“The Life Sciences, Biosecurity, and Dual-Use Research”

Brian Rappert & Malcolm Dando

UNIVERSITY of EXETER

UNIVERSITY OF BRADFORD

MAKING KNOWLEDGE WORK

What We are Doing

ESRC Project: Coding Research: Biological Weapons, Security & the Silencing of Science

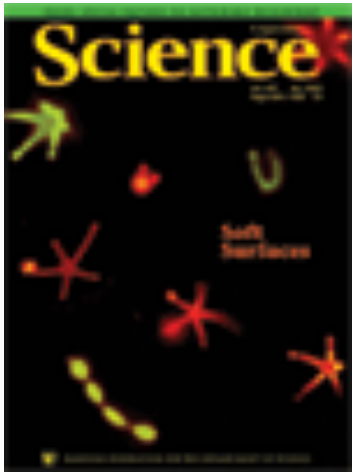
- How, if at all, might regulatory controls challenge the existing norms and conduct of research?
- How can policy makers develop new approaches for minimising bioweapon threats through engagement with bioscience communities?
- Can codes of conduct be a viable and effective policy option?

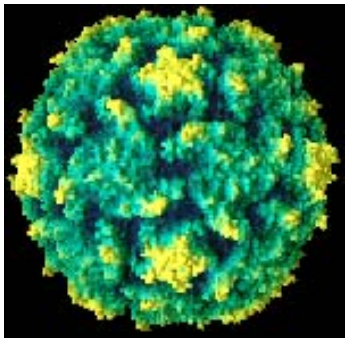
Starting Points: Importance of keeping the conversation going; testing out views

Ethics & Research: Information, consent, & contact

Cause for Concern?: Synthetic Polio Virus

- In 2002 Wimmer et al. (State University of New York) synthesised chemically polio virus
- Over a few years made to order DNA segments & public sequence info used to construct full-length cDNA version, then a viable virus
- Danger: Suggested technique for synthetically creating other viruses (e.g. Ebola *New Scientist*)
- Controversy: Novel? Necessary?





Should it have been done?

Cause for Concern?

- ‘I think it's inflammatory, without scientific justification...To purposely make a synthetic human pathogen is irresponsible.’ Venter, *NYT*, July 2002
- November 2003 Craig Venter et al. synthesise the bacteriophage phi-X174 from segments

• Improved process with less contamination, took 14 days
• Funded by US Department of Energy to find new ways of environmental clean-up

Is artificial synthesis still a good idea?

“We have the enabling technology to take us to these next exciting frontiers”
Dr Craig Venter

Mousepox: What Should be Done?

- 2001 Australian researchers employ mousepox to immunize mice against egg protein, insertion of the IL-4 gene to > antibody response
- Recombinant virus killed mice genetically resistant to mousepox and those immunized against it
- 'Unforeseen' potential for >> lethality of smallpox
- To publish or not to publish?

Should such experimental results have been widely circulated?

The British Reserve

- Officials reported that in late 1990s similar results to the Australian mousepox research were (unexpectedly) obtained
- Researchers informed HSE, but deliberately avoided discussing bioweapons implications
- Bembridge et al. *Journal of Virology* 1998 72: 4080-7???

  - IL-4 in vaccinia virus

  - Manipulation with IL-4 had definite negative effects on the course of recovery

How should researchers make their research results available to others?

Responding to Bioweapons Threats: Keeping Ahead Through Research

2001 -- Leaked US Initiatives

(1) Genetically enhance the potency of the bacterium that causes anthrax to test defenses

(2) Assembled and tested of an old Soviet cluster germ bomb (w/stimulant)

(3) Built bioweapon plant from commercially available materials (w/stimulant)

Should we always seek to 'run faster'?

US Fink Committee: What is Being Done

- New research controls: Post 9-11 and anthrax attacks in the US
- Recommendations include expansion of NIH rDNA review procedures for 'experiments of concern' including:
  - How to make vaccine ineffective
  - Alter host range of pathogen
  - Enhance virulence of pathogen
  - Confer resistance to useful antibiotics & antivirals
- Proposals submitted to Local Institutional Biosafety Committee, perhaps to national expanded RAC for 'assessment'
- Establishment of National Science Advisory Board for Biosecurity to review, survey and educate bioscientists

Is this oversight reasonable, dangerous, etc?

