Guidelines for the implementation of Action B2

EU CBRN action plan

March 2014

Contents

1. Foreword

On 24 June 2009 the commission adopted its communication on strengthening chemical, biological radiological and nuclear (CBRN) security in the European Union (EU). The EU CBRN Action Plan (1), which was based on the findings of a CBRN Task Force established by the Commission in February 2008, involved both public and private stakeholders.
The EU CBRN Action Plan is aimed at strengthening CBRN security in the European Union. Its overall goal is to reduce the threat and damage from CBRN incidents of accidental, natural and intentional origin. The EU CBRN Action Plan is broadly based on all-hazard approach, including terrorist threats, and contributes to the implementation of the EU Counter Terrorism Strategy (2).

The goal #2 "***Enhance the security of high risk CBRN materials and facilities***" of the first chapter (Prevention) of the EU CBRN action plan contains 4 specific biological actions (B1, B2, B3 and B4).

The B2 action is described as follow:

Action B.2

The Member States should establish:

• a registry of facilities possessing any of the substances on the EU list of high risk biological agents and toxins within each Member State while allowing access to law enforcement, taking security requirements into account;

• a process to verify whether security arrangements of facilities are adequate, including diagnostic laboratories handling and possessing any of the EU list of high risk biological agents and toxins;

• a mechanism within facilities storing biological agents and toxins on the EU list of high risk biological agents and toxins to regularly review the need of such biological agents and toxins while keeping a good record of stored materials.

Involved actors: MS/ Commission/relevant stakeholders
Implementation period: from 2010-2014

This document is a guide which was prepared in order to assist Member States to implement the B2 action and bring them into compliance with UN Security Council Resolution 1540 (UNSCR 1540) and the Biological and Toxin Weapons Convention (BTWC) (3-4). The recommendations described in this guide were developed by a group of European experts (all member of a public institution) from the following countries:
Denmark, France, The Netherlands, Sweden, the United Kingdom and Switzerland (as invited member). France was the leading country for this initiative and three workshops were organized in Paris in 2013 to elaborate this guide. The workshops were funded by the European Commission.

The final review/endorsement round for this document has been closed during the final workshop in Brussels on 25-03-2014.

Comments and suggestions from the Member States are welcome and should be addressed to the EC-Home Affairs DG (EC-HOME).

2. Introduction

Each Member State is free to determine its biosecurity policy, i.e. the degree/level of implementation of biosecurity guidelines, code of conducts and measures. Laws and executive orders are important to ensure a certain minimum biosecurity level and to allow penalties against offenders. Biosecurity legislation is needed to a certain extent to guarantee biosecurity and this is the choice of each Member State to implement the recommendations described in this guide.

This document must be seen as a toolkit of what can be added in the regulatory framework to reinforce biosecurity. It highlights some basic strategies for assisting Member States to:

- create a registry of facilities possessing any of the substances on the EU list of high risk biological agents and toxins (see appendix I),
- reinforce the law regarding those facilities, taking security requirements into account,
- define a process to verify whether security arrangements of facilities are adequate (assessment and/or inspection),
- persuade facilities to keep a good record of stored materials and encourage those facilities to regularly review the need of the high risk biological agents and toxins.

Those recommendations have been developed by a group of experts, representatives of the field of human, plant and animal pathogens. The objective was to develop guidelines for Member States to complement the CWA 15793 laboratory biorisk management standard (5) which describes a management system approach at the level of the organization to effectively identify, monitor and control the laboratory biosafety and biosecurity aspects of its activities. Those guidelines might not be relevant to enhance the overall security of plant pathogens, however they could help to reinforce biosecurity by using existing biosafety measures which are already implemented in the EU countries due to both 2000/29/EC and 2008/61/EG directives (6-7).

In the appended documents (appendix II), several models of biosecurity measures which are already applied in several European countries and in Switzerland, are presented.

3. Terms and definitions

Main sources: CWA 15793 CEN workshop agreement on laboratory biorisk management (5).
CWA 16335 CEN workshop agreement on biosafety professional competence (8)

Accident: unintended event giving rise to harm
Note: an accident is an incident which has resulted in harm.

Biorisk: combination of the probability of occurrence of harm and the severity of that harm where the source of harm is a biological agent or toxin
Note: the source of harm may be an unintentional exposure, accidental release or loss, theft, misuse, diversion, unauthorized access or intentional unauthorized release.

Biosafety: biosafety describes the containment principles, technologies and practices that are implemented to prevent the unintentional exposure to biological agents and toxins, or their accidental release

Biosecurity: biosecurity describes the protection, control and accountability for biological agents and toxins within laboratories, in order to prevent their loss, theft, misuse, diversion of, unauthorized access or intentional unauthorized release

Biosecurity manager: individual who has a broad range of competences and abilities to advice management and personnel on the secure use of biological material and to manage and support the development and implementation of relevant biosecurity management programmes or systems
Note: this individual may be employed under a variety of titles such as biosafety/biosecurity officer, biosafety/biosecurity advisor, biosafety/biosecurity manager, biosafety/biosecurity coordinator, biorisk management advisor.
(adapted from CWA 16335:2011)

Facility: operational unit and associated buildings and equipment used to manage high risk biological agents and toxins
Note: this includes the laboratory, together with the supporting infrastructure, equipment and services including ancillary rooms such as airlocks, changing rooms, sterilizing rooms and storage rooms.

Genetically modified microorganism (GMM): microorganism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination

Hazard: source, situation or act with a potential for causing harm

Incident: event with a potential for causing harm

Inspection: conformity evaluation by observation and judgement accompanied as appropriate by measurement, testing or gauging

Laboratory: room within a facility, designated for work on biological agents and/or toxins

Microorganism: microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material including viruses, viroids, animal and plant cells in culture

Organization: company, corporation, firm, enterprise, authority or institution, or part or combination thereof, whether incorporated or not, public or private, that has its own functions and administration
Note: for organizations with more than one operating unit, a single operating unit may be defined as an organization

Register: a database of facilities possessing a formal or official recording of items, names, or actions

Risk assessment: process of evaluating the risk(s) arising from a hazard(s), taking into account the adequacy of any existing controls and deciding whether or not the risk(s) is acceptable

Top management: top management includes officers (Director General, Chief Executive Officer, Chief Operating Officer, Chief Financial Officer, scientific manager of the operating unit) and Directors of the organization

Toxin: substance, produced by a biological system, which in small or moderate amounts produces an adverse effect in humans, animals or plants. This definition includes substances and materials which may be contaminated with toxins

4. Scope

4.1. Establishment of a national list

As the first step for the implementation of the B2 action, Member States need to define the scope of the biological material that is subject to governmental control. Each Member State should establish a list of biological agents and render it public by publication for instance in an executive order. There are several possibilities to design such a list:

1. The national list could be based on biosafety risk groups (e.g. risk groups 3 and 4). If a biological agent is included in one of the risk groups selected, it is automatically included in the list of materials that are under governmental control. However biological risk groups have been defined only for human pathogens and agents which represent a threat for animals or plants are not included. Moreover toxins which have potential for being used for malicious purposes are not listed in the risk groups (European directive 2000-54-EC (9)).
2. Several lists of high risk biological agents and toxins already exist and could be used by Member States. For instance the Australian Group (AG) list which has been developed for the harmonisation of export controls is broadly used. Moreover, Member States together with the Commission have also established their own list (see appendix I). This list has been designed for official use and can be shared with public (and private) stakeholders but on a need-to-know basis only. The use of the EU list could be useful in order to harmonize security arrangements

of facilities all over Europe, however not all EU countries have accepted and are using this list (see appendix II).

3. A specific national list could be designed on the base of a risk assessment analysis taking also into account the existing list developed for international regulation like the AG list or the EU list. The work may include an agreement on the criteria and methods to be used for establishing such a list, including quantitative thresholds for toxins. Specific national criteria (e.g. high sensitivity of the population to a specific pathogen, lack of counter measures against biological threats) could be used to define the list.

To be relevant and representative of special security concern, the list must be regularly reviewed. **We recommend to form an advisory board of biosafety and biosecurity experts to regularly reassess the list**. This advisory board should have an expertise in human, animal and plant pathogens and must be composed of public and private stakeholders. Adding a new high risk biological material in the list might generate extra workload for the administration in charge of controlling the facilities. The more extensive the list of agents included for regulatory oversight, the more complex and expensive the program will be (10). It would be one of the missions of the advisory board to asses the impact of adding a new agent in the list. It is important to define national criteria and to review frequently the list based on risk assessment results realize by the advisory board.

4.2. Genetically modified microorganisms and genetic elements

To supervise every facility with a potential biological threat, it would be also necessary to include Genetically Modified Microorganisms (GMM) in the scope. **We recommend as a first step to control GMM if a high risk microorganism from the list in place has been used as the recipient or if it is used as parental microorganism for the genetic modification**.

