The Biological Weapons Proliferation Threat: Past, Present, and Future Assessments and Responses

Strategic Insights, Volume VI, Issue 5 (August 2007)

by Catherine Rhodes and Malcolm Dando

Introduction

It has been argued that there have been many instances of the use of biological weapons in the historical record. However, when assessed against a realistic set of criteria few of these examples are credible (Wheelis 1999). On the other hand, as soon as the scientific analysis of infectious diseases began to be clarified in the latter part of the 19th century states began to examine and apply this new knowledge for hostile purposes. Indeed it is reasonable to suggest that the series of large-scale state offensive biological weapons programmes of the 20th century progressively utilised the developing understanding of microbiology: bacteriology in the First World War; aerobiology in the Second World War; industrial production and virology in the early Cold War; and, genetic engineering in the late Cold War (Dando 1999). Moreover, it is becoming ever clearer that after the Second World War the victorious states considered biological weapons to be as serious a threat as nuclear weapons and that it was only as nuclear weapons became available to states that the biological weapons programmes declined in importance (Wheelis *et al* 2006). In the Soviet Union, of course, a massive enhancement of the offensive programme began in the 1970s and at least two other states—Iraq and South Africa—are known to have had offensive biological weapons programmes late in the 20th century.

The response to this looming threat can only be characterised as grossly inadequate. Whilst the Polish delegation succeeded in adding “bacteriological methods of warfare” to the prohibition of use of chemical warfare in the 1925 Geneva Protocol, this agreement had many weaknesses, and the Biological and Toxin Weapons Convention (BTWC), negotiated some 50 years later, is widely acknowledged to be the weakest of the international treaties dealing with Weapons of Mass Destruction (WMD) (Goldblat 2002). That then was the unbalanced situation of threat and response when the growing understanding of the Iraqi and Soviet programmes began to alert policy makers to the spectre of biological warfare again in the early 1990s (Dando 1994).

Current Response: To “Bugs”

Given that the threat at that time was seen in terms of state-level programmes in which attacks by bacteria, viruses, fungi and toxins might be developed against humans, animals and plants, a “bug-based” response in which export controls on agents and equipment were important is understandable.

Thus the Australia Group export control mechanisms developed in response to potential chemical weapons proliferation were extended progressively to deal with possible biological weapons proliferation. Today the Australia Group Agents List is quite comprehensive as can be seen from the categories shown in Figure 1. Similarly the Australia Group equipment list is focused on key elements required to produce and weaponise microbial agents and toxins (Figure 2). Thus a request for export of a variety of equipment relevant to an offensive programme would be subject to careful consideration in an Australia Group country. Items 2, 3 and 4 in Figure 2 are concerned with the growth and concentration of agents and items 5 and 7 with agent preparation and aerosolisation. Protection and containment are, of course, required to work with dangerous agents. The Australia Group member that denies an export because of concerns about potential misuse also alerts other members, thus increasing the possibility that denials in one country will not be circumvented by the use of another country (Pearson 1999). Furthermore, although export controls cannot totally prevent a country determined on proliferation from succeeding in that goal, the historical record shows that tough export controls can be a hindrance and lax controls can be circumvented.

Figure 1: Australia Group Agent List Categories*

- Core List (Human Pathogens and Toxins)
- Viruses
- Rickettsiae
- Bacteria
- Toxins (and other sub-units)
- Genetic Elements and Genetically-Modified Organisms
- Core List (Plant Pathogens)
- Bacteria
- Fungi
- Viruses
- Genetic Elements and Genetically-Modified Organisms
- Core List (Animal Pathogens)
- Viruses
- Bacteria
- Genetic Elements and Genetically-Modified Organism

*From http://www.australiagroup.net.

Figure 2: Australia Group Equipment List Categories*

- Equipment
    - Complete containment facilities at P3 and P4 containment level
    - Fermenters
    - Centrifugal separators
    - Cross (tangential) flow filtration equipment
    - Freeze-drying equipment
    - Protective and containment equipment
    - Aerosol inhalation chambers
- Related Technology

*From http://www.australiagroup.net.

In the 1990s the Security Council developed a similar approach to possible sales to Iraq of equipment and agents that might be misused. An annex to the 1995 Security Council Resolution S/1995/208 gave a very detailed list of items that it wanted to be subject to control. The list is summarised in Figure 3. Thus special (HEPA) filters required for biological containment were item 2.4 under part 2 and aerodynamic particle-sizing equipment was item 9.3 under part 9 dealing with equipment suitable for the study of aerosols.

Figure 3: Summary of Items to be Reported*

1. Microorganisms, toxins, other organisms and genetic material (as listed separately)
2. Biohazard containment and decontamination items
3. Fermentation equipment
4. Equipment useable for processing, handling, transporting or storing microorganisms their products or components
5. Formulated powdered complex media or concentrated liquid complex media for growth of microorganisms
6. Detection and assay systems for microorganisms, toxins or genetic material and specially designed reagents (for the separately listed agents)
7. Equipment and reagents for use in molecular biology research and specially designed components thereof
8. Equipment capable of dispersing aerosols and specially designed components thereof
9. Equipment useable in the study of aerosols and specially designed components thereof
10. Equipment designed for the microencapsulation of living organisms, their products or components including toxins or other biological material
11. Vaccines for the microorganisms or toxins (listed separately)
12. Documents, information, software or technology for the design, development, use, storage, manufacture, maintenance or support of entries 1-11 listed above
13. Munitions, rockets or missile warheads capable of disseminating biological warfare agents

*From *S/1995/208*

Study of the text of the proposed Verification Protocol negotiated during the 1990s for the BTWC shows that the same types of items were focused on in the system put forward to help ensure confidence in compliance (Dando 2006). However, the protocol failed to achieve consensus amongst the States Parties and it seems unlikely that such an approach will be possible for some years to come. Discussions amongst the States Parties over the last three years have therefore been concerned with other matters rather than the issue of checking the compliance of States Parties with their obligations.

