THE STRENGTHENED BTWC PROTOCOL: IMPLICATIONS FOR THE BIOTECHNOLOGY AND PHARMACEUTICAL INDUSTRY

by Malcolm R Dando

Introduction

1. The mandate[1] for the Ad Hoc Group (AHG) is *"to consider appropriate measures, including possible verification measures, and draft proposals to strengthen the Convention"*. The mandate includes also the requirement that:

> *"Measures should be formulated and implemented in a manner designed to protect sensitive commercial proprietary information and legitimate national security needs."*

and that:

> *"Measures shall be formulated and implemented in a manner designed to avoid any negative impact on scientific research, international cooperation and industrial development."*

The Ad Hoc Group have throughout their deliberations kept these requirements at the forefront of their consideration of an effective regime to strengthen the Biological and Toxin Weapons Convention (BTWC).

2. The fifth version[2] of the draft Protocol was produced following the June/July 1998 AHG meeting at which there were clear indications of moves towards the consideration of clean texts in which only major points of difference remain. It has thus become apparent that the endgame of the negotiations has either already begun or is imminent. It is certainly true that the current version of the draft Protocol already contains all the essential elements of an integrated regime[3] to strengthen the BTWC.

3. Although some States have kept their national biotechnology and pharmaceutical industries informed of the developments in the negotiations, it is evident that in some countries the potential implications for industry are less well understood. The meetings in 1998 organised by the UK (in its capacity as holder of the EU Presidency) for European industry (Brussels, early May), and by the European Federation for Biotechnology (Vienna,

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[1] United Nations, *Special Conference 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*, BWC/SPCONF/1, Geneva, 19 - 30 September 1994.

[2] United Nations, *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*, BWC/AD HOC GROUP/41, Geneva, 16 July 1998.

[3] University of Bradford, *The Strengthened BTWC Protocol: An Integrated Regime*, Briefing Paper No. 10, July 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

late May)[4] to examine the implications for biotechnology of a strengthened BTWC Protocol were very timely.

4. This Briefing Paper examines the likely implications of the central elements of the Protocol for industry and considers the extent to which the negotiators have successfully met the objective of their mandate to devise measures designed to protect sensitive commercial proprietary information and to avoid any negative impact on industrial development. It is concluded that the draft Protocol will not impose a significant additional burden upon an industry that is already tightly regulated and controlled in most parts of the world.

The Draft Protocol

5. The central and essential elements of the Protocol to strengthen the BTWC are widely recognised[5] as comprising:

> Declarations of a range of facilities and activities of potential relevance under the Convention so as to enhance transparency;
>
> Provisions for visits to facilities in order to promote accurate and complete declarations and thus further enhance transparency and confidence;
>
> Provision for rapid and effective investigations into concerns over non-compliance, including both facility and field investigations; and
>
> A cost-effective and independent organisation, including a small permanent staff, capable of implementing the Protocol effectively.

These would be complemented with Articles in the Protocol addressing national implementation measures, confidentiality, and enhancing the implementation of Article X (peaceful cooperation) and of Article III (non-transfer) of the Convention.

6. The elements of the Protocol of greatest relevance to the biotechnology and pharmaceutical industry are the requirements for declarations, the procedures for visits to facilities, the facility investigations and the provisions for the safeguarding of confidentiality. The likely requirements in the Protocol for each of these is considered in turn.

Declarations

7. In the VEREX process mandated by the Thrid Review Conference in 1991, declarations were defined as *"Mandatory, periodic reporting on a regular basis of information considered to be of relevance for verification of the B[T]WC"* and were one of the 21 single measures

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[4]See Graham S Pearson, *A Strengthened BTWC: Three Specialist Conferences*, ASA Newsletter 98-4, 14 August 1998, issue number 67, p.10.

[5] See for example Working Paper BWC/AD HOC GROUP/WP. 296, 10 July 1996 submitted by 29 western and eastern States Parties including Argentina, Australia, Austria, Belgium, Bulgaria, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Netherlands, New Zealand, Norway, Poland, Portugal, Republic of Korea, Romania, Slovakia, Spain, Sweden, Switzerland, Turkey, United Kingdom and the United States.

evaluated.[6] At the third meeting of VEREX a working paper by the rapporteur, which provided the evaluation of declarations, stated that:[7]

> *"...Declarations were considered to be a major off-site measure from which national profiles or patterns of biological activity could be assessed against other sources of information. Using the declaration mechanism, nations could share information regarding biological activities and could, in effect explain to States Parties activities which may otherwise cause compliance concerns."*

The final report of VEREX stated that *"The measure "Declarations" was most frequently identified for application in combination with other measures."* and noted that *"...the view was expressed that declarations and on-site inspections might be further considered at a later stage."* At the Special Conference of States Parties in 1994 which considered the final report of VEREX, there was evidence of widespread understanding of the importance of declarations in a verification system for the BTWC.[8]

8. In considering the impact of declarations on the biotechnology and pharmaceutical industry it is important to distinguish clearly between the **trigger** for a declaration to be required and the **information** to be provided in a declaration. Thus, for example, in the confidence-building measures agreed at the Second Review Conference of the BTWC in 1986 and extended at the Third Review Conference in 1991 the **trigger** for CBM A Part I is a *"Facility having maximum containment laboratory meeting criteria for BL4 or P4"* whilst the **information** required to be submitted includes the name of the facility, its location, financing and so on.

9. Although there has been much discussion in the Ad Hoc Group of what should be the triggers for declarations, the language in the current Protocol is for declarations of the following range of activities and facilities:[9]

> *D. DECLARATIONS*
>
> *[(A) PAST OFFENSIVE/DEFENSIVE PROGRAMMES]*
> ....
>
> *[(B) CURRENT DEFENSIVE PROGRAMMES]*
> ...

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[6] United Nations, *Report of the Ad Hoc Group of Government Experts to Identify and Examine Potential Verification Measures from a Scientific and Technical Standpoint.* BWC/CONF.III/VEREX/9, Geneva, 24 September 1993.

