, afraid I would pass away," she said.

When Ms. Wei came around three days later, she was barely able to move, but remembers one doctor surnamed Kong telling her, around Dec. 21, that two other workers from Hua'nan market were at Tongji Hospital, another major one in Wuhan.

"He said your illness is really serious," she recalled.

By Dec. 21, there were about three dozen people showing similar symptoms who would later be identified as confirmed or suspected coronavirus cases, according to a study released on Feb. 18 from China's Center for Disease Control and Prevention, or CDC.

At the time, though, doctors had yet to establish the common link between them.

Zhang Jinnong, the head of Xiehe Hospital's emergency department, said he doesn't recall treating Ms. Wei, but remembers the first Hua'nan patients coming in between Dec. 10 and 16.

He said he was relatively unconcerned at first, because there were no signs of the virus spreading between people. "Back then, I wasn't afraid at all—I was even relaxed," Dr. Zhang said in a phone interview. "The early stages made us drop our guard."

Some doctors also didn't realize at first that they were treating patients from the market, making it less likely they would discern a pattern.

Another local hospital, Wuhan Central, received its first coronavirus case, a 65-year-old man with a fever but no other symptoms, on Dec. 16, although doctors didn't know it then, said Ai Fen, who runs the emergency department there, in an interview on Feb. 18.

A CT scan revealed infection in both his lungs, but antibiotics and anti-flu drugs wouldn't shift it. Only after he was transferred to another hospital did staff there learn that he worked at Hua'nan, Dr. Ai said.

It would be another 11 days before doctors started to make the connection between the Hua'nan cases. Dr. Ai was among the first.

On Dec. 27, she received a second patient with similar symptoms, and ordered a laboratory test. By the following day, she had seen seven cases of unexplained pneumonia, four affiliated with the Hua'nan market, including a vendor's mother.

This could be a contagious disease, she remembers thinking to herself.

She informed the hospital's leadership on Dec. 29, and it notified the China CDC's district office, which said it had heard similar reports from elsewhere in Wuhan, according to Dr. Ai.

A doctor at the Hubei Hospital of Integrated Traditional Chinese and Western Medicine had also raised the alarm on Dec. 27, state media would report later.

On Dec. 30, Dr. Ai got the results for the laboratory test she ordered. It said "SARS coronavirus," the same kind of virus that had killed 774 people world-wide after emerging in China in 2002.

Terrified, she immediately told her superiors. She also circled the result with a pink marker pen and sent a photo to a medical-school classmate, together with a video clip of lung scans from another patient.

That photo and video became the first evidence to be leaked to the public after they were passed to another doctor at Wuhan Central, Li Wenliang, whose death from the virus in February would trigger an outpouring of grief and anger at Chinese authorities.

In a group posting on the WeChat messaging app that afternoon, Dr. Li told more than 100 of his medical-school classmates "7 SARS cases confirmed at Hua'nan Seafood Market" and said the patients were "quarantined in the Emergency Department of our hospital."

One person warned that the chat group could be censored. Dr. Li responded with an update: "coronavirus confirmed, and type being determined." And he added "Don't leak it. Tell your family and relatives to take care."

By that night, the information was circulating widely on social media, until government censors swung into action.

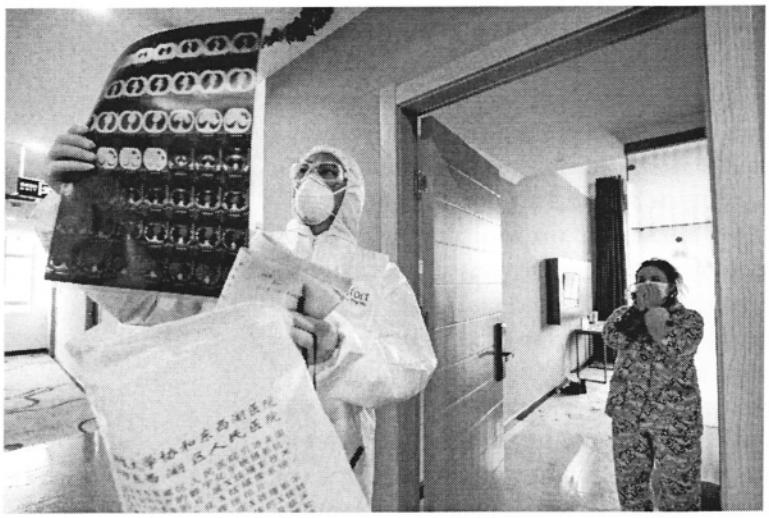
Hospital officials called Dr. Li to reprimand him. In a self-criticism letter confirmed by the Journal, he wrote that the leak "had a negative impact" on the National Health Commission's efforts to investigate the outbreak.

Meanwhile, evidence of human-to-human transmission was mounting.

Lü Xiaohong, a doctor at Fifth Hospital in Wuhan, became alarmed on Dec. 25 when she heard that medical staff at two hospitals had been quarantined after being infected with an unidentified form of viral pneumonia, she told the China Youth Daily newspaper.

Early in the morning on Jan. 1, another patient arrived at Dr. Ai's department from the Red Cross Hospital, where Ms. Wei was briefly treated nearly three weeks earlier. The owner of a private clinic near the market had become seriously sick after treating several patients suffering from fever.

Fearing her colleagues could be infected the same way, Dr. Ai once again alerted hospital authorities on Jan. 1, and ordered her own department to put on masks.



A doctor in Wuhan checked images for a patient on Feb. 3.

PHOTO: CHINATOPIX/ASSOCIATED PRESS

That night, the hospital's discipline department summoned her for a chat the next day. She was criticized for "spreading rumors," according to Dr. Ai. She tried to argue that the disease could be contagious. They said her action caused panic and "damaged the stability" of Wuhan.

The hospital's leadership also banned staff from discussing the disease in public or via texts or images, Dr. Ai said. Eight days later, a nurse in her department started to feel sick, and it was later confirmed she was infected by the coronavirus. By early March, three doctors at the hospital had died from the infection.

After warnings from local hospitals, the Wuhan office of the China CDC did a retrospective search for similar pneumonia cases with links to the Hua'nan market. It found several more, and reported those results on Dec. 30 to the national CDC headquarters, which sent a team of nine experts to Wuhan the next day.

The World Health Organization said its China office was informed on Dec. 31. Wuhan health authorities also issued the first official public statement on the outbreak that day, announcing 27 cases of suspected viral pneumonia related to the Hua'nan market.

"The investigation so far has not found any obvious human-to-human transmission or infection of medical staff," the statement from the Wuhan branch of the National Health Commission said. "The disease is preventable and controllable."

Medical authorities in Wuhan, meanwhile, were trying to get as many as possible of the suspected cases transferred to Jinyintan, the hospital that specializes in infectious diseases, where staff had built dedicated quarantine areas, fearing the virus could spread between humans.

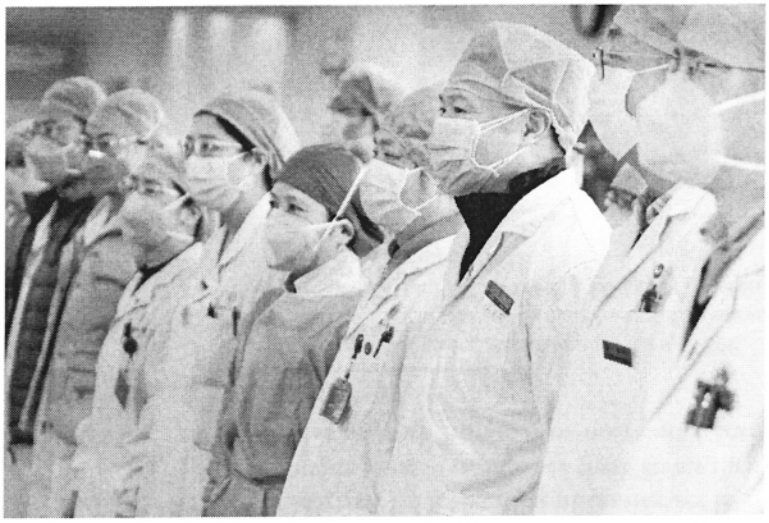
Zhang Li, a Jinyintan doctor, said she remembers receiving 15 patients from other hospitals on Dec. 30, and putting them in an empty, newly renovated area far from the children she was treating for flu. As more arrived, she separated Hua'nan workers from those who lived nearby, and checked if other hospitals' medical staff were infected, but was told none was.

"I was on alert because this was a new pneumonia and because I'd dealt with SARS," she said in a phone interview last week, adding that most early patients recovered well. "That also misled us."

Among those transferred to Jinyintan was a 41-year-old man who regularly shopped at the Hua'nan market and had gone to his local clinic after developing a fever and coughing up blood on Dec. 23, his wife said in an interview on Feb. 18.

He had been in Tongji Hospital since Dec. 27. After doctors there took a chest scan, they began to wear masks and protective gear, and placed him in quarantine, his wife said. He was put in an almost empty ward at Jinyintan on Dec. 31.

Overnight, about 40 patients arrived—all with the same symptoms, and all with a connection to the Hua'nan market.



Medical staff of Wuhan's Union Hospital on Jan. 22.

PHOTO: CHENG MIN/XINHUA/ZUMA PRESS

Some health experts say medical authorities made an error at that point by looking only for patients who had fever, direct Hua'nan market exposure and chest scans ruling out regular bacterial pneumonia.

In doing so, they overlooked those who had come in close contact with such cases, and other patients who had no direct exposure to the market, milder symptoms or illnesses other than pneumonia, the health experts said.

Back at Xiehe Hospital, Ms. Wei, the seafood vendor, had to undergo a new series of tests, including a throat swab and an endoscopy up her nose and down her airways. Like many other early cases, she couldn't be officially diagnosed with the virus because scientists had yet to genetically decode it and develop a test that would later be widely used.

Even so, her doctors treated her as a suspected case. They donned masks, isolated her and tried to move her to Jinyintan, but she refused, thinking they were trying to get rid of her because they suspected market workers were unhygienic.