Like the Chemical Weapons Convention (CWC) the BTWC is founded upon a “General Purpose Criterion” that forbids any use of biology apart from peaceful purposes. There is often confusion caused by the fact that the CWC does have an international verification system and an organisation with a technical secretariat to carry it out. But the fact remains that the international system checks but a small part of what might be misused and it is the national legal system and organisation that has the major responsibility for ensuring that the General Purpose Criterion is upheld. It is for this reason that the CWC States Parties have put such effort into an action plan designed to ensure that there is effective legislation in all member countries (Pearson & Sims 2006). Naturally, as concerns about the use of biological and toxin agents by sub-state groups have grown since 2001 there has been an increased interest in ensuring that the BTWC is adequately implemented in national legislation. Whilst the exact situation is not clear it seems very unlikely that the BTWC is better implemented than the CWC so there is clearly much that needs to be done. Certainly, the requirements for adequate national implementation of the BTWC are well beyond what is likely to be the situation in many countries (Figure 4). It is for this reason

that the detailed discussions of national legislation in the BTWC meetings of 2003 and the reporting under Security Council Resolution 1540 are to be welcomed (Security Council 2004). It is to be hoped that hard decisions on pushing forward with a timetable for effective universal implementation of BTWC national legislation will be agreed at the 2006 Review Conference.

Figure 4: Measures Necessary to Prohibit and Prevent under BTWC Article IV

- Penal legislation to:
  - Criminalise the development, production etc. as described in Article I of the BTWC
  - Criminalise biological and toxin weapons use
  - Criminalise the assistance, encouragement or inducement of others
  - Criminalise breaches of related regulations such as export controls
- Criminal procedural legislation to:
  - Ensure appropriate authority for law enforcement
  - Ensure application to state and non-state actors within the territory of the state, under its jurisdiction or control anywhere
  - Ensure appropriate jurisdiction over crimes for national courts
- Registration and licensing measures
- Export control legislation
- Measures to promulgate national biological weapons law, for example in education courses

However, just as the international community was perhaps getting a better grip on dealing with the possible misuse of microbiology by states and sub-state groups during the 1990s it was realised that the problem had undergone a dangerous mutation

Threats: Bugs and Beyond

In an age of “Molecular Biology” it has become more and more difficult to see the threat from chemical and biological weapons as being distinct, rather it is now necessary to consider a biochemical threat spectrum ranging from classical chemical weapons, through mid-spectrum agents such as toxins and bioregulators and on to traditional and genetically modified biological agents (Pearson 2006). Moreover, by the 1990s it was obvious that the mid-spectrum agents—particularly bioregulators—would pose an increasing problem (Dando 1996). Bioregulators are chemical signalling molecules in living organisms such as those that operate in the nervous, endocrine and immune systems of human beings. Disruption of the operation of these signalling systems, for example by the use of lethal nerve agents, can have catastrophic effects and it is likely that sub-lethal attacks on one of these systems will cause complex effects on the other systems because of their intimate connections (Kelle, Nixdorff and Dando 2006). Worryingly, it was also becoming clear that as technologies simplified and spread it would become easier, for example for sub-state groups, to misuse modern biology (Zilinskas and Dando 2005). Speculations were also being made as to the likely course of an offense-defence biological arms race over future decades. Clearly there were only a number of pathogens suitable for misuse and the defence might be able eventually to deal with these. Then again there were only a number of ways that those pathogens could be modified for misuse so again the defence might eventually be able to cope. The looming problem was that as our understanding of the physiology of living organisms expanded the attacker could switch from the agent to the target choosing any number of different ways to attack a wide range of targets. The final outcome looked bleak for the defence (Petro *et al* 2003).

Thus the rapid advances in civil biotechnology research were seen as driving the increasingly dangerous threat spectrum and greatly complicating any efforts at the control of proliferation.

Moreover, whilst previous advances had fuelled the potential for misuse of microbiology in state-level offensive programmes now advances in many areas of biology appeared to open up the possibility of misuse by states, sub-state groups or even, eventually, deranged individuals.

Recognition of the need to rethink the threat came first from individuals such as George Poste in his call for us to think "Beyond Bugs" (Poste 2002) but it was in two National Academies Reports—the Fink and the Lemon reports—that detailed analyses left little room for disagreement.

The Fink Report

Although the U.S. National Academies had produced numerous reports on national security issues, as the Fink Committee report "Biotechnology Research in an Age of Terrrorism" (Committee on Research Standards and Practices to Prevent the Destructive Application of Biology 2003) pointed out in its Preface "this is the first [report] to deal specifically with national security and the life sciences." The committee that produced the report under the chairmanship of Gerald Fink was charged particularly to:

> Recommend changes in… practices that could improve U.S. capacity to prevent the destructive application of biotechnology research while still enabling legitimate research to be conducted.

