

First → say DH asking now.

We're worried about new flu's DH → strategy to treat + prevent chem poisonings.

2 yrs ago → Inter Departmental Advisory - Gov tender in 2016. follicular tender - look at how to decontaminate skin + how if someone uses a chemical poison (worst)

Did also of work - published - at last technical advisory meeting

→ weeks & weeks at end of Nov.

↓
Decided to look at polar solvents - that could be used - psychological start toxic.

There could be dispersion of football match - does chem cold people access? - hot.

Gov £6,000 being used synthesis of ppt. doing a number of studies to decontaminate skin following exposure.

DH at later down - carrying human exposure studies.

↓
not allowed to use heat → that's where DR comes in because they can do In Vitro.

Gov Chief Scientist - ^{Chris} ~~Mark~~ Wittery & Nick Gant

nowhere like this is absorbed thru skin

DR

Gov involved - we decontaminate skin - idea of work re PPE will be pushed - new gov.

form a chemical think tank → looking to develop protocol for framework internationally.

and stocks - also in the right approach - DTR been
advised on this.

↳ limited area & compounded area \rightarrow if lost and we have
- strategy for reeling -

large effects - if it's a stadium - 5t of granoxane thrown
across a crowd \rightarrow area of project is looking at behaviour

↓
this is why ~~it~~ is looking at ~~for~~ again.

He I say (Apologies for some of the tone of the note)
 \rightarrow Martin Willis (work) - granoxane which had been rolled
out \rightarrow had overcome blockages.

Michael Voerman assured me that everything worked out
for effective use.

Water - survivability was ↑ at low end

He I say there was hope that this formulae could
be introduced into market \rightarrow he said is four main products

granoxane contained to x gelling agent

Different gelling agents
had higher level of smoke

Water in 3x standard level

Then came to present

Brian Fursey
Geoff Willis
Peter Buckley

| We \rightarrow may want should
be first choice
formulae.

[Interg for low sweet and sorced.]

Proposed our last few yrs that nothing further coming.

Synt index has been dropped on grounds of

- ① Bulk tanks - gelatin - required people to go in manually
- ② 2nd Int'l Synt Study concluded - no clear effect of formulation.

↓
Int'l banks dominated by us for self now.

Angela Boddy took desire to say where. (Head of Reg)

Convinced India no scope or table for development

now in 1980's + 90's did not make gelatin agar - needed sweet.

At TMC - categorically said - dropped emulsion program
at BH.

→ on 10% formulation → difficult formulation with emulsions

1-2% of sweet (not 0.25%)
as a 10% formulation

Fluorimeter tests

At rec meeting in White Horse 1988 - decided to go to magnesium 100% → and also of more - magnesium very cheap
magnesium L - 10% formulation.

TMC sourced 20% with minimal sweet + minimal gel

(3)

We had to present to when having

(3)

Magnon - 10% - we were talking about 20% -
loss of var

would we let us put out our paper



would have more gel + more sensitive.

They now → looked at FAD regulation:

With paper → there are published papers &
availability →

AC → Korea: as far as well know as far for

which roughly better than Granoxon - had some
benefit

No - threshold after

If we took when - was aware before making that this
was dropped.

Boris + Geoff - don't worry you will develop
high gel + high sensitive formulation

DJ - put in dry slides → not seeing degree of sensitivity

What does product have to do to get a license
for the product? FAD free.

France - before 1980 - dialogue - 1980 - Some H+T
+ Geoff - tried to persuade them not to drop
proposal - prof. Reinh (Committee de l'Europe)

(4)

(7)

by person's problems in Guadeloupe - France
- worked - by field work.

In France → introduced thickened formulae -
+ + smooth thickened formulae

↓
Smooth + standard ↓
↓

by too late - high smooth + thickened
Smallest - finest powder

- They did we never buy many charges for
the formulae in France?

FAD after the date to our concern - 11/7/97.

ICF 63197 → going to be a blockbuster - did multiple
clinical trials. → lots of indications. France noticed
evidence of vomiting

REXXA largest one

Bowl paper - going to have to develop / webbing
capacity at Huddersfield
(John Tunney believed that it was too expensive.
Also of debate around the cost of doing this.

↑ Europe alone is standard PEG formulae

FAD open species sheet

Type A - dropped smooth down to FAD open.

In global standard -

FAD open 2008 - It only has this not been amended

(8)

i lack of knowledge

At 2008 the spec repeller review one didn't work
rogue.

This conversation → not had few conversations with others
regarding - how things are

↓
Rising this is very new

Basis of its importance is security -

brought copies today -

Bob Morris - worked everything destroyed.

Hand

It all original does know
him.

signed disclosure by
same - don't
remember -

but not deeds after file in the bank

This belongs to Ferguson. Don't want to be - a post
live this has to be handled for

Or a scenario buyer - - want you guys to challenge me.

Before this goes out of company - I want you challenge me.

Want to know - Dan Mukherjee - Andy Gorver was
PA to Governor of Florida

He asked Andy Gorver as do you know anyone
who knows about GE melt - like Rose seethe lead. (6)

Andy Gove got Dan to Kelle.

Cal EPA Henry

I know we have close system.

I know people are still dying from strong
granite - I believe because level of smoke
is too low.

Exhibit 1 → Rose 1976 report ⇒ "R" revise.

↓

JH has original

First R = Revised.

Second R = Revised

This is a copy of original doc from Dr. Corning.

Brought it as a blue book. I could not work into
the bluebook give a highlight problem

Set of reports housed in library at A Park.

Never seen by people at DR to smog file. As well
as original reports. very interesting correspondence
between Mose, Exee, Bunnin.

So many findings around the world - ICI is per-
sonal smog was true gold dust.

A report - say big number + more, response

for every dose - does response in different species.

Data from papers #73. (Alan Burgess - Head of Safety + reviewers)

Percent fat of curve is $4/37$. - 11%.