Spanish Flu: What Should be Done?

- 1918 'Spanish' flu killed ~30 million
- 1997 US Armed Forces Institute of Pathology isolate and sequence nine fragments of viral RNA; full sequencing now near completion
- 2001+ Recombinant viruses of influenza formed using 1918 flu genes; molecular analysis possible
- 2004 1918 surface proteins substituted in mouse and human flu strains

Are there any limits on what should be done or how it is communicated?

Data Access and Genomics Research

Data access – info, biomaterials, etc. – as negotiated

e.g., Hilgartner, S. 1998. In *Private Science*

HGP Single Chromosome Workshops in 1990s

- 'Gene Hunters': to share or not to share?
- Strategic calculations: delayed release, not submit to Genome Data Base, decline to release clones
- Forced requirement for presented materials to be made public
- Other examples from Yeast Sequencing, Sequence-Tagged Sites

In practice does science work according to free and open communication?

Beyond Bugs

Fink Committee: 'The Committee has initially limited its concerns to cover those possibilities that represent a plausible danger… Over time, however, the Committee believes that it will be necessary to expand the experiments of concern to cover a significantly wider range of potential threats.'

<u>Bioregulators and Weaponry</u>

- US/UK historical interest in 'incapacitants' (e.g., 3-quinuclidinyl benzilate)
- Pennsylvania State University, *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique* (2000)

  Drug classes: Benzodiazepines, α_2 adrenergic receptor agonists, Dopamine D3 receptor agonists

Conflict between serving nation and not developing biochemical weapons?

A Code of Conduct?

- 'Codes of Conduct': Royal Society, Foreign Office, ICRC, BMA, and House of Commons Committees. House of Commons S&T Committee 'urge scientific learned societies to consider introducing an overt ethical code of conduct as a prerequisite of membership' into the scientific profession
- Why code?
- Biological Weapons Convention international meeting in 2005 about codes

  UK Foreign Office as chair

What individual and collective responsibilities should be included?

Forthcoming Codes

"If the scientific community does not take stronger action to regulate itself then it risks having ill-judged restrictions placed on it by politicians."

-- UK House of Commons Science & Technology Committee (2003)

"Every major technology - metallurgy, explosives, internal combustion, aviation, electronics, nuclear energy - has been intensively exploited, not only for peaceful purposes but also for hostile ones. Must this also happen with biotechnology, certain to be a dominant technology of the twenty-first century?"

Matthew Meselson
Professor of Molecular Biology, Harvard University

What steps might be taken by you as individuals and by bioscience bodies to avoid this happening?

Thank You

For further information:

www.ex.ac.uk/codesofconduct

B.Rappert@ex.ac.uk

Further References

Alberts, B. & May, R. 2002. 'Scientists Support for Biological Weapons Controls' *Science* (November 8):1135.

British Medical Association. 1999. *Biotechnology, Weapons and Humanity* London: Hardwood Academic.

Cello, C., Paul, A. & Wimmer, E. 2002. 'Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template' *Science* 297: 1016-8.

Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, Development, Security, and Cooperation. 2004. *Biotechnology Research in an Age of Terrorism* Washington, DC: National Research Council.

Dando M. 2001. *The New Biological Weapons* Boulder: Lynne Rienner.

Foreign and Commonwealth Office. 2002. *Strengthening the Biological and Toxin Weapons Convention* London: HMSO. http://www.bradford.ac.uk/acad/sbtwc/other/fcobw.pdf

Further References

Hilgartner, S. 1998. 'Data Access Policy in Genome Research' In *Private Science* A. Thackray (ed.) Philadelphia: University of Pennsylvania.

Jackson, R. Ramsay, A., Christensen, C., Beaton, S. Hall, D., & Ramshaw, I. 2001. 'Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox' *Journal of Virology* 75(3): 1205-1210.

National Science Advisory Board for Biosecurity. 2004. http://www.nap.edu/books/0309089778/html/

Poste, G. 2002. *Advances in Biotechnology: Promise or Peril*. Available at www.hopkins-defense.org/sympcast/transcripts/trans_post.html.

Rappert, B. 2003. 'Coding Ethical Behaviour: The Challenges of Biological Weapons' Science & Engineering Ethics 9(4) Available at http://www.ex.ac.uk/~br201/Research/Bioweapons/index.htm