13. Biological weapons and potential indicators of offensive biological weapon activities

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I. Introduction

Current and future threats are more complex and difficult to predict than the perceived security threats of the cold war. The 11 September 2001 terrorist attacks and the letters containing anthrax spores in the United States exemplify this. For states, the boundary between external and internal security threats is becoming less distinct. The threats are becoming more global, and traditional military threats are being replaced by asymmetric and transnational threats. The combination of the increased movement of people, knowledge and products across borders as well as the greater availability of expertise and information via the Internet have made it easier to acquire biological weapon (BW) materials and know-how. In addition, there is the risk of the use of BW in armed conflicts by states or non-state actors. The difficulties involved in gathering reliable intelligence and assessing whether a country is pursuing a BW programme have been clearly demonstrated in the case of Iraq.

Rapid developments in biotechnology could be a driving force encouraging states to pursue a BW capacity and opening new possibilities for potential future military or terrorist misuse.[1] Researchers now have standard methodologies for altering an organism's genetic make-up, including modifications for increased antibiotic resistance, heightened pathogenicity, increased aerosol stability or altering epitopes on organisms important for identification and diagnosis. Rapid progress in biotechnology could lead to a new class of biological warfare agents that will be engineered to target specific human biological systems at the molecular level, thereby shifting the focus from traditional biological warfare agents and making defence more difficult.[2]

In order to deal with future threats and create an effective non-proliferation policy the nature of biological weapons and possible ways to deal with them must be better understood. In section II the characteristics of biological

[1] US, Central Intelligence Agency, 'The darker bioweapons future' Unclassified report, Office of Transnational Issues, 3 Nov. 2003, URL <http://www.fas.org/irp/cia/product/bw1103.pdf>; Wheelis, M. and Dando, M., 'New technology and future developments in biological warfare', *Disarmament Forum*, no. 4 (2000), pp. 43–55; Petro, J. B., Plasse, T. R. and McNulty, J. A., 'Biotechnology: impact on biological warfare and biodefense', *Biosecurity and Bioterrorism: Biodefense Strategy, Practice and Science*, vol. 1, no. 3, (2003), pp. 1–8; and Geissler, E. (ed.), SIPRI, *Biological and Toxin Weapons Today* (Oxford University Press: Oxford, 1986).

[2] Petro, Plasse and McNulty (note 1); Fraser, C. M. and Dando, M. R., 'Genomics and future biological weapons: the need for preventive action by the biomedical community', *Nature Genetics*, vol. 29, (Nov. 2001), pp. 253–56.

weapons are outlined, including how they are defined. Section III discusses the border between defensive and offensive activities and possible potential criteria for identifying and evaluating 'sensitive' research. Section IV identifies potential discriminators that could be used to detect offensive activities. The conclusions are provided in section V.

II. What defines a biological weapon?

A common international understanding of the term biological weapon is essential in order to avoid confusion over terms such as 'bioterrorism' and the legality of biodefence programmes. The need to define biological weapons became obvious in the late 1960s during preparation for the negotiation of a convention covering biological and toxin weapons. One definition, made in a 1969 United Nations study for the Secretary-General, is still used: 'Bacteriological (biological) agents of warfare are living organisms, whatever their nature, or infective material derived from them, which are intended to cause disease or death in man, animals or plants, and which depend for their effects on their ability to multiply in the person, animal or plant attacked'.[3] Similar definitions are presented in a 1970 World Health Organization (WHO) report[4] and by SIPRI publications from the early 1970s.[5] These definitions do not include toxins in the term biological weapons. The negotiators of the 1972 Biological and Toxin Weapons Convention (BTWC) did not perceive the need for a narrow definition of biological weapons because their aim was to control technologies that were often dual use in character (i.e., that could be used both for warfare and for peaceful purposes).[6] They also wanted to cover any future scientific developments that could have an impact on the convention's prohibition. The concept agreed, the so-called general purpose criterion, defines the prohibition in Article I:

Each State Party to this Convention undertakes never in any circumstance to develop, produce, stockpile or otherwise acquire or retain:

[3] United Nations, Department of Political and Security Council Affairs, 'Chemical and bacteriological (biological) weapons and the effects of their use', Report of the Secretary-General, UN Document A/7575/Rev1, no. E.69 I. 24, New York, 1969.

[4] World Health Organization, *Health Aspects of Chemical and Biological Weapons: Report of a WHO Group of Consultants* (WHO: Geneva, 1970).

[5] The definition used by SIPRI was: 'Biological warfare means the wartime use against an enemy of agents causing disease or death in man, animals or plants following multiplication within the target organism. Biological warfare agents thus include pathogenic micro-organisms and infective materials derived from such micro-organisms'. SIPRI, 'The developing technology of CBW', *The Problem of Chemical and Biological Warfare*, vol. I, *The Rise of CB Weapons* (Almqvist & Wiksell: Stockholm, 1971), p. 25. See also the history of the negotiations leading up to the BTWC in SIPRI, *The Problem of Chemical and Biological Warfare*, vol. IV, *CB Disarmament Negotiations, 1920–1970* (Almqvist & Wiksell: Stockholm 1971), pp. 253–79, 290–321.

[6] The Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction is reproduced on the SIPRI Chemical and Biological Warfare Project Internet site at URL <http://projects.sipri.se/cbw/docs/bw-btwc-text.html>. Complete lists of parties, signatory and non-signatory states are available on the SIPRI CBW Project Internet site at URL <http://projects.sipri.se/cbw/docs/bw-btwc-mainpage.html>. See also annex A in this volume.

1. Microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes;

2. Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.[7]

It is thus important to know the intent of any activity involving biological agents or toxins. It is also clear that research is not included, which is why it has been possible for some to argue that offensive research is not covered. (The negotiators could not agree to include the word 'research' owing to the difficulty of distinguishing clearly between defensive and offensive research.) The first four BTWC review conferences dealt with the scope of Article I, including the 'types and quantities' issue and how developments in science and technology could affect it. The consensus reports of the review conferences, the Final Declarations, reflect the continuing satisfaction of the states parties with the provisions of Article I. For example, the 1996 Fourth Review Conference concluded in Article 1 of its Final Declaration: 'The Conference notes the importance of Article I as the provision which defines the scope of the Convention'.[8]

Article I was well drafted and still covers all advances in biotechnology. More specific wording would not have been able to do this, and thus most parties are satisfied that the definition will adequately address future scientific and technological developments. At the Ad Hoc Group's negotiations to strengthen the BTWC with a legally binding instrument, some parties proposed alternative definitions of terms in Article I and suggested linking it to lists of agents.[9] The possible value of such lists has been discussed for a number of years, and it has been debated whether they could help to clarify the boundary between permitted and prohibited activities, although this view has never received broad support. There is no evidence that the absence of lists of type and quantity of agents in Article I has reduced the effectiveness of the BTWC. Such lists would not be beneficial but instead would narrow the scope of Article I and require constant updating to keep pace with scientific developments and emerging infectious diseases. The absence of a list of agents ensures that any known agent or any which may emerge or be developed using genetic engineering will still be covered.

[7] BTWC (note 6).

[8] In addition, Article 6 noted: 'The Conference, conscious of apprehensions arising from relevant scientific and technological developments, *inter alia*, in the fields of microbiology, biotechnology, molecular biology, genetic engineering, and any applications resulting from genome studies, and the possibilities of their use for purposes inconsistent with the objectives and the provisions of the Convention, reaffirms that the undertaking given by the States Parties in Article I applies to all such developments'. United Nations, Fourth Review Conference of the Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, Geneva, 25 Nov.–6 Dec. 1996, Final Document, Part I, BWC/CONF. IV/9, Geneva, 1996.

[9] United Nations, 'Working paper submitted by the Russian Federation', The Ad Hoc Group of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, Fifteenth session, Geneva, 28 June–23 July 1999, BWC/AD HOC GROUP/WP.381, 29 June 1999.

The title of the BTWC makes it obvious that both biological and toxin weapons are covered. Since the 1975 entry into force of the convention the situation has become less clear because the term 'biological warfare agents' is frequently used to refer to toxins produced by any living organism (not only micro-organisms) or by any other means, including synthesis. Biological warfare agents are categorized as toxins by the USA (including by the Centers for Disease Control and Prevention, CDC), and by the North Atlantic Treaty Organization (NATO) and China.[10] On the other hand, at the BTWC Ad Hoc Group negotiations Russia, for example, proposed defining biological and toxin weapons as two types of weapon in keeping with the title of the BTWC.[11]

A more recent definition was used in a 2003 WHO report:

> biological weapons are those that achieve their intended target effects through the infectivity of disease-causing microorganisms and other such entities, including viruses, infectious nucleic acids and prions. Some of these biological agents may owe their pathogenicity to toxic substances that they themselves generate. Such toxins can sometimes be isolated and used as weapons. Since they would then achieve their effects, not as a result of infectivity, but of toxicity they will fall within the definition of chemical weapon, even though there would still be grounds for regarding them as biological weapons.[12]

Toxins are not included in the report's list of biological agents in Annex 3.[13] This was also the case in a report by the British Medical Association.[14] These examples illustrate that there is no agreement on whether toxins ought to be included in the category of biological weapons, and it is important to bear this in mind when using the term.

In order for one or more biological warfare agents to be used as a weapon, the agents must be filled in a suitable means of delivery or in munitions (bombs, grenades, spray tanks or other devices). For bioterrorism use the

[10] Geissler, E., 'Introduction', ed. Geissler (note 1), p. 5. According to NATO, a biological agent is 'a microorganism (or a toxin derived from it) which causes disease in man, plants or animals or which causes the deterioration of material'. Biological warfare is 'the employment of biological agents to produce casualties in man or animals and damage to plants or material'. A biological weapon is 'an item of material which projects, disperses, or disseminates a biological agent; including athropod vectors'. 'Part II. Biological', *NATO Handbook on the Medical Aspects of NBC Defensive Operations, AMedP-6(B)*, FM 8-9, NAVMED P-5059, AFJMAN 44-151 (US Department of the Army, the Navy and the Air Force: Washington, DC, Feb. 1996), available at URL <http://www.vnh.org/MedAspNBCDef/toc.htm>; Centers for Disease Control and Prevention (CDC), 'Bioterrorism agents/diseases', URL <http://www.bt.cdc.gov/agent/agentlist.asp>; and United Nations, 'Definitions for some items related to measures under discussion for strengthening the convention on biological weapons', Working Paper submitted by China, Ad Hoc Group of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, Second session, Geneva, 10–21 July 1995, BWC/AD HOC GROUP/ 27, 5 July 1995.

[11] United Nations, 'Working paper submitted by the Russian Federation' (note 9).

[12] World Health Organization, *Public Health Response to Biological and Chemical Weapons: WHO Guidance*, 2nd edn (WHO: Geneva, May 2004) URL <http://www.who.int/csr/delibepidemics/biochemguide/en/index.html>.

[13] World Health Organization (note 12), Annex 3, table A3.1, pp. 230–31.