The Committee's concerns were illustrated through a review of recent biotechnology research publications that had led to concern about their misapplication. For example the report reviews civil work carried out in Australia to try to prevent highly destructive plagues of mice and published in the *Journal of Virology* early in 2001 (Jackson *et al* 2001). The Australian researchers had the idea of modifying a benign mousepox so that its genome incorporated the gene for a mouse egg protein. Infected mice were expected to have an antibody response to their own eggs and therefore to reject them and thus the buildup of the mouse population would be halted. As the expression of the mouse egg protein was insufficient to lead to rejection they decided to also add the gene for the cytokine IL-4 (a bioregulator in the immune system) to the mousepox genome. This they hoped would enhance the response they desired to obtain. To their surprise the doubly modified mousepox shut down the cell-killing arm of the immune system and led to the results of concern. As the Fink Report put it: "The authors of this study used standard and quite simple procedures for incorporating the IL-4 gene into the mousepox genome.," which suggested others could easily do the same perhaps with an agent that affected human beings (for example smallpox or monkeypox).

The Fink report continued by pointing out that the authors of the mousepox study:

> then demonstrated that the engineered mousepox virus was more virulent than the parent virus and killed 60 percent of infected mice, even if the mice were from a genetically resistant strain.

Worse still:

> Even more unexpected was their observation that mice that had been vaccinated and were completely resistant to the parent virus, and even to a more virulent strain of mousepox, were now killed by the IL-4 gene-expressing virus.

Consideration of this and other examples led the committee to produce some tough conclusions (Figure 5).

Figure 5: Recommendations of the Fink Committee*

1. Educating the Scientific Community
2. Review of Plans for Experiments
3. Review at the Publication Stage
4. Creation of a National Science Advisory Board for Biodefense
5. Additional Elements for Protection Against Misuse
6. A Role for the Life Sciences in Efforts to Prevent Bioterrorism and Biowarfare
7. Harmonized International Oversight

*From the *Fink Committee Report*, 2003

Of particular interest is that the committee decided that there were at least seven categories of experiments of concern that required review before they were carried out. These classes of experiment are set out in Figure 6. The committee's view was that:

> We recommend that the Department of Health and Human Services (DHHS) augment the already established system for review of experiments involving recombinant DNA conducted by the National Institutes of Health to create a review system for seven classes of experiments [the Experiments of Concern] involving microbial agents that raise concerns about their potential for misuse.

It is important to grasp that the experiments were not to be reviewed on the grounds of biosafety but on the grounds of potential misuse of the results (biosecurity). In order "to provide advice, guidance and leadership for the system of review and oversight" they also proposed the setting up of a National Board. This recommendation was accepted by the Administration and the National Science Advisory Board for Biosecurity (NSABB) duly came into being in 2005 and is currently working on these issues.

Critics have pointed to the limitations of this system. It is voluntary not legal, does not apply to industry and the military, and is national not international (Steinbrunner *et al* 2005), but it certainly brought a different expanded perception of the threat to the fore.

Figure 6: Experiments of Concern*

Experiments of concern would be those that:

1. Would demonstrate how to render a vaccine ineffective;
2. Would confer resistance to therapeutically useful antibiotics or antiviral agents;
3. Would enhance the virulence of a pathogen or render a nonpathogen virulent;
4. Would increase transmissibility of a pathogen;
5. Would alter the host range of a pathogen;
6. Would enable the evasion of diagnostic/detection modalities;
7. Would enable the weaponization of a biological agent or toxin.

* From the *Fink Committee Report*, 2003.

The Lemon Report

The Lemon report titled "Globalization, Biosecurity, and the Future of the Life Sciences" was produced by the Committee on Advances in Technology and the Prevention of their Application to

Next Generation Biowarfare Threats in early 2006. The committee was co-chaired by Stanley Lemon and David Relman, and as the Preface to the report acknowledges, it builds on the work of the Fink Committee. However, the differences are also stressed, first in the global rather than the U.S. focus and secondly, as the Preface notes, "Our focus has been on advances in the life sciences and related convergent technologies that are likely to alter the biological threat spectrum over the next 5 to 10 years."

The committee concluded that to concentrate on traditional agents such as anthrax was to take a dangerously narrow view of the threat and that the rate of advance in the life sciences made it very difficult to be specific about how the threat might develop even over a 5 to 10 year period. For example, it cites the rapid appearance of RNAi technologies and the new Synthetic Biology as examples of developments that could not have been anticipated just a few years ago.

Thus the committee decided that it had to find a different approach to thinking about the future threat. Therefore, rather than trying to produce an expanded list of threats the committee "sought to define more broadly how continuing advances in life science technologies could contribute to the development of novel biological weapons and to develop a logical framework for analysts to consider as they evaluate the evolving technology threat spectrum." They suggested that the advances in the life sciences might usefully be grouped into four categories (Figure 7) and that this grouping could assist in the necessary continuing evaluation of the threat.

Figure 7: Lemon Committee Classification of Technologies*

1. Technologies that seek to acquire novel biological or molecular diversity;
2. Technologies that seek to generate novel but pre-determined and specific biological or molecular entities through directed design;
3. Technologies that seek to understand and manipulate biological systems in a more comprehensive and effective manner;
4. Technologies that seek to enhance production, delivery, and "packaging" of biologically active materials.

* From the *Lemon Report*, 2006.