"I thought to myself, I sell clean things," she said. "I sell live shrimp."

One of seven early cases at Hubei Integrated also refused to be transferred. Still, a doctor at Jinyintan got samples from the other six and sent them to the Wuhan Institute of Virology to try to identify the cause of the illness.

The institute would later reveal that it had identified a new coronavirus and mapped its genetic sequence by Jan. 2—critical steps toward containing the epidemic and designing a vaccine. But that wasn't made public at the time.

On Jan. 5, a medical research center in Shanghai notified the National Health Commission that one of its professors had also identified a SARS-like coronavirus and mapped the entire genome using a sample from Wuhan, according to an internal notice.

The virus was likely spreading via the respiratory tract, and "appropriate prevention and control measures in public places" were recommended, said the notice from the Shanghai Public Health Clinical Center. Lu Hongzhou, the center's director, confirmed its authenticity.

Still, Chinese authorities didn't publicly confirm an outbreak of a new coronavirus until Jan. 9, two days after The Wall Street Journal revealed it, citing people familiar with the findings. They didn't share the genome with the rest of the world until Jan. 12.

While WHO and Chinese officials have repeatedly trumpeted the swift sharing of the genome data as evidence of transparency in Beijing's response, some epidemiologists believe it should have happened at least a week earlier.

They, and many local doctors, also fault the government's repeated denials of human-to-human transmission in the first half of January.

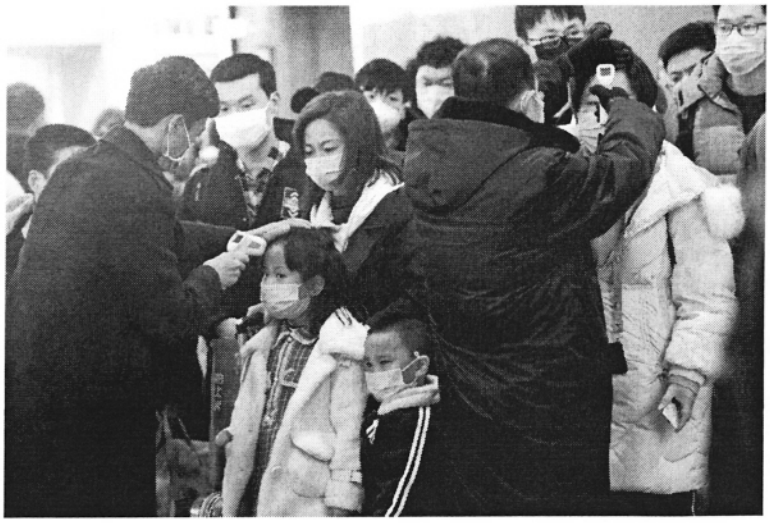
"We knew then that the government was lying," said one local doctor. "But we don't know why they needed to lie. Maybe they thought it could be controlled."

Only after a WHO official told a press conference on Jan. 14 that there could be "limited human-to-human transmission, potentially among families," did the Wuhan branch of the National Health Commission adjust its language to echo that position.

Even then, Li Qun, the head of the China CDC's emergency center, played down the threat, telling Chinese state television on Jan. 15: "After careful screening and prudent judgment, we have reached the latest understanding that the risk of human-to-human transmission is low."

Hubei province and Wuhan, its capital, were holding annual sessions of their local legislative and advisory bodies between Jan. 6 and 17. Local authorities routinely try to suppress bad news in such periods.

Between Jan. 5 and 17, no new cases were announced. And on Jan. 18, Wuhan went ahead with a yearslong tradition of hosting a mass Chinese Lunar New Year banquet, where families pose for group photos and use chopsticks to share dishes.



Travelers arriving on a train from Wuhan were checked at Hangzhou Railway Station on Jan. 23.
PHOTO: CHINA DAILY/REUTERS

The first public indication of Mr. Xi's involvement came on Jan. 20, when official media said he had ordered officials to contain the virus.

It now appears that he was in charge of the response since at least a Jan. 7 meeting of the party's top leadership, a change in the narrative that was made public in February as public anger mounted at a perceived lack of leadership from Beijing.

Chinese doctors and scientists said there were errors and foot-dragging by some experts sent by the government to Wuhan.

Among those sent in early and mid-January was Peking University's Wang Guangfa, who told official media on Jan. 10 that the virus had little capacity to cause illness and the epidemic was under control. Dr. Wang, who declined to comment, announced later that he had caught the virus.

Some of the experts had access to the first 41 confirmed cases at Jinyintan but were reluctant to share data with others before publication in a prestigious medical journal, according to some doctors and scientists involved in the response.

"Everyone was beginning to prepare for similar cases in other provinces and yet had no firsthand information on the virus and how it worked," said a doctor who repeatedly asked for more clinical details and was brushed off. "Doctors across China were really angry about this."

Another doctor involved said Chinese authorities had been looking solely for evidence that the virus was spreading from patients to medical workers, overlooking signs that it was moving between patients, their relatives and others they came into contact with.

With international concern mounting and China's health authorities receiving reports of fresh cases in Wuhan and some other cities, Beijing sent a new team of experts to Wuhan on Jan. 18, the day of the Lunar New Year banquet.

That team included an infectious disease expert from Hong Kong who had reported the day before that human-to-human transmission occurred in a family from the city of Shenzhen who had visited relatives in Wuhan but had not been to the Hua'nan market.

It also included Dr. Zhong, as the leader of the task force, who had played a key role in combating SARS. Among the evidence local doctors presented to Dr. Zhong was that of a single patient who had infected 14 medical workers at Xiehe Hospital, according to that hospital's emergency chief.

Zhong Nanshan, an epidemiology expert and head of the task force in Wuhan, visited Jinyintan Hospital on Jan. 19.

PHOTO: CHINA DAILY/REUTERS

Still, when President Xi made his first public statement on the crisis on Jan. 20, he made no explicit mention of human-to-human transmission, even as he told officials it was vital to contain the virus during the Lunar New Year travel period.

A few hours later, it was Dr. Zhong who announced on Chinese state television that the coronavirus was indeed spreading between people.

His team privately informed the Chinese leadership that the situation was more dire than they realized, and presented a series of recommendations, including as a Plan B, locking down Wuhan, according to a city official familiar with the discussions.

As a WHO committee met in Geneva to discuss whether to declare a global emergency, President Xi went for Plan B, imposing a cordon sanitaire on Jan. 23 on Wuhan and three other cities, affecting some 20 million people. By late February, new cases were slowing in China but rising sharply in other countries.

Looking back, Ms. Wei thinks she might have been infected via the toilet she shared with the wild meat sellers and others on the market's west side. She said the vendors next to her on both sides got sick, and the man kitty corner from her almost died. One of her daughters, a niece and the niece's husband caught the virus, too.

Ms. Wei was discharged in early January, having paid some 70,000 yuan, or about $10,000, in medical bills. She is unable to work, with the market still closed, and was unable to see her daughter in the hospital. Still, she considers herself lucky. "Some people spent so much money and still couldn't buy their lives," she said.

—Fanfan Wang and Lingling Wei in Beijing contributed to this article.

Write to Jeremy Page at jeremy.page@wsj.com, Wenxin Fan at Wenxin.Fan@wsj.com and Natasha Khan at natasha.khan@wsj.com

From:	<Robert.Kadlec@hhs.gov>
To:	Evaluation Only. Created with Aspose.HTML. Copyright 2013-2020 Aspose Pty Ltd.IBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>
Subject:	Fwd: Science: Mining coronavirus genomes for clues to the outbreak's origins
Date:	2020/01/31 22:04:19
Priority:	Normal
Type:	Note

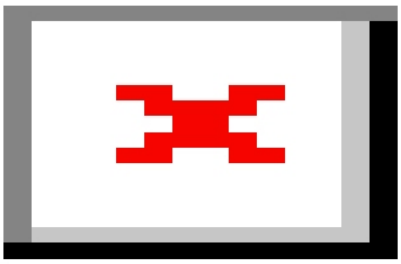
Sent from my iPhone

Begin forwarded message:

From: "Fauci, Anthony (NIH/NIAID) [E]" <(b)(6)
Date: January 31, 2020 at 9:48:59 PM EST
To: "Kadlec, Robert (OS/ASPR/IO)" <Robert.Kadlec@hhs.gov>
Cc: "Lane, Cliff (NIH/NIAID) [E]" <clane@niaid.nih.gov>
Subject: FW: Science: Mining coronavirus genomes for clues to the outbreak's origins

Bob:
This just came out today. Gives a balanced view.
Best,
Tony

From: Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>
Sent: Friday, January 31, 2020 8:43 PM
Subject: Science: Mining coronavirus genomes for clues to the outbreak's origins



As part of a long-running effort to see what viruses bats harbor, researchers in China collect one from a cave in Guandong.

EcoHealth Alliance

Mining coronavirus genomes for clues to the outbreak's origins

By Jon CohenJan. 31, 2020 , 6:20 PM

attaaaggtt tataccttcc caggtaacaa accaaccaac tttcgatctc ttgtagatct …

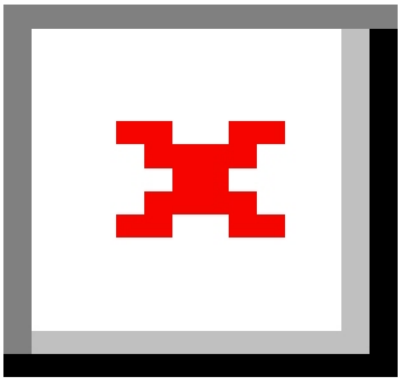
That string of apparent gibberish is anything but: It's a snippet of a DNA sequence from the viral pathogen, dubbed 2019 novel coronavirus (2019-nCoV), that is overwhelming China and frightening the entire world. Scientists are publicly sharing an ever-growing number of full sequences of the virus from patients—53 at last count in the Global Initiative on Sharing All Influenza Data database. These viral genomes are being intensely studied to try to understand the origin of 2019-nCoV and how it fits on the family tree of related viruses found in bats and other species. They have also given glimpses into what this newly discovered virus physically looks like, how it's changing, and how it might be stopped.

