

ANNEXES

A. DECLARATIONS

I. LISTS AND CRITERIA (AGENTS AND TOXINS)⁵²

1. The list of agents and toxins following below is for use with [specific measures in particular] Article III, section D, subsection I, paragraphs ... [and section F]. [In accordance with Article XI, this list shall not be interpreted as in any way modifying or amending the Convention.]⁵³

[In this context the following criteria were used as a basis to establish the list of agents and toxins during the discussions of the Ad Hoc Group:⁵⁴

52. The view was expressed that further consideration needs to be given to microorganisms carrying nucleic acid sequences coding for pathogenic properties of listed agents and toxins.

Another view was expressed that further consideration also needs to be given to nucleic acid sequences coding for toxins.

The view was expressed that live-attenuated microorganisms such as registered or recognized internationally vaccine strains should not be included as part of the lists.

53. This text was introduced during the seventeenth session of the Ad Hoc Group but not discussed.

54. A view was expressed that the lists of criteria are only aids to the Ad Hoc Group and should not be included in the Protocol. However, the Protocol should include procedures with defined time lines for the future review of the list of agents and toxins.

According to another view, criteria are important for selecting agents and toxins.

Whether criteria for human pathogens and toxins, for animal pathogens and for plant pathogens should be included in the Protocol together with the list of biological agents and toxins needs further discussion.

- Agents or toxins known to have been developed, produced or used as weapons;
- Agents or toxins which have severe public health and/or socio-economic effects;
- High morbidity, incapacity and/or mortality rates;
- Low infective/toxic dose;
- High level of transmissibility and/or contagiousness;
- Low effective or cost-effective prophylaxis, protection or treatment available;
- Ease of production and/or dissemination;
- Stability in the environment;
- Short incubation period and/or difficult to diagnose/identify at an early stage.]

2. Any State Party may propose modifications to the list. The Executive Council shall review such proposed modifications to the list of agents and toxins. Any changes to the list shall be made in accordance with Article XIV.⁵⁵

3. In reviewing the list of agents and toxins the Executive Council shall consider, *inter alia*, [the above-mentioned criteria as well as] the following factors:

[(a) The potential of individual agents and toxins for use as weapons, for example, whether they are known to have been developed, produced, stockpiled or used as weapons; would have severe adverse socio-economic and/or public health effects; are difficult to diagnose and identify; have short incubation and high morbidity, incapacity and/or mortality rates; have a lack or limited availability of effective and economical prophylaxis and/or treatment; have a low infective or toxic dose; are easily produced and/or disseminated; are stable in the environment; and/or are highly contagious or easily transmissible;]

(b) Scientific and technological developments that may affect the potential of individual agents or toxins for use as weapons;

55. The view was expressed that review of and change to the list shall be addressed in Article III, section A and Article XIV.

(c) Effects of potential inclusion or exclusion of an agent or toxin in the list on scientific and technical research and development.⁵⁶

4. The list is not exhaustive, it does not exclude the relevance for the Protocol of unlisted microbial or other biological agents or toxins [such as pests, arthropods and helminths]. [In accordance with Article XI, this list shall not be interpreted as in any way modifying or amending the Convention.]

[5. The microorganisms enumerated in the lists of human, animal and plant pathogens do not include live-attenuated strains which have been registered as such in official culture collections or are internationally recognized as such.]

6. Pathogens causing zoonotic diseases appearing in one section of the list shall also apply to the other sections.

A. HUMAN PATHOGENS

Viruses

1. Crimean-Congo haemorrhagic fever virus
2. Eastern equine encephalitis virus
3. Ebola virus
4. Sin Nombre virus
5. Junin virus
6. Lassa fever virus
7. Machupo virus
8. Marburg virus
9. Rift Valley fever virus
10. Tick-borne encephalitis virus
11. Variola major virus (Smallpox virus)
12. Venezuelan equine encephalitis virus
13. Western equine encephalitis virus
14. Yellow fever virus
15. Monkeypox virus

Bacteria

1. Bacillus anthracis
2. [Brucella abortus]
3. Brucella melitensis
4. [Brucella suis]

56. Ibid.

5. Burkholderia (Pseudomonas) mallei
6. Burkholderia (Pseudomonas) pseudomallei
7. Francisella tularensis tularensis
8. Yersinia pestis