[14] Assche, W. *et al.* (eds), British Medical Association, 'Table 3.3. the CBW spectrum' and 'Glossary' (definition of biological warfare), *Biotechnology Weapons and Humanity* (Harwood Academic Publishers: Amsterdam, 1999), pp. 43, 117.

means of delivery of agents can vary significantly and may include letters or other simple means.

Most infectious disease agents are not suitable as biological warfare agents for military use or even for use by terrorists. At least five requirements must be met to achieve an effective, usable agent. Such an agent must: (*a*) consistently produce a given effect, (*b*) be producible on a large scale, (*c*) be stable during production and storage in munitions and during transport, (*d*) be capable of efficient dissemination, and (*e*) remain stable after dissemination. In addition, it is preferable that: (*a*) the force using the agent is able to protect itself against the agent, (*b*) it would be difficult for a potential enemy to protect itself against the agent, (*c*) the agent has a short and predictable incubation period, and (*d*) the agent possesses a short and predictable persistency if the contaminated area is to be promptly occupied by friendly troops.[15]

This illustrative list of criteria indicates that the number of biological warfare agents suitable for large-scale military use is and will continue to be fairly limited. For terrorist use, the number of potential agents is higher, but many of the above factors are also valid at least for a bioterrorist group that aims to cause mass casualties.

Past offensive BW programmes have attempted to improve the performance of agents to allow them to be weaponized (i.e., prepared to be delivered as a weapon) by modifying the physical characteristics of agent preparation. This has been done by adding adjuvants or stabilizers, using micro-encapsulation techniques, genetically modifying an agent to change its characteristics or improving the methods and technology for dissemination. The methods for drying and milling in order to produce viable dry-agent powders of desired particle size have also been improved. For obvious reasons, information on this is not and should not be made public. However, many developments in civilian research and development (R&D) have the potential for misuse in this area.

III. Offensive and defensive biological warfare activities

It is important that a BW defence programme can demonstrate to its personnel and to outside observers that it is purely defensive. In the West, most such programmes are well aware of this need, but there is a danger that proper oversight of such programmes will become more difficult. In the USA, for example, biodefence work has increased significantly in scope and scale and now involves many US departments and subcontractors at universities or in industry. When intelligence organizations are also involved in a biological defence programme and much work is done in secrecy, outside observers will become concerned, especially if there is ambiguity about the nation's overall intentions. The only long-term solution is for biodefence programmes to be better focused, but smaller, and for their activities to be as transparent as

[15] SIPRI, *The Problem of Chemical and Biological Warfare*, vol. II, *CB Weapons Today* (Almqvist & Wiksell: Stockholm, 1973), p. 311.

possible. However, there will always be some types of work and analysis that, for security reasons, cannot be openly revealed. Only a few countries make any information available on their biological defence policy or programmes and then usually for domestic policy reasons in order to inform the legislative body or the public. The politically binding confidence-building measures (CBMs) of the BTWC stipulate that information on biodefence programmes, including past offensive and defensive programmes since 1946, should be submitted but too few countries do this annually. It has also become clear that the CBMs are inadequate and that the returns have been unsatisfactory. A proposal for dealing with the problem was made in the Ad Hoc Group's negotiations, which developed detailed formats for annual declarations of programmes, but because the negotiations collapsed in 2001 no proposal has been agreed.

The role of scientists in biodefence programmes is crucial. Under certain circumstances, research laboratories can drift from purely defensive research to offensive work for defensive reasons and then, through a gradual process, to purely offensive R&D work. This process can take place over a long period of time, and it can be difficult for individual scientists to recognize that it is happening—especially in large 'compartmental' programmes where only those working at the highest levels have the complete picture. In 1969, when the USA terminated its offensive BW programme, it stated: 'The United States bacteriological/biological programmes will be confined to R&D for defensive purposes (immunization, safety measures *et cetera*). This does not preclude research into the offensive aspects of bacteriological/biological agents necessary to determine what defensive measures are required'.[16] It would be very difficult to define what aspects of offensive research are needed for defensive measures, and which thus would be permitted by the BTWC. The limits for the future US biological defensive research were set out in the 1975 Scowcroft Memorandum, which defined the activities that were determined to be for prophylactic, protective or other peaceful purposes.[17] This compilation of activities is still valid for defining what might be included in a well-developed

[16] US National Security Council, 'National Security Decision Memorandum 35, United States policy on chemical warfare program and bacteriological/biological research program', 25 Nov. 1969, available at URL <http://www.gwu.edu/~nsarchiv/NSAEBB/NSAEBB58/>.

[17] '1. Prevention, diagnosis, or treatment of diseases of human beings, animals or plants, or research and development activities for the purpose of developing means and methods for the prevention, diagnosis, or treatment of disease; 2. Activities concerned with the protection of human beings, animals, plants, and materiel from the effects of exposure to microbial or other biological agents or toxins, including vulnerability studies and research, development and testing of equipment and devices such as protective masks and clothing, air and water filtration systems, detection, warning and identification devices, and decontamination systems; 3. Research, development, testing and use of equipment, devices and techniques for detecting the development, production, stockpiling, acquisition or retention of microbial or other biological agents or toxins; 4. Biomedical or other research for the purpose of increasing human knowledge and not intended for weapons development; 5. Research, development, production or use for the enhancement or protection of agriculture and the environment; 6. Use of biological processing techniques for non-weapons purposes, including use in chemical, pharmaceutical, food, mineral extraction and other industries, or in research and development of such techniques; and 7. Educational and instructional activities related to the above'. Editorial, 'Preventing the hostile use of biotechnology: The way forward now', *CBW Conventions Bulletin*, no. 57 (Sep. 2002), pp. 1–2.

biological defensive programme as well as for determining what might constitute potential offensive activities.