Geoff Hilli + 2 killed their pumps + filters.

"Majority" used a stand of "about 70%". (unni changes)

1976. → widely wanted to confirm as something
~~mostly~~ made available is easier by CRI's leadership.

ESC 729 - Agreements found. - Achieved by better grade.



Executive Development Committee



Syng → level of adder - crucial that 796 should
be added to grammar at the right level.

0.05% weight for rel. → RII is expected to produce
variety + level of response by the majority
(of lethal dose)

More fat poisonings result from small + more
sources: mostly 50ml.

Used here today as example.

Concluded further study was not necessary. - This paper
was good enough.

No worry about formulation of 796

In Table 1 is Board report

Forrest

Arthur Baum

Davies

Hughes

Ruth Bayliss.

AC summary:

Research report → CIR → went to Agency Board + agreed with Report

— mni box unfortunately dried = fracture

Deutscher made → per encre = P.R. (1975).

b

i) 15 ml of granulose 15% →

This paper gets cited in several literature.

Level of encre of mni lethal dose taken.

In frame it was identified

1978 - 87 → level of encre did not work.

Using this paper in panels → cited as CIR report.

It remains at so far p.t. (when it joined the country).

Historian of dollars spent on offering
(this b → per review of TH.)

It had access to Phineas report - have actual data from 1973 Bayliss report

~ Nov 25 1990 -

reviewed report & concluded

author named a number of odd things

0-05% recommendation

Lewis Smith

Mark Dugger

Rob [Marlow]

Gerry Silver

All those involved in design have gone.

~ then ad explosive with Paine - looked at Paines report (where minor date came from).



Date was fabricated - o-

Thank you to tell me I am wrong.

In lorsque as members work - he said (1991) →
he did not want to hear about this again.



Benny Kort + Geoff Wilks knew ~~the~~ someone worked
plus we knew existing level did not work but
we did not know why.

key piece of information → is in a pharmaceuticals report

other than your friend PAN or Lederle



Can give you copies + a stack with all files..

INTERVIEW:

not planning to raise it in meeting - prefer to discuss
with scientists ↳ "as part of the team"

~ 5.9.70

JH → HS → v. detailed table -

↓
→ 3 differences - don't count.

Don saying H/37 vomit response has replaced
don per = 0 response.

H/37 should be 0.3%.

H/1836

~ Not only 2 mg don expected it is not

8 mg/kg → 2 hours to vomiting has been ignored.

Indication of ~~ED~~ SO is difficult.

1990 JH → disagree with R₃₉₀

↓
same case for judge since dose was never
been judged correctly

↓
these findings remain undigested.

Note the note before board paper.

funny word is JH → "I think it has experiment".

Old studies - dog + new ones agreed with JH
new.

~~Result of cocaine~~

Raised to seniority & wages Jan 1990.

by senior change → few should have been
(↑ senior)

Very bad Rose decided he would get "flat rate" before

Answer replied ~ January 1990.

Oct 1990

→ H → PH → confirmed received news.
→ will ensure matter raised with HR
business.

Everyone copied - & note disappeared.

April 1991 PH → S. Rogers



CZ should review it [possibly] →
or truth recommending

Any you to Offenders:
1 Bob Frost

Gerry

to review due processes to ensure from day
of arrest & derive a new recommendation
issued.

Comprehensive, Considerate & formal thinking

1991 → Gerry + Leo light + Gerry appointed to Exec.

1991 → PP appointed Head of Anti-Ban → Gerry with

V.P.

(12)

Gerry + JT had a few meetings + number of memos
~ (over all) with JT

Gerry obviously looked in + thought their " "

of them + many + time - applications for company
→ knowing where did not work + non-
applications to business + this needs to be
managed effectively.

Conversations with Gerry →

newspaper + from all jobs lost - Gerry moved
to pharmaceuticals did not report a success.
↓
he moved to pharmaceuticals after 1991.

Has not reported a.

Lewis + JT have never spoken about this
ever again.

↳ need to find → outside the church. → more
time about this - big issue here

Where BT came from?

Mike Rose - left some of his notes + correspondence
file

Indee data → copied to Jagger

↓

out of 1000 add - not many remitted
several copies by single author (or two)

(13)

During the base study to provide evidence for ban.

Other teams problem was the cork.

I think he fabricated the 37 to make it look like more poison is now.

Base response curve is wrong.

P8: When P8 arrived H didn't receive report
and did not send to get fangs checked.

H never wrote & mixed with one peer reviewed
(Now you have nowadays).

Glyphosate issue - glass writing → did not
mention in glyphosate brief.

H said we did not tend to get fangs checked.

H not involved in peer reviewing the report.

H did not believe that we were sort of paid
to fabricate data.

He did not see graph? - after 1990.

↳ where 4f(37) come from.

Are you sure he did select 37 because they were
best quality data?

He pretty muched if there was pressure put to
some of the report.

Team's response → did not want to go through data
& focus on magnification

France does appear to smelt.

Had magnesium + water → it was kept well on the same door.

PB: Did ever remember OH

→ told by his manager to destroy file.

→ Geoff Hilli → threatening guy:

- Cover threatening Dug

↳ signed letter to senior manager

Any basis kept is to yourself (ST).

Confidential → told to keep confidential.

↓
Received magnesium + water → shake Dug

Low point we could because smelt built
several of.

From [1996] → had

Left
Contractor forced to use brittle or more expensive
because the base don't fit correctly.

Then went to TRL → 5 fold smelt

→

Told → no certain terms how we could not
exceed [3x]

Isometry as trilaterating the ED curves, are well set
for most of getting things right.

Re accident following as interior has gone

↓

→ You can sleep at night if further deaths due to accident.

How you ends?

→ Justice done.