Thus novel biological or molecular diversity can be obtained through use of technologies such as DNA synthesis, DNA shuffling or combinatorial chemistry. Directed design is increasingly possible by the use of rational drug design, synthetic biology and genetic engineering of viruses. We can understand and manipulate biological systems more precisely through the use of RNAi, computational biology and bioinformatics and systems biology. Finally, production, delivery and "packaging" of biological agents is becoming more likely through the use of plants for production, aerosol technology, microencapsulation techniques, and gene therapy.

As is evident from a summary of the committee's recommendations, they did not conclude that the advances in the life sciences could or should be slowed or halted (Figure 8) rather they suggested an approach which sought to maximise the benefits that the advances should bring whilst also trying to minimise the dangers of misuse.

Figure 8: Summary of Lemon's Recommendations*

1. Endorses and affirms policies and practices that, to the maximum extent possible, promote the free and open exchange of information in the life sciences.
2. Recommends adopting a broader perspective on the "threat spectrum."
3. Recommends strengthening and enhancing the scientific and technical expertise within and across the security communities.

4. Recommends the adoption and promotion of a common culture of awareness and a shared sense of responsibility within the global community of life scientists.
5. Recommends strengthening the public health infrastructure and existing response and recovery capabilities.

* From the *Lemon Report*, 2003.

What is crucial from the present perspective is the recognition in Recommendation 2 of the limitations of an agent specific approach and the committee's view that it is necessary to:

> 2b. Adopt a broadened awareness of threats beyond the classical 'select agents' and other pathogenic organisms and toxins, so as to include, for example, approaches for disrupting host homeostatic and defense systems and for creating synthetic organisms.

So, on this considered view, we face a multifaceted and rapidly evolving—probably unpredictably evolving—threat that could be manifest in attacks against animals, plants and humans carried out on a variety of scales, including WMD levels, by states, sub-state groups and even by individuals. It would seem quite evident on that analysis that the time for belated, *ad hoc*, response to the BW threat should be over. What seems necessary is a serious systematic and integrated response that could minimise all aspects of the potential threat. What might such a response be?

Web of Prevention

In dealing with the threat of the potential hostile use of modern biotechnology (either by states or non-state groups/individuals) a key concept that has been developed is the 'web of prevention' (also referred to as the web of deterrence, web of assurance or web of protection). The following quotes and Figure 9 outline some of the elements that would make up such a web and the logic behind its use:

> The web of prevention is expressly designed to foster synergy of action among all people in a position to limit the risk of poisoning and the deliberate spread of disease. (ICRC 20/01/04, (1)).

...implementation of these recommendations in aggregate will likely decrease the risk of inappropriate application or unintended misuse of these increasingly widely available knowledge and technologies, favour the early detection of malevolent applications and mitigate the loss of life or other damage sustained by society in both the short and long term, should the worse case scenario occur. (The Lemon Report 2006, 161).

The web of prevention will include essential elements at all levels from the local to the international. The current global context means that coordinated international action will be a vital part of the web, and this paper will focus on the international level. The paper will focus particularly on written rules and agreements including legally-binding treaties, voluntary standards, guidelines and codes. Other important elements of the web at the international level include transnational networks of scientists and other stakeholders, export control groups, early warning systems, and educational programmes.

Figure 9: Elements of the Web of Assurance*

- a. international and national regimes that totally prohibit chemical and biological weapons:
  - 1. the universality of the BTWC and CWC and the 1925 Geneva Protocol
  - 2. the withdrawal of all reservations to the Geneva Protocol
  - 3. a legally binding instrument to strengthen the effectiveness of the BTWC
  - 4. national implementing legislation for the BTWC and CWC in all countries
- b. controls on dangerous pathogens and chemicals:
  - 5. addressing handling, use, storage and transfer both nationally and internationally
- c. wide-ranging protective measures:
  - 6. preparedness, detection, diagnosis and medical countermeasures
  - 7. preparedness before and after release
- d. determined national and international response to use or threat of use of chemical or biological weapons
  - 8. diplomatic actions, sanctions, military intervention
  - 9. a recognition of their responsibilities by the five permanent members of the United Nations Security Council
  - 10. national prosecution of instigator

* From *Pearson*, 2006, 79.

A strong international web of prevention against the misuse of modern biotechnology will incorporate international agreements and control mechanisms not only in the area of arms control, but also across other issue areas including health and disease control, environmental protection, trade rules, and ethical guidelines. There are a range of existing agreements in these areas that are of relevance. Various key elements that the existing agreements have the potential to contribute to a web of prevention are shown in Figure 10, which shows that there is clear potential within existing international agreements to contribute to a broad and deep web of prevention.

Figure 10: Key Elements that Existing Agreements Can Contribute to the Web of Prevention

- Prohibitions
- Prescribed national implementing measures
- Verification mechanisms
- Review of scientific developments and anticipation of threats
- Promotion of licit and beneficial uses of science and technology
- Capacity-building for health care
- Capacity-building for licit scientific and technological development
- Capacity-building for strengthening regulatory and administrative capacities
- Surveillance and response to disease outbreaks (for human, animal and plant diseases)
- Laboratory biosafety and biosecurity measures
- Tracking and documentation of transboundary movements of infectious substances
- Promotion of increased awareness of risks
- Legitimate application of trade restrictions for the protection of health and national security
- Advanced informed agreement procedure for imports of genetically modified organisms
- Development of norms and ethical principles relating to scientific and technological advances and human rights

We will now look in more detail at where these elements can be found:

In the area of arms control:

The first key element in this area is the clear prohibitions on the development, production, stockpiling, transfer and use of weapons based on biological agents and toxins. These prohibitions extend to agents and toxins effective against humans, animals or plants, or that can be used for environmental modification during warfare. The prohibitions are contained within the 1925 Geneva Protocol, the Biological and Toxin Weapons Convention (BTWC), the Environmental Modification Convention (EnMod), and the Chemical Weapons Convention (CWC). To enforce these prohibitions states are required to take any national implementing measures necessary (see Article IV BTWC, Article IV EnMod, and Article VII CWC).