Rickettsiae

1. Coxiella burnetii
2. Rickettsia prowazekii
3. Rickettsia rickettsii

[Protozoa

1. Naegleria fowleri
2. Naegleria australiensis]

B. ANIMAL PATHOGENS

1. African swine fever virus
2. [Avian influenza virus (Fowl plague virus)]
3. [Classic swine fever virus (Hog cholera virus)]
4. [Contagious bovine (pleuropneumonia)/Mycoplasma mycoides var. mycoides]
5. [Foot and mouth disease virus]
6. [Newcastle disease virus]
7. [Peste des petits ruminants virus]
8. Rinderpest virus
9. [Teschen disease virus (Porcine enterovirus type 1)]
10. [Vesicular stomatitis virus]
11. [African horse sickness virus]
12. [Blue tongue virus]

C. PLANT PATHOGENS

1. [Colletotrichum coffeanum var. virulans]
2. [Dothistroma pini (Scirrhia pini)]
3. [Erwinia amylovora]
4. [Ralstonia solanacearum]
5. [Puccinia graminis]
6. [Sugar cane Fiji disease virus]
7. Tilletia indica
8. Xanthomonas albilineans
9. [Xanthomonas campestris pv citri]
10. [Sclerotinia sclerotiorum]
11. [Peronospora hyoscyami de Bary f.sp. tabacina (Adam) skalicky]
12. [Claviceps purpurea]

[Thrips palmi Karny
Frankliniella occidentalis]⁵⁷

D. TOXINS

Bacteriotoxins

1. Botulinum toxins
2. Clostridium perfringens toxins
3. Staphylococcal enterotoxins
4. Shigatoxins

Phycotoxins

1. Anatoxins
2. Ciguatoxins
3. Saxitoxins

Mycotoxins

1. Trichothecene toxins

Phytotoxins

1. Abrins
2. Ricins

Zootoxins

1. Bungarotoxins

[Definition of some terms]

Morbidity: Ratio of [new] cases of disease to total population over certain period of time in the infected area;

Contagiousness: Capability to be communicable;

57. It was suggested that since these items are not agents or toxins they should be discussed in an appropriate section.

Incapacity: Lack of physical or intellectual power;

Mortality: Ratio of dead to total population over certain period of time in the infected area.]

II. LIST OF EQUIPMENT⁵⁸

The following list of equipment shall be a component of the reporting format for facilities declared pursuant to Article III, section D [and as an illustrative list of equipment in the context of a facility investigation]. [It may also be used as provided for in Annex D, section III, paragraph 38.]

[1. Dynamic, static and explosive aerosol chambers designed or used for the dissemination of aerosols of microorganisms [or toxins of particles mass median diameter not exceeding 10 micrometres].

(a) Total chamber working volume range which applies to equipment present:

up to 0.2 m ³	Yes / No
0.2 - 1.9 m ³	Yes / No
2 - 4.9 m ³	Yes / No
5 - 10 m ³	Yes / No
over 10 m ³	Yes / No

(b) Have any been operated at any time during the year

under high biological containment	under maximum biological containment
Yes / No	Yes / No

[1 *bis* Aerosol chambers designed or used for the dissemination of aerosols of microorganisms or toxins [and simulants].]

(a) Are dynamic aerosol chambers present:

Yes / No

If Yes, complete the following:

(i) Specify volume(s) of chamber(s) present:

58. A list of equipment may also have utility in the context of [any] guidelines on [all] transfers of dual-use items.

less than 0.2 m ³	Yes / No
0.2 - 5 m ³	Yes / No
5 - 30 m ³	Yes / No
over 30 m ³	Yes / No

- (ii) Were any of the aerosol chambers used at any time during the previous calendar year:

under high biological containment	under maximum biological containment
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Yes / No

Yes / No

- (b) Are static aerosol chambers present:

Yes / No

If Yes, complete the following:

- (i) Specify volume(s) of chamber(s) present:

up to 0.2 m ³	Yes / No
0.2 - 1.9 m ³	Yes / No
2 - 4.9 m ³	Yes / No
5 - 10 m ³	Yes / No
over 10 m ³	Yes / No

- (ii) Were any of the aerosol chambers used at any time during the previous calendar year:

under high biological containment	under maximum biological containment
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Yes / No

Yes / No

- (c) Are explosive aerosol chambers present:

Yes / No

If Yes, complete the following:

(i) Specify volume(s) of chamber(s) present:

less than 0.2 m ³	Yes / No
0.2 - 5 m ³	Yes / No
5 - 30 m ³	Yes / No
[30 - 100 m ³	Yes / No
over 100 m ³	Yes / No]

(ii) Were any of the aerosol chambers used at any time during the previous calendar year:

under high biological containment	under maximum biological containment
Yes / No	Yes / No

]

[1 *ter* Aerosol chambers (either static, dynamic, or explosive)

Present
 Utilized
 Used in high biological containment or higher
 Not present

If present or utilized, respond to the following questions:

(a) Indicate the type(s) of activities conducted by or in these aerosol systems or chambers.