"One of the biggest takeaway messages [from the viral sequences] is that there was a single introduction into humans and then human-to-human spread," says Trevor Bedford, a bioinformatics specialist at the University of Washington, Seattle. The role of Huanan Seafood Wholesale Market in Wuhan, China, in spreading 2019-nCoV remains murky, though such sequencing, combined with sampling the market's environment for the presence of the virus, is clarifying that it indeed had an important early role in amplifying the outbreak. The viral sequences, most researchers say, also knock down the idea the pathogen came from a virology institute in Wuhan.

In all, 2019-nCoV has nearly 29,000 nucleotides bases that hold the genetic instruction book to produce the virus. Although it's one of the many viruses whose genes are in the form of RNA, scientists convert the viral genome into DNA, with bases known in shorthand as A, T, C, and G, to make it easier to study. Many analyses of 2019-nCoV's sequences have already appeared on virological.org, nextstrain.org, preprint servers like bioRxiv, and even in peer-reviewed journals. The sharing of the sequences by Chinese researchers allowed public health labs around the world to develop their own diagnostics for the virus, which now has been found in 18 other countries. (*Science*'s news stories on the outbreak can be found here.)

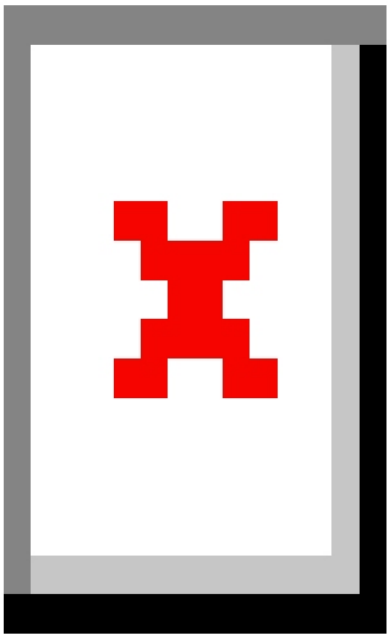
When the first 2019-nCoV sequence became available, researchers placed it on a family tree of known coronaviruses—which are abundant and infect many species—and found that it was most closely related to relatives found in bats. A team led by Shi Zheng-Li, a coronavirus specialist at the Wuhan Institute of Virology, reported on 23 January on bioRxiv that 2019-nCoV's sequence was 96.2% similar to a bat virus and had 79.5% similarity to the coronavirus that causes severe acute respiratory syndrome (SARS), a disease whose initial outbreak was also in China more than 15 years ago. But the SARS coronavirus has a similarly close relationship to bat viruses, and sequence data make a powerful case that it jumped into people from a coronavirus in civets that differed from human SARS viruses by as few as 10 nucleotides. That's one reason why many scientists suspect there's an "intermediary" host species—or several—between bats and 2019-nCoV.

According to Bedford's analysis, the bat coronavirus sequence that Shi Zheng-Li's team highlighted, dubbed RaTG13, differs from 2019-nCoV by nearly 1100 nucleotides. On nextstrain.org, a site he co-founded, Bedford has created coronavirus family trees (example below) that include bat, civet, SARS, and 2019-nCoV sequences. (The trees are interactive—by dragging a computer mouse over them, it's easy to see the differences and similarities between the sequences.)



Bedford's analyses of RaTG13 and 2019-nCoV suggest that the two viruses shared a common ancestor 25 to 65 years ago, an estimate he arrived at by combining the difference in nucleotides between the viruses with the presumed rates of mutation in other coronaviruses. So it likely took decades for RaTG13-like viruses to mutate into 2019-nCoV.

Middle East respiratory syndrome (MERS), another human disease caused by a coronavirus, similarly has a link to bat viruses. But studies have built a compelling case it jumped to humans from camels. And the phylogenetic tree from Shi's bioRxiv paper (below) makes the camel-MERS link easy to see.



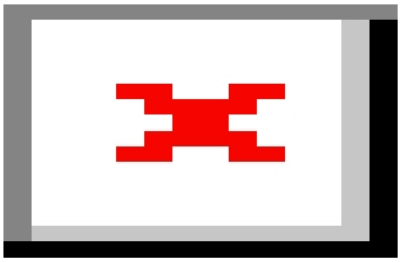
The longer a virus circulates in a human populations, the more time it has to develop mutations that differentiate strains in infected people, and given that the 2019-nCoV sequences analyzed to date differ from each other by seven nucleotides at most, this suggests it jumped into humans very recently. But it remains a mystery which animal spread the virus to humans. “There’s a very large gray area between viruses detected in bats and the virus now isolated in humans,” says Vincent Munster, a virologist at the U.S. National Institute of Allergy and Infectious Diseases who studies coronaviruses in bats, camels, and others species.

Strong evidence suggests the marketplace played an early role in spreading 2019-nCoV, but whether it was the origin of the outbreak remains uncertain. Many of the initially confirmed 2019-nCoV cases—27 of the first 41 in one report, 26 of 47 in another—were connected to the Wuhan market, but up to 45%, including the earliest handful, were not. This raises the possibility that the initial jump into people happened elsewhere.

According to Xinhua, the state-run news agency, “environmental sampling” of the Wuhan seafood market has found evidence of 2019-nCoV. Of the 585 samples tested, 33 were positive for 2019-nCoV and all were in the huge market’s western portion, which is where wildlife were sold. “The positive tests from the wet market are hugely important,” says Edward Holmes, an evolutionary biologist at the University of Sydney who collaborated with the first group to publicly release a 2019-nCoV sequence. “Such a high rate of positive tests would strongly imply that animals in the market played a key role in the emergence of the virus.”

Yet there have been no preprints or official scientific reports on the sampling, so it’s not clear which, if any, animals tested positive. “Until you consistently isolate the virus out of a single species, it’s really, really difficult to try and determine what the natural host is,” says Kristian Andersen, an evolutionary biologist at Scripps Research.

One possible explanation for the confusion about where the virus first entered humans is if there was a batch of recently infected animals sold at different marketplaces. Or an infected animal trader could have transmitted the virus to different people at different markets. Or, Bedford suggests, those early cases could have been infected by viruses that didn’t easily transmit and sputtered out. “It would be hugely helpful to have just a sequence or two from the marketplace [environmental sampling] that could illuminate how many zoonoses occurred and when they occurred,” Bedford says.



A research group sent fecal and other bodily samples from bats they trapped in caves to the Wuhan Institute of Virology to search for coronaviruses.

EcoHealth Alliance

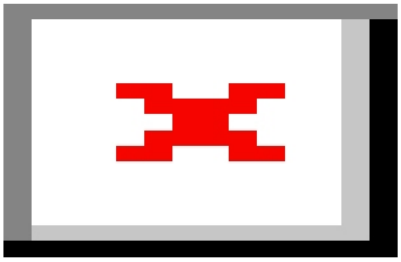
In the absence of clear conclusions about the outbreak’s origin, theories thrive, and some have been scientifically shaky. A sequence analysis led by Wei Ji of Peking University and published online by the *Journal of Medical Virology* received substantial press coverage when it suggested that “snake is the most probable wildlife animal reservoir for the 2019-nCoV.” Sequence specialists, however, pilloried it.

Conspiracy theories also abound. A CBC News report about the Canadian government deporting Chinese scientists who worked in a Winnipeg lab that studies dangerous pathogens was distorted on social media to suggest that they were spies who had smuggled out coronaviruses. The Wuhan Institute of Virology, which is the premier lab in China that studies bat and human coronaviruses, has also come under fire. “Experts debunk fringe theory linking China’s coronavirus to weapons research,” read a headline on a story in *The Washington Post* that focused on the facility.

Concerns about the institute predate this outbreak. *Nature* ran a story in 2017 about it building a new biosafety level 4 lab and included molecular biologist Richard Ebright of Rutgers University, Piscataway, expressing concerns about accidental infections, which he noted repeatedly happened with lab workers handling SARS in Beijing. Ebright, who has a long history of raising red flags about studies with

dangerous pathogens, also in 2015 criticized an experiment in which modifications were made to a SARS-like virus circulating in Chinese bats to see whether it had the potential to cause disease in humans. Earlier this week, Ebright questioned the accuracy of Bedford's calculation that there are at least 25 years of evolutionary distance between RaTG13—the virus held in the Wuhan virology institute—and 2019-nCoV, arguing that the mutation rate may have been different as it passed through different hosts before humans. Ebright tells *Science*Insider that the 2019-nCoV data are "consistent with entry into the human population as a natural accident."

Shi did not reply to emails from *Science*, but her longtime collaborator, disease ecologist Peter Daszak of the EcoHealth Alliance, dismissed Ebright's conjecture. "Every time there's an emerging disease, a new virus, the same story comes out: This is a spillover or the release of an agent or a bioengineered virus," Daszak says. "It's just a shame. It seems humans can't resist controversy and these myths, yet it's staring us right in the face. There's this incredible diversity of viruses in wildlife and we've just scratched the surface. Within that diversity, there will be some that can infect people and within that group will be some that cause illness."



A team of researchers from the Wuhan Institute of Virology and the EcoHealth Alliance have trapped bats in caves all over China, like this one in Guangdong, to sample them for coronaviruses.
EcoHealth Alliance

Daszak and Shi's group have for 8 years been trapping bats in caves around China to sample their feces and blood for viruses. He says they have sampled more than 10,000 bats and 2000 other species. They have found some 500 novel coronaviruses, about 50 of which fall relatively close to the SARS virus on the family tree, including RaTG13—it was fished out of a bat fecal sample they collected in 2013 from a cave in Moglang in Yunnan province. "We cannot assume that just because this virus from Yunnan has high sequence identity with the new one that that's the origin," Daszak says, noting that only a tiny fraction of coronaviruses that infect bats have been discovered. "I expect that once we've sampled and sampled and sampled across southern China and central China that we're going to find many other viruses and some of them will be closer [to 2019-nCoV]."