The actual technology allows to recreate an infectious agent *in vitro* solely by following instructions from a written sequence (11). The sequences of high risk biological agents are available on the web without any restriction access and could be used for non pacific purposes. In this context it might therefore be necessary, to include genetic elements (from synthetic or biological origin) in the scope of the materials that should be under governmental control. The council regulation n°428/2009 (12) setting up a Community regime for the control of exports, transfer, brokering and transit of dual-use items and which is based on the AG list includes Genetically Modified Organisms (GMO) or genetic elements that contain nucleic acid sequences associated with pathogenicity. Genetic elements that contain nucleic acid sequences coding for any of the toxins specified or even sub-units of toxins are also included.
Based on a risk assessment, each Member State should decide if it is relevant for them to include genetic elements in their own list.

4.3. Exemptions

It might be necessary for Member State to refine the list in order to implement a security program that is not too intrusive and that may not inhibit essential scientific productivity. However the impact of every exemption implemented must be evaluated from a security point of view. Every Member State should be able to justify the reason of the exemptions. Among European countries, the following exemptions to the legislation are frequently encountered:

- toxins which are pharmaceutical specialties as soon as they are under a licensing system for human or animal use in the treatment of diseases and which is permitted by a governmental authority to be marketed as a pharmaceutical product,
- pathogens which are modified to be used as pharmaceutical specialties as soon as they are under a licensing system for human or animal use in the treatment of diseases and which is permitted by a governmental authority to be marketed as a pharmaceutical product (e.g. vaccines),
- a limited amount of toxin which is not lethal for human,
- a toxin which consists only as an immunotoxin,

and for diagnostic:

- any animal, alive or dead or anything that was part of it which is not deliberately infected by a pathogen or carries a pathogen as a deliberate act, and when not stored for more than 30 days,
- any human corpse or any part of it who is not deliberately infected by a pathogen or carries a pathogen as a deliberate act, and when not stored for more than 30 days,
- any food, food source or feeding stuff which is not deliberately infected by a pathogen or carries a pathogen as a deliberate act and when not stored for more than 30 days,
- any environmental sample which is not deliberately infected by a pathogen or carries a pathogen as a deliberate act and when not stored for more than 30 days.

5. Inventory of facilities

5.1. How to establish a national registry

The first objective of the B2 action is to set up a registry of facilities possessing any of the substances from the scope. Each Member State is responsible for the establishment and the maintenance of its own register. To establish this register, the biological agents may be imported, held, produced, used and stored only if a relevant permit has been obtained or if notification has been done. Permits and authorization must be delivered by authorities who are under the supervision of one or several competent ministries, for instance:

- the ministry of health,
- the ministry of home affairs,
- the ministry of foreign affairs,
- the ministry of economical affairs,
- the ministry of environment
- the ministry of research
- the ministry of justice
- the ministry of defence,
- the ministry of agriculture.

Local or governmental authorities in charge of delivering the licence or receiving the notifications must maintain the register. The register (database) should contain all the information regarding the licences and notifications. Every Member State could assign the mission to a pre-existing authority or even create a specific agency to address this question. As mentioned in the previous chapter, delivering permits and authorization or receiving notification can represent an extra workload for an already existing administration. Member States can choose to share the responsibility between different authorities (e.g. one being in charge of human and animal biological threats and one being in charge of plant pathogens).

To be relevant, the licence could be delivered to a legal entity that has professional and legitimate grounds for obtaining a permit. **We recommend that the permit mentions at least, the following information**:

- the complete address of the facility. It is important to mention the precise location of the facility (name of the building, level floor etc.),
- the name of a single point of contact, responsible for biosecurity management and/or for scientific management (top manager).

To be functional the register must be updated regularly. **It is recommended to deliver licences which are time limited**.
Since the register must contain all data regarding the facilities possessing the high risk biological substances, the access to this register must be restricted to a limited number of persons. According to national criteria, the register might be classified.
The administration in charge of maintaining the register must be clearly identified. **Moreover, it is recommended that the authorities publish the information regarding the national regulatory scheme on her website in order to advice relevant stakeholders**.

5.2. Diagnostic laboratory

For diagnostic laboratories, different regulations may be in place. Diagnostic labs are important to maintain a public health policy. To allow these laboratories to respond rapidly in case of a pandemic, the biosecurity regulatory framework should be more flexible for them. On the other hand, some diagnostic labs need to store temporally the samples to confirm the investigation. To confirm the diagnostic it may be necessary to conserve some material that can be used as a positive control. **We recommend diagnostic labs to be included in the registry as soon as they keep the samples and/or the culture of the microorganism more than 30 days. Otherwise they can send the material to registered reference labs.**

6. Assessment and security plan

The second objective of the B2 action is to establish a process to verify whether security arrangements of facilities are adequate. To achieve this goal, Member States should promote the implementation of a biorisk management policy (as described in the CWA 15793 laboratory biorisk management standard (5)) at the level of each organization possessing any of the high risk biological agents. The first step is to identify hazards and to perform a risk assessment to identify risks and biosecurity gaps (13).

6.1. Biosecurity assessment

There are different methodologies available for assessing biorisk. **We recommend that each organization implements and maintains a suitable methodology of risk assessment to identify and categorize risks that need to be eliminated or controlled to maintain a good level of biosecurity**. Such a classification can be achieved through the use of a risk matrix identifying likelihood and consequence categories, ordered to illustrate those falling into high, moderate and low zones (5).
However before obtaining such a classification, the hazards must be identified and documented. It is useful to involve in this process a work team with experts in security management. A hazard identification exercise could consist to work on different scenarios/cases like:

- a biological agent, loss, theft or misuse,
- an unauthorized access to the facility,
- an intentional release of a biological agent,
- a vandalism action in the facility executed by activists,
- inside threat,
- civil unrest and war,
- screening and isolation of suspect packages,
- putting pressure on staff to obtain biological agents,
- compromising data regarding the location of the biological agents.

A biosecurity toolkit has been developed in the Netherlands in collaboration with biosafety professionals and other experts. The toolkit aims to enhance biorisk management inside organizations dealing with hazardous biological materials. This toolkit is freely available at www.biosecuritytoolkit.com in English and can be used by an organization as a self-check instrument. The toolkit covers different themes (awareness, personnel reliability, information security, physical measures etc.) which might be useful to identify biosecurity hazards within an organisation working with high risk pathogens.

6.2. Physical security

When vulnerabilities have been identified, the next step is to implement and maintain physical security measures for the cultures, specimens, and the samples potentially contaminated with high risk biological agent.
The top management of the organization is in charge of reinforcing the overall security of the facility. However **we recommend that every Member State develops a process to verify the consistency**

of the physical measures in place in every facility possessing substances from the list. To achieve this, the authorities in charge of delivering licences and authorizations or receiving notifications should also develop, with national experts, physical security guidelines. Though the list of the materials which are under control contains the most dangerous biological agents, the level of physical security required might be different between the substances. **We recommend to develop several security subgroups on the base of the intrinsic hazard of each biological agent and to apply physical security guidelines relating to each security group** in order to ensure national continuity in the way organizations secure their dangerous substances. Where multiple substances are stored or used, security requirements must be achieved in line with the highest risk substance.

The main concepts to secure high risk substances are to implement (a) physical measures to slow down any non-authorized person to access to the substance and (b) reinforce effective controls and monitoring mechanisms to detect any attempt to do so. In other words, access controls are used to limit access to restricted areas only to individuals who have proper authorization and keep track of traffic in and out these areas.

According to the security groups which have been defined, control and monitoring mechanisms should be implemented:

- at the level of storage (fridge, freezer or liquid nitrogen tank),
- and/or at the level of the facility,
- and/or the level of the building.

6.3. Information security

Every organization should identify sensitive information regarding high risk biological agents they possess. Just like the physical measures, vulnerabilities regarding information must be identified and categorized on the base of a risk assessment. Examples of sensitive information may include facility security plans and inventories (written or electronic records), and storage location of high risk biological agents (14). The objective is to limit the access to individuals on a need to know basis. Therefore, the top management of the organization should develop appropriate policies that govern the marking and handling of information and how that information is gathered, maintained, distributed, documented, accessed, shared and stored within the facility and with appropriate counterparts.

Similar to the physical measure, we recommend that every Member State develops a process to verify the consistency of the information security measures in place in every organization possessing substances from the list.

7. Personnel

Top management is mainly concerned by security requirements of a facility possessing substances from the list. It is necessary for the top management of the organization to define the roles and responsibilities of laboratory employees who need to handle, use, store, transfer and/or transport high risk biological agent and the manner in which the organization ensures that individuals are appropriate for their position within the organisation. Recruitment and training are important topics to achieve this. Top management must be trained on biosecurity aspect to be aware of the potential biological threat (8).

On the other hand, it is recommended that Member States implement a process to verify the reliability of those persons. Appropriate controls must be implemented for security evaluation of persons working with specified biological substances. We recommend that every organization appoints a biosecurity manager who can be contacted by the competent authorities for up-to-date information. This person is in charge of implementing effective laboratory biosecurity measures and should liaise with other personnel.

7.1. Personnel recruitment and training

Personnel recruitment and training is the responsibility of the top management of the organization. They have to ensure that qualification, experience and aptitudes relating to biorisk are considered as

part of the recruitment process (together with scientific skills). As mentioned above, the key person for the implementation of a biosecurity culture in the facility is the biosecurity manager. Since this person must play a primordial role in the organization, his recruitment must be a priority for the top management.