In France → desire of committee d'Enquête →
reviewing grammars

↓

EU committee set up to review
effectiveness of smecte.

Not so formalized

Dr Uno - Not working in Japan → Japanese did
not believe in effectiveness of smecte.

Any invasion in Europe would have significant cost
implications.

As:

France - Dose limit increased to 40 g / l
- formally

Why did we make the first field review?

Not sure of people did know what was going on.

Not set off loaded it - told by Lewis that buyers
by news would be informed.

Conversation with Ian Robbie - 1991ish → "Do you think
mistakes were made" - Yes - "Please - Please all
of us to learn from you".

(16)

Geoff Willis apparently hit the roof - when heard
from Bob.

↓
when was June ~ 2005 - 2007.

Bank notes has gone

Dear response curve is not valid - explanation
for higher we prepared.

We now have a simulation → if no more human
data →

We need to do something about this

↓
multi rates is over by a factor of 10. → however
is increase of
spec for Lp + gamma is needed

AE: We don't apply generic all prospect \Rightarrow we are
a more plaus

It would be extremely interested in involve
by dog & monkey and a live drama
between three is false.

KT: If data is many - parts a and slight in

AB: full benefit of hindsight \rightarrow [possible for
revert of outcome] \rightarrow we could have been
to derive a lower level of generic \rightarrow but
some of assumptions from modelling is deg

It did no comment at all \rightarrow the original Langford
report. (13)

LS → did not see report before & went on.

JH: responded to ST w/ a signed note.

If JH comes across more accidental
passing off

no longer have access to scientific
way of doing things.

need to have no action from
meeting

(files)

not going to bring them in + destroy
them all.

Eric Rose → Apr ~ 1984/86 - want to file this.

ME was neither head of Andy Court.

"Think of how information was stored & retrieved" →
"Do you have got it wrong?"

What do you think should be done?

level

If FAD spec should be changed

↳ to what

↳ effectiveness of measures

↳ withdraw the product.

↳ compilation of laboratory outcomes & firms
from who have published

↳ need to ↓ dealers from accidental passings.



- PB: the product is mixed \Rightarrow we recognise that
the product is harmful \Rightarrow ~~harm~~ if we notice
the outcomes - we are telling the same thing that the
pesticides don't all follow the leg spec \Rightarrow don't
adapt to novel legislation

↓
Rowlett asked us to take an stance.

- Medical opinion is different in terms of reducing
cases - cases of pesticide poisoning \rightarrow opinion
 \rightarrow now not to reduce cases.

Evidence from Health & Safety UK sharp
curves is effective.

AC: sharp is medical opinion against curves \rightarrow more
related to of type incidents.

PA: 5000 + 10 50 cases are send - you need to get
get it out.

Thank you to say you have it wrong.

PA: working with JH
DoH/ESF - work on other ones - party to inform him
that the level is very - can't live with that.

Orange report from 1990 \rightarrow compiled for JH.
(from ICI pharmaceuticals)

↓

Need to get hold of Langford staff - PB: can't do.

e.g. second member of Agchem aware - does sees this
mean from the Agency perspective?

(P)

Rbei Diskussions Akt \rightarrow if there is a danger to health
 \Rightarrow you have an obligation.

It felt that we had off loaded the issue.

↓

→ said lets drop the idea Rose stuff \rightarrow focus on magnesium

↓

could be put forward because we have made an advance on the safety of the product.

Only few people involved.

↓

Not for i'm still does not know

Only person discussed it with us in Jakarta \Rightarrow ~~not~~
~~other doctor - suspect~~

want to give opportunity of working with you to discuss my + your need

But \rightarrow own important to do this.

↓

close ~~follow~~ transfer.

If nothing is done - what concerns one in the past -
of the situation is that we had the wrong kind,

strategy \Rightarrow now is closed transfer.

\Rightarrow go from having - new committee as partners
is so that no one compromises greatly

\rightarrow

~~XXXXXXXXXXXXXX~~

We have devised - the park.

We accept that we should not be invading the fishing people.

Our absent guides who must follow close
→ close / far away.

It is best solution California EPA



end of 'coca cola' bottles.



use of containers deeper in park.

The containers we will have → US are not accessible
except by dock + keep.

JH: To me - that strategy does not affect JH position -
we are talking about human safety, the

We think the step change comes through the
fertilizers rather than by formulation.

Mark our general concern about metric

level is 'product of 10% too low, 5% higher -
plus denum'

PB: likely to agree with you position → sides more of
pass probability.

↳ Having aircraft passing JH thru
close system

JH: PB sounds like John Fetter.

PR: We are investing money & preventer rather than cure.

Calyptor: Delete option

JH → push for the cure connected to pharmaceutical company does.

JH: Cannot leave FAD specification as it is.

FAD specification → any manufacturer can come forward.

PR: If made a proposal to FAD to removal of ~~suspect~~
statement → ^{JH:} It would not help at a human safety level

↓

Star level of警戒 does work.

Key thing you guys have to manage

Got to off load the file somewhere - not far or any family to have this.

Andy Vahl (meridian + vahl) → carry in ADL

JH: After this meeting → never it to be managed on a pharmaceutical basis → otherwise I cannot settle on this.

All files on stick

Got to be a more positive - got to be comfortable the pharmaceutical aspects have been managed.

JH: told many years ago - please do we keep
control over smecti → supply to others.

↓
litigation

↓

SyC provided route of agreement of smectic

PB: could we be assured of not doing smectic.

↓

"light step in the wrong direction"

JH: can sleep at night in Puri. That calyptra thing → very
distracted

- TBSAT
- DIALOGUE.

Rob Morse (NJ#)

↳ Pigeon + Strelitzia → decision request (late 1990's)

→ no memo

~~Stock Agreements~~ → no reasons given.

JH Not threatened by anyone

SyC / cethart

Die Dillinger → was this not forged?