It's not just a "curious interest" to figure out what sparked the current outbreak, Daszak says. "If we don't find the origin, it could still be a raging infection at a farm somewhere, and once this outbreak dies, there could be a continued spillover that's really hard to stop. But the jury is still out on what the real origins of this are."

Posted in:

- • Asia/Pacific
- • Health

- Coronavirus

doi:10.1126/science.abb1256

Jon Cohen

Jon Cohen

Jon is a staff writer for *Science*.

- Email Jon
- Twitter

Sender:	<Robert.Kadlec@hhs.gov>
Recipient:	Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>
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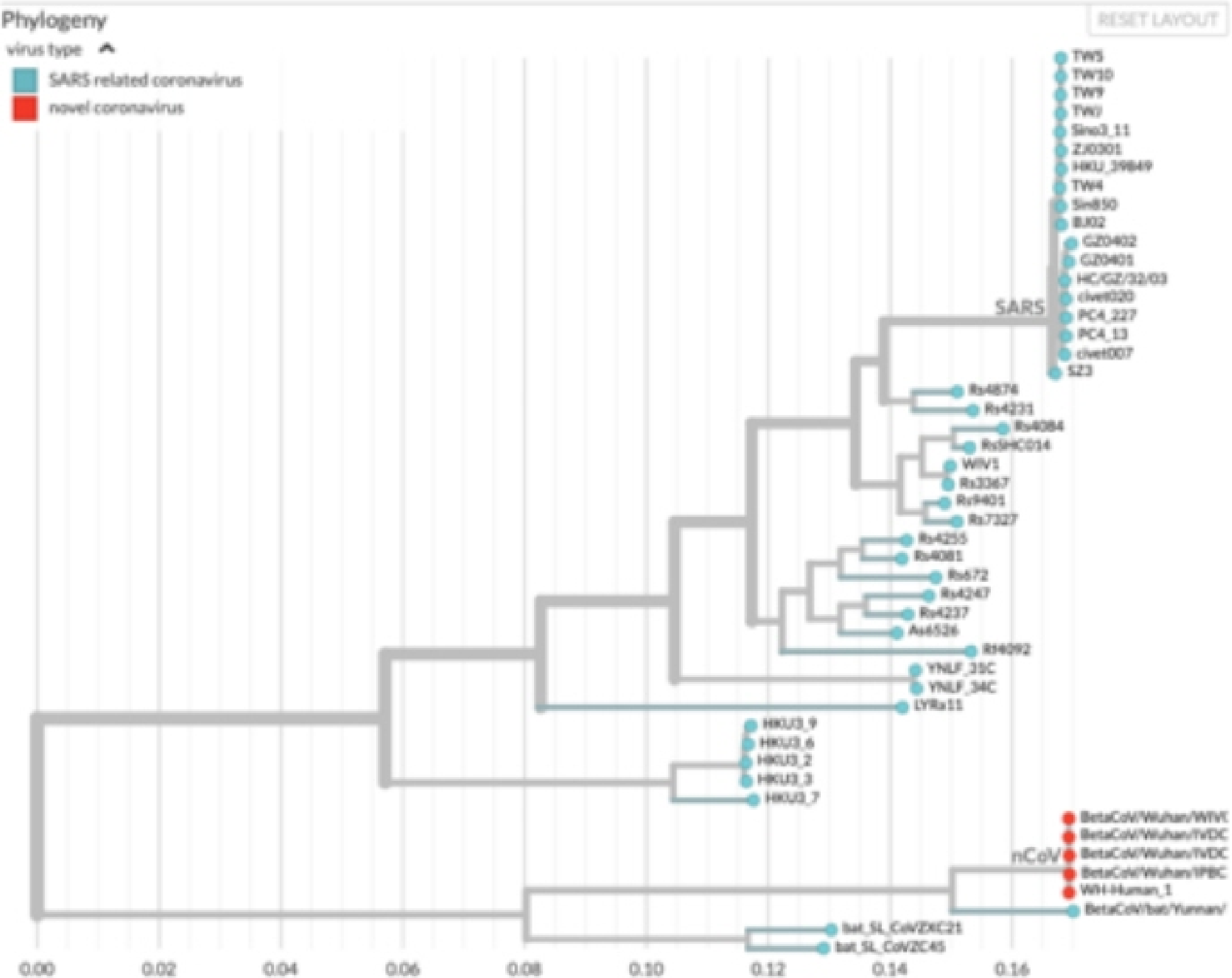
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virus type
SARS related coronavirus
novel coronavirus
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TW10
TW9
TW7
Sino3_11
ZJ0301
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TW4
Sin850
BJ02
GZ0402
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nCoV
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bat_SL_CoVZC45
0.00
0.02
0.04
0.06
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0.12
0.14
0.16

“All documents”
1 - DHS Master question list for COVID-19, March 18 2020
40 - same, March 25 2020

“Opaque - FEMA and OGA IR8”
1 - Fwd: China (WIV) wants to patent Gilead’s experimental covid drug
10 - Mention of EcoHealth, not COVID-related (plague in DR of Congo)

“Final Opaque DOS 17 pages”
1 - Forwarding Chinese study about origin
7 - From State to Kirk McConnell (senate - Armed Services) and Brian Walsh (senate - Intelligence), March 19 2020. RE: Some Russian expert opinion on “Wuhan virus”

“Final Opaque FDA 78 pages”
Emergency Use Authorization for Gilead COVID drug
Almost all pages withheld under b4.

“Final Opaque IOS 95 pages”
1 - Alex Azar schedule and briefing materials. Nothing about origins.
83 - Senator Martha McSally and Representative Matt Gaetz write to the Secretary to urge cutting connections with WIV and to clarify extent of NIH connection with WIV.

“Final Opaque Records IR3 USRTK”
1 - 2015 paper by Vincent Menachery, Baric, Shi Zheng-li, et al.

“Final Opaque Part 1 IR2 combined” - this was in an earlier production, I’ve read it before
NAS standing committee meeting briefing materials - Andersen, Fauci, Daszak, Mazet a part
1 - all published reports
180 - Red dawn rhapsodizing - 6 pages left white
211 - DHS Master Question List

“FNL Records IR4 (nih cdc)”
1- WSJ article about covid early missed cases
15 - January 2020, Fauci to Kadlec, Science article “gives balanced view” on origins

“OGA 4 pages IR7 Opaque”
1 - “Draft cable to China on consultations under Article V of BWC”. All meaningful content b5 redacted.

From:	Grigsby, Garrett (HHS/OS/OGA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7CD78B4810D44B17B8711AAEDE9A9023-GRIGSBY, GL <Garrett.Grigsby@hhs.gov>
To:	Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>
CC:	Kerr, Lawrence (HHS/OS/OGA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8ce9de2e7497472bb758f8fd6e262c86-Kerr, Lawre <Lawrence.Kerr@hhs.gov>
Subject:	FW: IMPORTANT: Draft cable to China on consultations under Article V of the BWC
Date:	2020/12/29 16:39:27
Importance:	High
Priority:	Urgent
Type:	Note

Dr. K,

(b)(5)

(b)(5) Let us know how we can support you. Thanks!

From: Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>
Sent: Tuesday, December 29, 2020 3:56 PM
To: Grigsby, Garrett (HHS/OS/OGA) <Garrett.Grigsby@hhs.gov>; Mciff, Colin (HHS/OS/OGA) <Colin.Mciff@hhs.gov>; Burr, Mara (HHS/OS/OGA) <Mara.Burr@hhs.gov>; Elvander, Erika (OS/OGA) <Erika.Elvander@hhs.gov>
Subject: FW: IMPORTANT: Draft cable to China on consultations under Article V of the BWC
Importance: High

(b)(5)

From: Danskin, Kathleen (OS/ASPR/SPPR) <Kathleen.Danskin@hhs.gov>
Sent: Tuesday, December 29, 2020 3:43 PM
To: Watson, Ian (OS/ASPR/SPPR) <Ian.Watson@hhs.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>

Cc: Lawrence, Theresa (OS/ASPR/SPPR) <Theresa.Lawrence@HHS.GOV>; Perkins, Dana (OS/ASPR/SPPR) <Dana.Perkins@hhs.gov>; Fernandez, Jose (OS/OGA) <Jose.Fernandez@hhs.gov>
Subject: IMPORTANT: Draft cable to China on consultations under Article V of the BWC
Importance: High

Hello;

(b)(5)

We're happy to hop on a call later today or tomorrow to discuss an HHS response – just let us know if there is a good time.