The Chemical Weapons Convention contains strong verification measures including: verification of destruction of chemical weapons and production facilities; routine inspections; and challenge inspections. Ideally such strong verification measures would be in place for the BTWC too, however at the moment this is an area of significant weakness in the BW control regime.

Review of scientific developments is provided for in the BTWC, CWC and EnMod Convention. For example, Article 12 of the BTWC instructs states parties to: “take into account any new scientific and technological developments relevant to the Convention..” It has been repeatedly emphasised in the final declarations of the BTWC Review Conferences that the prohibitions of the Convention cover all scientific and technological developments, including those in the field of biotechnology.

The BTWC and CWC prohibit transfer of agents and related equipment, however trade restrictions must not be used unjustifiably and cooperation on continued research and development for peaceful purposes is encouraged:

> This Convention shall be implemented in a manner designed to avoid hampering the economic or technological development of States Parties to the Convention or international cooperation in the field of peaceful bacteriological (biological) activities. (Article X.2, BTWC)
>
> The provisions of this Article shall be implemented in a manner which avoids hampering the economic or technological development of States Parties, and international cooperation in the field of chemical activities for purposes not prohibited under this Convention. (Article VI.11 CWC)

There are also provisions on capacity-building for scientific and technological development which can be found in Article X.1 of the BTWC and Article XI.2 of the CWC. For example:

> The States Parties to this Convention undertake to facilitate, and have the right to participate in, the fullest possible exchange of equipment, materials and scientific and technological information for the use of bacteriological (biological) agents and toxins for peaceful purposes. (Article X.1, BTWC)

Possible developments in the BW control regime that may contribute to the web of prevention include those items that have been discussed during the BTWC Review Conference Interim Process:

> i. the adoption of necessary national measures to implement the prohibitions set forth in the Convention, including the enactment of penal legislation;

ii. national mechanisms to establish and maintain the security and oversight of pathogenic microorganisms and toxins;
iii. enhancing international capabilities for responding to, investigating and mitigating the effects of cases of alleged use of biological or toxin weapons or suspicious outbreaks of disease;
iv. strengthening and broadening national and international institutional efforts and existing mechanisms for the surveillance, detection, diagnosis and combating of infectious diseases affecting humans, animals and plants;
v. the content, promulgation, and adoption of codes of conduct for scientists. (ICRC 20/01/04 (2))

Discussion of these issues can be found in many of the papers in the Second Series of Bradford Briefing Papers on Strengthening the Biological Weapons Convention (see: http://www.brad.ac.uk/acad/sbtwc/briefing/bw-briefing.htm).

In the area of health and disease control:

In this area there are guidelines and mechanisms for surveillance of and response to outbreaks of diseases that affect humans, animals and plants. These are contained within, respectively: the World Health Organisation's International Health Regulations (2005 Edition); the Office International des Epizooties' Terrestrial and Aquatic Animal Health Codes (TAHC and AAHC); and the Food and Agriculture Organisation's International Plant Protection Convention (IPPC).

The International Health Regulations of 2005 require that all 'public health emergencies of international concern' are reported to the WHO. These are defined in Article 1 of the IHR as:

> an extraordinary event which is determined, as provided in these Regulations:
>
> (i) to constitute a public health risk to other States through the international spread of disease, and
>
> (ii) to potentially require a coordinated international response.

Once an outbreak is reported the WHO will follow set procedures to determine whether an emergency is occurring and if so which measures to recommend to counter the outbreak. The IHR require states to develop core capacities for: surveillance; detection; verification; notification; determination of control measures and response (Annex I, IHR) and at 'designated points of entry' for dealing with infected or suspect travellers or materials.

The IPPC established National Plant Protection Organisations (NPPOs) in its member states. The NPPOs are responsible for surveillance of plant pests and diseases, for risk analysis, and for imposing control measures (Article IV.2). NPPOs are also responsible for issuing international phytosanitary certificates which must accompany all exports of plants and plant products to show that they have been inspected and are free of any pests specified by the importing state (Annex—Model Phytosanitary Certificate).

The Terrestrial and Aquatic Animal Health Codes of the OIE also make use of an international certification scheme (referred to as the international veterinary or international animal health certificate). These certificates show that exported animals/animal products meet the requirements of the importing state (e.g. for examination, testing or vaccination). Veterinary administrations in each OIE member state are responsible for reporting any disease outbreaks to the OIE Central Bureau, and for conducting risk analysis and management for imports of animals/animal products.

There are some provisions in the disease control agreements on capacity-building for health care, for scientific and technological development, and for regulatory development. These include Article XX of the IPPC on technical assistance for meeting obligations under the Convention, and Article 44 of the IHR on collaboration and assistance.

Guidelines on laboratory biosafety and biosecurity are provided by the WHO and the OIE. The WHO Laboratory Biosafety Manual was revised in 2004 and now contains advice on Laboratory Biosecurity Concepts in Chapter 9. There is also biosafety guidance provided in Chapter I.1.6 of the OIE's Manual of Diagnostic Tests and Vaccines for Terrestrial Animals and in Chapter 1.4.5 and Section 3.4 of the Terrestrial Animal Health Code.