JH: "Please tell to your position."

do
Gerry operated to far enquiry on this → got memo to
say on informed.

JH corp memory is still sharp.

Hank & Dave manager not confidential memo is never
are - copied - fed + start

(23)

All people in board → should have been aware.

Planned to turn off demand in

Next steps

→ Can measure of org. that is confidence

→ Give our info to Holt that we have had this disaster

→ Over months / years → if nothing done - what we want to do

— END OF MEETING

KHM → HMIS FILE AND SOURCE

Li 29/11/2018 Rose - acting - severe → did not prescribe date.

Dog studies '85

→ as published by severe - dog survived.

}

(subsequently refuted by a vet?)

TH reported '86

Described all of emetic - needed

to prevent liver damage ! After conservative -

* TH says "solved the issue".

vs formulae - no soft evidence

- anecdotal evidence that much softer is expected
among the toxicity

When it was soft lead to ↑

TH would switch from Red Morris → Ag.

TH alleged

Invitation from Bob Morris to destroy the file or be passed on
for profit - true and the former German lawyer

(2A)

Jumped in against Correa - undermine his opinion.
It did not say it's right → need to decide what it is
He felt should be 3x higher

Not going to jump to a different conclusion until there was evidence
from - concerned response - don't want to do that

The LGR - did not have all of info. But has had never
been served by
not good enough evidence.

In behind the passed policies regarding telecom spending

Data from 1976.

Study of some public companies

85 new Pan Am - does worse than
3x revenue.
Failed to justify it.

Arg not a clear comparison.

It was not substantially efficient if it is lower

Then attempts to defend regulatory standards.

Other government didn't give any answer to answer the question.

Wrong - unacceptable

- people do same almost frequently - airline is good at making you wait.
- good airline → user, just does not fare well.

New analysis of PP796 human census data

↳ organia

BEST estimate of dose giving 50% chance of reaching 5 mg enzatic ~ 10 mts. of formation.

RAO : requirement to vomit with 30 minutes = majority of cases.

JH - working on FQT at DTR

↳ 3 or 4 days (+ soak)

Want to focus on hydrophilic portions (eg FQT).

- initial epithelial response
- secondary epithelial response.

FQT.

JH tried to get involved at Glaxo for project.

↳ give after faecalising.

Actually showed to get interested in RQT again → retained files.

Talked with writing a report.

Denis Tolley - Methyl Salicylate

Print a table - we weedkiller.

Sought in more labelled QT → Dant's Soother.

Then show for concerned about RAO & see having 0.5 mg enzatic.

Basically which has been pulled.

Wean 3x enzatic + gel rather than 5x enzatic. → big drove to keep enzatic level down.

Got JH fired up because the current RAO spec is incorrect

(26)

low study used to identify level of smoke needed to induce vomiting in 50% of cases - 30 min.

original Rose Report

No definitive answer on what level of smoke needed to induce vomiting response.

Rose report came from Dugan Report

Probably fabricated data (Mike Rose)

4/37 - 4 people vomited across trials

Nov 37 - should be 1356.

4/37 fitting was sigmoidal curve.

Crooks - Dunce - 3 volunteers - no vomiting.

LT - historical details - that we should be trying to eliminate.

↓

- poss. purpose in enucleate was to deal with accidental deaths.

JH - in France - ↑ smoke forced accidental + deliberate deaths

so suggestion that high enucleate fat products should be evaluated

(LT → not seen Mike Rose notebook before)

Recent TGA → enucleate oil dying accidentally

~~Mike Rose Report~~

JH → "company has endorsed a level of smoke that Mike Rose has duly fabricated"

"Having been aware of information in 1990 that data was
f fabricated" → FAO specifies & still the same.

4/37 → a report that was circulated -

JH says date was fabricated



presented to Purchase, Oliver etc.

In the day, they were not prepared to grow back out.

FAO spec → Company ~~must~~ are also of 400:1



H "Good enzuki but did not give Iverin."

FAO specification is not based on this. → cited Herditch + Vail.

JH - says enzuki did work in Sri Lanka

~~11/16/1994~~

FAO specification - just FAO spec that refers to enzuki - sees our

- generalized areas of properties

- next 796

- FAO spec based on Herditch + Vail

FAO spec - ~~for~~ former claimed date used to FAO spec.

LS → a date like this

→ completely fabricated to make man look like monkey
+ fig.

FT
~~18/3/98~~

With a pretty poor data set - you come up with similar conclusion
as we've done.

TA - specifies of that is effective dose in man is incorrect

↓

KA not disagree.

LS - got more than 50% of patients vomiting - 30 minutes.

↓

the get to bottom end of tube, that's

TH - Synth making a product knowing all on ineffective level of emetic

- Kui has shown concern with hospital data

↳ how are mis-parsed the data..

Taper →

AC ~~etc~~ → Company spent \$ on getting safety systems → not a \$ issue

between the event worked - miffed them we are defending the wrong level of emetic in 2019

LS:

• If want to do something about accidental cases - should ↑ level of emetic.

• lots of people are complaining too much emetic in fact.

• LS - 50% of calls area - how do I stop patient vomiting?

↓

really worried about people vomiting + causing damage

• In terms of just putting emetic up - had a lot of problems from clinicians.

• Claims from Alstom Vail → no emetic → TH working with shorter Vail

(2)

PB - You just said we endorse portions of these dose - we don't.

KT → start with lowe



LS - If look retrospectively - then 60% of patients required - it will hit the target



if want to treat the bottom end of the curve

earliest vomiter or those who take a large quantity of ppt

LS - published paper - shows early concentration of ppt in the plasma ↗

→ presented at May meeting -

→ got to get lethal dose out of Codex - 36 minutes.

LS - not the person who earned them. → difficult to reach consensus.

TH

TH - agree that I understand Sygen is not supporting the lowe conclusion.