[7] United Nations, *Declarations (Rapporteur: Ms A. Duncan)*, BWC/CONF.III/VEREX/9, Geneva, 1993, pages 166-173.

[8] University of Bradford, *Discriminating Triggers for Mandatory Declarations*. Briefing Paper No. 3, September, 1997. Available on the web at http://www.brad.ac.uk/acad/sbtwc

[9] United Nations, *Procedural Report of 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*, BWC/AD HOC GROUP/41, Geneva, 16 July 1998.

[(a) Activities

(i) The presence/absence of [military] [civilian] [national] [biological] defence programmes [against biological and toxin weapons];
[(ii) Any additional information related to past offensive and/or defensive activities not provided in the initial declaration.]]

(b) Facilities

(i) [Which as their main task are] [taking part in] [military] [civilian] [national] [biological] defence [facilities taking part in] programme(s) [against biological and toxin weapons [as per listed agents or toxins]] [and conducting work on microorganisms or toxins as well as material imitating their properties].

[(C) VACCINE PRODUCTION FACILITIES]

(ii) Which produce vaccines [and/or toxoids/anatoxins] [licensed by the State Party] for the protection of humans [against listed agents or toxins] [with a production capacity as specified in Annex ...] [with primary production containment];

(iii) Which produce vaccines [and/or toxoids/anatoxins] [licensed by the State Party] for the protection of animals [against listed agents or toxins] [with a production capacity as specified in Annex ...] [with primary production containment];

[(iv) Which produce plant inoculants and/or biological control agent(s) and have a plant quarantine capability [with primary production containment];]

....

[(D) MAXIMUM BIOLOGICAL CONTAINMENT LABORATORIES]

(v) Which have any maximum containment laboratories meeting criteria designated as [Biosafety Level 4 ((BL4) according to WHO Classification) or P4 (according to WHO Classification) or equivalent standards] [maximum containment];

....

[(E) HIGH BIOLOGICAL CONTAINMENT FACILITIES]

[(vi) Containing areas protected [by high containment] [according to Biosafety Level 3 (BL3) [as specified in the 1993 WHO Laboratory Biosafety Manual]] [and working with listed agents or toxins] but excluding purely diagnostic [and medical] facilities;]

[(F) WORK WITH LISTED AGENTS]

(vii) Which

[work with listed agents or toxins with the exclusion of facilities involved only in diagnostic and/or medical treatment activities;]

or

[have an aggregate fermenter capacity of 100 litres or more and work with or produce listed agents;]

or

[conduct any of the following activities with any of the agents or toxins listed in Annex A excluding those involved only in diagnostic and/or medical treatment activities:

[- research and development, including on detection or identification methods [and with an aggregate production capacity on site of 100 litres or more] [and with [high containment] [certain containment characteristics including negative air pressure]];]

[- production of such agents or toxins [and/or of vaccines against them] [with an aggregate production capacity on site of 100 litres or more] [and with [certain containment characteristics including negative air pressure] [primary production containment]];]

[- maintain culture collections [registered and designated by the government] and provide professional services on demand;]

[- apply genetic modification techniques] [[to enhance pathogenicity, virulence or resistance to environmental factors/antibiotics] [focussing on genetic elements containing nucleic acid sequences coding for the determinants of pathogenicity of listed microorganisms or toxins for introduction into agents not listed in Annex A]];

[- aerobiology];]

....

[(G) NON-VACCINE PRODUCTION FACILITIES]

[(viii) Other microbiological production facilities [including development facilities] not working with listed agents which have an aggregate fermenter production capacity of [100] [1000] litres or more

[with primary production containment;]

[- which produce by fermentation (i) medicines and/or

(ii) antibiotics or (iii) other microorganisms in closed systems].]

[(ix) Not working with listed agents or toxins which

[- possess aerosol [explosive] test chambers of ... m^3 or above for work with microorganisms or toxins;]

[- possess equipment for aerosol dissemination in the open air with a particle mass median diameter not exceeding [10] microns [excluding those for purely routine agricultural [, health or environmental] use];]

[- conduct research and development with microorganisms containing nucleic acid sequences coding for determinants of pathogenicity or toxicity of listed agents or toxins;]

[- conduct genetic modification [to enhance pathogenicity and virulence [or resistance to environmental factors/antibiotics]] [with BL3 containment or equivalent standard] [with high containment] [and have an aggregate production capacity of 100 litres or more].]]

....

[(H) TRANSFERS

[(I) APPEARANCE OF OUTBREAKS OF DISEASE OR EPIDEMICS

[(J) DECLARATIONS ON THE IMPLEMENTATION OF ARTICLE X OF THE CONVENTION

[(K) NATIONAL LEGISLATION AND REGULATIONS

10. Clearly, declaration requirements under several of these headings are of little or no concern to the civil biotechnology and pharmaceutical industry. In addition, careful examination of the draft Protocol indicates that one of the above triggers which would require declarations from industry -- namely

[(E) HIGH BIOLOGICAL CONTAINMENT FACILITIES]

[(vi) Containing areas protected [by high containment] [according to Biosafety Level 3 (BL3) [as specified in the 1993 WHO Laboratory Biosafety Manual]] [and working with listed agents or toxins] but excluding purely diagnostic [and medical] facilities;]

-- is not elaborated further unlike the other triggers in the draft Protocol. It is therefore reasonable to assume that this trigger will not be included in the final Protocol.

11. As might be expected, several of the States Parties engaged in the Ad Hoc Group negotiations have carried out surveys of their national microbiological capabilities in order to gain an appreciation of how many facilities would indeed have to be declared should such triggers be incorporated into the Protocol. An analysis of these surveys, which have largely

been made by developed countries, last year led to the broad conclusion[10] that:

> "...**the number of facilities in each country that would need to be declared under triggers chosen to capture those facilities of most relevance to the Convention would be relatively limited with numbers in the order of 10s in each country**..."