It has also been proposed that some activities should not be regarded as justified under Article I of the BTWC.[18] In a working paper at a 1992 meeting of the Ad Hoc Group of Governmental Experts to Identify and Examine Potential Verification Measures from a Scientific and Technical Standpoint (VEREX) Iran proposed guidelines to differentiate between prohibited and permitted activities.[19] Experts have also discussed whether it would be possible to define 'potentially dangerous' biotechnology based on ideas presented during the BTWC Ad Hoc Group negotiations.[20] In 2002 a proposal was made to establish certain controls on the publication of 'sensitive' research on select agents (as defined by the US CDC). Such agents would aim to achieve one or more of six weaponization-related goals: (*a*) to enhance pathogen infectivity, pathogenicity, antibiotic resistance or resistance to host immunological defences; (*b*) to improve the ability of a microbial pathogen to remain viable and virulent during prolonged storage and/or after release into the environment; (*c*) to facilitate the dissemination of biological agents as a fine particle aerosol; (*d*) to facilitate the dissemination of a biological agent by contamination of food or water sources; (*e*) to create a novel pathogen or one whose characteristics have been altered to evade current detection methods or host immune defences; and (*f*) to assemble oligonucleotides to synthesize the genome of a pathogenic micro-organism.[21]

Perhaps some of the most serious threats arise not from lone terrorists or organizations with limited scientific expertise but from scientists working in sophisticated, well-funded national BW programmes or affluent terrorist organizations with access to outside expertise. Such experts read the scientific literature and are capable of using basic research findings to pursue weapon-related developments.[22] The US National Research Council of the National Academies has recommended that some experiments 'of concern' be added to

[18] Wright, S., 'Responding to the problems of defensive biological warfare programs: beyond confidence-building and verification', eds E. Geissler and R. H. Haynes, *Prevention of a Biological and Toxin Arms Race and the Responsibility of Scientists* (Akademie-Verlag: Berlin, 1991).

[19] United Nations, 'Guidelines to differentiate between prohibited and permitted activities', Working paper by Islamic Republic of Iran, Ad Hoc Group of Governmental Experts to Identify and Examine Potential Verification Measures from a Scientific and Technical Standpoint, BWC/CONF.III/VEREX/WP.28, 7 Apr. 1992. The text is available at Department of Peace Studies, University of Bradford, 'Strengthening the Convention, VEREX: session 1', URL <http://www.opbw.org/>.

[20] Dando, M., 'Defining "potentially dangerous" biotechnology research', Paper presented at the conference on The Possible Use of Biological Weapons by Terrorist Groups: Scientific, Legal and International Implications, International Centre for Genetic Engineering and Biotechnology and Landau Network–Centro Voltà, Rome, 15 Apr. 2002.

[21] Zilinskas, R. A. and Tucker, J. B., 'Limiting the contribution of the scientific literature to the BW threat', Paper presented at the Workshop on Guidance for the Publication of Scientific Research Potentially Related to Biological and Toxin Warfare, Washington, DC, 12 Aug. 2002, Center for Nonproliferation Studies (CNS), Monterey Institute of International Studies, available at URL<http://cns..miis.edu/pubs/week/021216a.htm>; and Zilinskas R. A. and Tucker J. B., 'Limiting the contribution of the open scientific literature to the biological weapons threat', Report from the Workshop on Guidance for the Publication of Scientific Research Potentially Related to Biological and Toxin Warfare, Washington, DC, 12 Aug. 2002, CNS, Monterey Institute of International Studies, *Journal of Homeland Security*, Dec. 2002, URL <http://www.homelandsecurity.org/journal/Articles/Tucker.html>.

[22] Zilinskas and Tucker (note 21)

the existing oversight process used by the US National Institutes of Health (NIH) to ensure that biotechnology research is conducted safely. However, these guidelines do not apply, for example, to the Department of Defense (DOD).[23] In December 2001 the American Society for Microbiology adopted a policy whereby editors of major scientific journals screen papers in the light of security concerns.[24]

It can also be questioned whether the USA crossed the border between offensive and defensive BW research when a CIA project, Clear Vision, secretly built and tested a model of a Soviet BW cluster bomb.[25] According to a White House spokesman, 'this is purely bio-defensive research, which is allowed under the Biological Weapons Convention'.[26] The US Federal Bureau of Investigation (FBI) has also tried to produce dry powder of weapon-grade anthrax through reverse engineering of anthrax of the quality that was used in the October 2001 anthrax-contaminated letters as part of its investigation of the incident.[27] In addition, it is known that for years the US DOD has produced small quantities of weapon-grade anthrax bacteria for testing detection and protection equipment, and similar tests within the limits of the BTWC are probably being carried out in several biodefence programmes. The US Defense Intelligence Agency (DIA) initiated Project Jefferson[28] to produce small amounts of a genetically modified antibiotic-resistant strain of anthrax to mimic a strain that Soviet scientists claimed to have constructed in the Soviet BW programme.[29] (For several years the USA has tried to obtain the strain from Russia without success.) The US Defense Threat Reduction Agency's Project Bachus involved the construction, in secret, of a small production facility from commercially available equipment at a remote test site in the

[23] Steinbrumer, J. D. and Harris, E. D., 'When science breeds nightmares: dangerous research', *International Herald Tribune*, 3 Dec. 2003; US National Research Council of the National Academies, *Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma* (National Academies Press: Washington, DC, 2003), URL <http://books.nap.edu/catalog/10827.html>; and Epstein, E. L., 'Controlling biological warfare threats: resolving potential tensions among the research community, industry, and the national security community', *Critical Reviews in Microbiology*, vol. 27, no. 4 (2001) pp. 321–54.