LS - Speculation was a retrospective file to show data actually demonstrated.

LS - when look at the decisions you have to build in what was going on



can't spend lots of money on a product that is absolutely not guaranteed to make a difference.

TH - France - ↑ metric + diluted it → better data.

AC - not able to give data on "Duckbill" formulations

TH - understanding was that this made a difference - isolates - early 1980s (3)

LS - early 1980s - was pet product manager.

JH - consistency between dog & human census:

Until evaluated Interon in Arthasha - did not know.

Markell

LS - Not sufficient evidence to write at 0.05 as a dose.



but think you think for being so clever for getting the dose right.

- 1985 - believe that census may be suspended (mid 80s)

Frolic Forum 1991

Reason why magnozone did not work.



Interon → do we know drug 3x in Interon.

Rob Merson - safer formulations possible (aper - 1990)



Magnozone 5x

Interon ⇒ three ways it does it protects you.

All of discussion with Steve Dugger was about 1 capacity of smelt
plants at Huddersfield. → new smelt plant came on stream -
1996.

Enquiry never took place (graphs, 4/37)

LS - problem is you keep coming back to 4/37 as answer for
everything else.

I8 - what happened early on is irrelevant

P3 - full benefit of hindsight a better programme could have been made out of the poor data

I8 of view that ~~there~~ there would be deaths & loss of ~~losses~~ ~~injuries~~

Influenced by authority or basis of loss-making

I5 - A FAO to report on mercury & vinyl

JH - Most of our regulatory refinement was based on loss findings

I5 - I hold we human data to conclude it was a good metric.



JH - Does not know what is right level of metric.

I5 - Government of their would work

↳ looks like good substitute

JH - They only wanted an independent enquiry



KT - review evidence & look at right amount of metric.

JH - Why did first pos = 0.5?

↳ I5 - Guess.

↳ JH - fabrication

I5 - Consensus of intervention > 50% of people worked.

I5 - Have been to business to say level of metric too low

- Geoff Willis got angry over the continued discussion on level of metric.

JH - inform relevant regulatory authorities + inform them of
- effective level being suspect.

~~REGULATORY~~

Most of regulation advice was based on the study.

Original paper to Agency Board - recommended adding 57. + they
- end it

[why instead \rightarrow 3%]

- Do you accept that. 60% \leq 30 minutes \rightarrow Yes.

Fact sheet 0.5%.

↓

Want up to 5% after the agency board paper (Mycosane)

JH - manufacture + 2 had a gentlemen's agreement on this - he was
- except on this point \rightarrow if this sort of information - it could
be twisted

- if said original decision was fabricated \Rightarrow
how would this be received externally

Part / Regulator

KT - Possibly by over interpreting the data we have and if -
- better place with

HS - Mike Ron - not stupid - depressed when he found out that A776
not working

HS - Data (A775) suspect but we knew that we had to \uparrow enzime
- HS presented 1983/84 \rightarrow should \uparrow enzime
- No doubt
- Enzyme increased 5x with Mycosane

(33)

By 1990 company was now relying on 1975 data

Leave for note meeting with customers because agreement with law has been broken

JH → never showed it to the lab notebooks from Nine Rose

JH - Rose that now agreed that the dose response is wrong -
"it has been fabricated".

BT - now discuss about level of evidence - 1 evidence makes
a difference a lot end of the course.



no proof about the level of evidence being low

0', 11, 50, 100 → table used in regulatory purposes
piece of evidence.

5 Sept 1990 → news to BT →

But their minor data is misleading

Date

4/37 was replaced a 0/? response

4/1356

JH → 0.05 not being used now.

JH → sooner we get to grips + inform the regulators authorities → say
that the original data was wrong.

BT → challenge is that we now have to decide what
the message is regarding the

JH - no answers from BT from Sept - no replies from Bob
Pardosawski who asked

(34)

JH - Complete disagreement between you + ATL?

Why would Dan purchase

↳ buy down or

↳ buy down the company.

| 21 Sept.
1998 - due
2 yrs ago

Comments will ask what happened on 15th November.

JH - feels uncomfortable going back to EPA & saying "not"

LS - End April 1991 → company never shipped long anything based on memory except Chromatographing.

JH - If go back to colleagues w/ EPA → Safety Data Sheet (SDS) → EPA have got all the data.

Reini agrees with JH. → Category 4 →

If have deliberations w/ EPA → JH recommends where that

JH - obviously not appear by what has been said.

PS - Disagrees if there was no intention of some of these controls.

lets have a enquiry about the level of control.



The old data → didn't see parts of.

PB Iran

TH Tony Elliott presented Iran

PB → From a safety perspective Iran did not live up to powers & obligations

TH → Y/1/first dose/absence

Y/1/absent/2/absent

Carrying information → withdrawn from any engagement with IAEA

→ lots of concerns

→ lots of angles add up

→ very uncomfortable about that

TH → until today → TH did not know HS had not raised

↓

thorough and less:

to majority of findings would be valid if
based on the current product

Do wake up at night - I am only person - world who can
take this forward to regulators →

I am the only person
who can do that

Got evidence/original documents - reasons both + others

PB never look at 2 paper together + S. Korea does -� benefici
benefit ⇒ at low end of the dose response curve.

↓

consequence of those, not evidence

PB

By day full dose response as compared to monotherapy
with ibuprofen → no difference (statistically) → contrary to what had
been said to regulators

(36)

- JH → film of sumo to cont got criticized w/ performance review for
team not working.

PB This was to answer specific leg question about relevance of defining
↓
Project did not deliver on its original goal

Relevant v. 1986 was to safer generation → Wx Safety with
Union.

Representations to US EPA 5x but we could not demonstrate 2x.

LS told us the problems causing problems with Union.

PB Is there one now per the BPA any more or less safe - no
↓
nothing to do either →

JH Note that Union not super yet the control → up to
128 -

JH What are we going to do about information to regulators?