This view was confirmed by the Austria/UK contribution[11] to the EU seminar for the pharmaceutical industry in May 1998 which stated that *"**the number of facilities in individual EU countries that would need to be declared can probably be measured in tens rather than hundreds**"*.

12. The total numbers of facilities to be declared world-wide can thus be estimated[12] as being of the order of 1600 to 3200 assuming a figure of 10 to 20 facilities is taken as the average for 160 States Parties. This total is consistent with the number of 2500 estimated by others[13]. It is thus clear that whilst some commentators[14] may have given the impression that all possible civil industrial facilities would have to be declared, this is incorrect and that as others such as Douglas J. MacEachin (former Deputy Director for Intelligence of the US Central Intelligence Agency) have argued recently[15], it is important is **to design triggers** that will require declaration of those sites that are "especially relevant to possible weapons purposes".

13. Careful examination of the draft Protocol shows why such relatively small numbers of facilities are likely to be required to be declared. Those triggers which might be expected to produce large numbers of industrial declarations are combined with exemptions which will reduce the numbers of facilities to be declared. For example, the Protocol reads, in regard to facilities to be declared:

> *"[(E) High Biological Containment Facilities]*
>
> *[(vi) Containing areas protected [by high containment] [according to Biosafety Level 3 (BL3) [as specified in the 1993 WHO Laboratory Biosafety Manual]] [and working with listed agents or toxins] but **excluding purely diagnostic [and medical] facilities;]"** [Emphasis added]*

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[10] University of Bradford, *Discriminating Triggers for Mandatory Declarations*. Briefing Paper No. 3, September, 1997. Available on the web at http://www.brad.ac.uk/acad/sbtwc

[11] Austria and the United Kingdom, *Industry and Declarations*, UK Presidency and the European Commission: The BWC and the Pharmaceutical Industry, 13 May 1998.

[12]University of Bradford, *The Strengthened BTWC Protocol: An Integrated Regime*, Briefing Paper No. 10, July, 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

[13]Federation of American Scientists Working Group on BW Verification, *Estimate of the Number of Declared Facilities*, revised September 1997.

[14] Taylor, T. and Johnson, L. C., *The Biotechnology Industry of the United States: A Census of Facilities*. Center for International Security and Arms Control, Stanford University, 1995.

[15] MacEachin, D. J., Routine and Challenge: Two pillars of verification. *The CBW Conventions Bulletin*, **39**, 1-3, 1998.

although, as noted above, this trigger is unlikely to appear in the final Protocol, and:

> *"[(F) Work with Listed Agents]*
>
> *(vii) Which*
>
> *[work with listed agents or toxins* ***with the exclusion of facilities involved only in diagnosis and/or medical treatment and activities;****]*

and, under *"G. Non-Vaccine Production Facilities"*, in paragraph 15 of the current draft, the requirement is for an initial declaration and annual declarations of facilities which at any time in the previous year have:

> *"Produced medicines, antimicrobials, pesticides, plant inoculants, enzymes, ...peptides or amino acids, nucleic acids or genetic elements, microorganisms for use in biotransformation processes; or produced microorganisms in areas protected by high containment,*
>
> *when*
>
> *(a) This involved [possession] [use] of a fermenter/bioreactor exceeding [300] litres in capacity, or smaller fermenters/bioreactors with an aggregate capacity exceeding [300] [1000] litres, or continuous or perfusion fermenters/bioreactors with a flow rate capable of exceeding [2] [20] litres per hour;*
>
> *or*
>
> *(b) This involved production by other methods with an annual consumption exceeding [...] embryonated eggs or [...] litres of tissue culture medium or [...] litres of other medium."*

However, the text goes on in the following paragraph to state that:

> "A facility should not be declared under paragraph 15 if:
>
> ***The [fermenters/bioreactors were] [facility was] solely [possessed] [used] for bioremediation or waste treatment, or for manufacture for sale or use of soap, cosmetics, detergents, fertilizers, or foods or beverages for humans or animals [, or of single cell proteins].****"*

In short then, it would appear that the negotiators are succeeding in crafting a set of triggers for mandatory declarations that will not impact most of civil industry at all.

14. Although Annex A on Declarations consists of six sections:

> *"[I. Definitions*
> *II. Lists and Criteria (Agents and Toxins)*
> *III. List of Equipment*
> *IV. [Thresholds]*
> *V. Programmes and Facilities*

VI. Declaration Formats."

there is, as yet, no text for section V or, particularly, for section VI on Declaration Formats. However, Section III, List of Equipment, is useful in the insight it gives into the level of detail that might eventually be required in declarations. The current langauage makes it clear that attention is being given to devising a format that will be clear and straightforward to complete using a multiple choice Yes/No approach where possible.

15. Some detail of the kinds of **information** to be provided in declarations is covered in the following Appendices to the Protocol:

"A. [Information to be Provided in Declarations of [Biological] Defence Programmes [Against Biological Weapons]]

B. Information to be Provided in Declarations of Facilities taking Part in [Biological] Defence Programmes [Against Biological Weapons]

C. Information to be Provided in Declarations of Past Biological and Toxin Offensive and/or Defensive Research and Development Programmes

D. [Information to be Provided in Declarations of Other Facilities]."

The title of Appendix D carries a footnote (No 131) pointing out that it is an interim step in the design of declaration formats and that, whilst it is useful to consider two categories of trigger (stand-alone and combinations), the dichotomy is suggested as a temporary expedient in working towards "*the ultimate objective of declaration format(s) based on a simple uniform relationship between the trigger and the focus of information required*". This goal has not yet been achieved but, despite that indeterminacy, it is quite clear that confidential proprietary information is intended to be fully protected as the footnote goes on to state :

*"**Declared information will be passed to all States Parties to the Protocol. Accordingly, the design of the declaration formats is intended to avoid reference to confidential proprietary information or national security information**..." [Emphasis added]*

This intention to fully protect confidential proprietary information has also been recognised elsewhere[16]. However, the nature of the information that will eventually be required in declarations can be seen from the current text in this Appendix.