Static tests (*Study of aerosol properties*)
 Dynamic tests (*Study using aerosol flows*)
 Explosive tests (*Explosive/shock wave dissemination of aerosols*)
 Other (specify)

(b) What is the volume of the largest chamber used?

Static

Equal to or less than 10 cubic metres
 More than 10 cubic metres
 Not applicable, no static chambers used

Explosive

- Equal to or less than 10 cubic metres
- More than 10 cubic metres
- Not applicable, no explosive chambers used

Dynamic

- Equal to or less than 10 cubic metres
- More than 10 cubic metres
- Not applicable, no dynamic chambers used]

2. Equipment designed or used to generate aerosols of microorganisms or toxins [and simulants].

(a) Form of source material used to generate aerosol(s) (check all that apply):

- liquid
- solid
- not applicable

(b) Mass median diameter of aerosol particles generated (check all that apply):

- less than 10 microns
- 10 - 20 microns
- over 20 microns

(c) For which purpose was the equipment used:

- | | |
|---------------------------|----------|
| Aerosol chambers | Yes / No |
| Open-air release | Yes / No |
| With experimental animals | Yes / No |
| Not applicable | |

3. Aerosol analytical equipment to determine the size of particles up to 20 micrometers in diameter.

Present: Yes / No

[4. Aggregate fermenters/bioreactors capacity.

(a) Volume range.

Specify which range applies:

up to 100 litres	Yes / No
101-1,000 litres	Yes / No
1,001-10,000 litres	Yes / No
10,001-100,000 litres	Yes / No
over 100,000 litres	Yes / No

(b) Specify the volume of the largest fermenter/bioreactor.]

5. Fermenters/bioreactors for batch operation with a volume over [300] litres.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

primary production containment	under high biological containment	under maximum biological containment
Yes / No	Yes / No	Yes / No

[5 bis Indicate the presence, utilization, and containment usage of the following equipment at the declared facility (check where applicable):

(a) Fermenter(s) with total/internal volume exceeding [50] litres:

- Present
- Utilized
- Used in high biological containment or higher
- Not present

(b) Bioreactor(s) with total/internal volume exceeding [50] litres:

- Present
- Utilized
- Used in high biological containment or higher
- Not present

(c) Chemical reactors:

- Present
- Utilized
- Used in high biological containment or higher
- Not present]

6. Equipment for continuous or perfusion growth of microorganisms with a volume over ... litres.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

primary production containment	under high biological containment	under maximum biological containment
Yes / No	Yes / No	Yes / No

7. Self-sterilizable centrifuges for continuous or semi-continuous operation with a throughput capacity of over 100 litres per hour.

(a) Present: Yes / No

(b) Have any been operated at any time during the previous calendar year

primary production containment	under high biological containment	under maximum biological containment
Yes / No	Yes / No	Yes / No

[7 bis Continuous centrifuge(s) that are self-sterilizable, with throughput capacity greater than 100 litres per hour:

- Present
- Utilized
- Used in high biological containment or higher
- Not present]

8. Cross-flow or tangential filtration equipment with a filter area of over 2.5 m².

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
Yes / No	Yes / No	Yes / No

[8 bis Cross-flow filtration equipment with filter area of over 5 square metres:

Present
 Utilized
 Used in high biological containment or higher
 Not present]

[8 ter Tangential filtration equipment with filter area of over 5 square metres:

Present
 Utilized
 Used in high biological containment or higher
 Not present]

9. Freeze-drying equipment with a condenser capacity of over 5 kg of ice in 24 hours.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
Yes / No	Yes / No	Yes / No

(c) With steam sterilization: Yes / No

[9 bis Freeze dryer(s) with condenser capacity of over 5 kg of ice in 24 hours:

- Present
- Utilized
- Used in high biological containment or higher
- Not present]

10. Cell disruption equipment capable of continuous operation without the release of aerosols with a flow rate greater than 10 litres per hour.

- (a) Present: Yes / No
- (b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
Yes / No	Yes / No	Yes / No

11. Spray drying equipment.

- (a) Present: Yes / No
- (b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
Yes / No	Yes / No	Yes / No

[11 bis Spray dryer(s):

- Present
- Utilized
- Used in high biological containment or higher
- Not present]

[12. Drum drying equipment.