Thank you-
Katie Danskin

From: Couch, Johnny N <(b)(6)
Sent: Tuesday, December 29, 2020 2:26 PM
To: (b)(6); (b)(6) DiPietro, Maxwell D Lt Col USAF JS J5 (USA) (b)(6); Miller, Jennifer J5 <(b)(6); ISN-BPS-DL <(b)(6); Seedorff, Jennifer E <(b)(6); Cohen, Mark J <(b)(6); Perina, Alexandra H <(b)(6); Park, Christopher J (T) (b)(6) Chafin, Kelly (EOP.GOV) <(b)(6); Jones, Adam M <(b)(6) Brown, Douglas <Douglas.Brown@bis.doc.gov>; Wood, Robert A (Geneva) (b)(6); wcp_cbw@ucia.gov; Danskin, Kathleen (OS/ASPR/SPPR) <Kathleen.Danskin@hhs.gov>; Perkins, Dana (OS/ASPR/SPPR) <Dana.Perkins@hhs.gov>; (b)(6) (b)(6) @dhs.gov; (b)(6) @hq.dhs.gov; 'Kouts, Jodi' <Jodi.Kouts@nnsa.doe.gov>; (b)(6) @ostp.eop.gov; Peruski, Leonard F. (CDC/DDPHSIS/CGH/DGHP) <czn1@cdc.gov>; Vega, Jose M <(b)(6); Morrow, Grant H <(b)(6); Switzer, Bryan R (Rick) (b)(6); Feith, David <(b)(6)
Cc: Wright, Janey F <(b)(6); DiNanno, Thomas G (b)(6); Gibbs, Jeffrey J (b)(6); Jih, Rongsong (b)(6)
Subject: Draft cable to China on consultations under Article V of the BWC

Good Afternoon and Happy New Year,

Clearance Request: (b)(5)

(b)(5)

(b)(5)

Thanks in advance,

Neil

Neil Couch
Director, Office of Verification, Planning, and Outreach
Bureau of Arms Control, Verification and Compliance
U.S. Department of State
(b)(6)
(b)(6)

SENSITIVE BUT UNCLASSIFIED

Sender:	Grigsby, Garrett (HHS/OS/OGA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7CD78B4810D44B17B8711AAEDE9A9023-GRIGSBY, GL <Garrett.Grigsby@hhs.gov>
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Subject:	Fwd: Bloomberg: China Wants To Patent Gilead's Experimental Coronavirus Drug
Date:	2020/02/05 09:52:36
Priority:	Normal
Type:	Note

FYI

Sent from my iPhone

Begin forwarded

China Wants To Patent Gilead's Experimental Coronavirus Drug

- • 04:59 AM ET 02/05/2020

Chinese researchers have applied for a local patent on an experimental **Gilead Sciences** (GILD) drug that they believe might fight the novel coronavirus.

The Wuhan Institute of Virology— based in the central Chinese city at the epicenter of the epidemic — has applied for a patent in China for the use of the antiviral drug, know as remdesivir, in treating the ailment. The application was made on Jan. 21 along with a military academy, according to a Feb. 4 statement on the institute's website.

The move is a sign that China wants more say over a drug it deems one of the most promising candidates against the infection that has killed almost 500 people. The decision to seek a patent, instead of invoking the heavy-handed "compulsory license" option that lets nations override drug patents in national emergencies, underscores the delicate balancing act before China as it signals commitment toward intellectual property rights alongside curbing the virus outbreak.

"The fact that they have applied for a patent means there's growing awareness about this in the country," said Wang Yanyu, a senior partner at AllBright Law Offices in Beijing. "The government is

compelled to avoid using the compulsory license because it has been making efforts to show China respects intellectual property rights and the abuse of compulsory licensing will draw international criticism."

Makes Sense

It is not clear if or when China's intellectual property authorities will approve the institute's application. The patent filing will need to prove that the drug works on this coronavirus strain, 2019-nCoV, in a way that's different from how it works on other viruses in the same category.

Filing of the patent application by a stakeholder in China, however, makes sense, according to Wang. "Most of the patients are here, rather than in the U.S. which makes it unlikely that Gilead will do all these tests," he said.

While Gilead's experimental drug isn't licensed or approved anywhere in the world, it is being rushed into human trials in China on coronavirus patients after showing early signs of being highly effective. It may go into clinical trials in China as early as next week in patients with moderate and severe symptoms of the novel pathogen, said Merdad Parsey, Gilead's chief medical officer.

Chinese scientists have found Gilead's remdesivir, and chloroquine, an 80-year-old malaria drug, "highly effective" in laboratory studies at thwarting the novel coronavirus, they said Tuesday in a paper in the journal Cell Research. The two drugs' efficacy on humans required further clinical tests, the institute said in the statement.

Wants Access

China is capable of manufacturing chloroquine and now wants access to remdesivir.

If this patent is granted, Gilead will have to negotiate with Chinese patent owners when it wants to sell the drug for treating the novel coronavirus infection outside China.

"The good thing in having a patent is that it would lead to cross-licensing situations that give China more bargaining chips in negotiating the licensing fee with Gilead," said Wang. "And when Gilead wants to sell the drug to other countries for fighting new coronavirus, it will have to negotiate with China as the country who owns the patent for that specific purpose."

Gilead will retain the global rights to market the antiviral medication — once approved — for treating other illnesses such as Ebola and SARS that the drug was originally aimed for.

The Wuhan institute said in its statement that it made the patent application out of national interest, and won't exercise its patent rights if foreign pharmaceutical firms work together with China to curb the contagion.

At its end, Gilead is shipping enough doses to treat 500 patients and is ramping up supply in case the clinical trials work.

While the drug is challenging to produce, Gilead is working as fast as possible to produce more, according to Parsey. "It has been very no-holds-barred on our side," he said.

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Date:	2021/01/06 07:05:44
Priority:	Normal
Type:	Note

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HHS Executive Summary: Wednesday, 06Jan21

1. HHS

Today's Noteworthy Topics:

COVID-19 (Novel Coronavirus)
As of 1253ET on 05Jan21, the CDC confirmed and presumptive positive U.S. cases of COVID-19 have reached 20,732,404 across 50 states and DC, Guam, PR, CNMI, and USVI; deaths 352,464. WHO reported: global cases: 84,780,071; global deaths: 1,853,525 (as of 0338ET, 06Jan20). WHO member countries and areas with cases: 222. Testing: 250,479,467 cumulative tests include samples tested by State/Local Public Health Laboratories, Commercial Laboratories, Hospital Laboratories, CDC, and VA.

Daily Operational Schedule:
0830 – FEMA Daily Operations Brief
0900 – JCC/SOC Stand Up

Public Health Emergency of National Significance:
Opioid Crisis, Nationwide: 08Jan21
Novel Coronavirus (COVID-19): 23Jan21

HHS Response Status Summary:
HHS SOC: Level I (Full Activation)
CDC EOC: COVID-19 (Agency-Wide Response)
CDC EOC: Level III (Polio)
FDA EOC: Level I (Escalated Response Operations)

Emergency Support Function (ESF) Activation:
ESF – 8: Activated
ESF – 6: Activated

Recovery Support Function (RSF) Activation:
H&SS RSF: Activated Region II (2017 Irma/Maria, Puerto Rico projected end date of 10Mar21)

H&SS RSF: Activated Region X (2020 Oregon Wildfires projected end date of 28Feb21)

HHS Deployments: (Total = 237)
ASPR: 180 – (177) COVID-19, (1) Irma/Maria Recovery, (2) Laura
CDC: 57 – (57) COVID-198

New Mission Assignments (MA): NSTR

Active Situations (3):

- • Irma/Maria, Puerto Rico, &USVI (Recovery)
- • Novel Coronavirus (COVID-19)
- • California Wildfires

U.S. International Health Regulation National Focal Point Status: 30Dec20, a potential Public Health Emergency of International Concern has been declared for COVID-19 variant B.1.1.7. The final USG EIS text submitted to WHO/PAHO.

2. FEMA:

Interagency Response Status Summary:
NWC: Monitoring
NRCC: Level III
National IMATs: Red – Mission Capable; White – NRCC; Blue – Mission Capable; Gold – Mission Capable
Regional IMATs: Region V, Virtual COVID-19; Region IX-2, CA; Region X, OR

Significant National Weather:
The active western pattern will bring additional rain on saturated soils that could cause flooding and brings an enhanced threat of landslides, especially, in western Washington. Other hazards include mountain snow, gusty winds, and high surf. Wintry conditions are possible in the Northern and Central Plains with showers, locally heavy, and thunderstorms, some strong, in the South.

3. OPDIV/STAFFDIV Overnight Reports:

CDC:

- • COVID-19 – 222 locations – Update
- Plague – Democratic Republic of the Congo – New
- Yellow Fever – Guinea – Update
- Influenza [Animal (High Pathogenic)] – Slovenia – New

FDA:

- Coronavirus Disease 2019 (COVID-19)/ML/2019
- *Salmonella* Potsdam/Seafood(suspect)/December 2020

Prepared by:

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U.S. Department of Health and Human Services (HHS)

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ASPR

CDC Daily Report: As of 7:00 a.m. EST, Tuesday, January 05, 2021

SIGNIFICANT EVENTS:

- **<u>Note</u>: Operational updates described within the CDC Daily Report may not be inclusive of all response activities that are occurring.**

MONITORED EVENTS:

** Asterisks denote updates to monitored events/responses*

- Ebola
- Hepatitis-A Outbreak

RESPONSE STATUS:

- COVID-19 (Agency-wide Response) *
- Polio (Level III)

CDC DEPLOYMENTS:

- Domestic
  - COVID-19 (**52**)
- International
  - Polio (0)
  - COVID-19 (1)

  Total Personnel: (**53**)

RESPONSE UPDATES:

- **<u>COVID-19 United States</u>**
  - CDC's website provides the latest resources for community, healthcare professionals and information regarding United States COVID-19 cases: https://www.cdc.gov/coronavirus/2019-ncov/index.html.
  - Confirmed and probable U.S. cases of COVID-19: **20,558,489 (+212,117)** as of January 4.
  - U.S. deaths reported to CDC: **350,664 (+1,418)** as of January 4.