The organization should establish laboratory biosecurity training for staff working with high risk biological agents and responsible staff involved in ensuring the security of the laboratory facility. The biosecurity manager and/or the scientific manager shall have sufficient knowledge on training principles in order to understand training needs and to develop, deliver and validate an internal biosecurity training programme.

In order to develop a laboratory biosecurity culture, **we recommend that Member States promote the implementation of a biosecurity academic training for scientists. Such training would help to understand the need for protection of high risk biological agents, equipment, knowledge and the rationale for the laboratory biosecurity measures adopted. It should also include a review of relevant national policies. This would favour the creation of a network within the scientific community to address biosecurity problems and improve the overall security in facilities. The authorities in charge of delivering authorizations or receiving notifications must be involved in the development of a national training program.**

7.2. Personnel reliability

Personnel reliability is an important topic to avoid inside threat and to guarantee the security of the facility and the storage of the substances. Although many organizations regard personnel security as an issue resolved during the recruitment process, it is a discipline that needs to be maintained throughout a member of staff's time in employment.
Although this is the mission of the biosecurity manager and/or the scientific manager to develop a biosecurity culture, they might be limited to perform all security checks for in depth screening of personnel reliability. However the biosecurity manager should know exactly who has access to the high risk biological agents stored in the facility concerned. **We recommend that each Member State implement a formal system for the assessment of personnel reliability. To achieve this, the biosecurity manager should <u>regularly</u> inform the national authorities with the details of the persons having access to the dangerous substances. Authorities must have a process in order to control:**

- **the identity,**
- **references**
- **the immigration status,**
- **the criminal records,**
- **the financial probity.**

It might be necessary for authorities in charge of those security checks to work together with intelligence services, in particular if international scientists work in the facility concerned. Moreover, the intelligence services must be able to verify if the employees are members of an organization hostile to biological research or otherwise fundamentally rejecting social, economic or religious values. Sensibilisation of authorized staff by security services must be useful to create a common culture of security.
If an employee does not comply with security requirements established by the authorities, authorized access to the facility for this employee and the information relating to the facility must be denied immediately by the biosecurity manager.

7.3. Non-core personnel

Particular attention must be paid to non-core personnel (contractors, visitors, students and suppliers) who might have temporarily access to the facility where high risk biological agents are stored. In that case the organization shall ensure that they do not compromise biorisk management of the facility. It is not necessary to transmit the details regarding non-core personnel to competent authorities in order to carry out security checks however, physical security measures or escort procedures should be implemented at the level of the organization to guarantee facility security and sensitive information protection.

8. Biological agents and toxin inventory and information

The third objective of the B2 action is to implement a mechanism within facilities possessing high risk biological agents and toxins to keep a good record of stored material and regularly review the need of possessing such substances. **To set up an effective mechanism, we recommend that Member States encourage the organizations concerned to establish and maintain inventories of the biological substances defined in the scope**. Every Member State can be free to render (or not) mandatory the use of a specific inventory (database) within every organization concerned, but **we recommend that the annual reporting of stocks to the competent authorities to be statutory.**

Records relating to the inventory of high risk biological agents must be stored securely with adequate backup provision.
Establishing an inventory may also present an advantage for the organization on a scientific point of view. In fact scientists working in one of those facilities would have access to the database and decide which strains they could use for scientific experiments.

8.1. Information that should be reported

If the organization is willing to establish a register in order to report to the national authorities, this database must be designed to contain at least the following items:

- the activities of the facility and the quantity of biological substances stored within the facility, including cultures, specimens and other sources (e.g. infected tissues / samples or deliberated infected animals) when stored for more than 30 days,
- any purchase, sale, transfer or disposal of those materials.

To be effective, the inventory must be updated on an ongoing basis. Any authorized substances registered must be related to permits and authorizations delivered by the competent authorities (see chapter 5). This database might also contain the information regarding location of the material and a reliable identification system of the material (e.g. a bar code and/or an identification number if for biosecurity reasons the name of the biological agent is not mentioned on the tube).
In order to encourage the implementation of a register, the competent authorities could design a common database which is then distributed to all organization possessing the high biological agents. Such a tool has the advantage to oblige all the organization licensed to work with a common template for the annual reporting.

8.2. Monitoring of theft, loss and release

To complement the biosecurity regulatory scheme, **we recommend that each Member State sets up a formal mechanism to oblige the organization to inform the competent authorities in case of theft, misuse or loss of the high risk biological agents and toxins.** The system can also be used to monitor accidents or incidents (e.g. suspicion of a release of the authorized substances) within each facility. Monitoring events could give an idea of the behaviour of the registered facilities over time and identify potential recurrent problems (15). Just like a reduction in laboratory accidents may be an indication of better safety practices, a reduction in incidents of loss or theft at biological facilities may be an indication of better security. This monitoring system would help to measure the effectiveness of a biological laboratory monitoring program.

9. Inspection-control

We recommend that Member States ensure that the competent authorities organise onsite facility inspections and other control measures (accreditation) to certify that organizations comply with the biosecurity recommendations described here and to prevent any undesirable consequences. Inspections and controls shall be conducted regularly to determine if the requirements described here are effectively implemented and maintained. Follow up inspections must include the verification of the action taken and the reporting of verification results. Random and unannounced inspections are useful to ensure compliance at all times, not just in time for scheduled inspections.

Whether there is a need to create a specific biosecurity inspection body depends on the organisational structure and priorities in the country. Biosafety inspectors and/or inspectors in charge of controlling the measures for the contained use of GMM (16) may be involved for the biosecurity controls as well. Biosafety and biosecurity complement each other for the management of biorisk and both aspects could be examined during the same inspection.
Inspections must be performed by competent individuals who have no conflict of interest with the organization being inspected. Inspectors must be trained to become competent both on biosafety and biosecurity. Otherwise inspections must be realized by a team of inspectors with different but complementary background (e.g. a biosafety inspector with a security officer).

10. Non-compliance

A biosecurity program established by law and regulations should also clearly describe the penalties for non-compliance. **We recommend that any organization that does not comply with the requirements prescribed by the competent authorities can be exposed to penalties**. Penalties may vary from an administrative decision (e.g. authorization removal) leading to a loss of opportunity to penal sanctions (fines and and/or imprisonment). Opportunity loss might include loss of research grants, or authority to purchase, sale, transfer import or export high risk biological agents. **We recommend also that penalties must be proportional to the regulation violation. Penalties and administrative decisions must be clearly described and well defined in the regulatory corpus**.

11. Costs and benefits of the implementation of the B2 action

Before implementing the B2 action Member Sates would probably examine the costs and benefits of a biological laboratory monitoring program. In the following table the costs and the benefits that the B2 action would generate for organizations and Member States (countries) are listed.

Costs	Benefits
For the organizations	
Administrative fees for licences (if required)	Increases the awareness and the culture of biosecurity
Cost for the implementation of a biorisk management system : • personnel training, • record maintenance, • management.	Improves the biosecurity and biosafety culture
Cost of infrastructure, security should be implemented from the beginning (before the construction of the facility)	Corporate Social Responsibility (CSR)
A case of incident or theft may result in damage to organization reputation	
For Member States	
Personnel costs	Promotion of the global security awareness Compliance with BTWC and UNSCR 1540
Clerical support functions	Reinforces the counter terrorism strategy

National register development and maintenance	Improves the overall biological security of biological laboratory
Travel expenses (for onsite inspection)	Awareness of the high risk biological agents and toxins available on the territory. Critical tool to manage biorisk at the level of the country.

For Member States, implementation and management of an effective biological facility monitoring program can serve to meet the requirement of the Biological and Toxin Weapons Convention (BTWC) which was opened for signature in 1972 and entered into force in 1975 (3) and the United Nations Security Council resolution 1540 which was adopted on April 28 2004 (4).

12. Conclusion

The present document contains recommendations for the implementation of the B2 action from the EU CBRN action plan. It offers Member States a toolbox to help them to develop a biological laboratory monitoring program which is based on the 3 objectives of the B2 action previously mentioned. Examples of a biosecurity measures already implemented in several countries are presented in appendix (see appendix II).

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APPENDIX I

EU List of high risk biological agents[1][2]

This list has been designed for official use and can be shared with public (and private) stakeholders but on a need-to-know basis only.

Threats to humans
Agents:
Bacillus anthracis
Brucella spp.
Burkholderia mallei
Burkholderia pseudomallei
Congo-Crimean haemorrhagic fever virus
Coxiella burnetti
Eastern equine encephalitis virus
Ebola virus
Francisella tularensis A
Japanese encephalitis virus
Junin virus
Lassa fever virus
Machupo virus
Marburg virus
Monkey pox virus
Nipah virus
Sars corona virus
Variola virus
Venezuelan equine encephalitis virus
Vibrio cholerae
Western equine encephalitis virus
Yersinia pestis

Toxins:
Abrin
Botulinum toxins
Clostridium perfringens toxins
Ricin
Saxitoxin
Staphylococcus aureus toxins

Threats to animals
Agents:
African Swine Fever Virus
Bacillus anthracis
Capripoxvirus
Foot and Mouth Disease Virus
Influenza type A Virus (Highly Pathogenic Avian Influenza H5 H7)
Peste des petits ruminants (Morbillivirus)
Rinderpest virus (Morbillivirus)
Vesicular stomatitis virus

Threats to plants
Agents:

[1] The Danish delegation did not participate in the establishment of the list of high risk biological agents with respect to threats to humans.
[2] Switzerland which is member of the B2 working group did not participate in the establishment of the EU list.