- (a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
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Yes / No	Yes / No	Yes / No
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]

[12 bis Drum dryer(s):

Present
 Utilized
 Used in high biological containment or higher
 Not present]

13. Biological safety cabinets Class III or Class I with accessories for conversion to Class III.

Present: Yes / No

14. Flexible film isolators or other cabinets with air handling characteristics equivalent to Class III and anaerobic boxes.

Present: Yes / No

[15. Biological safety cabinets Class II.

Present: Yes / No]

16. Equipment for microencapsulation of microorganisms or toxins.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
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Yes / No	Yes / No	Yes / No
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[16 *bis* Microencapsulation equipment:

- Present
- Utilized
- Used in high biological containment or higher
- Not present]

[17. Automatic DNA sequencing equipment.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
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Yes / No	Yes / No	Yes / No
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[18. Automatic DNA synthesizer.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
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Yes / No	Yes / No	Yes / No
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]

[19. Automatic peptide sequencing equipment.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary production containment]	under high biological containment	under maximum biological containment
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Yes / No

Yes / No

Yes / No

]

[20. Automatic peptide synthesizer.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary
production
containment]

under high
biological
containment

under maximum
biological
containment

Yes / No

Yes / No

Yes / No

]

21. Milling equipment having a capacity of milling grain with mass median diameter less than 10 micrometres.

(a) Present: Yes / No

(b) Has any been operated at any time during the previous calendar year

[primary
production
containment]

under high
biological
containment

under maximum
biological
containment

Yes / No

Yes / No

Yes / No

[21 *bis* Milling equipment with grain size capacity of less than 10 micrometres:

___ Present

___ Utilized

___ Used in high biological containment or higher

___ Not present]

22. Plant inoculation cabinets/chambers providing quarantine.

Total cabinet/chamber working volume range which applies to equipment present:

up to 1 m³

Yes / No

1-3 m ³	Yes / No
over 3 m ³	Yes / No

23. Cabinets/chambers designed or used for rearing insects.

(a) Total cabinet/chamber working volume range which applies to equipment present:

up to 3 m ³	Yes / No
over 3 m ³	Yes / No

(b) Have any been operated at any time during the previous calendar year under quarantine

Yes / No

[24. Indicate the presence, utilization, and containment usage of the following equipment at the declared facility (check where applicable):

(a) Incubator(s):

- Present
- Utilized
- Used in high biological containment or higher
- Not present

(b) Autoclave(s):

- Present
- Utilized
- Used in high biological containment or higher
- Not present

(c) Self-contained breathing apparatus for other than fire-fighting purposes:

- Present
- Utilized
- Used in high biological containment or higher
- Not present]

III. [THRESHOLDS]

[Specific threshold quantities of biological materials stored at facilities for the purposes of developing and testing means of protection against BW shall be established on the basis of the following characteristics:

- Characteristic “a” - effective dose (ED₅₀)⁵⁹ of an agent with the highest virulence (cells or plaque forming units)⁶⁰;
- Characteristic “b” - genuinely achievable concentration of the agent in biological material (cells/ml or plaque forming units/ml)⁶¹;
- Characteristic “d” - maximum quantity of biological material containing this agent, which can be held at the facility at one time (kg)⁶².

Based on these values the ED₅₀ quantity of this agent (“K” value) which can be held at the facility at one time shall be calculated as follows:

$$K = d \times 1000 \times b/a$$

The quantity of another biological material containing another agent, or the same one with a different virulence or concentration, that can be held at the facility at one time shall be determined by way of inserting the actual concentration and ED₅₀ of the agent (ED₅₀ values are given in table) into the following formula:

$$M = K \times ED_{50}/C \times 1000, \text{ where}$$

59. ED is an effective dose of a biological agent (LD₅₀, ID₅₀) determined through experiments on model animals with the use of certain means of infection under normal conditions.

60. Specific value of the parameter is to be agreed upon in advance.

61. Ibid.

62. Ibid.

- M is the quantity of biological material containing the agent of a given virulence and concentration which can be held at the facility at one time (kg);
- C is the concentration of the agent in biological material (cells/ml or plaque forming units/ml).