16. The information to be provided in declarations of "other facilities", which are clearly of most concern to industry, falls into two categories. First some general information about the name, location and ownership of the facility and secondly some more specific information about the triggered function/activity.

17. The general information is for each **facility** under the following headings:

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[16]See, for example, Austria and the United Kingdom, *Industry and Declarations*, UK Presidency and the European Commission: The BWC and the Pharmaceutical Industry, 13 May 1998 and Fidler, D. P., *Legal Measures for the Protection of Confidential Information in the January 1998 Rolling Text of the Proposed BWC Protocol*. Federation of American Scientists, Washington D.C., March 1998.

"[For vaccine production facilities...]

[For facilities producing vaccines and/or anatoxins to protect humans and animals against listed agents or toxins...]

[For facilities with BL4 protected areas (Biosafety Level 4 (BL4) according to WHO Classification) or P4 (according to WHO Classification) or equivalent standard...]

[For facilities that work with listed agents or toxins and have a production capability on site and other production facilities not necessarily working with listed agents or toxins...]

[For facilities (except for diagnostic facilities) at which work is carried out on listed agents or toxins...]

[For facilities with equipment for production in the open air of aerosols with particle size not greater than 10 micrometres of any microorganisms or toxins, as well as materials that imitate their properties...]"

As an example, the information required for the last group of facilities detailed above is as follows:

"1. Name of facility.
2. Location (address and geographical location).
3. Ownership (government department or company).
4. List the microorganisms or toxins, as well as materials that imitate their properties, on which work is being carried out.
5. Indicate the main areas of activity of the facility (development of means and methods of prophylaxis, detection and isolation; genetic manipulation; aerobiology; toxicology; disinfection and other activities related to the purposes of the Convention)."

Clearly, provision of such information will be straightforward and is unlikely to be an excessively onerous task.

18. More specific information is required in regard to **functions or activities** at the site. In Part A, information is required under the following headings:

"Information is required for [facility activities] [the following functions/activities at the site] not involving commercial proprietary or national security information:

[(a) The triggered function/activity, that is the function/activity at the site which has been triggered for declaration.

[[(b) Specified linked functions/activities...]

[(c) Other activities at the site. A general description only is required...]]"

There then follow 21 questions under three general headings which have to be completed for each triggered function or activity. The first eight questions under the heading *"General Information About the Triggered Function/Activity"* cover matters such as the location,

ownership, funding, staffing, possession of animal holding units or waste treatment/dispersal plants and general description of work. Questions 9 to 20 come under the heading *"Scientific and Technical Information"* and request the following information:

"[Information for the triggered function/activity

Fields of activity]

9. Trigger: Specify which trigger applies.

10. Is this triggered function/activity involved in work in any of the following subject areas? Such work may be, inter alia, research, development, testing, evaluation or production. Purely diagnostic work, for example in a medical, veterinary or food hygiene context, need not be declared. Work performed purely in order to set up standard operating procedures for equipment at the facility need not be declared.

(a)	*Vaccines*	*Yes / No*
(b)	*Other prophylaxis or therapy techniques for humans or animals*	*Yes / No*
(c)	*Plant inoculants*	*Yes / No*
(d)	*Pathogenicity, virulence, infectivity or stability in the environment of microbial or other biological agents or toxins, or resistance to antimicrobial agents*	*Yes / No*
(e)	*Toxicity*	*Yes / No*
(f)	*Studies involving genetic modification*	*Yes / No*
(g)	*Aerobiology*	*Yes / No*
(h)	*Detection, identification or diagnostic techniques*	*Yes / No*
(i)	*Physical protection techniques*	*Yes / No*
(j)	*Decontamination/disinfection techniques*	*Yes / No*
(k)	*Insect/pest control techniques for use in agriculture/horticulture*	*Yes / No*
(l)	*Production using fermenters*	*Yes / No*
(m)	*Production of microbial or other biological agents or toxins other than in fermenters*	*Yes / No*

11. If the triggered function/activity includes work with biological agents or toxins on the list at Annex, specify the agents worked with by annotating the corresponding entry in the list [as 'T'].

[Information for any specified linked functions/activities

12. Does the triggered function/activity have any links involving the cooperative handling of microbial or other biological agents or toxins, with the following areas at this site:

(a)	*Laboratories*	*Yes / No*
(b)	*Animal houses*	*Yes / No*
(c)	*Production areas*	*Yes / No*
(d)	*Waste treatment areas*	*Yes / No*

[If yes, indicate whether such linked areas:

[- Work in any additional subject areas on the list at question 10. If so, indicate which areas by annotating the corresponding entry in the list as 'A'.]

[- Handle any additional biological agents or toxins in the list at Annex. If so, indicate which agents or toxins by annotating the corresponding entry in the list at Annex as 'A'.]]]

[Information for all the above declared functions/activities]

13. If vaccines are produced, list them.

Containment areas

14. (a) Does the facility have rooms/other enclosures with a maximum level of biological containment for human or animal pathogens, BL4 (as specified in the 1993 WHO Laboratory Biosafety Manual) or equivalent?

Yes / No

[If Yes, specify the floor area of the working areas (for example, excluding shower areas) in ranges [up to 30 sq.m. / 31-100 sq.m. / over 100 sq.m.].]

(b) Does the facility have rooms/other enclosures with a high level of biological containment for human or animal pathogens, BL3 (as specified in the 1993 WHO Laboratory Biosafety Manual) or equivalent?

Yes / No

[If Yes, specify the floor area of the working areas (for example, excluding shower areas) in ranges [up to 30 sq.m. / 31-100 sq.m. / over 100 sq.m.].]

(c) Does the facility have rooms/other enclosures with a high level of biological containment/quarantine for plants or plant pathogens?