[24] Vastag, B., 'Openness in biomedical research collides with heightened security concerns', *Journal of the American Medical Association*, vol. 289, no. 6 (12 Feb. 2002), pp. 686–90; and Fox, J. L., 'Bioterrorism threat could make some research too "sensitive" to disclose', *American Society of Microbiology News*, vol. 69, no. 3 (2003), pp. 112–14.

[25] Miller, J., Engelberg, S. and Broad, W., *Germs: The Ultimate Weapon* (Simon & Schuster: New York, 2001), pp. 208–209, 219; and Leitenberg, M., 'Biological weapons and "bioterrorism" in the first years of the 21st century', Paper prepared for Conference on the Possible Use of Biological Weapons by Terrorists Groups: Scientific, Legal, and International Implications (note 20), available at URL <http://disarm.igc.org/bioweapDeanart.htm>.

[26] Agence France-Presse, 'US Plans to produce new anthrax strain for testing: Pentagon', 4 Sep. 2001, URL <http://www.commondreams.org/headlines01/0904-05.htm>.

[27] Matsumoto, G., 'Anthrax powder: state of the art?', *Science*, vol. 302, no. 5650 (28 Nov. 2003), pp. 1492–97.

[28] Miller, Engelberg and Broad (note 25), pp. 308–10.

[29] Pomerantsev, A. P. *et al.*, 'Expression of cereolysine AB genes in *Bacillus anthracis* vaccine strain ensures protection against experimental hemolytic anthrax infection', *Vaccine*, vol. 15, no. 17/18 (Dec. 1997), pp. 1846–50 (translated from Russian); Stepanov, A. V. *et al.*, 'Development of novel vaccines against anthrax in man', *Journal of Biotechnology*, vol. 44 (1996), pp. 155–60, (translated from Russian); and Broad, J., 'Gene-engineered anthrax: is it a weapon?', *New York Times*, 14 Feb. 1998, section A, p. 4.

Nevada desert. This was done in order to test whether a simulant for a BW agent could be produced by terrorists, for example, and to learn what kind of signatures such a facility would emit and whether they would be detected. Technicians placed sensors outside the facility to monitor heat and discharges into the air and soil. It was concluded that it would be fairly easy for a person with limited technical knowledge to construct and run such a facility and that it would be difficult for even the most sophisticated sensors to detect it.[30] It was also disclosed that the US Army has studied explosive and non-explosive means for the delivery of dangerous pathogens. The chambers used were explosive test chambers that had been used in the US chemical weapon (CW) programme.[31]

Other examples of sensitive research may exist in the privately funded research sector or may cross the border between defence and civil research. One such example was the construction of a synthetic poliovirus using published information on the genetic sequences of poliovirus that is freely available. The scientists discovered that the new strain had become 10 000 times less pathogenic than the natural version. However, the research demonstrated that synthetic viruses can be constructed and this may pose risks in future. Terrorists would not attempt to replicate this research because of its complexity and the need for sophisticated equipment and know-how. In addition, it is not easy to predict the effect of introducing mutations.[32] It has also been indicated that Ebola haemorrhagic fever and the 1918 Spanish flu virus strain could be recreated using the same technique,[33] and scientists have accidentally created a more virulent form of tuberculosis when trying to alter its genetic structure.[34]

Another experiment involved the engineering, from published DNA sequences, of an enzyme produced by the smallpox virus which defeats the immune system. Potentially, the results could provide information on how to increase the virulence of vaccinia virus.[35] In another case scientists attempted to sterilize mice using a modified mousepox virus (which contained genes for mouse egg proteins and an immune regulatory protein, interleukin 4 (IL-4) as part of a contraceptive vaccine). They discovered that their modified virus defeated the rodents' immune systems and thus became more virulent.[36] US

[30] Miller, Engelberg and Broad (note 25), pp. 297–99.

[31] Leitenberg, M., 'Distinguishing offensive from defensive biological weapons research', *Critical Reviews in Microbiology*, vol. 29, no. 3 (2003), pp. 223–57; and Koch, A., 'USA exposes previously secret work on biological warfare', *Jane's Defence Weekly*, vol. 36, no. 11 (12 Sep. 2001).

[32] Cello, J., Paul, A. V. and Wimmer, E., 'Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template', *Science*, vol. 297, no. 5583 (Aug. 2002), pp. 1016–18.

[33] Pagàn Westphal, S., 'Ebola virus could be synthesised', *New Scientist*, 17 July 2002, URL <http://www.newscientist.com/news/news.jsp?id=ns99992555>.

[34] Shimono, N. *et al.*, 'Hypervirulent mutant of *Mycobacterium tuberculosis* resulting from disruption of the mcel operon', *Proceedings of the National Academy of Sciences*, vol. 100, no. 26 (Dec. 2003), pp. 15918–23.

[35] Rosengard, A. M. *et al*., 'Variola virus immune evasion design: expression of a highly efficient inhibitor of human complement', *Proceedings of the National Academy of Sciences*, vol. 99, no. 13 (June 2002), pp. 8808–13.