Value of effective doses of biological agents

Biological agent	Experimental animal	Method of infection	Effective dose
1	2	3	4
Crimean-Congo haemorrhagic fever virus	white mice	intracerebrum	0,1 PFU ⁶³
Chikungunya virus	white mice	intracerebrum	0,5 PFU
Eastern encephalitis virus	white mice	intracerebrum	0,1 PFU
Ebola virus	white mice guinea pigs	intracerebrum intraperitoneum	0,3 PFU 0,1 PFU
Hanta virus	rats	aerogenic	0,5 PFU
Japanese encephalitis virus	white mice	intracerebrum	0,01 PFU
Junin virus	guinea pigs	intraperitoneum	0,02-150 PFU
Lassa fever virus	guinea pigs	hypodermic	0,3 PFU
Machupo virus	guinea pigs	hypodermic	2 PFU
Marburg virus	guinea pigs	intraperitoneum	0,1 PFU
Rift Valley virus	white mice white mice white mice	intracerebrum intraperitoneum aerogenic	0,03 PFU 3 PFU 0,2-0,3 PFU
Tick-borne encephalitis virus (Russian spring-	white mice white mice	intracerebrum	0,01 PFU

63. PFU - plaque forming unit.

Biological agent	Experimental animal	Method of infection	Effective dose
1	2	3	4
summer encephalitis virus)		intraperitoneum	0,1 PFU
Variola virus (Smallpox virus)	rabbits	aerogenic	15 PFU
Venezuelan encephalitis virus	white mice guinea pigs	hypodermic intraperitoneum	0,3 PFU 3 PFU
Western encephalitis virus	white mice white mice	intracerebrum intraperitoneum	0,03 PFU 1 PFU
Yellow fever virus	M. mulatta	aerogenic	0,5 PFU
Kyasanur Forest fever virus			
Bacillus anthracis	white mice guinea pigs	hypodermic hypodermic	10 cells 30 cells
Brucella spp.	white mice	hypodermic	5 ... 20 cells
Chlamydia psittaci	chicken embryo		1000 cells
Clostridium botulinum			
Francisella tularensis	white mice	hypodermic	1..10 cells
Pseudomonas mallei	golden hamsters	hypodermic	10..100 cells
Pseudomonas pseudomallei	white mice golden hamsters guinea pigs	hypodermic hypodermic hypodermic	10 cells 10 cells 10 cells
Yersinia pestis	rats white mice	hypodermic hypodermic	5 cells 15 cells
Coxiella burnetii			
Rickettsia prowazekii			

Biological agent	Experimental animal	Method of infection	Effective dose
1	2	3	4
Rickettsia rickettsii			

]

[For toxins, three general categories could be considered based on their LD₅₀. Accordingly for the specific measure of declaration, the following thresholds could be envisaged for each category of the toxins:

Group 1: Toxins with LD₅₀ of less than 1 microgram/kg, such as:

- Botulinum toxin;
- Neurotoxin (Shigella toxin);
- Tetanus toxin (Clostridium tetani).

Declarations are required for more than 5 milligram of these toxins.

Group 2: Toxins with LD₅₀ of between 1 and 5 microgram/kg, such as:

- Abrin (A. precatorius);
- Enterotoxin (Staphylococcus aureus);
- Ricin (Ricin communis);
- Saxitoxin (Ganyaulax catanella).

Declarations are required for more than 100 milligram of these toxins.

Group 3: Toxins with LD₅₀ of between 5 and 15 microgram/kg, such as:

- Tetrodotxin (Spheroides rufripes);
- Trichothecene mycotoxin.

Declarations are required for more than 500 milligram of these toxins.

(The level of toxicity and/or LD₅₀ is based on the experiment on the animals.)⁶⁴

[Threshold quantities of toxin containing materials stored at facilities for the purposes of developing and testing means of protection against BW shall be determined on the basis of the following characteristics:

64. The toxins have been selected among those reflected in the list of pathogens and serve only as examples.

- a - Effective dose (ED₅₀) of the toxin reduced to 100 kg mass (micrograms);
- b - Threshold quantity of effective doses of the toxin stored at the facility;
- c - Toxin concentration in biological material (microgram/ml);
- m - Threshold quantity of toxin containing material (kg).

With these characteristics in mind, the quantity of a toxin containing material that can be stored at a facility at one time shall be calculated as follows:

$$m = b \times a/c \times 1000.$$

Values of “a” and “b” parameters shall be agreed upon in advance.

Example:

The ED₅₀ value of botulinum toxin has been agreed upon at the level of 100 micrograms.

The agreed threshold quantity of effective doses of toxins authorized for storage at a facility at one time shall be 300 ED₅₀.

Actual toxin concentration in the material shall be 10 microgram/ml.

Inserting the appropriate values into the formula we arrive at:

$$m = 300 \times 100/10 \times 1000 = 3 \text{ kg.}]$$

IV. PROGRAMMES AND FACILITIES

V. DECLARATION FORMATS