Bursaphelenchus xylophilus
Candidatus Liberibacter spp.
Clavibacter michiganensis subsp. Sepedonicus
Fusarium graminearum
Leptinotarsa decemlineata
Microcyclus ulei
Phytophthora ramorum
Puccinia graminis
Puccinia striiformis
Ralstonia solanacearum races 2 and 3
Synchytrium endobioticum
Tilletia indica
Xanthomonas campestris
Xylella fastidiosa

APPENDIX II

Models of biosecurity regulation already applied in several EU countries and Switzerland

Biosecurity measures in France

Since 2001 France has implemented a regulation system to register facilities possessing substances from the French list of the Microorganisms and toxins (MOT). The scope of the legislation is the control of MOT use which is likely to be a public health risk. The list mentions high risk agents and toxins that have been determined to have potential for use as bioweapons. It is closely related to the first part of the EU list (threats to human). For each facility, a person responsible of the biological material should be identified. This person should ask a specific authorization to the French National Agency for Medicines and Health Products Safety (ANSM) in order to handle and/or to store the material. The licenses are valid for a maximum of 5 years and mention 3 main data:

- the name of the older of the license (the person legally responsible of the material),
- the name of the micro-organism or the toxin,
- the address of the facility.

If any of these 3 points changes, the licence is no longer valid.
Before delivering a license, ANSM performs an assessment which contains three steps (Figure 1):

1. reviewing of the criminal record of the applicant, the manager of the facility and the person who will be working with the microorganism or the toxin,
2. assessing competences and skills of those persons,
3. assessing the biosafety and the biosecurity risk control measures of the entity.

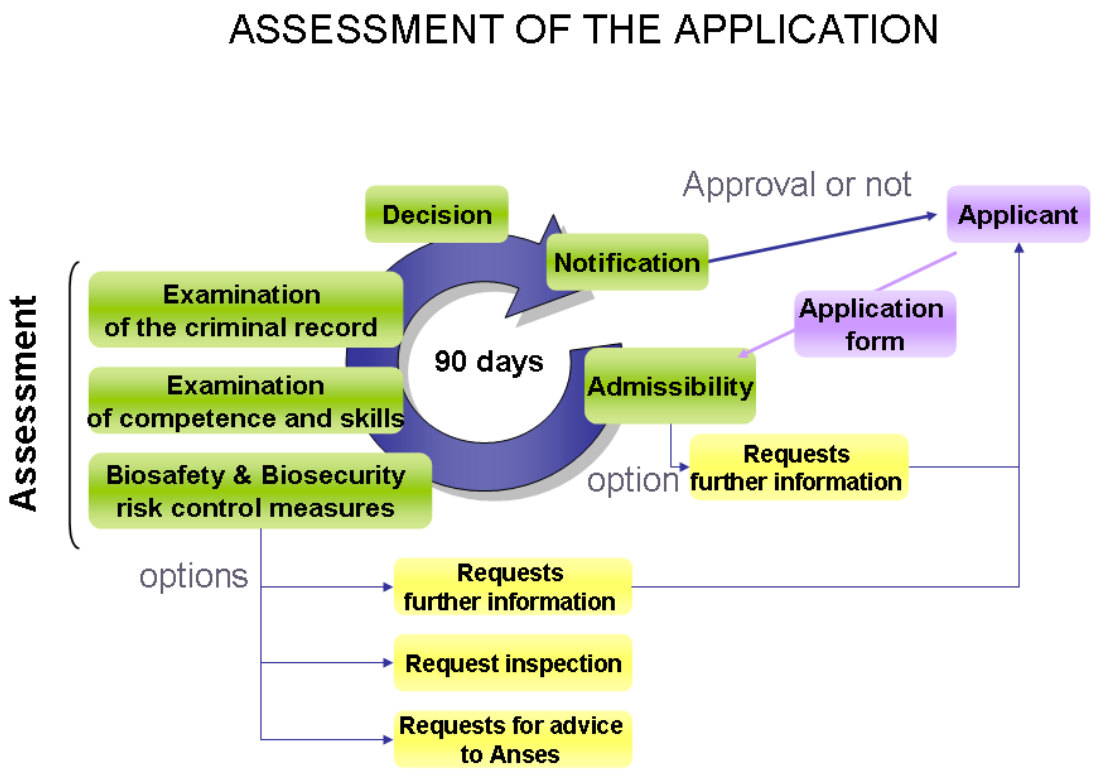


Figure 1: Assessment process before the delivery of a license.

(1) If the applicant, the manager of the facility or any person who will use a MOT in this facility, has committed a crime which is registered in the section 2 of the French criminal record, the license won't be delivered. Section 2 contains a record of most of the crime and offence committed. This section is delivered by the ministry of justice only to the civil service. If the holder of the license or the manager of the establishment commits a crime or an offence after

the issue of the license, this license is no longer valid and the micro-organism and toxin should be disposed or transferred to another facility.

(2) To obtain the license, the applicant should justify of a minimal level of competences and skills. The regulation requires they should have a degree either in medicine, veterinary medicine, pharmacy or biological science (PhD) and that they can justify of 2 years of practice in the field of microbiology during the last 5 years. Otherwise, if an applicant has only a 2 years degree in the field of biology and is able to justify of a 5 years of practice in microbiology over the last 7 years, he has also the possibility to get a license for a microorganism. However the applicant doesn't need to justify of any experience for a license concerning a toxin.

(3) The assessment of biosafety and biosecurity risk control measures is the main part of the assessment. Laboratory biosafety describes the containment principles, technologies and practices that are implemented to prevent the unintentional exposure to MOT, or their accidental release. Laboratory biosecurity describes the protection, control and accountability for MOT within facilities, in order to prevent their unauthorized access, loss, theft, misuse, diversion or intentional release. ANSM has designed a Biorisk Assessment Tool (BAT) which is based on the Failure Modes and Effects Analysis (FMEA) method. This BAT has been designed to help the applicant to identify and quantify the risk in both biosafety and biosecurity aspects. Based on the result of the biorisk assessment, ANSM can request (i) more information to the applicant, (ii) advice from the Agency in charge of animal disease control in France (Anses) or even (iii) inspect the facility.

The decision (approval or rejection of the authorization) should be notify to the applicant in less than 90 days. No response from ANSM after this period means that the application has been rejected.

ANSM has also an inspection body which allows to control on site the security arrangements of the facilities. The inspection could be announced or unannounced, which could be useful for inspectors in case of suspicious activity. During their missions, inspectors control the security protection and the traceability of the biological material. Inspectors realize security assessment of the building, the facility and of the storage condition.
The holder of the license must monitor the biological material which is stored and review it once per year. After this review, he must inform ANSM (before mid of February) of the amount of material stored in the facility. Any theft, loss or release of MOT should be immediately reported to ANSM. The monitoring system, the record of stored material and the adequacy to the annual declaration is also examined during inspection.

ANSM has the possibility to suspend authorizations if the security arrangements are inappropriate or insufficient for storage or use of the microorganisms and toxins. In that case the biological material must be destroyed or sent to another authorized facility. Any person holding or using a high risk micro-organism or a toxin mentioned in the French list without the required license could be sentenced to 3 years in prison and is susceptible to pay penalties (up to 45 000 €).

Biosecurity measures in the Netherlands

Recognizing the need to strengthen biosecurity, the Dutch government has initiated several processes to implement a coordinated biosecurity regime for organizations that work with hazardous or dual-use biological agents to prevent proliferation and misuse.
The Dutch approach to biosecurity involves a coordinated biosecurity regime with several elements including a continuously updated overview of locations in the Netherlands where human, plant, and animal pathogens are stored; overview and adaptation of the current regulatory framework; improved ways of anchorage of biosecurity in organizations, secure sharing of critical information to first responders during a incident and coordination of supervision.

List and inventory
In previous years a national database was established containing an inventory of biological facilities holding listed agents. It comprises human pathogens, animal pathogens and plant pathogens, both genetically modified and wild-type. A practical decision was made for the list of agents, as the EU list was not yet completed at the starting point of the project. The decision was taken to attune to the national lists and to focus on risk groups 3 and 4 agents (a grouping commonly used for biosafety aspects).

Implementation of biosecurity in several national legislations
An overview of the current regulatory framework was made in 2011. The Netherlands are currently exploring how to implement biosecurity into legislation. The following elements will be included in this exploration:

- Mandatory notifications by facilities working with listed agents.
- A standard for security measures at facilities. Starting point is that facilities are primary responsible to apply appropriate biosecurity measures within their organization.
- Obligation to appoint a Biorisk professional, a single point of contact within an organization for all biosecurity-aspects.

Biosecurity Office as national contact point
Recently, the Dutch Biosecurity Office, a national focal point for biosecurity has been installed. This office is tasked to maintain the national inventory of facilities and to raise compliance with the novel Biosecurity-regime. This will be achieved by an active outreach program aimed to assist facilities to raise awareness and resilience to biosecurity risks. The office aims to incorporate good practices from other initiatives, both national and international, such as the BTWC, the EU CBRN Action Plan, CEN CWA 15793 and the Dutch Code of Conduct.