Yes / No

[If Yes, specify the floor area in ranges [up to 30 sq.m. / 31-100 sq.m. / over 100 sq.m.].]

Equipment

OPTION A

Indicate any of the specified types of equipment that are present in the facility, regardless of whether or not the equipment is operational. For each item, indicate Yes or No, or indicate the size range that applies, as appropriate.

OPTION B

Facility equipment information should be provided according to the trigger(s) that applies:

When the trigger ... applies, answer equipment questions ..... only.

When the trigger ... applies, answer equipment questions ..... only.

When the trigger ... applies, answer equipment questions ..... only. etc.

Scale of production

15. If the answer to questions 10 (l) or (m) was "Yes", provide the following information:

- Specify the type(s) of product: antibiotic/pesticide/insecticide/plant inoculant/human or animal foodstuff/human or animal food additive/enzyme or enzyme source/fine chemical or fine chemical source/proteins other than enzymes/other (specify).

- If more than one product applies, indicate which type constitutes the major activity.

- State, if any items were produced for general sale or use, either directly or after further processing, formulation or packaging.

Information on aggregate capacity of fermenters has been provided above under "Equipment". Provide the following additional information:

16. Scale of use of tissue culture media used in the previous year.

Specifiy which range applies: [up to a 1000 litres / 1000s of litres / 10,000s of litres].

17. Scale of use of inoculated eggs for growth of microorganisms used in the previous year.

Specifiy which range applies: [up to a 1000 eggs / 1000s of eggs / 10,000s of eggs].

18. Chemical reactors above 100 litres in capacity.

State aggregate reactor capacities, in ranges [101-1000 litres / over 1000 litres].

[Vaccination requirements

19. Are there any areas which can only be entered by personnel who have been vaccinated?

Yes / No

If yes, are these areas in laboratories/production areas/downstream processing areas/other (specify). [List any vaccines that apply.]]

[International collaboration/cooperation

20. List any projects/activities funded or supported in any way by [international organizations] [by other states and/or intergovernmental or non-governmental organizations].]"

Question 21 asks for general information on sites other than those declared above and Part B requires limited information on activities which are projects supporting national biological defence programmes.

Analysis

19. It is thus evident that the numbers of facilities that will need to be declared will be of the order of 10s per country, the information to be declared will **not** require any disclosure of commercial proprietary information and the level of detail and amount of information required in the envisaged declarations will be **not** be an undue burden on what is an already highly regulated industry.

Visits

20. The draft Protocol includes provision for a limited range of visits. The current text addresses visits in Article III F. Visits and Investigations with additional detail in Annex B. Random and Clarification Visits. Article III F considers four types of visits: random; clarification; voluntary; and voluntary confidence-building. As the last two would only occur with the prior agreement of a facility, they are therefore not considered further here.

21. Consideration of the likely structure of the Protocol and size and operation of the likely BTWC organisation makes it clear that there will never be large numbers of random visits. It can justifiably be argued[17] that

> "...of the 100 visits and inspections each year, 20 would be to biological defence facilities and 10 to past BW facilities. The remaining 70 would be for random visits, clarification visits and voluntary visits..."

In the early years of implementation of the Protocol:

> "...it is likely that there could be a number of Voluntary Visits to assist States Parties in compiling their national and facility declarations and that there could also be a number of Clarification Visits to resolve ambiguities, uncertainties, anomalies and omissions in declarations. It is suggested that there might be some 50 visits, both Voluntary and Clarification, in the early years which could be expected to reduce in number in later years as States Parties gained experience in compiling their declarations..."

Thus it follows that:

> "...the number of Random Visits thus might be some 20 a year in the early years and would increase as the numbers of Voluntary and Clarification Visits reduced but would be unlikely to exceed 70 a year should the numbers of Voluntary and Clarification Visits reach zero..."

Any one state is therefore unlikely to receive more than a very small number of visits in total in any one year. Moreover, it is clear from the Protocol that the nature of the visits will be

[17]University of Bradford, *An Optimal Organisation*. Briefing Paper No. 5, January 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

carefully circumscribed to minimise the impact on legitimate operations.

22. Although industry has voiced strong concerns[18,19] about the idea of visits to its facilities, it appears that these concerns predated the present development of the Protocol and the appreciation of the probable numbers of declared facilities and of visits. Certainly, the current text makes it clear that visits will usually only be to a small number of declared sites. A careful analysis of the requirements for an effective Protocol suggests that visits are a necessary complement to declarations and challenge investigations[20]. As MacEachin has argued:[21]

> *"...Absent a regime for subjecting legitimate activities to a high degree of transparency, the best way for a violator to carry out a covert programme would be to bury it - piggy-back it - inside a legitimate programme..."*

But if declared facilities are also subject, without the right of refusal, to non-challenge visits then a violator is always at risk of discovery in using the declared site. However, to move the covert activity to an undeclared site means that **all** signs of the activity, not just its illegal purpose, have to be kept secret as the undeclared site will be potentially subject to a challenge investigation. It seems most unlikely that the negotiators can afford to forego the powerful combined regime - declarations, visits, and investigations. Their task therefore has been to craft visits in such a way as to protect legitimate industrial and national security concerns. A range of reasons have been put forward to justify the inclusion of Non-Challenge Visits in the Protocol.

23. It also seems that the negotiators are most unlikely to propose anything other than a professional inspectorate with clear loyalty to the BTWC organisation -- and this is something that the pharmaceutical and biotechnology industry can be expected to welcome. Only by utilizing a professional inspectorate can maximum protection of confidential information be assured. Consideration of the likely structure and finance of this organisation again leads to the very important conclusion that its staffing and operations are going to be at a much lower level than that of the OPCW, and thus that there are likely to be relatively small numbers of visits to any one country and infrequent visits to any particular industrial site[22,23].

