A generative compliance culture for emerging pathogen research

Prof Andreas Suhrbier,
QIMR Berghofer
Medical Research Institute,
Brisbane, Queensland, Australia

Group Leader; Inflammation Biology QIMR B
-PRF NHMRC Australia
-Prof Griffith University & James Cook University
-Adj Ass Prof University of Queensland.
-Member; Australian Infectious Disease Res. Centre.

TEL +61 7 3362 0415
email Andreas.Suhrbier@qimrberghofer.edu.au

http://www.qimrberghofer.edu.au/lab/inflammation-biology/

Why am I here?

Thanks Helen!
Restricted PC2
Zika virus

PC3
Chikungunya virus
PC2
Ross River virus

PC2
Ebola virus treatment (no agent)
CONTROLLING EXPORT OF INFORMATION THAT MAY FACILITATE DEVELOPMENT OF BIOLOGICAL WEAPONS

Defence Trade Controls Act 2012.

Lead case study in the Pilot Program. Five formal reports & 3 round table meetings. These activities significantly influenced federal legislation and substantially minimised the considerable negative impacts on Australian medical research of the DTC Act (2012), leading to the Defence Trade Controls Amendment Act (2015).

I now hold permits

(i) to export information to listed parties overseas for

DOD/DT-T/16275806T Dengue
DOD/DET/16291840 Chikungunya
DOD/DET/16726225 Ebola

The Defence and Strategic Goods List

All new recipients must be added to the permit before information can be sent.

(ii) to transport computers, mobile phones etc with such information overseas to designated countries. Dual use DSGL software technology

DOD/AUSGEL1/16213411
DOD/AUSGEL1T/16908042
DOD/AUSGEL2/16272785
DOD/AUSGEL5/16840706

Penalties include imprisonment

YOUNG RESEARCHERS
WHAT FIELD SHOULD I WORK IN?

CANCER?

INFECTIONOUS DISEASE?

- High regulatory burden
- Higher risk of penalties
- Reagent exchange very difficult
- Extra training requirements
- Productivity reduced (e.g., PC3)

  - Lower publication output
  - Less grant success
  - Higher risk of unemployment
Our Investment will support efforts to prevent and contain disease outbreaks that have the potential to cause large scale economic impacts on a national, regional or global scale.

Zika, chikungunya, SARS, MERS, AIDS, tuberculosis, malaria, Nipah, Antimicrobial resistance etc

Climate change, rapid population growth, urbanisation, regional conflicts, travel
$1.384B in capital raised in 2016

Australia’s ASX-listed life sciences sector is valued at $100.042 billion and comprises of around 100 companies

4.4% expected annual average growth

Expected to grow at an average annual rate of 4.4 per cent, reaching $8.67 billion in aggregate revenues by 2021

Robust and rapidly growing industry
Does not even mention the biotech sector which has more regulation than any other sector.

Red Tape is escalating UNCHECKED, UNMENTIONED

Does not mention red tape
Some key principles
“It is when we all play safe that we create a world of utmost insecurity”

Dag Hammarskjold

Secretary-General of the United Nations, from April 1953 - September 1961.
What is perceived as **high risk** today may be **low risk** tomorrow

Liao Ning virus – associated with lethal encephalitis in China (1 paper) – High risk

What if Liao Ning virus is abundant in Australian mosquitoes and Liao Ning virus is unable to replicate in any vertebrates (PAPER WAS WRONG) - Low risk

What is perceived as **low risk** today may be **high risk** tomorrow

Self amplifying vaccines (SAMs) - latest in RNA based vaccine technology. Deemed very safe as not DNA thus cannot integrate. - Low risk

What if SAMs can be taken up from injection sites by mosquitoes and recombine with viruses in the mosquito to make new “Frankenviruses” – High risk?
A patient claps his hands every ten seconds. Asks why, his explanation was

“Its to scare away elephants”
- "Elephants? But there aren't any elephants here!"

To which he responds “you see, it works”
An example of the “hand clap” principle

Quarantine rules requires that inside the PC3 facility (i.e. in full containment) we must count & report how many mosquitoes/snails we have in each PC3 cage/aquarium.