As part of the biosecurity regime a Biosecurity Toolkit was developed in collaboration with biosafety professionals and other experts. The Toolkit aims to enhance Biorisk management inside organizations dealing with hazardous biological materials. The Toolkit, freely available at www.biosecuritytoolkit.com in English and Dutch, can be used inside organizations as a self-check instrument. The outcome of the tool includes suggestions that may improve the biosecurity level of the organization concerned. Results are not stored; information is exclusively available for the user. The Dutch Biosecurity Office has no task in inspection. This is organized by the inspections of several adjacent legislations.

Dual use
In 2007, the Dutch government, together with the Royal Dutch Academy of Arts and Sciences (KNAW) published a “Code of Conduct for Biosecurity”. This code of conduct addresses the biosecurity topics awareness, research and publication policy, accountability and oversight, shipment and transport, etc. for science. In December 2013, the KNAW published the advisory report ‘Improving biosecurity; assessment of dual-use research’ which advices on how to assess dual use research of concern and by whom.

Biosecurity measures in the United Kingdom

Legislation: Part 7, Anti Terrorism Crime and Security Act 2001.

The purpose of the Anti Terrorism Crime and Security Act is to help ensure that Government has the necessary powers to counter the terrorist threat to the UK.

Part 7 and Schedule 5 of the Act sets out the obligations on occupiers and managers of laboratories and other premises keeping or using stocks of specified disease causing micro organisms and toxins (listed in Schedule 5). The legislation currently encompasses human and animal pathogens but not plant pathogens, pests or toxic chemicals. The following is a brief summary of the Act:

Pathogens and toxins are covered:

- Annex A set out the pathogens and toxins included within the scope of the Act.
- The pathogens and toxins on the list are considered by an expert panel who consider a range of factors including: the extent to which the UK population is vulnerable to infection by the pathogen; how infectious the pathogen is when spread by air or through contamination of food or water supplies; the extent to which the disease caused by the pathogen is transmitted from person-person; the availability of measures, such as vaccines, to deal with potential incidents; the severity and duration of illness caused by the pathogen, including the availability of treatment; how long the pathogen is able to survive in the environment; and how easy it is to grow, and store, the pathogen.
- Consideration is also given to existing lists including the 'Australia Group' list of animal pathogens for export control; other organisms from the UK Advisory Committee on Dangerous Pathogens (ACDP) Categorisation of Pathogens; and the OIE (World Organisation for Animal Health) list of animal pathogens.

Requirements of the legislation:

- It is the duty of a site occupier to make a notification to the Secretary of State prior to keeping or using and Schedule 5 Dangerous substances. This must be done one month prior to taking possession of the dangerous substance and must include details of the premises of the intended use or storage and also of any building to which the premises is attached.
- Information about the security of the dangerous substance must be provided to police. This details substance which is kept there and any measures taken to ensure the security of it.
- Managers of laboratories and other premises, on request, must provide police with details of persons with access to the dangerous substances held there. In some cases, depending on the containment level of the material, individuals with access may require security vetting.

Powers:

- If the current security of the premises is not considered to meet the required standard following an inspection then a police office can require improved security measures be put in place.
- Where there are reasonable grounds to believe that security measures are not being implemented, the Secretary of State may require the dangerous substance to be disposed of.

Exemptions:
There are exemptions to the legislation which are provided for by the Statutory Instrument 1281 of 2002.

- A pathogen or toxin which exists in the form of a medicinal product.
- A pathogen which is modified for use to be administered to one or more human beings or animals for a medicinal purpose.
- A pathogen which is kept in a way that it is no longer in a state that will allow it to be propagated.
- A pathogen which forms part of a clinical specimen for diagnostic purposes.

- A diagnostic specimen which is kept for no longer than is reasonably practicable after diagnosis. (there is no specified time limit for this).
- A toxin which is less than 5 milligrams
- A toxin which consists only as an immunotoxin.
- Any animal, alive or dead or anything that was part of it.[3]
- Any human corpse or any part of it.[1]
- Any food, food source or feeding stuff.[1]

Practical Implementation:

Notifications of intention to keep or work with Schedule 5 Dangerous substances are made to the Secretary of State via email to the Home Office[4]. This notification is passed to the National Counter Terrorism Security Office[5] (NaCTSO), who contacts the individual responsible for the notification to ascertain their intentions, which dangerous substance is to be kept and determine that the notification has been properly submitted. Once the legitimacy of the notification is established, NaCTSO forward the initial details of the request to the police Counter Terrorism Security Advisor (CTSA) department within the police force area covering the premises.

All substances listed on Schedule 5 which are worked with at Containment levels 2 and 3 have been grouped within 3 Security groups A, B and C to ensure high risk pathogens are dealt with in a risk commensurate way. NaCTSO have developed physical security guidelines[6] relating to each of the Security groups, which ensures national continuity in the way laboratories secure their dangerous substances. Where multiple substances are stored or used, security requirements must be achieved in line with the higher risk substance. i.e. If a site has Group A and Group C pathogens then the security must satisfy the requirements of Group A. It should be noted that Schedule 5 substances which are worked at within containment level 4 laboratories, are not included in these Security groups. They will receive bespoke advice directly from NaCTSO.

On receipt of new notification details, a CTSA will visit the premises to survey the existing security measures. This visit will generate a comprehensive written report detailing the findings of the visit. If the security measures fall below those required to satisfy NaCTSO guidelines for the Security group associated with the Dangerous substance to be held, the report will contain requirements and recommendations to bring the overall security up to a standard commensurate with the risk involved with holding the material.

Until the security improvements have been made by the site and inspected by the CTSA, the site is not able to hold or work with the Schedule 5 substance. Once the CTSA has approved the completed security measures to a satisfactory standard then the site is considered to be “Under Notice” and is able to work with dangerous substances up to the Security Group detailed in the survey. The CTSA will then inform NaCTSO that they have a site containing a Schedule 5 Dangerous substance and this will be added to the National list of sites which they manage. Whilst NaCTSO maintain a list of sites containing Schedule 5 material, they do not collate what substances are held at which site, as the purpose of the list is to collate sites and assess security, not to manage individual substances.

CTSAs will then visit the site on an annual basis in order to assess the continuing effectiveness of the security measures. No further notification is needed for subsequent pathogens or toxins taken onto a site as long as they fall within or in a lower risk Security group. Should the site wish to work with a material which is in a higher Security group, then the CTSA should be notified directly in order for a new survey of security measures to be carried out.

[3] Does not apply if the occupier knows or ought to have reasonably known that the subject had been deliberately infected by a pathogen or carries a pathogen as a deliberate act.
[4] Home Office is the lead government department for immigration and passports, drugs policy, crime policy, and counter terrorism and work to ensure visible, responsive and accountable policing in the UK.
[5] NaCTSO is a police unit co-located within the Centre for Protection of National Infrastructure (CPNI.) It is funded by a Home Office grant and works to the Office for Security and Counter Terrorism (OSCT) reporting activity to the Association of Chief Police Officers (Terrorism and Allied Matters) (ACPO TAM).
[6] Security Requirements for Pathogens and Toxins is a restricted document produced by NaCTSO containing physical security standards for Schedule 5 substances. Available from NaCTSO on request.

Biosecurity measures in Switzerland

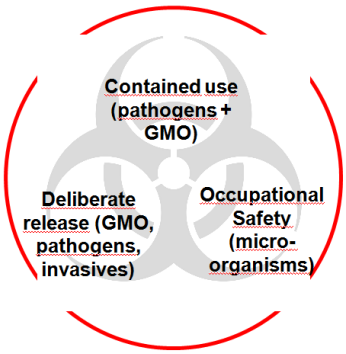
Switzerland has a very good biosafety culture. Since 1999 three Ordinances regulate the handling of organisms in contained systems (contained use), the handling of organisms in the environment (deliberate release) and the protection of employees from dangerous microorganisms (occupational safety). All three Ordinances are closely aligned with the corresponding EU guidelines.

The notification system for activities with organisms subject to a containment obligation (GMO, pathogens and invasive, alien organisms) is very well established. The Biosafety enforcement is supported by an effective and efficient IT system (www.ecogen.ch):

- The project leaders send their notifications (risk class 1 and 2) and applications for authorisation (risk class 3 and 4).
- The enforcement authorities at the federal and cantonal level communicate their opinions
- The competent office files its decision or the authorisation as well as correspondence.
- The cantonal inspection authorities can use ECOGEN in order to document inspection reports.
- The information on all notified and authorised activities that according to the law have to be made public are made accessible in a public module.

The responsible federal authorities (Federal Office for the Environment, Federal Office of Public Health) are aware of the companies that work with high-risk organisms. Specialised cantonal services carry out periodic inspections in the companies; the frequency and scope of the inspections depend on the risks associated with the activities. The specialised cantonal agencies know the companies from inside and in emergencies can coordinate hazardous situations with the intervention forces.