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[18] Smithson, A. E., Man versus microbe: The negotiations to strengthen the Biological Weapons Convention. In A. E. Smithson (ed.), *Biological Weapons Proliferation: Reasons for Concern, Courses of Action*. The Henry L. Stimson Center, Washington D.C., 1998.

[19] Dando, M. R., *Implications of a Strengthened Biological and Toxin Weapons Convention for the Biotechnology Industry*. Paper presented to a meeting on 'A Strengthened Biological and Toxin Weapons Convention: Potential Implications for Biotechnology', organised by the Working Party on Safety in Biotechnology of the European Federation of Biotechnology, Vienna, 28-9 May 1998.

[20] University of Bradford, *The Necessity for Non-Challenge Visits*. Briefing Paper No. 2, September 1997. Available on the web at http://www.brad.ac.uk/acad/sbtwc

[21] MacEachin, D. J., Routine and Challenge: Two pillars of verification. *The CBW Conventions Bulletin*, **39**, 1-3, 1998.

[22] Chevrier, M. I., *The Cost and Structure of a BWC Organization*. Federation of American Scientists, Washington D.C., June 1998.

[23] University of Bradford, *An Optimal Organisation*. Briefing Paper No. 5, January 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

In short[23]:

> "...**if 100 visits and investigations were carried out annually and if visits to the assumed 40 biological defence facilities were to occur more frequently, say once every two years, then the number of visits to other declared facilities would be some 80 visits each year - or an average of one such visit to a State Party every two years**." [Emphasis added]

Another study of the future organization has shown that if an assumption is made of an average of four people per inspection team and an average two days per visit, then the cost of significantly increasing the numbers of visits and the consequential expansion of the organisation would be large enough[22] to suggest that it is unlikely to happen.

24. In regard to the nature of **Random Visits**, the Protocol in Article III F. Visits and Investigations makes clear in paragraph 2 that:

> *"[The BTWC Organization] shall conduct, in accordance with [this Article and] the detailed provisions contained in the Annex [on Implementation of Random Visits] [...], a limited number per year of Random Visits [which shall be non-confrontational [and confidence-building] in nature] to declared facilities.* ***These visits shall be [designed to confirm] [limited to confirming], in cooperation with the State Party to be visited that the declarations are consistent with the obligations under this Protocol****."* [Emphasis added]

This strict limitation to cooperative confirmation of the declaration during the visit, for which a standard mandate will be issued, is reinforced in the following paragraph:

> *"[3. The visits shall be conducted in the least intrusive manner [and shall not affect or interrupt [in any way] the activities taking place in the facility].]"*

and, as reviewed[24] previously, by strict conditions for the reasonable and fair distribution of random visits between States Parties.

25. **Clarification Visits** necessarily have a more limited purpose than Random Visits. The current Protocol states that:

> *"8. [The BTWC Organization] [may] [shall] also conduct, [with the consent of the State Party to be visited and] in accordance with the provisions of this Article and the detailed provisions contained in [Annex B],* ***Clarification Visits in order to resolve any ambiguity, uncertainty, anomaly or omission in the declarations of a State Party and to promote accuracy and comprehensiveness in future declarations***." [Emphasis added]

This strict limitation to matters related to resolving specific issues related to the declaration is reinforced in paragraph 12 which states:

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[24] University of Bradford, *The Strengthened BTWC Protocol: An Integrated Regime*. Briefing Paper No. 10, July 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

"The Director General shall [, in cooperation with the State Party to be visited,] [in accordance with [Annex B] [...]] [issue] [prepare] ***a mandate which shall be limited to confirming that declarations are consistent with the obligations under this Protocol and resolving the identified ambiguity, uncertainty, anomaly or omission****..."* [Emphasis added]

Again there are, in regard to Clarification Visits, provisions for non-interruption of the work of the facility and fair distribution of such visits between States. Additionally, there is a provision for prior consultation, clarification and cooperation under Article III. E (paragraphs 6 or 7). Paragraph 11 of Article III. F also allows for the possibility of Clarification Visits to **undeclared** facilities after such consultation processes.

26. The carefully circumscribed nature of both Random and Clarification Visits is further reinforced by the Protocol in Annex B. The Pre-Visit Procedures note, for example, that:

"...Members of the Visit Team shall be drawn from the permanent staff of the Technical [Secretariat] [Body]. The size of the Visit Team shall be kept to the minimum necessary for the proper fulfilment of the mandate, and shall not exceed [4] [6] persons..."

and:

"...The duration of a Random Visit [the visit] shall not exceed [48] hours, unless extended by agreement of the Visit Team and the Visited [State Party] [facility]..."

On arrival the equipment of the Visit Team (listed in Appendix E) is subject to inspection and approval by the visited State Party and during the visit representatives of the visited State Party and the facility accompany the Visit Team *"throughout the duration of the visit to the facility"*.

27. The Visit Team is allowed to carry out interviewing, visual observation, identification of key equipment and auditing. Sampling and identification may only be conducted if offered by the visited facility and then *"mutually agreed sampling and analysis [shall] may be performed by facility personnel"*, but in the presence of the Visit Team. Most notably, managed access procedures can be used:

"(E) MANAGED ACCESS

26. The visited State Party shall have the right, in accordance with the obligation to demonstrate compliance and the right, if necessary, to protect sensitive information as set out in ..., to take specific measures which may include but are not limited to the following:

(a) Removal of sensitive papers from direct view;

(b) Shrouding of sensitive displays, stores, and equipment;

(c) Shrouding sensitive pieces of equipment, such as computer or electronic systems;

(d) Logging off of computer systems and turning off data indicating

devices;

(e) Using random selective access techniques whereby the team is requested to select a given percentage or number of buildings of their choice to investigate; the same principle can apply to the interior and content of sensitive buildings or documents;

(f) In exceptional cases, limiting the number of team members who have access to certain parts of a facility; and limiting the viewing angle; the reasons for such limitations shall be stated;

(g) Limiting the time team members may spend in any area or building, while allowing the team to fulfil its mandate; and limiting the viewing angle; the reasons for such limitations shall be stated;"

The Protocol adds that:

> *"(h) The visited State Party may at any time during the visit identify products and processes in which it has a proprietary interest in order to help the team respect the visited State Party's right to safeguard proprietary information. It may request that if a specific piece of information is released to the team, it should be accorded the most stringent protection measures by the Organization."*

The draft report of the visit is to be submitted to the visited State Party which has the right to comment and, if appropriate to impose confidentiality.