PROGRAM UPDATES:

GLOBAL DISEASE DETECTION OPERATIONS CENTER (GDDOC):

- **COVID-19 – 222 locations – Update to the GDDOC report dated December 31, 2020**

- Source: CDC; NCIRD/DVD; WHO Headquarters; WHO Regional Offices; Ministries of Health
- As of 4 January, 5:33 pm CET / 11:33 am ET, WHO has reported a global cumulative count of 83,910,386 cases and 1,839,660 deaths for an increase of 583,907 cases and 7,957 deaths over the preceding 24 hours.
- The cases are distributed in the six regions as follows: Region of the Americas [36,674,670 cases (337,231 new cases) / 876,031 deaths (3,545 new deaths)]; European Region [27,059,283 cases (173,812) / 591,792 deaths (3,022)]; South-East Asia Region [12,077,882 cases (26,868) / 184,941 deaths (448)]; Eastern Mediterranean Region [5,000,203 cases (22,351) / 122,472 deaths (411)]; African Region [1,978,166 cases (16,932) / 44,038 deaths (446)]; and Western Pacific Region [1,119,437 cases (6,713) / 20,373 deaths (85)]. Among the 222 affected locations, 138 reported new confirmed cases with the highest number of new cases from United States, United Kingdom, Russia, India, Brazil, Italy, France, South Africa, Colombia, Turkey, Germany, and Netherlands. As of 4 January 2021, media sources reported that 16 European and 20 additional countries have reported the new UK COVID-19 variant, VOC 202012/01. At the same time, three European and seven additional countries have reported cases of the new South African variant 501Y.V2.
- For further details on case counts and deaths by location, please see the WHO COVID-19 Situation Reports, Dashboard, Weekly Epidemiological and Operational Updates and Weekly Situational Updates. The official WHO case and death counts of confirmed COVID-19 cases may be intermittently updated; thus, differences among WHO reports with varying cutoff times and between WHO reports and other sources of COVID-19 data, using different inclusion criteria, are to be expected.
- CDC has established a COVID-19 Incident Management System and the CDC Emergency Operations Center is activated to provide ongoing support to the COVID-19 response. CDC COVID-19 Travel Recommendations for the locations with and without restrictions on entry to the United States are posted and will continue to be updated. The CDC maintains the Health Alert Network (HAN) and a dedicated CDC COVID-19 website, including recent postings on vaccinations, epidemiological studies, scientific updates, control measures, as well as a COVID-19 RSS Feed. On 4 January 2021, CDC updated its posts on Considerations for Election Polling Locations and Voters and Federal Register Notice: Temporary Halt in Residential Evictions to Prevent the Further Spread of COVID-19.

- **Plague – Democratic Republic of the Congo – NEW**
  - Source: United Nations Children's Fund (UNICEF)
  - The Global Disease Detection Operations Center (GDDOC) has learned of an outbreak of plague in the Democratic Republic of the Congo (DRC).
  - According to a UNICEF report, 286 cases of bubonic plague, including 27 deaths (case-fatality proportion = 9.44%), were reported since August in Ituri Province. Rethy and Biringi health zones have the highest number of cases, with 210 registered cases, including 15 deaths. This is the largest number of plague cases in DRC since 2009, when 618 cases and 27 deaths were reported; subsequent outbreaks have reported only 152 cases or fewer. Ituri province also borders both South Sudan, many of whose residents

are currently refugees in DRC, and Uganda, which had a case of plague imported from DRC in 2019.

- According to information from EcoHealth Alliance, on 21 December 2020, a team from Biringi and Aru health zones, including the Biringi zone chief medical officer, the Aru health zone nurse supervisor, and the laboratory technician from Aru General Hospital, investigated 58 cases and 5 community deaths reported at the Azumba and Kumbuku health centers. They took nine samples of bubo aspirate, which were sent to the national reference laboratory, Institut National de Recherche Biomedicale (INRB), six of which have tested positive with a rapid diagnostic test for plague. The team visited the villages of Azumba and Onu Oyia (Biringi health zone), where 41 additional cases were identified among the population with the help of the volunteer community relay (RECO). In addition, rat epizootics were reported in the immediate vicinity of the outbreak areas around the beginning of November 2020 in Onu Ayia, Odhu, Linya, and Ayaya villages.
- In Ituri Province, UNICEF, through its implementing partner Caritas Mahagi, has supported the Provincial Health Division of Ituri in its efforts to stem the transmission of bubonic plague through awareness campaigns on plague prevention measures. In response to the bubonic plague in Ituri province, UNICEF trained 20 managers from the seven Central Zone Offices (BCZ), 12 of them on community engagement and the process of setting up CACs (Cellule d'Animation Communautaire), on facilitation in the promotion of awareness messages through different communication channels (community dialogues, educational talks, popular forums, radio broadcasts, printed materials), and on mobilizing the population and communities against the epidemic.

- **Yellow Fever – Guinea – Update to the GDDOC report dated December 28, 2020**
  - Source: CDC - Guinea; NCEZID/DVBD; WHO; Guinea Ministry of Health
  - As of 2 January 2021, 80 suspected cases of YF and 15 deaths reported from 13 districts, with nine districts newly reporting cases. This represents a 54% (28) increase in cases and 7% (1) in deaths since the previous GDDOC report, with data as of 15 December 2020. Fifty-five (69%) cases and all deaths were reported from the health district of Koundara in north west Guinea, of which 38 were tested, and eight were IgM positive and unvaccinated for YF. Seroneutralization testing at the Institut Pasteur de Dakar (IPD) in Senegal confirmed that seven of the eight were positive for Yellow Fever, as well as IgM positive for at least one of the following: dengue, West Nile virus, and/or Zika. Confirmatory testing for Dengue is ongoing. Among the 15 deaths, four samples were taken, and all were negative for YF. The geographic distribution of the cases are as follows: Koundara 55 suspected cases, 38 tested, seven confirmed, 15 deaths; Kouroussa, nine suspected cases; Lelouma, four; two suspected cases each in Koubia and Fria; and one each in Mandiana, Télémélé, Dubréka, Forécariah, Faranah, Dabola, Yomou, and N'Zérékoré. All seven health areas of Koundara were affected, with the majority of cases in three health areas: Sambailo (23 suspected cases, 3 confirmed, and 6 deaths); Kamabi (10 cases, 1 confirmed, and 1 death); and Koundara Center, an urban commune (7 cases, 1 confirmed, and 3 deaths). The yellow fever vaccination status for the 55 Koundara cases is as follows: 2 (4%) vaccinated (without card); 34 (62%) unvaccinated; and 19 (34%) unknown status. Of the 52 Koundara cases with demographic information, 34 (65 %) were male and the most affected age group was 5-

14 years of age with 32 cases (58%), followed by 1-4 years of age with 14 cases (25%) and more than 15 years of age with nine cases (16%). Out of 15 registered deaths, nine occurred at a hospital and six in the community.

- Guinea is a high risk endemic country according to the EYE (Eliminate Yellow fever Epidemics) global strategy classification. However, the risk assessment at the regional level is classified as moderate because of the proximity of the cases to the borders of Senegal and Guinea Bissau, which have unvaccinated populations, and activities between the three countries which are conducive to spread of YF. The country has routine vaccination for children from nine months of age, international travelers, and also organizes preventive and mass campaigns according to the epidemiological context, with the last one completed in 2010. According to WHO-UNICEF estimates, the vaccination coverage for yellow fever in Guinea has been 40% for the years 2016 to 2019, while a survey in Koundara district found that coverage is only 16%. This low coverage suggests that a high proportion of the population is at risk, particularly children born after the 2005 mass vaccination campaign in Boke and any older person who was missed in past vaccination campaigns. Koundara is also noted to have documented *Aedes* species, parks inhabited by monkeys, and forests extending into Guinea Bissau and Senegal, the latter of which is also reporting cases of YF in this contiguous area. In response to the current outbreak, the Koundara Public Health Department activated its Emergency Operations Center and implemented active case finding, clinical management, vector control, risk communication, community engagement, and the development of an ongoing response plan. In addition, 2,912 children (9-59 months) have been vaccinated against yellow fever. A request for YF vaccine has been submitted to the International Coordinating Group on vaccine provision, and a mass campaign targeting 144,430 people between nine months and 60 years of age is planned for 11-17 January 2021.

- **Influenza [Animal (High Pathogenic)] – Slovenia - NEW**
  - Source: World Organization for Animal Health (OIE)
  - The GDD Operations Center (GDDOC) has learned of highly pathogenic avian influenza (HPAI) A (H5N5) virus identified in a wild bird in Koper, Slovenia.
  - According to OIE, a mute swan found injured in Koper was euthanized and subsequently tested positive for HPAI (H5N5) virus by PCR at the National Veterinary Institute, Slovenia's national laboratory. The source of the infection is unknown.
  - This is the first report of HPAI H5N5 from Slovenia. The GDDOC will provide additional information as it becomes available.

EOC 24 HOUR CALL DATA:

Category	Total Count
COVID-19 (DoH)	3
COVID-19 (Other)	67
Administrative	39
COVID-19 Vaccine Adverse Event	6
DGMQ - QPHO	1
DGMQ - QPHO - Artesunate	1
DGMQ - QPHO - Blood/Tissue Importation	1
DGMQ - QPHO - hBAT	1
DGMQ - Travel Restrictions - DNB/LO - TRIA	2
HBAT	1
Import, Export, Permits-Etiologic	1
ITSO	1
Logistics Assistance - DEO	1
Malaria	1
MIS-C - Multisystem Inflammatory Syndrome in Children	1
Naegleria fowleri infection (Primary Amebic Meningoencephalitis)	1
NOC - DHS: Secure Ops Center	3
On-Call Updates	1
Other	2
Vaccine Safety Questions	1
VAMS	7
Total Calls:	**142**

FDA OFFICE OF EMERGENCY MANAGEMENT
HHS FDA REPORT – January 5, 2021

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UPDATES

Adverse Events Associated with Methanol in Hand Sanitizer/ML/June 2020
No updates. OEO, via the Methanol in Hand Sanitizer Strike Team, will continue to monitor and provide updates.