The well-established Biosafety system likewise ensures that a large part of the Biosecurity requirements are fulfilled. Shortcomings in Biosecurity are identified and the adjustments in laws and ordinances are progressed. In this regard, information, persuasion and pragmatic solutions should take priority over rigid regulations. The institutions to be regulated (academic and private research laboratories, production companies and diagnostic laboratories) should be restricted as little as possible in their freedom of research and innovation.



There is no need for extensive or urgent action. At present the following elements of Biosecurity are in discussion, but no decisions have been taken so far concerning the changes in ordinances or acts:

1. *Threat assessment*
   There is still no binding national list of biological high-risk materials which the Biosecurity discussion can focus on. Present alternatives are the *Australia group list* and other published national "select agent lists".
   Various federal offices, agencies and commissions in several departments deal with questions of Biosecurity. A newly created *Biosecurity Platform* facilitates communication and coordination.

2. *Physical security*
   The cantonal Biosafety inspectors check the physical and organisational access controls. However, minimum requirements for physical barriers that allow access to the laboratory or to the production only to authorised personnel are lacking. These requirements should be defined in an implementing ordinance, e.g. by means of a corresponding adjustment of the *contained use ordinance* or in another appropriate ordinance.

3. *Personal security*
   The responsibility for the security clearance of individuals should remain with the companies that work with high-risk organisms. This obligation should be anchored in an adequate ordinance. The cantons would check for compliance in the course of their inspections. In support of this, the Federal Intelligence Service has already embarked on an awareness campaign in various companies.

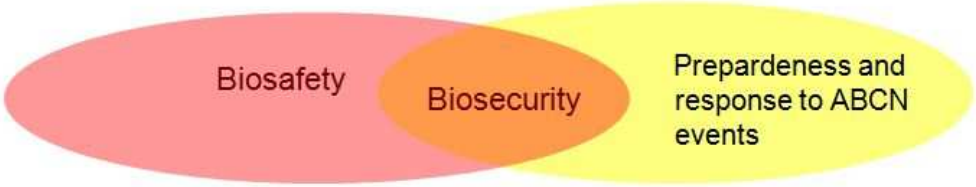
4. *Material control and accountability*
   The storage of high-risk organisms in a physically robust environment with restricted access should be self-evident. This obligation as well as keeping an inventory and an accounting system for cultures (stocks, reference cultures) should likewise be defined in an appropriate ordinance. The inspection would be carried out by the cantonal Biosafety inspectors.

5. *Transport security*
   The transport of organisms on public ways is regulated by the detailed national transport regulations that were adopted from the European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR).
   In contrast to animal and plant pathogens, the importation of high-risk human pathogenic organisms into Switzerland is not subject to authorisation. However, an amendment to the law is under preparation.

6. *Information security*
   Many researchers are often not even aware of the dual-use character of their research that they publish in printed, oral and digital form in project descriptions, raw data and results. The Arms Control B-Service of the Federal Office for Civil Protection (FOCP) and the Federal Intelligence Service have developed awareness programmes that aim to raise Biosecurity awareness in research.

Swiss authorities involved in biosecurity

Federal Departments	Home Affairs	Environment, Transport, Energy+Com.	Economics Education + Research	--	Defence, Civil Protection + Sport	Justice and Police
Federal Offices	Public Health	Environment	Agriculture	National Accident Insurance Fund	Civil Protection	fedpol
	Veterinary		Economic Affairs		Spiez Lab. National ABC Protection	
					Intelligence Service	
Federal Commissions	Expert Committee for Biosafety	Ethics Commit. on Non-Human Biotechnology			ABC Protection	
26 Cantons: Coordination Plattform ABC						



Biosecurity measures in Denmark

Executive Order on securing specific biological substances, delivery systems and related materials[1]

Pursuant to Article 1, Article 2, Paragraph 2, Article 4, Paragraph 1 and Article 6, Paragraphs 2 and 3 of Act No. 474 of 17 June 2008 on securing specific biological substances, delivery systems and related materials, the following has been laid down:

Application

Article 1. The provisions in this Executive Order apply to the biological substances, delivery systems and related materials specified in Annex 1, which are included in the system of export controls specified in the regulation on the European Community system of controls for dual-use items (products and technology), which can be used in association with attacks against people and therefore represent a danger to public safety.
Paragraph 2. The Centre for Biosecurity and Biopreparedness can fully or partially exempt specific biological substances, delivery systems and related materials from being included by the provisions in this Executive Order.

Article 2. The Ministry of Health and Prevention can introduce provisions that stipulate that the provisions set forth in this Executive Order are also to include biological substances, delivery systems and related materials that are not included in Article 1, if the biological substances, delivery system and related materials are considered to be usable in association with biological attacks on people and therefore represent a danger to public safety.
Paragraph 2. Resolutions to include other biological substances, delivery systems and related materials, cf. Article 1, are introduced on the basis of professional guidance from The Centre for Biosecurity and Biopreparedness.

Definitions

Article 3. The following definitions apply in this Executive Order:

1) Biological substances: these include human pathogens, zoonoses and toxins in the form of viruses, rickettsiae, bacteria, toxins or sub-units of toxins, some fungi and specific genetic elements and genetically modified organisms which can be used in association with biological attacks against people and therefore represent a danger to public safety.
2) Possession: to own or have custody of biological substances, delivery systems or related materials included by the Executive Order.
3) Dual use: that biological substances, delivery systems or related materials can be used for both legitimate and offensive purposes.
4) Delivery systems: spraying equipment and other unmanned systems which are capable of disseminating certain biological substances.
5) Storage unit: single unit for storing specific biological substances, i.e. a closed test tube containing a bacterial culture.
6) Professional purpose: research, diagnostics or commercial purposes, which can involve both private and public entities, i.e. university departments, hospital laboratories, biotechnology companies, pharmaceutical entities etc.
7) Related materials: materials, equipment and technology which are covered by the relevant international treaties and agreements or included in national control lists and

[1] The draft Executive Order has been notified in accordance with Directive 98/34/EC of the European Parliament and the Council (the Information Procedure), as amended by Directive 98/a48/EC.

which can be used in the design, development, production or use of biological weapons and their delivery systems.

8) Security plan: plan of the measures or precautions to be implemented to prevent, detect and respond to the theft or misuse of certain biological substances, delivery systems and related materials.
9) Vulnerability assessment: identification of the threats and security weaknesses associated with the possession, production, use, storage, purchase, sale, transport, transfer and disposal of certain biological substances, delivery systems and related materials.
10) Entity: physical or legal entity (an owner and/or independent person), which is responsible for specific biological substances, delivery systems and related materials, including hospitals, institutions, production entities etc. or departments thereof.

General regulations

Article 4. The biological substances, delivery systems and related materials included in the Executive Order may be held, produced, used and stored only if a relevant permit has been obtained.

Permit to hold, produce, use and store etc. certain biological substances, delivery systems and related materials

Article 5. Permits in pursuance of Article 4 are obtained from The Centre for Biosecurity and Biopreparedness.
Paragraph 2. Permits are to be applied for using the forms prepared by The Centre for Biosecurity and Biopreparedness. The forms can be obtained from The Centre for Biosecurity and Biopreparedness or www.biosikring.dk.
Paragraph 3. Permit applications are to be signed by the manager responsible, cf. Article 6. The application is to contain at least the following information:

1) Name and address of person, entity, institution or similar.
2) Department in which the biological substance, delivery system or related materials are present.
3) Name and training of the person responsible for security, cf. Articles 11 and 12.
4) Purpose and required scope of permit, cf. Articles 6 and 7.
5) Information on security circumstances, cf. Article 17.
6) Information on storage circumstances, cf. Article 15.

Article 6. Permits can be issued only to persons, including legal entities, who have professional and legitimate grounds for obtaining a permit for the substances etc. included in Articles 1 and 2.
Paragraph 2. Legal entities are to appoint a natural person who, together with the legal entity, shall be responsible for ensuring compliance with the provisions on the biological substances, delivery systems and related materials included in Articles 1 and 2, cf. Article 11.

Article 7. Permits can be issued for a single biological substance, delivery system or related material or for groups of biological substances, delivery systems or related materials.
Paragraph 2. Permits can be issued for a limited period, or for as long as the activity for which the permit is issued continues, cf., however, Article 9.
Paragraph 3. Permits can also be issued for diagnostic investigations which involve the biological substances included in the Executive Order, cf. Annex 1. These biological substances are to be disposed of within 14 days of the completion date of the investigation, unless permits for the specific biological substances have been obtained.

Article 8. The Centre for Biosecurity and Biopreparedness can, in association with the issuing of permits, set special requirements relating to the storage, disposal, stocking, security circumstances and training of personnel, including persons responsible for security, which supplement the requirements specified in the Executive Order.

Article 9. Changes in an entity's activities which have a significant importance for permit issuance are to be reported to The Centre for Biosecurity and Biopreparedness.

Paragraph 2. The Centre for Biosecurity and Biopreparedness can fully or partially suspend permits issued in accordance with Article 4 if the requirements set pursuant to Article 8 are not complied with or if it is established that the entity no longer complies with permit eligibility conditions.
Paragraph 3. The Centre for Biosecurity and Biopreparedness can fully or partially suspend or change previously issued permits if warranted by significant public safety considerations.
Paragraph 4. The deadlines for the disposal of substances etc. after permits have expired are set by The Centre for Biosecurity and Biopreparedness, cf. Article 8.