Analysis

28. The net impact of visits on the civil pharmaceutical and biotechnology industry would therefore appear to be small. In the first instance visits are directed, with very limited exceptions in extreme circumstances, only at declared facilities, and, as we have seen, most industry facilities will simply not be declared. Then the size of the probable organisation is such that only a very small number of visits by small teams of professional inspectors is likely to take place in any one country. Furthermore, any random or clarification visit will be limited to checking the declaration of the visited facility and carried out under managed access controlled by the facility. Finally, it is clear from the text that sampling and analysis are not under consideration unless offered by the visited facility.

Facility Investigations

29. There is little dissent over the need for an effective Protocol to include Challenge Investigations[25]. However, despite that fact, and the clear indications that very few such investigations are likely to occur[24], considerable concerns remain in the industrial world about the potential loss of commercial proprietary information during intrusive facility

[25] University of Bradford, *The Importance of On-Site Investigations.* Briefing Paper No. 1, July 1997. Available on the web at http://www.brad.ac.uk/acad/sbtwc

investigations[26]. This has led to attempts to argue that investigations should be first approved under 'green light' procedures. The reasons why there is a strong case for an Executive Council to have the power to stop an investigation but not be required to approve its initiation has been cogently argued[27].

30. In considering the concerns expressed by industry, the question that has to be asked first, however, is: **How likely is it that an industrial facility in a country with a strong BTWC and associated national legislation could ever be under any credible threat of receiving a Challenge Investigation under any procedure?** Article III E. of the Protocol deals with Consultation, Clarification and Cooperation in regard to Compliance Measures. The text indicates that if there is any question of concern preliminary efforts should be made to resolve the matter between States Parties:

> *"3. [Without prejudice to the right of any State Party to request an investigation] States Parties [should] [shall] [,whenever possible,] [,as a rule,] first make every effort to clarify and resolve, amongst themselves or with or through [the Organization], any matter which may cause concern about possible non-compliance with the obligations of this Protocol or the Convention, or which gives rise to concerns about [a matter which may be considered ambiguous] [the implementation of the provisions of this Protocol]."*

31. Should such a consultation process in regard to an industrial facility **not** result in a resolution of the concern, and should the BTWC Organization itself becomes involved, then there is provision in the Protocol for the Executive Council to request the Director General to consult appropriate experts and report to the Executive Council:

> *"10. For the purposes of obtaining further clarification requested...the [Executive] [Consultative] [Council] may call on the Director-General to [consult the Scientific Advisory Board and] establish [on the basis of equitable geographical distribution [if possible]] a group of experts from the Technical [Secretariat] [Body] [, or if appropriate staff are not available in the Technical [Secretariat] [Body], from the list of [ad hoc] [part-time] experts nominated for designation by States Parties in accordance with procedures as set out in Annex...and approved in advance], to examine all available information and data relevant to the situation causing concern. The group of experts shall submit a factual report to the [Executive] [Consultative] [Council] on its findings."*

32. Against that background it needs to be recalled that, during the necessary consultation and technical evaluation process, information should also become available from the national framework of regulations and controls relating to industry[28] as well as from the requirements

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[26] Woollett, G. R., Industry's role, concerns, and interests in the negotiation of a BWC Compliance Protocol. In A. E. Smithson (ed.), *Biological Weapons Proliferation: Reasons for Concern, Courses of Action*. The Henry L. Stimson Center, Washington D.C., 1998.

[27] University of Bradford, *Non-Compliance Concern Investigations: Initiation Procedures,* Briefing Paper No. 15, October 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

[28] University of Bradford, *Article X: Pharmaceutical Building Blocks.* Briefing Paper No. 8, July 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

of the national legislation under Article X of the Protocol[29]. Article X requires that each State Party shall take necessary measures to:

> *"[(a) Prohibit natural and legal persons anywhere on its territory or in any other place under its jurisdiction as recognized by international law from undertaking any activity prohibited [to a State Party] under the Convention [, including enacting penal legislation with respect to such activity];]*
>
> *[(b) Prohibit natural and legal persons from undertaking any such activity anywhere under its control; and]*
>
> *[(c) Prohibit, in conformity with international law, natural persons possessing its nationality from undertaking such activity anywhere.]]"*

33. The kind of capabilities that recent developments in the US legal system have given to the authorities attempting to control the misuse of pathogens and toxins in the United States[30] illustrates the powers and requirements for information that States Parties should acquire. In such circumstances the mounting of a successful argument that a Challenge Investigation of an industrial facility is necessary seems to lack any semblance of credibility. In a State Party with effective national monitoring of industry (such as, for example, the FDA in the United States) linked to international agreements such as the Pharmaceutical Inspection Cooperation Scheme and Mutual Recognition Agreements,[28] backed up by national legislation to implement the BTWC Protocol, a mass of information to demonstrate compliance could be provided by the particular State Party to convince other States of the reality of their compliance. Moreover, as the Protocol is implemented, such legislation is likely to grow stronger and more integrated, thus decreasing the risk of abusive/frivolous challenge investigations still further.

Analysis

34. It is concluded that an industrial facility that is in fact in compliance with the BTWC in a country with strong BTWC legislation and with a strong infrastructure of controls of health and safety as well as of its pharmaceutical industry will not be the subject of a credible investigation request. Furthermore, it is considered that the provisions in the Protocol for the prevention of frivolous or abusive investigation requests will be effective in preventing such requests in regard to facilities in such a country being implemented.