As the WHO explains, while the concepts are different, effective biosecurity depends on good biosafety, particularly as it highlights areas of risk:

> Effective biosafety practices are the very foundation of laboratory biosecurity activities. Through risk assessments, performed as an integral part of an institution's biosafety programme, information is gathered regarding the type of organisms available, their physical location, the personnel who require access to them, and the identification of those responsible for them. This information can be used to assess whether an institution possesses biological materials that are attractive to those who may wish to use them improperly. (Laboratory Biosafety Manual, 47)

It is expected that an institution's biosecurity programme would identify, report, investigate and take action on any breaches of biosecurity (Laboratory Biosafety Manual, 48).

There are also measures in this area for tracking and documentation of transboundary movements of infectious substances. Brief guidance can be found in Chapter 1.4.5 of the Terrestrial Animal Health Code on International Transfer and Laboratory Containment of Animal Pathogens, but more detailed information is provided in the WHO's Guidance on Regulations for the Transport of Infectious Substances. This provides summarised information, specific to infectious substances, from the rules contained within the UN Model Regulations on the Transport of Dangerous Goods. There are also regulations on the transport of dangerous goods that are specific to each mode of transport (the International Maritime Dangerous Goods Code; the Technical Instructions for the Safe Transport of Dangerous Goods by Air; the Regulations Concerning the International Carriage of Dangerous Goods by Rail; and the European Agreement Concerning the International Carriage of Dangerous Goods by Road). These are all based on the UN Model Regulations.

The WHO Guidance provides information on the safe packaging and handling of infectious substances, including appropriate labelling and marking. It distinguishes between Category A infectious substances which are "in a form that, when exposure to it occurs, is capable of causing permanent disability, life threatening or fatal disease in otherwise health humans and animals" (p.3), and Category B infectious substances which do not fit that definition. More stringent requirements are applied to Category A substances.

In the area of trade:

International trade agreements within the WTO trading system permit the application of scientifically justified trade restrictions for the protection of health and national security. The Sanitary and Phytosanitary Agreement (SPS), for example, states in Article 2 that:

> Members have the right to take sanitary and phytosanitary measures necessary for the protection of human, animal or plant life or health, provided that such measures are not inconsistent with the provisions of this Agreement.

And the Technical Barriers to Trade Agreement (TBT), in Article 2.2, states that:

> technical regulations shall not be more trade-restrictive than necessary to fulfil a legitimate objective, taking account of the risks non-fulfilment would create. Such legitimate objectives are, *inter alia*: national security requirements; the prevention of deceptive practices; protection of human health or safety, animal or plant life or health, or the environment.

There are also extensive provisions on technical assistance, including for capacity-building, in both of the agreements (see Articles 9 & 10 SPS, and Articles 11 & 12 TBT).

In the area of environmental protection:

The Cartagena Protocol on Biosafety to the Convention on Biological Diversity contains an 'advance informed agreement' procedure for transboundary movements of living modified organisms (LMOs), which it defines as: "any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology." (Article 3). It covers: "the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health." (Article 1). It does not apply to LMOs that are pharmaceuticals, in transit or for contained use.

Importing states must consent in writing before the first import of a particular LMO. The Protocol contains provisions on capacity-building specifically in the field of biotechnology:

> Cooperation in capacity-building shall, subject to the different situation, capabilities and requirements of each Party, include scientific and technical training in the proper and safe management of biotechnology, and in the use or risk assessment and risk management for biosafety, and the enhancement of technological and institutional capacities in biosafety.(Article 22.2)

In regard to ethical guidelines:

There has been recent work on developing international norms and ethical principles relating to scientific and technological developments that have significant social impacts, particularly in the field of human genetics. Over the past ten years four international declarations of principles have been adopted: the Universal Declaration on the Human Genome and Human Rights (UDHGHR); the International Declaration on Human Genetic Data (IDHGD); the Universal Declaration on Bioethics and Human Rights (UDBEHR); and the United Nations Declaration on Human Cloning. Most of the work in this area takes place within United Nations Educational, Scientific and Cultural Organisation and its International Bioethics Committee and Intergovernmental Bioethics Committee. The development of these principles includes elements that will assist in raising awareness of potential risks of misuse:

> States should take appropriate steps to provide the framework for the free exercise of research on the human genome with due regard for the principles set out in this Declaration, in order to safeguard respect for human rights, fundamental freedoms and human dignity and to protect public health. They should seek to ensure that research results are not used for non-peaceful purposes. (Article 15, UDHGHR)

> States should take appropriate measures, both at the national and international levels, to combat bioterrorism and illicit traffic in organs, tissues, samples, genetic resources and genetic related materials. (Article 21.5, UDBEHR)

Capacity-building is strongly promoted in the declarations for health care, scientific and technological development and regulatory strengthening. For example:

In the framework of international co-operation with developing countries, States should seek to encourage measures enabling:

> i) assessment of the risks and benefits pertaining to research on the human genome to be carried out and abuse to be prevented;
>
> ii) the capacity of developing countries to carry out research on human biology and genetics, taking into consideration their specific problems, to be developed and strengthened;
>
> iii) developing countries to benefit from the achievements of scientific and technological research so that their use in favour of economic and social progress can be to the benefit of all;
>
> iv) the free exchange of scientific knowledge and information in the areas of biology, genetics and medicine to be promoted. (Article 19.a, UDHGHR)

Public education and awareness raising programmes are specifically recommended by the declarations (see Articles 20 & 21 UDHGHR, Article 22 UDBEHR, and Article 23, IDHGD).