Accountability and training

Article 10. Entities are responsible for complying with the regulations specified in the Executive Order and with any conditions or requirements set out in issued permits.

Article 11. Entities are responsible for ensuring that one or more of the entity's staff is appointed as security manager. Such employees are also to be approved by The Centre for Biosecurity and Biopreparedness. Documentation is to be submitted confirming that the staff responsible for security consent to information being obtained on any criminal record they may have.
Paragraph 2. The entity is responsible for ensuring that a suitable replacement is appointed before a security manager leaves his/her position, and that this person is approved by The Centre for Biosecurity and Biopreparedness.

Article 12. The person appointed as security manager by the entity is to attend a training course offered by The Centre for Biosecurity and Biopreparedness. This is provided free of charge.
Paragraph 2. The person appointed as security manager by the entity is to ensure that all persons who have access to the biological substances, delivery systems and related materials included in the Executive Order are familiar with the regulations in the area as well as with the guidelines issued by The Centre for Biosecurity and Biopreparedness. These guidelines can be obtained from The Centre for Biosecurity and Biopreparedness or www.biosikring.dk.

Paragraph 3. The person appointed as security manager by the entity is to record anyone who has access to the biological substances included in the Executive Order. The list should be available to The Centre for Biosecurity and Biopreparedness on request at all times.

Article 13. Unregistered persons are to be permitted access to biological substances included in the Executive Order only if accompanied by a registered person, cf. Article 12, Paragraph 3, whereby the responsibility shall be borne by the registered person.

Article 14. The Centre for Biosecurity and Biopreparedness may require a security evaluation of persons working with specified biological substances, delivery systems or related materials for which a permit has been issued in accordance with Article 4 if the work directly relates to weapons production or testing.

Storage and transport

Article 15. Biological substances, delivery systems and related materials included in the Executive Order are to be stored in such a way so as to prevent theft and misuse.

Article 16. Biological substances included in the Executive Order, cf. Article 1 are to be transported in accordance with current regulations for the transport of hazardous goods. For road transport, ADR's (European Agreement concerning the International Carriage of Dangerous Goods by Road) regulations for class 6.1 and 6.2 apply (UN numbers 2814, 3373, 3172 and 3462); for railway transport, RID's (Regulations concerning the International Carriage of Dangerous Goods by Rail) regulations for class 6.1 and 6.2 apply (UN numbers 2814, 3373, 3172 and 3462); for sea transport, IMDG's (International Maritime Dangerous Goods Code) regulations for class 6.1 and 6.2 apply (UN numbers 2814, 3373, 3172 and 3462), and for air transport, ICAO-TI 's (Technical Instructions for the Safe Transport of Dangerous Goods by Air) regulations for class 6.1 and 6.2 apply (UN numbers 2814, 3373, 3172 and 3462).

Paragraph 2. The entity is to ensure that the carriers, forwarding agents etc. used by the entity are aware of their responsibility to secure the goods in their custody.
Paragraph 3. Carriers, forwarding agents etc. must ensure that shipments of biological substances, delivery systems and related materials included in this Executive Order are transported, stored whilst in transit and transferred to the recipient in such a way as to prevent theft, misuse and loss. They must also ensure that unauthorised persons cannot come into contact with such biological substances, delivery systems and related materials.

Security

Article 17. Entities which apply for permits are to prepare a vulnerability assessment and a security plan, which will be included in the permit application evaluation. The assessment and plan are to be prepared on a designated form which can be obtained from The Centre for Biosecurity and Biopreparedness or www.biosikring.dk.
Paragraph 2. The security plan is to include:

1) Registration procedures in association with stocks.
2) Disposal procedures.
3) Accident procedures.
4) Access control systems.
5) Technical security barriers, including alarm systems, technical inspections of alarms etc.
6) Security evaluation of selected persons where required, cf. Article 14.
7) Securing of sensitive information, including storage of information relating to technology, storage of substances etc. and personnel and visit information (IT/document security).
8) Drills/training.

Paragraph 3. The security plan is to be maintained on an ongoing basis and must be available to The Centre for Biosecurity and Biopreparedness on request.

Registration and disposal of biological substances, delivery systems and related materials

Article 18. The entity is to maintain registers/inventories of the biological substances, delivery systems and related materials included in this Executive Order for which it is responsible. The register/inventory is to be updated on an ongoing basis, at least once a quarter. Registers and other documents relating to permits are to be stored for a minimum of five years.
Paragraph 2. The entity is to report stock levels to The Centre for Biosecurity and Biopreparedness at least once a year. Stock movements are to be registered in accordance with the procedure stipulated by The Centre for Biosecurity and Biopreparedness.
Paragraph 3. The entity must make registers/inventories available to The Centre for Biosecurity and Biopreparedness on request.

Article 19. Any purchase, sale, transfer or disposal of biological substances, delivery systems and related materials included in this Executive Order is to be reported to The Centre for Biosecurity and Biopreparedness within 14 working days of the purchase, sale, transfer or disposal, specifying the type, volume and shipper/recipient.
Paragraph 2. The entity is responsible for ensuring that disposal takes place in such a way that biological substances, delivery systems and related materials cannot represent a danger to human safety.
Paragraph 3. The entity must set out procedures for the disposal of the biological substances, delivery systems and related materials included in the Executive Order, cf. Article 17, Paragraph 2.

Accidents and loss

Article 20. The Centre for Biosecurity and Biopreparedness is to be immediately informed if the following occurs:

1) Theft, misuse or loss of the biological substances, delivery systems and related materials included in the Executive Order.
2) Suspicion of release of the biological substances included in the Executive Order.
3) Discovery of or suspicion of the presence of biological substances, delivery systems and related materials included in the Executive Order.

Paragraph 2. Unauthorised persons are to be kept out of all areas where there are uncontrolled occurrences of biological substances included in the Executive Order, until The Centre for Biosecurity and Biopreparedness has ensured that measures have been implemented to counter the potential danger.

Control

Article 21. The Centre for Biosecurity and Biopreparedness monitors and carries out inspections to ensure compliance with the provisions in this Executive Order.

Article 22. The Centre for Biosecurity and Biopreparedness may prohibit the possession, production, use and storage of the biological substances, delivery systems and related materials included in the Executive Order, until the requirements set by The Centre for Biosecurity and Biopreparedness are complied with.

Appeals, penalties, entry into force and transition provisions

Article 23 Decisions made by The Centre for Biosecurity and Biopreparedness in accordance with this Executive Order may be appealed within four weeks to the Ministry of Health and Prevention.

Article 24. Violations of Article 4, Article 8, Article 9, Paragraphs 1 and 4, Articles 10–16, Article 17, Paragraph 3, Articles 18–20 and Article 22 will be fined, unless other legislation deems that other penalties apply to the violation.
Paragraph 2. The penalty for violations of Article 4, Article 8, Article 9, Paragraphs 1 and 4, Articles 15–16 and Article 19, Paragraphs 1–2 can, if aggravating circumstances exist, rise to imprisonment for up to 2 years, if the violation has been committed intentionally or through the exercise of gross negligence, where the violation results in persons being significantly injured, property being significantly damaged or the environment being significantly harmed or results in the risk of these occurring, or a financial benefit for the persons involved or others, including savings, is achieved or intended to be achieved.
Paragraph 3. Entities etc. (legal entities) can be deemed to bear a criminal liability in accordance with the regulations in chapter 5 of the Penal Code.

Article 25. The Executive Order shall come into effect on 1 October 2009.
Paragraph 2*.* Entities in possession of biological substances, delivery systems and related materials included in the Executive Order upon entry into force of this Order are to submit a permit application within 6 months of the date of entry into force if they wish to continue to remain in possession thereof. Otherwise, the biological substances, delivery systems or related materials are to be destroyed in a safe way, cf. Article 19.
Paragraph 3. Entities which have submitted an application within the period specified in Paragraph 2 have a temporary permit, which will apply until The Centre for Biosecurity and Biopreparedness has reached a decision relating to the application.