↓
What am I going to do?

↓
"minimize scenario = node"

↓
no definitive level in men?

→ meet FRA spec for another reason.
→ going to have to think about
what to do about history data

LS It looks like JH has said - consider also do about
how to use loss data as argument for reducing the margin 37

FB It was a discussion we had with Dave French
+ Bruce MacFarland.

Initial ITC was a discussion with Dave French + Bruce
MacFarland.

OH Have to sort family quickly now

- ↓
 - no press or P&G
 - Office of Females became Colleagues
- ↓
- ~~presser~~

I am an only person

Agreed the date is wrong → career is the date
wrong

Sorry though French + others

Some kind of (FFSA)

Published paper registered in Palma

Do it review work needs to be completed

SOT → March 2020 → will be discussed in terms of
P&T + the U.P.

Jasper Barnes + John H have a few short - Syntec -

Andy Gower → consider taking him in.
(Pharm)

↳ Responsible for DR going to keel.

↳ AG agrees Japhis date sufficient to determine date in man

(30)

Early home is said since Rose almost wanted to
find myself a job.

TH thought world should not in case something happened to it

At god point to children of TH.
↓

saying to her that the answer of today is

then he said that happened in Rose study in
Barbados.

L5 → knew AG + NL did not get on well

1978 → lot of deaths to present

Why not ~~die~~ ^{rained} in 2006?



"Because rain this in 1990."



I heard that last bull is hit
the reef.

Then there are scars Deep sea.

Early connected with some robbery people -
have friends aware.

TH → do you understand ^{my} need to speak regular?



feel need to get off these to regular

feel so much better when TH was with letter to

One of former employees has made strong challenges to
spec of meter in lot.



PB we have spoken to COO of Crop Protection

TH - Andy Gove → agreed "fabricated data".



notified to agchem branch at the time.



evidence to suggest the data was fabricated.

Andy Cook - spoke directly to him → shortly after the meeting.

Took seriously



we need to make COO aware of situation.

AB - no one has spoken to Geoff Willis.

John Doe was not aware of conversation regarding

Andy Cook spoke to Tom lot (not enough)

- Formally fallen by way side + 'feeling slightly compromised'



PB Not that we have seen nothing in



not sure what the EPA would do.

This was the inquiry they had done a few days



Hired for you but you will go ahead.



PROVIDED BY
JON HEYLINGS
15-1-2019

Addition of the Emetic Agent PP796 to Paraquat Products

Jon Heylings

Dermal Technology Laboratory Ltd
Keele, United Kingdom

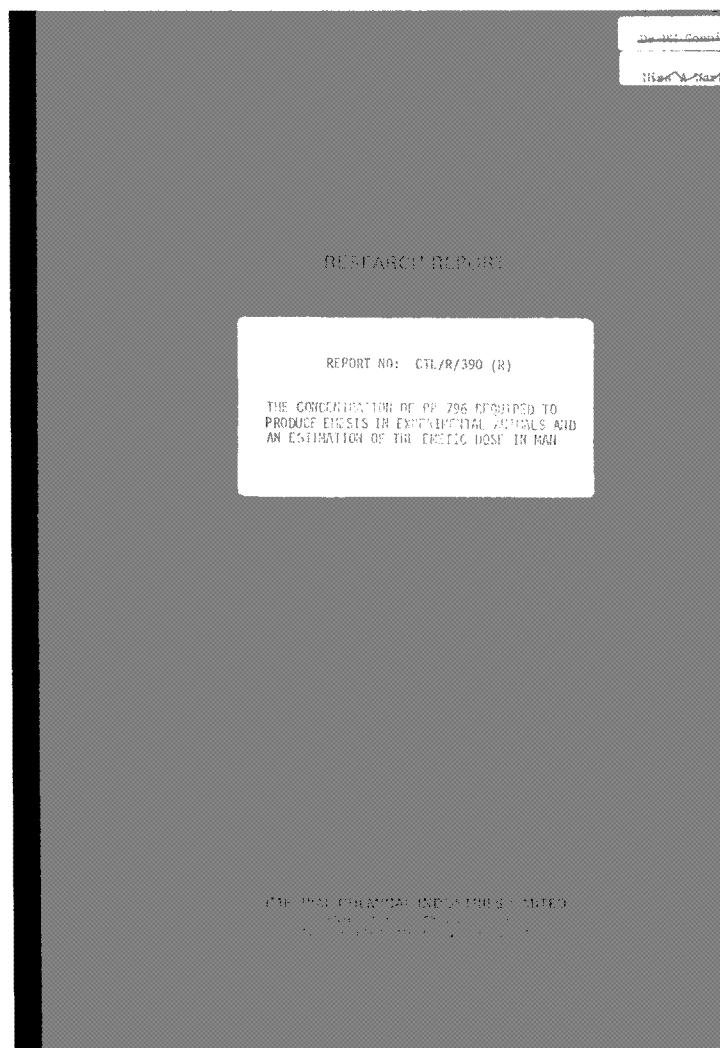


Why has the Emetic concentration in PQ products re-surfaced now?