***Burkholderia* Cepacia Complex Clusters/ML/October 2020**
No updates. OEO will continue to coordinate.

Coronavirus Disease 2019 (COVID-19)/ML/2019
FDA continues to work with WHO, US government partners (e.g., FEMA, NSC, HHS, ASPR, BARDA, CDC, NIH, DoD), state partners and medical product developers as necessary to support response efforts to the novel coronavirus outbreak/pandemic, COVID-19. Since FDA's previous report on 12/31/2020, FDA provided the following updates and information to the public and industry:

- **FDA Commissioner, Stephen Hahn, and the Center for Biologics Evaluation and Research (CBER) Director, Peter Marks, provided a joint *statement* on following the authorized dosing schedules for COVID-19 Vaccines. In summary, FDA is aware of discussions about changing the dosing schedule or dose based on a belief that changing the dose or dosing schedule can help get more vaccine to the public faster. However, making such changes that are not supported by adequate scientific evidence may ultimately be counterproductive to public health.**
- **FDA *alerted* patients and health care providers of the risk of false results, particularly false negative results, with the *Curative SARS-Cov-2* test. Risks to a patient of a false negative result include: delayed or lack of supportive treatment, lack of monitoring of infected individuals and their household or other close contacts for symptoms resulting in increased risk of spread of COVID-19 within the community, or other unintended adverse events. To reduce the risk of false negative results, it is important to perform the test in accordance with its authorization and as described in the authorized labeling, e.g., the *Fact Sheet for Healthcare Providers*. When the test is not performed in accordance with its authorization or as described in the authorized labeling, there is a greater risk that the results of the test may not be accurate.**
- **FDA published a new *toolkit* to help stakeholders communicate in English and Spanish about hand sanitizer safety and use during the COVID-19 pandemic. New**

materials include social media messages and graphics, consumer information, and health professional messaging. Furthermore, a new *COVID-19 Communication Toolkits webpage* provides links to all FDA toolkits on COVID-19 topics to help everyone communicate accurate and timely information to patients, the public, and health care professionals.

- **In a new *FDA Voices* entitled, *2020 at FDA: A Year of Unparalleled Contributions to Public Health*, FDA Commissioner Dr. Hahn, highlights a sampling of FDA's achievements, many COVID-19-related, from this past year.**
- **The agency published online a new infographic, *COVID-19 Tests and Collection Kits Authorized by the FDA in 2020*, that provides a visualization of the wide variety of tests authorized.**
- **Warning letters for unapproved and misbranded products related to COVID-19 were issued by FDA to *Sparrow & Health Performance LLC* and Riverstone LLC.**
- **FDA approved two abbreviated new drug applications (ANDAs), or generics, for heparin sodium injection. The agency continues to work to help patients suffering from COVID-19 by reviewing and approving generic medicines, such as anti-coagulants, used in the prevention and treatment of blood clotting.**
- **Testing updates:**
    - **Currently, 309 tests and sample collection devices are authorized by FDA under emergency use authorizations (EUAs). These include 235 molecular tests and sample collection devices, 63 antibody tests, and 11 antigen tests. There are 32 molecular authorizations that can be used with home-collected samples. There is one molecular prescription at-home test, one antigen prescription at-home test, and one over-the-counter (OTC) at-home antigen test.**

To review FDA's current response activities, click: *FDA's COVID-19 Current Response Activities*. OEO, via the 2019-nCoV IMG, will continue to monitor and provide updates.

***E. coli* O157:H7/Produce/September 2020**
No updates. FDA's Coordinated Outbreak Response and Evaluation Network (CORE) will continue to coordinate.

***Salmonella* Potsdam/Seafood(suspect)/December 2020**
FDA's traceback investigation is ongoing. CORE will continue to coordinate.

ON THE RADAR

First Amendment Activity/Washington DC/January 2020
The Washington DC Metropolitan Police Department (MPD) has advised that due to First Amendment Activity beginning on 1/5/2020 – 1/7/2021, several streets will be restricted to vehicular traffic. Motorists could encounter possible delays if operating in the vicinity of downtown area and may wish to consider *alternative routes*. OEO is monitoring the situation and information being provided by federal agencies and sharing it with FDA's Baltimore District Office. OEO will continue to monitor and report updates as necessary.

M6.1 Earthquake/Alaska/January 2020

On January 3, 2021, the USGS reported a 6.1 magnitude earthquake approximately 146 miles west-southwest of Adak, AK. No tsunami warning, advisory, or warning was issued. OEO notified out local district office of the event. No impact on FDA employees, facilities, or regulated industry is expected. OEO will continue to monitor, but no further reporting is expected.

FEMA National Situation Report

As of 3:00 a.m. ET, Wednesday, January 6, 2021

This report is published twice daily, 3:00 a.m. and 5:00 p.m. ET

Common Operating Picture

FEMA HQ

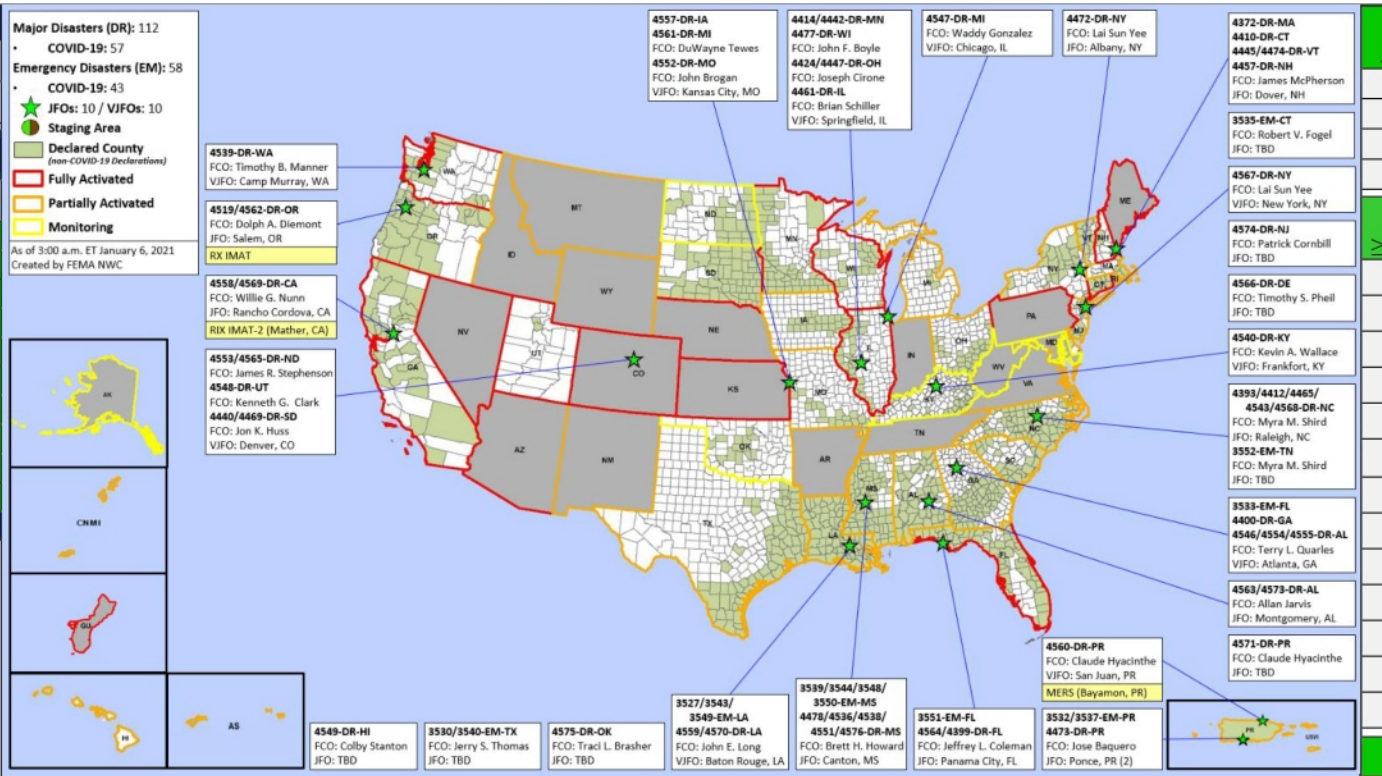
NWC	NRCC
Monitoring	Level III

FEMA REGIONS

WATCH		RRCC
Monitoring	I	Level II
Monitoring	II	Level III
Monitoring	III	Level III
Monitoring	IV	Rostered
Monitoring	V	Level III
Monitoring	VI	Level III
Alt. Location	VII	Rostered
Monitoring	VIII	Rostered
Monitoring	IX	Rostered
Monitoring	X	Level III

Notes:

NRCC / RRCCs: COVID -19 Response	All State EOCs, activated for COVID-19 (except SD and OR) PR: Earthquakes LA: TC Laura/Delta/Zeta IA: Derecho CA & CO: Wildfires AK: Flooding & Landslides



N-IMATs

3 Teams Available

Red	
White	NRCC
Blue	
Gold	

R-IMATs

≥ 7 Teams Available

I	
II	2
III	3
IV-1	
IV-2	
V	Virtual COVID-19
VI-1	
VI-2	
VII	
VIII	1
IX-1	
IX-2	CA
X	OR

FMC	PMC
NMC	Deployed

Team: Status	US&R >66%	MERS >66%	FCOs ≤1 Type I	FDRCs ≤1	IM Workforce
Assigned:	28	36	47	10	14,029 (+14)
Unavailable:	1	0	4	0	2,401 (-15)
Deployed:	0	0	38	10	5,665 (+28)
Available:	**27**	**36**	**5**	**0**	**43% / 5,963 (+1)**

Incident Management Cadre Availability Summary

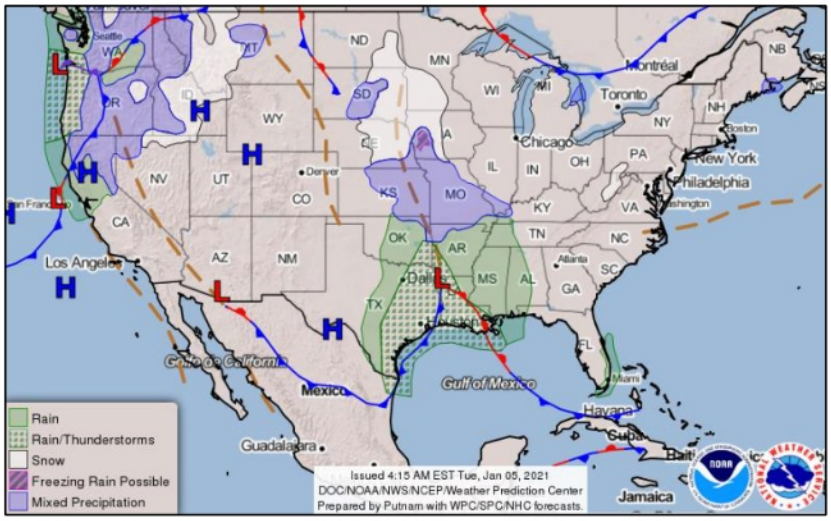
Cadres with 25% or Less Availability

FL 25% (40/159); PA 22% (713/3,199)