Ministry of Health and Prevention,

Jakob Axel Nielsen

/ John Erik Pedersen

List of biological substances, delivery systems and related materials

1. Biological substances

Human pathogens, zoonoses and toxins as follows:

a. Viruses, whether natural, enhanced or modified, in the form of isolated live cultures or of materials, including living materials which are intentionally inoculated or contaminated with such cultures, as follows:

1. Chikungunya virus;
2. Crimean-Congo virus (Crimean-Congo hemorrhagic fever);
3. Dengue fever virus;
4. Eastern equine encephalitis virus;
5. Ebola virus;
6. Hantaan virus;
7. Junin virus;
8. Lassa fever virus;
9. Lymphocytic choriomeningitis virus;
10. Machupo virus;
11. Marburg virus;
12. Monkey pox virus;
13. Rift Valley fever virus;
14. Tick-borne encephalitis virus (Russian spring-summer encephalitis);
15. Variola virus;
16. Venezuelan equine encephalitis virus;
17. Western equine encephalitis virus;
18. White pox (Variola minor);
19. Yellow fever virus;
20. Japanese encephalitis virus;
21. Kyasanur Forest disease virus;
22. Louping ill virus;
23. Murray Valley encephalitis virus;
24. Omsk haemorrhagic fever virus;
25. Oropouche virus;
26. Powassan virus;
27. Rocio virus;
28. St Louis encephalitis virus;
29. Hendra virus (Equine morbillivirus);
30. South American hemorrhagic fever virus (Sabia, Flexal, Guanarito);
31. Hemorrhagic fever with lung and renal syndrome virus (Seoul, Dobrava, Puumala, Sin Nombre);
32. Nipah virus.

b. Rickettsiae, whether natural, enhanced or modified, either in the form of isolated live cultures or of materials, including living materials, which are intentionally inoculated or contaminated with such cultures, as follows:

1. Coxiella burnetii;
2. Bartonella quintana (Rochalimaea quintana, Rickettsiae quintana);
3. Rickettsiae prowazekii;
4. Rickettsiae rickettsii.

c. Bacteria, whether natural, enhanced or modified, in the form of isolated live cultures or of materials, including living materials, which are intentionally inoculated or contaminated with such cultures, as follows:

1. Bacillus anthracis;
2. Brucella abortus;

3. Brucella melitensis;
4. Brucella suis;
5. Chlamydia psittaci;
6. Clostridium botulinum;
7. Francisella tularensis;
8. Burkholderia mallei (Pseudomonas mallei);
9. Burkholderia pseudomallei (Pseudomonas pseudomallei);
10. Salmonella typhi;
11. Shigella dysenteriæ;
12. Vibrio choleræ;
13. Yersinia pestis;
14. Epsilon toxin produced types of Clostridium perfringens;
15. Enterohemorrhagic Escherichia coli, serotype O157 and other verotoxin produced serotypes.

d. The following toxins and sub-units of these toxins:

1. Botulinum toxins;
2. Clostridium perfringens toxins;
3. Conotoxin;
4. Ricin;
5. Saxitoxin;
6. Shiga toxin;
7. Staphylococcus aureus toxins;
8. Tetrodotoxin;
9. Verotoxin and shiga-like ribosome activated proteins;
10. Microcystin (Cyanginosin);
11. Aflatoxins;
12. Abrin;
13. Cholera toxin;
14. Diacetoxyscirpenol toxin;
15. T-2-toxin;
16. HT-2-toxin;
17. Modeccin;
18. Volkensin;
19. Viscum album Lectin 1 (Viscumin).

Note 1:
No controls are imposed on botulinum toxins or conotoxins in product form, which comply with all of the following criteria:

1. *they are pharmaceutical specialties for human use in the treatment of diseases;*
2. *they are fully pre-packaged for distribution as pharmaceutical products;*
3. *they are permitted by a governmental authority to be marketed as a pharmaceutical product.*

Note 2:
No controls are imposed on vaccines or immunotoxins.

e. Fungi, whether natural, enhanced or modified, either in the form of isolated live cultures or of materials, including living materials, which are intentionally inoculated or contaminated with such.

1. Coccidioides immitis;
2. Coccidioides posadasii.

Genetic elements and genetically modified organisms as follows:

a. Genetically modified organisms or genetic elements which contain nucleic acid sequences associated with the pathogenicity from the organisms specified under points a–c and e in the above list of biological substances.

b. Genetically modified organisms or genetic elements which contain nucleic acid sequences as coding for any of the toxins specified under point d, or sub-units of toxins of these.

Note 1:
Genetic elements include chromosomes, genomes, plasmids, transposons and vectors, whether genetically modified or not.

Note 2:
For nucleic acid sequences associated with the pathogenicity from each of the microorganisms specified under points a–c and e in the above list of biological substances, each sequence is understood to be specific to the micro-organism specified, and which:

a. in itself or via its transcription or translation products represents a significant risk to human health; or

b. is known to make a specified micro-organism (or any other organisms in which it can be inserted or integrated in other way) more able to cause serious harm to human health.

Note 3:
Limitations do not apply to nucleic acid sequences which are associated with the pathogenicity from enterohemorrhagic Escherichia coli, serotype O157, and other verotoxin produced strains in addition to those which code for verotoxin or sub-units thereof.

2. Delivery systems

Spray or mist systems which are specifically designed or modified for installation on aircraft, craft which are lighter than air or unmanned aircraft, and specially constructed components for these, as follows:

a. Complete spray or mist systems which, based on a liquid suspension, can produce initial drops 'VMD' of less than 50 μm at a flow velocity of more than two litres per minute;

b. Spray systems or combinations of aerosol generating units which, based on a liquid suspension, can produce initial drops with a 'VMD' of less than 50 μm at a flow velocity of more than two litres per minute;

c. Aerosol generating units which are specially designed for installation in the systems specified under point a and b.

Note 1:
Aerosol generating units are devices which are specially designed or modified for installation on aircraft, i.e. jets, rotating drum atomizers and equivalent devices.

Note 2:
Controls are not imposed on spray or mist systems and associated components which have been proven not to disseminate biological agents in the form of infectious aerosols.

Note 3:
The drop size for spray equipment or jets which are specially designed for use on aircraft, craft which are lighter than air or unmanned aircraft are measured in accordance with one of the following methods:

a. doppler laser method;

b. forward laser diffraction method.

Note 4:
'VMD' is the volume mean diameter, and for water-based systems it is equivalent to the mass mean diameter (MMD).

3. Related materials

Equipment and technology which can be immediately used in the handling of pathogenic biological materials including toxins as follows:

a. Complete facilities for biological containment at containment level BSL3 or BSL4;

Note:
The specifications in Danish Working Environment Authority Executive Order No. 864 of 10 November 1993 on biological agents and working environments apply to containment level P3 and P4 (BSL3, BSL4, L3, L4).

b. Fermentors which can be used for the cultivation of pathogenic microorganisms, viruses or which can produce toxins without deriving aerosols and which have a total capacity of minimum 20 litres;

Note:
Fermentors include bioreactors, chemostats and systems with continuous through flow.

c. Centrifugal separators which can carry out continuous separation without the derivation of aerosols, with all the following properties:

1. flow velocity of more than 100 litres/hour;
2. components of polished stainless steel or titanium;
3. one or more seals in the steam containment area; and
4. can be sterilized in place in the closed state.

Note:
Centrifugal separators include decanting vats.

d. Filtration equipment with cross (tangential) flow and components as follows:

1. Filtration equipment with cross (tangential) flow, which can carry out the separation of pathogenic microorganisms, viruses, toxins or cell cultures without deriving aerosols, with both of the following properties:
   a. a total filtering area of at least 1 m^2; and
   b. can be sterilized or disinfected in place;

Note:
In association with d.1.b, sterilising means the elimination of all viable microbes in the equipment using physical agents (i.e. steam) or chemical agents. Disinfection means the destruction of the potential infecticity of microbes in the equipment using germicidal chemical agents. Disinfection and sterilisation differ from sanitation, sanitation being cleaning procedures which are implemented to reduce microbe levels in the equipment, without this necessarily leading to the total elimination of the infecticity or viability of the microbes.

2. Filtration components with cross (tangential) flow (i.e. modules, elements, cassettes, cartridges or plates) with a filtering area of at least 0.2 m2 for each component and which is designed to be used in the filtration equipment with cross (tangential) flow specified in point. d1;

Note:
Controls are not imposed on equipment for reverse osmosis as specified by the manufacturer.

e. Freeze drying equipment which can be sterilised by steam, with a condensation capacity of more than 10 kg of ice in 24 hours and under 1,000 kg of ice in 24 hours;

f. The following protection and encapsulation equipment:

1. Protective suits (fully or partial) or hoods with permanently attached external air supply in stationary systems which operate under positive pressure;

Note:
Controls are not imposed on suits which are to be used with built-in breathing equipment.

2. Class III biological safety cabinets or isolation equipment with similar performance standards;

Note:
Isolation equipment includes flexible isolators, drying chambers, anaerobic chambers, glove boxes and laminar flow hoods (closed with vertical flow).

g. Chambers designed for aerosol challenge testing using microorganisms, viruses or toxins and with a capacity of at least 1 m3.

h. Biological detection systems which have been specially developed or modified for the detection or identification of biological weapons for use in warfare and specially developed components thereof.

i. Technology which can be directly used for the development of biological weapons or for offensive usage. The technology required for the development, production or use of products which are controlled in this annex is controlled in accordance with the provisions for these products.

Technology which is required for the development, production or use of a controlled product, remains controlled even when used in a product which is not controlled.

There are no controls on technology which is required as a minimum for the installation, operation, maintenance (inspection) and repair of products which are not subject to control, or which have been previously issued with a permit.

There are no controls on information which is already in the public domain or represents basic scientific research, or which is required as a minimum for patent applications.

Note:
Technology is defined as specific information required for the development, production or use of a product. Information is 'technical data' or 'technical assistance'. 'Technical assistance' can take different forms such as instructions, skills, training, practical experience and consultant services and can include the transfer of technical data. Technical data can take the form of drawings, plans, diagrams, models, formulae, tables, design plans and specifications, manuals and instructions written or stored on other media or equipment such as diskettes, tape or ROMs.