Confidentiality

35. Article IV of the draft Protocol sets out the Confidentiality Provisions. This article, in its first paragraph, states that the organisation shall:

> *"...take every precaution to protect the confidentiality of information on civil and military*

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[29]University of Bradford, *National Implementation Measures*, Briefing Paper No. 4, January 1998 and *National Implementation Measures: An Update,* Briefing Paper No. 14, October 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc

[30] Ferguson, J. R., Biological weapons and US law. *Journal of the American Medical Association*, **278** (5), 357-60, 1997.

activities and facilities [including such information coming to its knowledge] in the implemention of this Protocol and, in particular, shall abide by the confidentiality provisions set forth in this Protocol."

The Director-General is required to establish and maintain a stringent regime for handling confidential information. This regime is to include provisions relating to:

"(i) The implementation of general principles for the handling of confidential information, including the establishment of appropriate classification levels on the basis of the sensitive nature of the information;

(ii) Conditions of staff employment relating to the protection of confidential information;

(iii) Measures to protect confidential information [obtained] in the course or as a result of on-site activities;

(iv) Procedures in cases of breaches or alleged breaches of confidentiality;

(v) Procedures [including procedures for archiving] to protect confidential information;

(vi) Procedures for archiving of confidential information."

Whilst the confidentiality regime is still being developed the Protocol already contains considerable detail. Annex E on Confidentiality Provisions has sections with detailed text on all but the last of this list. This regime, incorporating rules to prevent the unauthorised release of confidential information as well as rules that punish breaches, has many similarities to that agreed for the Chemical Weapons Convention[31].

36. Nevertheless, as Kellman has pointed out in regard to the Chemical Weapons Convention, in the extreme case confidential proprietary information could still be lost[32]. The biotechnology and pharmaceutical industry has argued that such a loss poses more of a financial risk to them than it does to the chemical industry[33]. However, in considering the risk that a strengthened BTWC might pose to the biotechnology and pharmaceutical industry it has to be asked whether this is of a different order from that posed by the possibility, for example, of challenge inspections already accepted under the Chemical Weapons Convention[34]. Indeed last year I found[35], as have other investigators[36], that the position taken

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[31] Fidler, D. P., *Legal Measures for the Protection of Confidential Information in the January 1998 Rolling Text of the Proposed BWC Protocol*. Federation of American Scientists, Washington D.C., March 1998.

[32] Kellman, B. *et al*., Disarmament and disclosure: How arms control verification can proceed without threatening confidential business information. *Harvard International Law Journal*, **36** (1), 71-126, 1995.

[33] Tucker, J. B., Verification provisions of the Chemical Weapons Convention and their relevance to the Biological Weapons Convention. In A. E. Smithson (ed.), *Biological Weapons Proliferation: Reasons for Concern, Courses of Action*. The Henry L. Stimson Center, Washington D.C., 1998.

[34] University of Bradford, *The CWC Verification Regime: Implications for the Biotechnological and Pharmaceutical Industry,* Briefing Paper, No. 11, July 1998 and *The Importance of On-Site Investigations.* Briefing Paper No. 1, July 1997. Available on the web at http://www.brad.ac.uk/acad/sbtwc

[35] Dando, M. R., *Implications of a Strengthened Biological and Toxin Weapons Convention for the Biotechnology Industry*. Paper presented to a meeting on 'A Strengthened Biological and Toxin Weapons

by the leadership of the industry in the United States was influenced strongly by factors other than direct concern over loss of confidential proprietary information. In my interviews, scientists working in the US industry did not appear well informed about the Ad Hoc Group's work but, given the threat of biological weapons and the amount of regulation they already worked under, were supportive of the measures being developed to strengthen the Convention especially if these were to be constructed so as to augment the controls that they already had[37].

Conclusion

37. It is evident from the current draft Protocol that the Ad Hoc Group negotiators have done an excellent job in meeting the requirements of their mandate to devise measures designed to protect sensitive commercial proprietary information and to avoid any negative impact on industrial development. The declaration triggers will lead to declarations of tens rather than hundreds (let alone thousands) of facilities in major industrial states. The information required for declarations will **not** require the provision of any confidential proprietary information from the small number of sites declared. Visits to this small number of declared sites will be infrequent - of the order of one site visit per state every two years - and will be carried out to confirm the accuracy of declarations with carefully designed provisions, such as managed access, to ensure that confidential proprietary information is protected. Whilst challenge investigations would necessarily be more intrusive than such visits, it seems most unlikely that a state with a strong BTWC regime in place alongside other national and international regulatory frameworks could ever have a credible challenge request sustained against a facility. Finally, the arrangements in regard to confidentiality in the current draft Protocol mirror closely those already accepted under the Chemical Weapons Convention which already includes the possibility of a challenge inspection at any facility.

38. It is concluded that the central elements of the Protocol of greatest concern to the biotechnology and pharmaceutical industry - the requirements for declarations, the procedures for visits to facilities, the facility investigations and the provisions for the safeguarding of confidentiality - will not impose a significant additional burden upon industry. Moreover, in view of growing appreciation world-wide of the danger of misuse of biological materials, it is probable that these extra regulations and controls will be quite acceptable to those working in what is already a very highly regulated industry.

Convention: Potential Implications for Biotechnology', organised by the Working Party on Safety in Biotechnology of the European Federation of Biotechnology, Vienna, 28-9 May 1998.

[36] Smithson, A. E., Man versus microbe: The negotiations to strengthen the Biological Weapons Convention. In A. E. Smithson (ed.), *Biological Weapons Proliferation: Reasons for Concern, Courses of Action*. The Henry L. Stimson Center, Washington D.C., 1998.

[37]University of Bradford, *The BTWC Protocol Implementation: Practical Considerations,* Briefing Paper No. 16, October 1998. Available on the web at http://www.brad.ac.uk/acad/sbtwc