National Current Operations and Monitoring

Weather Threats

- Locally heavy rainfall continues along the coasts of Washington, Oregon, and northern California
  - Up to 3 inches of rain in some areas expected; 6-12 inches of snow anticipated across the Olympic and Cascade mountains
- Mixed precipitation continues over the Northern/Central Plains
- Moderate to heavy rainfall expected across portions of the Southern Plains and Lower Mississippi Valley



(NOAA Forecasts: NWS | WPC | SPC)

Joint Preliminary Damage Assessments

Region	State	Event / Date	Type	Counties		Start – End Dates
				Requested	Completed	
IV	NC	Tropical Cyclone Eta Nov 12-19	IA	0	0	N/A
			PA	15	0	12/9 – TBD

Declaration Activity

Declaration Requests in Process: 10 (CO, GA, LA, MD (Appeal), UT, TX, CT, WA, Poarch Band of Creek Indians (COVID-19), & Navajo Nation (COVID-19)

(Declared Disasters: fema.gov)

Joint Field Office Status Updates

No changes over the last operational period

(JFO listing available on NWC SharePoint Site)

Regional Current Operations & Monitoring

Region I

RRCC: Level II (day shift – COVID-19)
WATCH – *Maynard MOC:* Monitoring (24/7)
- No significant activity

IMAT: FMC / Available
LNOs: CT, MA, ME, NH, RI, VT, & 1 Tribe
EOCs:
- CT, ME, & NH: Full Activation (COVID-19)
- MA, RI, & VT: Partial Activation (COVID-19)

Regional Continuity Status: Not activated

Region II

RRCC: Level III (day shift – COVID-19)
WATCH: Monitoring (24/7)
- No significant activity

IMAT: FMC / Available
EOCs:
- PR: Partial Activation (Earthquake & COVID-19)
- NY, NJ & USVI: Partial Activation (COVID-19)

Regional Continuity Status: Partially Activated (Telework/COVID-19)

Region III

RRCC: Level III (day shift – COVID-19)
WATCH: Monitoring (24/7)
- First Amendment Demonstrations in D.C.

IMAT: FMC / Available
EOCs:
- PA: Full Activation (COVID-19)
- DC, DE, & VA: Partial Activation (COVID-19)
- MD & WV: Monitoring (COVID-19)

Regional Continuity Status: Not Activated

Region IV

WATCH: Monitoring (24/7)
- No significant activity

IMAT-1: FMC / Available
IMAT-2: FMC / Available
EOCs:
- FL: Full Activation (COVID-19)
- AL, GA, MS, NC, SC, & TN: Partial Activation (COVID-19)
- KY: Monitoring (COVID-19)

Regional Continuity Status: Not Activated

Region V

RRCC: Level III (day shift – COVID-19)
WATCH: Monitoring (24/7)
- No significant activity

IMAT: Virtually Deployed all states (COVID-19)
LNOs: IL, IN, MI, MN, OH, & WI
EOCs:
- IL, MN, & WI: Full Activation (COVID-19)
- IN, MI, & OH: Partial Activation (COVID-19)

Regional Continuity Status: Not Activated

Region VI

RRCC: Level III (day shift – COVID-19)
WATCH – *Denton MOC:* Monitoring (24/7)
- Heavy Rainfall (see above)

IMAT-1: FMC / Available
IMAT-2: FMC / Available
LNOs: NM, TX, OK, AR, & LA
EOCs:
- LA: Partial Activation (TC Laura, Delta, Zeta, & COVID-19)
- NM, TX, & AR: Partial Activation (COVID-19)
- OK: Monitoring (COVID-19)

Regional Continuity Status: Partially Activated (Telework/COVID-19)

Region VII

WATCH: Monitoring (24/7); Alt Location
- Winter Weather (see above)

IMAT: FMC / Available
LNOs: NE, KS, IA, & MO
EOCs:
- NE & KS: Full Activation (COVID-19)
- IA: Partial Activation (Derecho & COVID-19)
- MO: Partial Activation (COVID-19)

Regional Continuity Status: Partially Activated (Telework/COVID-19)

Region VIII

WATCH – *Denver MOC:* Monitoring (24/7)
- Winter Weather (see above)

IMAT: FMC / Available
EOCs:
- CO: Full Activation (Wildfires & COVID-19)
- UT: Full Activation (COVID-19)
- MT & WY: Partial Activation (COVID-19)
- ND: Monitoring (COVID-19)

Regional Continuity Status: Not Activated

Region IX

WATCH: Monitoring (24/7)
- Heavy Rainfall (see above)

IMAT-1: PMC / (Portion of team deployed to CA; COVID -19 support)
IMAT-2: Deployed / CA (Wildfires)
IMAT-A: AZ, CA, HI, NV, AS, CNMI, GU, & Navajo Nation
EOCs:
- CA: Full Activation (Wildfires & COVID-19)
- AZ, NV, & GU: Full Activation (COVID-19)
- HI, AS, & CNMI: Partial Activation (COVID-19)

Regional Continuity Status: Partially Activated (Telework/COVID-19)

Region X

RRCC: Level III (day shift – COVID-19)
WATCH – *Bothell MOC:* Monitoring (24/7)
- Winter Weather (see above)

IMAT: Deployed / OR (Wildfires)
EOCs:
- WA: Full Activation (COVID-19)
- AK: Partial Activation (Flooding/Landslides & COVID-19)
- ID: Partial Activation (COVID-19)

Regional Continuity Status: Partially Activated (Telework/COVID-19)

FEMA National Situation Report Acronyms & Abbreviations

Front Page – Common Operating Picture

NWC:	National Watch Center
NRCC:	National Response Coordination Center
EX (State):	Exercise (Location)
FCO:	Federal Coordinating Officer
FDRC:	Federal Disaster Recovery Coordinator
FMC:	Fully Mission Capable
IM:	Incident Management
ISB:	Incident Support Base
MERS:	Mobile Emergency Response Support
N-IMAT:	National Incident Management Assistance Team
NMC:	Non-Mission Capable
PMC:	Partially Mission Capable
R-IMAT:	Regional Incident Management Assistance Team
RRCC:	Regional Response Coordination Center
RWC:	Regional Watch Center
US&R:	Urban Search & Rescue

Front Page – Force Laydown Map

CAD:	Caribbean Area Division
CNMI:	Commonwealth of the Northern Marianas Islands
DC:	Distribution Center / District of Columbia
DR:	Major Disaster Declaration (Stafford Act)
EM:	Emergency Declaration (Stafford Act)
EOC:	Emergency Operations Center
FCO:	Federal Coordinating Officer
IST:	Incident Support Team
JFO:	Joint Field Office
LNO:	Liaison Officer
TF:	Task Force
VJFO:	Virtual JFO

Front Page – Incident Management Cadres

ACQ:	Acquisitions
ADR:	Alternative Dispute Resolution
DI:	Disability Integration
DEC:	Disaster Emergency Communications
DFTO:	Disaster Field Training Ops
DSA:	Disaster Survivor Assistance
EHP:	Environmental Planning and Historic Preservation
ER:	Equal Rights
EA:	External Affairs
FL:	Field Leadership
FM:	Financial Management
HR:	Human Resources
IA:	Individual Assistance
IT:	Information Technology
OCC:	Office of Chief Counsel
LOG:	Logistics
HM:	Hazard Mitigation

Other Acronyms & Abbreviations

ARC:	American Red Cross
CBRN:	Chemical, Biological, Radiological and Nuclear
CDC:	Centers for Disease Control and Prevention
CIKR:	Critical Infrastructure / Key Resources
DCO:	Defense Coordinating Officer
DFA:	Direct Federal Assistance (Stafford Act program)
DIRS:	Disaster Information Reporting System
DLA:	Defense Logistics Agency
DoD:	Department of Defense
DOE:	Department of Energy
DRC:	Disaster Recovery Center
EAGLE-I:	Environment for Analysis of Geo-Located Energy Information (DOE)
EF:	Enhanced Fujita (Tornado scale)
EPA:	Environmental Protection Agency
ESF:	Emergency Support Function
FMAG:	Fire Management Assistance Grant
GIS:	Geospatial Information Systems
GOATs;	Generator on a trailer
HHS:	Health & Human Services
HM:	Hazard Mitigation (Stafford Act program)
IA:	Individual Assistance (Stafford Act program)
IMAAC:	Interagency Modeling & Atmospheric Assessment Center
IOF:	Initial Operating Facility
IPAWS:	Integrated Public Alert & Warning System
IST:	Incident Support Team
JTWC:	Joint Typhoon Warning Center
MCOV:	Mobile Communications Operations Vehicle
MEOV:	Mobile Emergency Operation Vehicle (MERS)
MCC:	Movement Coordination Center
MMI:	Modified Mercalli Intensity (Earthquake scale)
MOC:	MERS Operations Center
NHC:	National Hurricane Center
NG:	National Guard
NOAA:	National Oceanic & Atmospheric Administration
NWS:	National Weather Service
PA:	Public Assistance (Stafford Act program)
PAGER:	Prompt Assessment of Global Earthquakes for Response
PDA:	Preliminary Damage Assessment (Joint FEMA/State)
PSPS:	Public Safety Power Shutoff
RATs:	Repeater and trailer
ROC:	Response Operations Cell (part of the NRCC)
SEAR:	Special Event Assessment Rating
SLTT:	State, Local, Tribal, and Territorial (*Governments*)
SMT:	Staging Management Team
USACE:	U.S. Army Corps of Engineers
USAID:	U.S. Agency for International Development
USCG:	U.S. Coast Guard
USGS:	U.S. Geological Survey

(More FEMA Acronyms: FAAT Book)