Impossible to be accurate.
E.g. 123, 324, 231, 237 mosquitoes (changes daily as they die)
Or 634, 346, 587 snails (changes daily as they breed and become visible)

Considerable burden imposed on tax-payer-funded research
- to what safety benefit?

NOTHING EVER ESCAPES (YES BECAUSE ITS IN THE PC3!)

You see counting works!
Regulators

- Permanent job
- High level authority
- Limited urgency
- Limited autonomy
- Happy with certainty
- Respect rules

Research Scientists

- 1-5 year contracts
- Limited right of reply
- Deadlines the norm for grants & papers
- High level autonomy
- Exist because of uncertainty
- Respect evidence and logic (not rules)
DO WE HAVE AN EVIDENCE BASED SAFETY SYSTEMS?

“Common sense is rarely common and only occasionally sensible”

WE NOW HAVE EVIDENCE BASED HEALTH INSURANCE!

Eg from 1 April 2019, cover for natural therapies will be removed from private health insurance products: Alexander technique, aromatherapy, Bowen therapy, Buteyko, Feldenkrais, herbalism, homeopathy, iridology, kinesiology, naturopathy, Pilates, reflexology, Rolfing, shiatsu, tai chi, and yoga.

Humanity and bureaucracy frequently does things which have very poor cost benefit!
OTT regulations create perverse incentives

New viruses – Zika, chikungunya, flu strains etc

Knowledge is scarce so importation is very difficult, permits very slow, many over-the-top post-import requirements.

IBC assesses risk and approves *de novo* construction of wild-type virus

Virus generated *de novo* from synthetic oligonucleotides.
Two weeks work
AU$ 10,000.
Sensible limited IBC restrictions.

=  

Same virus imported (9 month to get import permit), under quarantine, stipulated inactivation protocols, storage documentation, restricted uses, no transfers etc etc
Some very silly things
Instruction in safety manual for PC3 operations

“Went the alarm goes off put away your work and leave the facility”

The alarm sounds and the staff member continues to work away quite happily!*#?!?

ASKED WHY ON EARTH HE/SHE DID NOT DO AS INSTRUCTED IN THE SAFETY MANUAL?
“The alarm had not gone off! It was still on!”

Verb “to go off”
- to go off on a tangent
- to go off the road
- to go off half-cocked
- to go off the rails
- to go off the deep end
- to go off on someone
- fruit goes off

We are a multicultural society – safety instruction need to be clear and free of idioms or phrases that can be easily misinterpreted.

≈30% of Australians do not speak English at home.
Never use the lift, they are inherently dangerous because there is always the possibility of fire.

Clear
Material Safety Data Sheet
Sodium chloride MSDS

Section 7: Handling and Storage

Precautions:
Keep locked up.. Do not ingest
If ingested, seek medical advice immediately

Storage: Keep container tightly closed.
A solution:

A generative safety culture for infectious disease research
A typology of organisational cultures

R Westrum

---

Pathological
Power oriented *(dictatorial, do what I say)*
Opinions from minions ignored
Blame focused
Capricious policing
Novelty crushed

Bureaucratic
Rules oriented *(by the book)*
Values paper work *(sign off and we’re safe)*
Rules unresponsive to reality *(“silly I know, but thats the rule”)*
Policing focused on correct paper work
Novelty/change largely buried

Generative
Productivity oriented *(improve organisational outputs)*
High levels of cooperation/consultation
Cross-discipline respect
Largely systems-level inquiry and policing
Novelty/change sought - timely implementation

Applied to biomedical research regulatory cultures

---

Table 1 How organisations process information

<table>
<thead>
<tr>
<th>Pathological</th>
<th>Bureaucratic</th>
<th>Generative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power oriented</td>
<td>Rule oriented</td>
<td>Performance oriented</td>
</tr>
<tr>
<td>Low cooperation</td>
<td>Modest cooperation</td>
<td>High cooperation</td>
</tr>
<tr>
<td>Messengers shot</td>
<td>Messengers neglected</td>
<td>Messengers trained</td>
</tr>
<tr>
<td>Responsibilities shirked</td>
<td>Narrow</td>
<td>Risks are shared</td>
</tr>
<tr>
<td>Bridging discouraged</td>
<td>Bridging tolerated</td>
<td>Bridging encouraged</td>
</tr>
<tr>
<td>Failure—&gt;</td>
<td>Failure—&gt;</td>
<td>Failure—&gt;</td>
</tr>
<tr>
<td>scapegoating</td>
<td>justice</td>
<td>inquiry</td>
</tr>
<tr>
<td>Novelty crushed</td>
<td>Novelty—&gt; problems</td>
<td>Novelty implemented</td>
</tr>
</tbody>
</table>