- Department of Health project won by DTL (2018-2020) to assess the skin decontamination of Methyl Salicylate (hydrophobic) and Paraquat (hydrophilic) poisons
- Review of the toxicity of the chemicals, lethal dose in man, oral vs skin exposure and prevention measures currently in force
- Collaboration with PHE, DSTL at Porton Down and Technical Review Group of Poisons Experts
- DTL acquired radiolabelled PQ and is studying the absorption from various formulations
- Reviewed the current status of PQ Registrations in 2018 and FAO Specifications for the Technical Concentrate and Gramoxone

FAO Specification

- Paraquat concentrates must contain the triazolopyrimidine compound PP796, as stipulated by the FAO for agricultural pesticides
- Important that it is included at an appropriate concentration in order to be effective in human poisoning cases
- The FAO specification as required by EPA/PMRA stipulates that "*emesis must occur in about half an hour in at least 50% of cases*"
- For the US TK (320g/L) the PP796 concentration must be at least 0.8g/L. This is equivalent to 0.5g/L (or 0.05%) in standard Gramoxone which contains 200g/L paraquat ion
- The ratio of 400 : 1 (PQ ion : emetic) is based on an estimation of the effective dose of PP796 in man by Rose (CTL/R/390R) in 1976
- This was ratified by the Agrochemicals Board and published
- Surprisingly this has not changed since it was pointed out that the emetic was ineffective in animals and human poisoning surveys back in 1990



Emetic Action of PP796 in Man

Data from Table 1 (CTL/R/390)

	mg	mg/kg	n	Nos vomiting	% vomiting response
1	0.015	2	0	0	0
2	0.03	37	4	11	
4	0.06	2	1	50	
8	0.11	1	1	100	

Complete Data from Clinical Report PH20992

	mg	mg/kg	n	Nos vomiting	% vomiting response
0.25	0.0035	1	0	0	0
0.5	0.007	1	0	0	0
1	0.015	2	0	0	0
2	0.03	3	0	0	0
3	0.04	2	0	0	0
4	0.06	2	1 (at 30min)	50	
8	0.11	1	1 (at 2hr)	100	

CATEGORY C REPORT

CLINICAL PHARMACOLOGY SECTION
GSK - HUMAN PHARMACEUTICALS

PH20992.C

11

Possible side effects

These are shown below:-

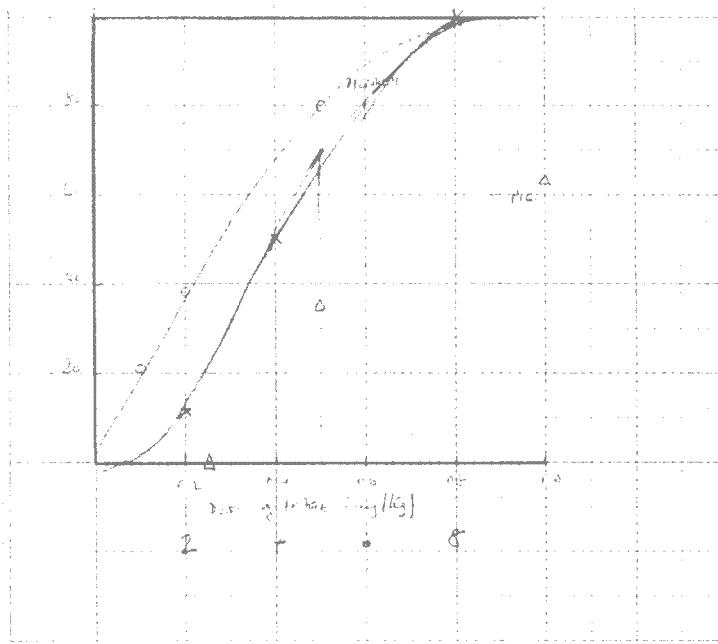
No.	Dose(mg.)	Possible side effects
1	0.25	Nil.
2	0.5	Mild nausea and light headedness.
3	1.0	Nausea at 1 hour.
4	1.0	Severe dizziness at 15 minutes. Felt as if he had taken "pop pills" from 1 - 4 hours.
5	2.0	Mild nausea.
6	2.0	Nil.
7	2.0	Dizziness and sweating at 30 minutes followed by some nausea.
8	3.0	Dizziness and nausea marked ½ - 2 hours.
9	3.0	At 30 minutes dizzy, pale, sweating. Nausea marked.
10	4.0	Nausea and flushing at 15 minutes. Vomited at 30 minutes. Light headedness for 2 - 3 hours.
11	4.0	Dizziness, flushing of face, sweating from ½ - 2 hours.
12	8.0	At 30 minutes sweaty, flushed and light headed. Vomited at 2 hours.

DISCUSSIONS

No clearly defined results emerged from this study, although certain suggestive ones were seen. The following points may be made:-

- (1) The half life of ICI 63,197 in the human, following a single oral dose is between 1½ and 2½ hours.
- (2) No clear effect was seen on pulse rate, although a slight fall was seen in some subjects. Similarly, no clear effect was seen on blood pressure, although in some subjects a fall was seen in the 2 - 4 hour period.

Mike Rose's Lab Book with a hand drawn graph of the human dose response to PP796, fitting the Pharms volunteer data between the primate and pig CTL data.



Human Action of PP796

Mike Rose's lab book annotation to generate the 11% incidence of emesis in man at the 2mg dose

Species	Dose		% emetic response	
	Dose	Max %	Dose	Max %
Pig	0.1 mg/kg	5/8	0.2 mg/kg	6/8
	0.2 mg/kg	1/8	0.4 mg/kg	3/8
	0.4 mg/kg	1/8	0.6 mg/kg	3.5/8
	0.6 mg/kg	1/8	0.8 mg/kg	6.8/8
Monkey	0.1 mg/kg	7/19	0.2 mg/kg	4/19
	0.2 mg/kg	4/16	0.4 mg/kg	5.5/16
	0.4 mg/kg	4/15	0.6 mg/kg	10/15
Man	0.05 mg/kg	7/37	0.1 mg/kg	11/37
	0.06 mg/kg	1/2	0.11 mg/kg	5/2
	0.11 mg/kg	1/1	0.2 mg/kg	100/1

- a) Number of animals
- b) Incidence of brachial emesis
- c) Human cannot tolerate a single formulation > 10 mg/mg
- d) Maximum emetic dose = 0.2 mg/kg in man < 10 mg/mg
- e) Human is already sensitive to 0.1 mg/kg
- f) Brachial dose was likely to be ~ 10 mg/mg
- g) Brachial emesis from multiple emetics

Clinical Trials with ICI 63197 (Bayliss 1973 PH 20992B)

All Trials used a dose of 2mg ICI 63197 (PP796).