[36] Jackson R. *et al.*, 'Expression of mouse interleukin-4 by a recombinant ectromelia virus suppresses cytolytic lymphocyte responses and overcomes genetic resistance to mousepox', *Journal of Virology*, vol. 75, no. 3 (Feb. 2001), pp. 1205–10.

scientists also recently created a highly lethal form of mousepox virus by splicing a single gene for interleukin 4 into an unimportant region of the virus DNA. It has been stated that the motivation for the research was to create a more lethal form of the virus in order to develop countermeasures against it and to deter terrorists. The scientists claimed that the mousepox virus research did not pose any human health risks. They have also stated that they have modified cowpox virus to better understand whether it would be possible to similarly modify smallpox virus to make it more lethal.[37]

IV. Ways of identifying weapon-related activities

What indicators might point in the direction of an offensive programme or activities? Are there adequate safeguards that the work being done will only be used for peaceful purposes, and is biological defensive research sufficiently 'transparent' to enable an 'outsider' to readily ascertain its defensive intent?[38] It has been argued that defensive research is based on different postulates and hypotheses to research directed towards offensive needs. This was clearly the view of Colonel David Huxsoll, former commander (1983–86) of the US Army Medical Research Institute of Infectious Diseases (USAMRIID), who, in testimony before the US Senate, presented a diagram illustrating the differences between vaccine production and the production of biological warfare agents.[39] Although this was useful as an illustration, it oversimplified the problems encountered in a large programme in which activities are compartmentalized, as in the Soviet BW programme.

A state may also possess a secret mobilization capacity that can be used when large amounts of agent are needed. In such a case, when an agent has been successfully developed and weaponized, only the required documentation for standardized large-scale production/weaponization and 'starting vials' (vials containing initial strains for laboratory work) are maintained in storage under the strictest security. These dedicated facilities for biological warfare agent/toxin production could be used for legitimate peaceful production but could also be mobilized on very short notice for agent production.

The BTWC does not mention offensive or defensive biological warfare activities or programmes. With reference to Article I of the BTWC, there has, however, been discussion of whether permitted activities can be distinguished

[37] Broad, W. J., 'Bioterror research builds more lethal mousepox', *New York Times*, 1 Nov. 2003, section A, p. 5; 'Team creates vaccine-evading virus', *Bioterrorism Week*, 24 Nov. 2003, p. 9, URL <http://www.NewsRx.net>; MacKenzie, D., 'US develops lethal new viruses', *New Scientist*, 29 Oct. 2003, URL <http://www.newscientist.com/news/news.jsp?id=ns99994318>; and Buller, M., 'The potential of genetic engineering to enhance orthopoxviruses as bioweapons', Paper presented at the Smallpox Biosecurity Summit, Geneva, 21–22 Oct. 2003.

[38] Zilinskas, R. A., 'Introduction', ed. R. A. Zilinskas, *The Microbiologist and Biological Defense Research: Ethics, Politics and International Security* (New York Academy of Sciences: New York, 1992).

[39] Huxsoll, D., Testimony, *Hearings on Germ Wars: Biological Weapons Proliferation and the New Genetics*, US Senate, Committee on Governmental Affairs and Permanent Subcommittee on Investigations of the Committee on Governmental Affairs, 17 May 1989 (US Government Printing Office: Washington, DC, 1990).

from prohibited activities by using quantitative thresholds for agents and toxins used for peaceful purposes. The Ad Hoc Group's negotiations to strengthen the BTWC with a legally binding instrument addressed this question thoroughly. For example, Russia proposed that up to five kilograms (kg) of any agent should be permitted at any facility. This quantity would also include permitted amounts of live agents that could be used for testing protective equipment.[40] Iran proposed threshold quantities for toxins based on three categories depending on their lethal dose.[41] The main shortcoming of this proposal was that it would require separate threshold quantities for every agent and that large quantities of agent may be produced over a very short period of time using small initial stocks. It was also proposed that upper and lower threshold quantities of biological materials be established for each listed agent which a state party could store in a facility taking part in a programme for protection against biological weapons.[42] Many years would probably be needed to reach agreement, if that is possible, on the method of calculation, not least on how the values of the effective doses had been established. After several years of discussion, the idea was rejected of using quantitative thresholds for an agent in order to define the justifiable amount of such an agent or the justifiable scale of work. Quantities for peaceful purposes cannot be defined independently of the particular circumstances of their use. Technically informed judgements can only be made on a case-by-case basis about the credibility of claims that activities are justifiable, and many factors would have to be taken into account in each case. The scale of a permitted defensive programme and that necessary for a small offensive programme would also overlap. If the relatively small quantities which terrorists or criminals might use are also considered this becomes even more difficult.

Publicly available, open-source information can indicate whether there is cause for concern about potential offensive activities but it cannot provide certainty. In some cases, this type of information is based on intentional or unintentional leaks by intelligence organizations. In other cases, it is fabricated information. The most extensive information on prohibited programmes has so far been supplied by defectors and the intelligence services.

The VEREX meetings during the BTWC negotiations evaluated 21 potential verification measures. VEREX concluded that, from a technical and scientific standpoint, no single measure was able to distinguish conclusively between

[40] United Nations, 'On determining the quantity of microorganisms and toxins required for protective purposes', Working Paper, Russian Federation, Ad Hoc Group of Governmental Experts to Identify and Examine Potential Verification Measures from a Scientific and Technical Standpoint, BWC/CONF.III/WP.95, 4 Dec. 1992.

[41] United Nations, 'Threshold quantities for toxins', Working paper submitted by the Islamic Republic of Iran, Ad Hoc Group of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, Third session, Geneva, 27 Nov.–8 Dec. 1995, BWC/AD HOC GROUP WP 40, 5 Dec. 1995.