Analysis

This more detailed view also clearly shows that there is great potential in the existing international agreements that are relevant to the control of the applications and impacts of modern biotechnology to contribute to a strong web of prevention. However, this potential is not being fulfilled.

For the potential contribution of these agreements to be realised weaknesses in the individual regulations (such as the lack of verification mechanisms in the BTWC) need to be resolved. In addition to this, efforts must be made to enhance the coherence of the regulations as a set of controls.

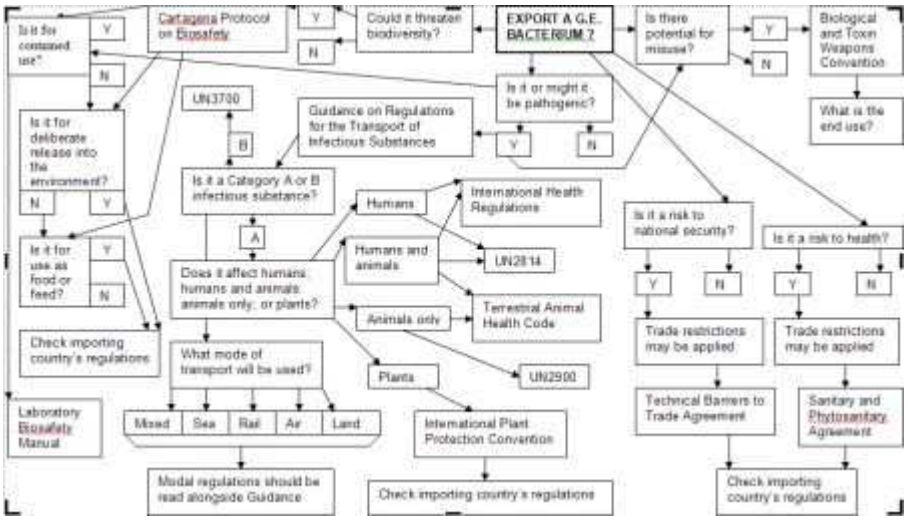
There are several examples of coherent regulatory sets at the international level which coordinate international action for a particular issue area. Prominent among these are the Geneva Conventions. Examination of such coherent regulatory sets allows the identification of certain key characteristics that form a model to which other regulatory sets (such as those which relate to biotechnology) can be compared (Rhodes 2006). This can assist policy makers in identifying elements that need strengthening in order to enhance coherence.

Currently, the various international regulations that apply to the applications and impacts of biotechnology do not form a coherent set, instead they are highly fragmented. They developed at different times and for different purposes. Few were designed specifically to control applications and impacts of modern biotechnology, instead they generally do this as a sub-issue to a wider purpose. The regulations vary in status from voluntary guidance and political declarations to legally-binding treaties. Participation by states varies widely. Some of the regulations have much stronger verification and enforcement mechanisms than others resulting in significant imbalances. There is a general lack of awareness of the connections between these agreements in their relevance to the control of biotechnology. And there is no guidance provided to states, groups and individuals on how they should prioritise compliance.

As an illustration of the problems this fragmentation can cause, take the example of a developing country with low domestic regulatory capacities which is considering whether to allow the export of a genetically engineered bacterium. In looking to the international rules for guidance, should that state apply rules on: arms control; disease control; the transport of dangerous goods; environmental protection; or a combination of some or all of these? (Assuming the state is aware of the existence of all these rules). How should the state prioritise compliance, i.e. which rules should it apply first? The same situation faces private and public groups and individuals. Whatever their individual strength, regulations that are fragmented in this way cannot effectively coordinate international action against common threats.

An overview of the complexity of this situation is shown in Figure 11.

Figure 11: Complexity of a Decision on the Export of a Genetically Modified Bacterium



Conclusion

There is great potential within existing international regulations to provide a firm foundation for the web of prevention against misuse of biotechnology. An important step in realising this potential will be to improve the coherence of the regulations as a set. This may be achieved by, for example, increasing awareness of the current situation among key actors; establishing regulatory priorities; and increasing interaction between the key international organisations involved in these areas of regulation (the OPCW, WHO, OIE, FAO, WTO, CBD Secretariat, UNESCO, etc.). Coherence must also extend to the other elements of the web of prevention, to all levels of the web of prevention, and operate between levels as well (Grotto & Tucker 2006).

About the Author

Dr. Catherine Rhodes is a Research Fellow in the Department of Peace Studies, University of Bradford in England. Malcolm Dando is a member of the Department of Peace Studies at the University of Bradford in England. He has a doctorate in neurophysiology from the University of St. Andrews in Scotland and is a professor of international security at Bradford. He also heads Bradford's program on strengthening the Biological and Toxic Weapons Convention.

For more insights into contemporary international security issues, see our *Strategic Insights* home page. To have new issues of *Strategic Insights* delivered to your Inbox, please email ccc@nps.edu with subject line "Subscribe." There is no charge, and your address will be used for no other purpose.

References:

1925 Geneva Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare, text provided by Harvard Sussex Program on CBW Armament and Arms Limitation.

CBD Secretariat. October 2000. *Cartagena Protocol on Biosafety to the Convention on Biological Diversity—Text and Annexes*.

Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology. 2003. *Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma*. Washington D.C.: The National Academies Press.

Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction, text provided by Harvard Sussex Program on CBW Armament and Arms Limitation.

Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on Their Destruction, text provided by the Organisation for the Prohibition of Chemical Weapons.

Convention on the Prohibition of Military or Any Other Hostile Use of Environmental Modification Techniques, text provided by Multilaterals Project, the Fletcher School, Tufts University.

Dando, M.R. 1996. *A New Form of Warfare: The Rise of Non-Lethal Weapons*. London: Brassey's.

Dando, M.R. 2006. *Bioterror and Biowarfare*. Oxford: Oneworld.

Dando, M.R. 1994. *Biological Warfare in the 21st Century*. London: Brassey's.

Dando, M.R. 1999. The Impact of the Development of Modern Biology and Medicine on the Evaluation of Offensive Biological Warfare Programs in the Twentieth Century. *Defense Analysis* 15, no. 1, 43-62.

Goldblat, J. 2002. *Arms Control: The New Guide to Negotiations and Agreements*. London: Sage Publications (for the International Peace Research Institute, Oslo and the Stockholm International Peace Research Institute).

Grotto, A.J. & J.B. Tucker. June 2006. *Biosecurity: A Comprehensive Action Plan*. Washington D.C.: Center for American Progress.

ICRC. 20/01/04 (1). *Responsibilities of actors in the life sciences to prevent hostile use*.

ICRC. 20/01/2004 (2). *Rules prohibiting poisoning and deliberate spread of disease*.

Institute of Medicine and National Research Council of the National Academies. 2006. *Globlization, Biosecurity and the Life Sciences, 'The Lemon Report'* (Washington, DC: National Academies Press, Prepublication Copy.)

IPPC Secretariat. 1997. *International Plant Protection Convention, 1997 Revised Version*.

Jackson, R.J. *et al*. 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: 1205-1210.

Kelle, A., K. Nixdorff, and M.R. Dando. 2006. *Controlling Biochemical Weapons: Adapting Multilateral Arms Control for the 21st Century*. Basingstoke: Palgrave/Macmillan.

OIE. 2005. *Aquatic Animal Health Code, 8th Edition*.

OIE. 2004. *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, 5th Edition*.

OIE. 2005. *Terrestrial Animal Health Code, 14th Edition*.

Pearson, G.S. 2006. Public perception and risk communication in regard to bioterrorism against animals and plants. *Review of Science and Technology*, Office International des Epizooties, 25(1):71-82.

Pearson, G.S. 1999. *The UNSCOM Saga: Chemical and Biological Weapons Non-Proliferation*, Basingstoke: Macmillan Press.

Pearson, G.S. and N.A. Sims. 2006. *Successful Outcomes for the BTWC Sixth Review Conference, Review Conference Paper No. 16*. Bradford University.

Petro, J.B. *et al*. 2003. Biotechnology: Impact on biological warfare and biodefence. *Biosecurity and Bioterrorism* 1, no. 3, 161-168.

Poste, G. 2002. *Advances in biotechnology: Promise or peril*.

Rhodes, C.A. 2006. *Control of the Biotechnology Revolution: Assessing the coherence of the international regulatory response to the challenges and opportunities of modern biotechnology*. Bradford University.

Security Council. 1995. *Plan for Future Monitoring and Verification of Iraq's Compliance with the Relevant Parts of Section C of Security Council Resolution 687 (1991)*. S/1995/208, 17th March, New York: United Nations.

Security Council. 2004. *Resolution 1540*. S/RES/1540 (2004), New York: United Nations.

Steinbrenner, J., E.D. Harris, N. Gallagher, and S. Okutani. 2005. *Controlling Dangerous Pathogens: A Prototype Protective Oversight System*.

UNECE. 2005. *Model Regulations—UN Recommendations on the Transport of Dangerous Goods, Fourteenth Revised Edition*.

UNESCO. 16/10/03. *International Declaration on Human Genetic Data*.

UNESCO. 19/10/05. *Universal Declaration on Bioethics and Human Rights*.

UNESCO. 11/11/97. *Universal Declaration on the Human Genome and Human Rights*.

UN General Assembly, 59th Session. 08/03/05. *A/RES/59/280, United Nations Declaration on Human Cloning*.

Wheelis, M.L. 1999. "Biological warfare before 1914," 8-34 in *Biological and Toxin Weapons: Research, Development and Use from the Middle Ages to 1945*, eds. van Courtland Moon J.E. and Geissler, E. (Oxford: Oxford University Press for the Stockholm International Peace Research Institute, 1999).

Wheelis, M.L., L. Rozsa, and M.R. Dando, eds., 2006. *Deadly Cultures: Biological Weapons Since 1945*. Cambridge, Mass: Harvard University Press.

WHO. September 2005. *Guidance on Regulations for the Transport of Infectious Substances, WHO/CDS/CSR/LYO/2005.22*.

WHO. 23/05/05. *International Health Regulations* (2005).

WHO. 2004. *Laboratory Biosafety Manual, 3rd Edition*.

WTO. 1995. *Agreement on Technical Barriers to Trade*.

WTO. 1995. *Agreement on the Application of Sanitary and Phytosanitary Measures*.

Zilinskas, R. and M.R. Dando. 2005. Biotechnology and Bioterrorism, 63-75 in Pilch, R.F. and R. Zilinskas, eds., *Encyclopedia of Bioterrorism Defense*. New Jersey: Wiley-Luss.