Trialist	Centre	Disease	Nos Patients or Volunteers	Nos of Doseings to each person	Vomiting Incidences
Crooks	Dundee	Normal Vol	3V	1	0/3 ~
Javies	Manchester	Endocrinology	8V	1	1/6 at 45M
Davies	Manchester	Glucose Tol	2V	1	0/2 ~
Kerr	Glasgow	Asthma	4P	1	1/4 no time quoted
Palmer	Aberdeen	Asthma	4P	1	1/4 no time quoted
Pemmer	Utrecht	Emphysema	12P	1	0/12 ~
Eccleston	Edinburgh	Depression	4P	63	0/252 21 day study TDS
Hagnus	Birmingham	Schizophrenia	6P	21	0/126 7 day study TDS
Hagnus	Birmingham	Anxiety	5P	21	1/105 Vomited once then settled 7 day study TDS
Zacharias	Bebington	Hypertension	3P	112	0/336 28 day study QDS
Davies	Manchester	Obesity	4P	126	0/504 6 week study TDS

TOTALS 55

% incidence by dosing
4/1356 or 0.3%

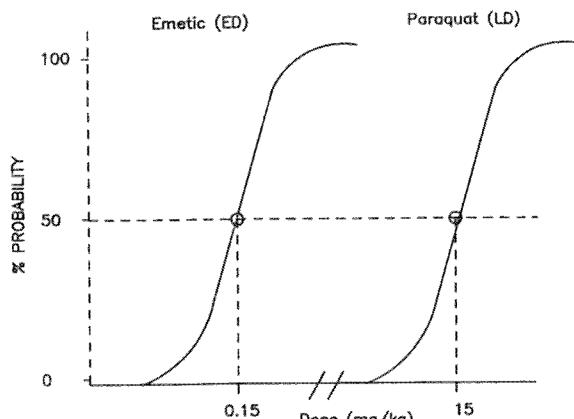
% incidence of individuals
4/55 or 7%
(but disease may predispose
or exacerbate nausea/vomiting)

The 4/37 (or 11% value) is based on 4 volunteers vomiting at 2mg but not taking into account that they didn't vomit on the subsequent occasions they were given this dose. There was no emesis at 2mg in either of the 2 Normal volunteer studies. This should be 4/1356, not 4/37 in any case

The ED dose response for the emetic and the LD curve for PQ are both quite steep. Unique position of having both in multiple species including man.

Bringing these together by either diluting the product or raising the emetic to an effective level in the current product is likely to provide a significant improvement in survival in both accidental and suicidal poisoning.

PARAQUAT TO EMETIC RATIO



Dog data suggests the above ratio for effective emesis following a lethal paraquat dose.

$$\text{ie } \frac{\text{PARAQUAT}}{\text{EMETIC}} = \frac{15}{0.15} = 100$$

$$\text{GRAMOXONE (1977)} \quad \frac{\text{PARAQUAT}}{\text{EMETIC}} = \frac{20}{0.05} = 400$$

$$\text{GRAMOXONE X5 EMETIC} = 0.25\% \text{ RATIO} = \frac{20}{0.25} = 80$$

$$\text{or GRAMOXONE L X 2.5 EMETIC} = 0.12\% \text{ RATIO} \frac{10}{0.12} = 83$$

Safer Formulation Strategy

- No disagreement that a higher emetic concentration in paraquat products should be evaluated
- Magnoxone delivered the PSAC requirements. It contained 5X emetic built and higher gel built into a 200g/L product
- Cost constraints of circa £30m /annum plus a new emetic plant forced a reduction to 3X emetic (1.5g/L) and lower gelling capacity that were finally used in Inteon
- Improvement in survival was demonstrated in Sri Lanka and was in line with expectations
- A new Inteon with 2.5 g/L emetic would further improve survival but questions would be raised on the selection of the original concentration of 0.5g/L

Recent publication from EPA shows that there are still a significant number of accidental poisonings in children. If an effective emetic concentration had been present in the product that met the FAO specifications and regulatory requirements then these children may well have survived!

1/9/2019 Paraquat Dichloride: One Sip Can Kill | Occupational Pesticide Safety and Health | US EPA
An official website of the United States government

Due to a lapse in appropriations, EPA's websites will not be regularly updated. In the event of an environmental emergency involving an immediate threat to the safety of human life or where necessary to prevent certain programs at EPA from being disrupted by lapses in appropriations, EPA will take action to protect public health and the environment. Please note that all information on the EPA website may not be up to date, and transactions and inquiries submitted to the EPA website may not be processed or responded to until appropriations are enacted.

Close

We've made some changes to EPA.gov. If the information you are looking for is not here, you may be able to find it on the EPA Web Archive or the January 19, 2017 Web Snapshot.



Paraquat Dichloride: One Sip Can Kill

en español



On this page:

- The accidental poisoning problem
- Recent deaths from the accidental ingestion of paraquat
- Paraquat use profile
- EPA incident investigation
- True stories
- EPA response
- The solution is you
- Paraquat dichloride information resources

The Accidental Poisoning Problem

The California Poison Control System and the Central California Children's Hospital reviewed data from 1998-2009 and identified more than 1,400 cases of accidental poisonings caused by storage of non-food substances in soda bottles, unmarked bottles, cups or glasses. Several of the deaths involved the accidental ingestion of pesticides, including paraquat.¹

Recent Deaths from the Accidental Ingestion of Paraquat

The California Poison Control System and the American Association of Poison Control Centers (AAPCC) recently sent letters of concern to EPA regarding a series of deaths from accidental ingestion of the pesticide paraquat in the San