[42] United Nations, 'Procedural report', Ad Hoc Group of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological(Biological) and Toxin Weapons and on their Destruction, Twenty-third session, Geneva, 23 Apr.–11 May 2001, BWC/AD HOC GROUP/56-1, 18 May 2001, Annex A, p. 26; and section III, p. 207.

permitted or prohibited activities. Various combination of measures could, however, serve this function. Off-site measures such as monitoring from satellites or aircraft as well as visual observation from outside a facility were found to be of limited value to differentiate between prohibited and permitted activities in such a facility.[43] A survey of biotechnology industries concluded that finding discriminators between permitted and prohibited activities would require thorough knowledge of the activities involved. These discriminators were of both an economic and a technical nature. Biotechnology products such as vaccines, diagnostics and pharmaceuticals must meet rigorous quality standards, which often require containment provisions. Industrial containment is usually directed at protection of the product rather than of the personnel, and the containment facilities therefore operate under positive atmospheric pressure (i.e., the atmospheric pressure inside the plant is higher than that outside it). This contrasts with the containment provisions required for the handling of pathogens. The downstream processing (concentration, separation, purification testing, packaging, etc.) of products has so many characteristic technical features that experts in the field can easily identify and interpret discriminators. Neither is it difficult to determine whether a downstream processing line has been used.[44]

Examples of distinguishing activities

Complete lists of crucial points in the development and production phase of a programme do not exist, but examples can be given of how possible indicators of offensive intentions could be detected.[45] It is very difficult to compile lists of activities in a facility that would differ between a legitimate facility and a 'BW facility'.[46] Barend ter Haar has compiled a list of activities indicating

[43] United Nations, 'Report, including final report', Ad Hoc Group of Governmental Experts to Identify and Examine Potential Verification Measures from a Scientific and Technical Standpoint, BWC/CONF.III/VEREX 9, Geneva, 1993.

[44] Gerbrandy, J. I. F., 'Search for discriminators between permitted and prohibited activities in technical microbiology', Presentation by TNO Medical Biological Laboratory, Rijswijk, the Netherlands at Seminar of the Ad Hoc Group of Government Experts to Identify and Examine Potential Verification Measures from a Scientific and Technical Standpoint, Seminar on On-site Inspections, Stockholm, 16–17 Oct. 1992.

[45] 'Appendix 2. Verification of CB disarmament', SIPRI, *The Problem of Chemical and Biological Warfare*, vol. V, *The Prevention of CBW* (Almqvist & Wiksell: Stockholm, 1971), p. 142; and Anchuleta, M. G. *et al*., 'Proliferation profile assessment of emerging biological threats', Air Command and Staff College research paper ACSC/DEA/012/06-04, Apr. 1996, available at URL <www.fas.org/irp/threat/cbw/96-012.pdf>.

[46] Hart, J., 'The ALSOS Mission: a case study of evaluation of intent and its relation to the Biological and Toxin Weapons Convention (BTWC) protocol', Paper presented at Workshop on On-site Inspection in Arms Control and Disarmament Regimes: Theory and Practice, London, 8–9 Mar. 2001; Leitenberg, M., 'Biological weapons arms control', *Contemporary Security Policy*, vol. 17, no. 1 (Apr. 1996), pp. 57–58; Leitenberg, M., 'Distinguishing offensive from defensive biological weapons research', *Critical Reviews in Microbiology*, vol. 29, no. 3 (2003), pp. 223–57; Center for Counterproliferation Research, *Towards a National Biodefense Strategy: Challenges and Opportunities* (National Defense University: Washington, DC, Apr. 2003), table 1; Robinson, J., P., 'Some Lessons for the Biological Weapons Convention from preparations to implement the Chemical Weapons Convention', ed. O. Thränert, *Enhancing the Biological Weapons Convention* (Verlag J. H.W. Dietz Nachfolger: Bonn, 1996), p. 111, table 1, 'Acquiring offensive biological-warfare capability'; and US Congress, Office of Technology Assessment, *Technologies Underlying Weapons of Mass Destruction*, OTA-BP-ISC-115

those which are permitted and those which are prohibited. The main criteria used by ter Haar for making the distinction was the purpose of the activity.[47] In 1993 the Russian Intelligence Service published a list of specific indicators of offensive BW programmes. Among these were the existence of programmes for training troops, special sub-units or intelligence and sabotage groups for operations involving the use of BW, the development of secret research programmes, and the presence of secret, special and military facilities.[48] Past military BW production programmes have been large, and this would still be true for possible future large-scale state programmes.[49] For a non-state actor the amount of agent needed would be much less, and small, unsophisticated equipment and facilities would be adequate. These facilities would not generate any easily detected signatures. A non-state actor would not rely on extensive testing of an agent but would probably use the agent and then evaluate its effects. There are few indicators that could be monitored by aircraft or satellites (e.g., test sites, storage areas, enlargement or modification of known facilities, aerial images of known facilities, etc.). The USA, however, was able to use overhead imaging photographs to identify specific features of Soviet BW facilities in the mid-1970s,[50] although facilities built later were not identified. Milton Leitenberg has discussed specific indicators in a facility that can be used to differentiate between prohibited and permitted activities. He focused on five categories of activity such as safety precautions, whether equipment was placed in biosafety areas or not, the presence or absence of commercial products, and so on.[51] The following paragraphs present lists of potential indicators of offensive BW activities, based on the above examples.

For *R&D, testing and evaluation* the following would be indicators of such activity: (*a*) R&D and evaluation in BW-related areas or technologies of concern, for example, specific agents (increased virulence, multi-antibiotic resistance, increased survival in the environment, production and recovery processes, etc.), defence links and international cooperation; (*b*) the number, category and type of expertise in a facility/laboratory; (*c*) the presence of large aerosol chambers including those for explosion tests and studies in chambers with live agents; (*d*) test area/proving grounds, outdoor grids, position markers, animal transporters and dispersal equipment in the area, weapon remains, tests with pathogens and weapons, grids for survival tests, buildings to house animals, animal incinerators, meteorological instruments, aerosol/explosive chambers, refrigerated bunkers, equipment for large-scale decontamination

(US Government Printing Office: Washington, DC, Dec. 1993), table 3-2, 'Biological weapons program signatures and concealment', pp. 112–13.