---


---

i.e. competitive grants and publications and employment

NHMRC Project success rate 15%
ORGANISATIONAL EFFORT

<table>
<thead>
<tr>
<th>Compliance strategy</th>
<th>Help to Comply</th>
<th>Make it Easy</th>
<th>Full Force of Law</th>
<th>Deter by Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>19%</td>
<td>80%</td>
<td>0%</td>
<td>1%</td>
</tr>
</tbody>
</table>

- Hire policemen & investigators
- Hire communicators & systems specialists

We are not here to help, we are here to police!

URGENT Action Required

Dear Dr Miscreant,

- It has been >60 days since the Safety Committee requested action on PROJECT 5414
- If no action is taken forthwith, the project will be deactivated and work must terminate.
- The Director and Senior Management have been notified.
- Revise and resubmit now

REMINDER Project 5414

Dear Professional,

- It has been >60 days since the Safety Committee requested action on PROJECT 5414
- If you are having problems, or do not understand, the requested action please contact Ext 4031 weekdays between 9 am and 5 pm.
- You can also request that our team undertake an activity that is purely administrative on your behalf and we will do our best to be of assistance.
- We would be grateful if you could complete this task within 30 days.
Shaping attitudes

- Policing, penalties etc does not move researchers down the pyramid
- “Help to comply” and “Making it easy” does!

WHY RESEARCHERS STUMBLED

<table>
<thead>
<tr>
<th>Proximate cause</th>
<th>Ultimate cause of researcher lapse</th>
<th>% of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of attention</td>
<td>Overextended, not detail-oriented or distracted by personal problems.</td>
<td>72%</td>
</tr>
<tr>
<td>Unsure of rules</td>
<td>An increase in regulations since researcher began career, lack of mentoring or cultural differences.</td>
<td>56%</td>
</tr>
<tr>
<td>Did not prioritize compliance</td>
<td>Failed to recognize seriousness of violations, biased thinking or cultural differences.</td>
<td>56%</td>
</tr>
<tr>
<td>Relationship problems, political</td>
<td>Communicated aggressively or worked with difficult personalities.</td>
<td>36%</td>
</tr>
<tr>
<td>tensions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Another problem

AQIS import permits

- DNA vaccines for horses – not issued
- Ebola glycoprotein – not issued
- Zika virus – 9 month delay (made our own in 2 weeks)
- Chikungunya vaccine ≈3 months
- Chimp adenovirus vaccine ≈3 months

Human adenovirus approved but is a human adenovirus
a. An adenovirus that can infect humans?
b. An adenovirus isolated from humans?
c. An adenovirus whose enzootic host is humans?

- Delays in R&D contracts
- Contracts dependent on approvals of import permit
- Projects cancelled due to inability to import
- Excessive organisation resources dedicated to applications
Another solution

• AQIS takes formal advice from registered and qualified institutional IBC. They have already assessed safety and understood the project.

• AQIS rubber stamps items deemed low risk by IBC. >80% of items are low-zero risk.

• AQIS restricts itself to assessing medium to high risk imports.
Meganasty virus remerges and starts infecting Australians in March 2019

- Just missed NHMRC grant round
- Must wait till 2020 to apply for research money
- Awarded in 2021 (2 years later)

- No knowledge about Meganasty virus
  - Import permits for vital reference material not issued
  - Compliance applications take a year to be approved

- Many Australians die.
  Diagnostic and treatment modalities imported from USA.

- Rapid targeted funding allocated
  (no NHMRC-style application process)

- Safety guidelines rapidly established and universally accepted
  (no application – rejection -re application-rejection -re application processes).

- Low risk imports immediately approved (<5 days including weekends & bank holidays).

- Many Australians do not die.
  We lead the world in diagnostics and treatment