[47] ter Haar, B., Center for Strategic and International Studies, *The Future of Biological Weapons*, Washington Papers, no. 151 (Praeger: New York, 1991), table 1, p. 63.

[48] Russian Federation, 'Proliferation issues: a new challenge after the cold war: proliferation of weapons of mass destruction', Foreign Intelligence Service Report, 3 Mar. 1993, Joint Publication Research Service TND-93-007, pp. 15–16, available at URL <http://svr.gov.ru/material/2-1.html>.

[49] 'Appendix 2. Verification of CB disarmament' (note 45), pp. 147–54.

[50] Lexow, W. E. and Hoptman, J., 'The enigma of Soviet BW', *Studies in Intelligence*, vol. 9 (1965) pp. 15–19.

[51] Leitenberg, (note 46).

and disposal of test animals and waste; and (*e*) BL3(P3) or BL4(P4) containment units and their area of coverage, and equipment (e.g., fermenters and sets of equipment that can be used to micro-encapsulate micro-organisms or toxins).

For *agent production and storage* the following would be indicators of offensive biological warfare activities: (*a*) funding and any budget discrepancies; (*b*) procurement (use of covert or complicated structures of companies) of specific equipment, types of acquired production equipment and specific culture media and ingredients that differ from stated civil production; (*c*) presence and use that differ from stated intentions, type of equipment and configuration, scale and number of fermenters, cell cultivation or egg incubators, downstream processing (e.g., filtration, separators/decanters, freeze dryers and spray dryers), steam generators, water purifier (quality used and controls), containment hoods or laboratories, protective suits, refrigerated containers for transport, oversized refrigerated storage, other storage/transport tanks, incinerators (for large and many animals), steam-generating capacity and culture media used (type and quantity); (*d*) level of worker safety, immunization of personnel, acquired or developed vaccines or serums, inoculations given, use of protective suits, decontamination showers, safety manuals, medical records, accident records and unusual outbreaks near a facility; (*e*) process parameters that differ from the stated process, negative pressure, raw materials that do not match the stated output, equipment that has been diverted from other facilities in country, use of locally manufactured equipment instead of commercially available equipment, residues of biological warfare agents in or outside a facility, omission of costly measures for purity and sterility quality programme (good laboratory practice, GLP, and good manufacturing practice, GMP) of stated pharmaceutical products, waste treatment, high-efficiency particulate air (HEPA) filters/air incineration for outflow air and packaging capacity/equipment; and (*f*) security, including fences, guard towers and military presence, restricted access, clearance required to visit, facility divided into several security zones, safety precautions used to protect humans, quarantine facilities and regulations.

For *weapons, delivery systems, R&D, test, filling and storage* the following would be indicators of offensive BW activities: (*a*) filling devices of special design, storage areas/bunkers with agents in bulk or filled weapons, weaponization of agents and transfer of agents or weapons in special containers or lorries; (*b*) weapons, munitions, missiles, unmanned air vehicles (UAV) or other means of delivery, various types of aerosol generators, spray tanks for different types of vehicle or aircraft, conventional munitions that could be modified for use with BW and proving ground or similar type of area; and (*c*) dispersion models, manuals for use and dissemination, deployment doctrines, military training manuals, military exercises/training involving biological warfare defence training (with live agents), equipment for BW defence and BW-protected buildings or vehicles, military mass vaccination programmes and preparation for mass vaccination.

From the above listings it can be concluded that there are very few activities that alone indicate offensive intentions. A systematic analysis of many types of information is needed, which together can point in the direction of offensive intentions. When activities move from the research phase to production and later to testing it is easier to distinguish offensive activities from defensive ones. The value of satellites or aerial surveillance is limited. For many of the factors listed above information from inside a facility is required in order to make a reliable judgement.

V. Conclusions

The perceived biological weapon threat is changing rapidly, not least because of political changes, the risk of mass casualty, transnational terrorism and the rapid developments in biotechnology.

The examples of sensitive research discussed above demonstrate how difficult it is to distinguish between permitted and prohibited activities under the BTWC. All of the examples given of such research can be motivated for defensive reasons and thus are permitted. There is, however, the problem of how and by whom these research results may later be used. The scientists who work in a biodefence programme have a crucial role to play in preventing their research from passing the limits set by the BTWC and in ensuring that ethical codes for scientific work are observed. In addition, they should monitor research activities to prevent any drift towards offensive work, which can occur if oversight and transparency are inadequate.

If visits or inspections that take into account provisions for managed access are not allowed, it is very difficult to externally monitor activities to ensure that no offensive activities are being carried out, although a number of potential indicators can be monitored together with other sources of information. In the downstream part of a production phase it is easier to identify indicators of prohibited activities. Each potential indicator of offensive activities can, together with other indicators, point towards offensive biological warfare activities, and this is why careful monitoring is required. It should be remembered that in most such cases information from inside the facility would be needed, and in actual situations this would be extremely difficult to obtain without some type of access to the facility.

Transparency in the rapidly developing field of biodefence R&D, in particular, is crucial in order to build confidence between states that new technologies are not being misused. Further elaboration of the BTWC's CBM information exchanges and converting them to mandatory declarations of current and past defensive and offensive biological weapon programmes could help to build such confidence. The fight against the proliferation of WMD will continue to remain high on the political agenda as should the work to strengthen the BTWC.