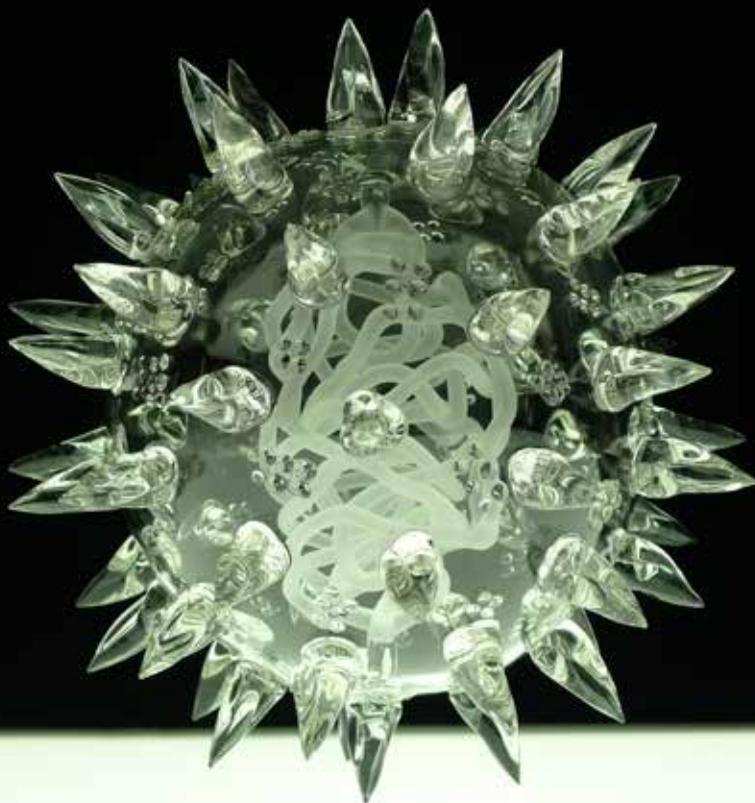




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AKADEMIE VAN WETENSCHAPPEN

# IMPROVING BIOSECURITY

## ASSESSMENT OF DUAL-USE RESEARCH



ADVISORY REPORT

# IMPROVING BIOSECURITY ASSESSMENT OF DUAL-USE RESEARCH

Royal Netherlands Academy of Arts and Sciences  
Biosecurity Committee  
December 2013



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# FOREWORD

The potential risks of science suddenly became world news last year. It happened when Rotterdam-based virologist Ron Fouchier wanted to publish a paper on the mutations that make the H5N1 virus – better known as the bird flu virus – transmissible between mammals. There were alarming reports in the media about the potential misuse of his research results by ill-intentioned parties. A heated debate ensued, focusing on the tricky balance between academic freedom on the one hand and the interests of public health and security on the other. The Royal Academy had already pointed out the possibility of misuse to life science researchers in 2007 with its *Code of Conduct for Biosecurity*. The debate that raged in scientific and political circles about the bird flu virus made clear that it was time to think seriously about the usefulness and necessity of additional policy measures.

This led the Dutch State Secretary for Education, Culture and Science to ask the Royal Netherlands Academy of Arts and Sciences to advise on dual-use research. The Academy Board inaugurated a Biosecurity Committee to prepare the present advisory report. The report builds on the work of the Academy Biosecurity Working Group, which drafted the Code of Conduct in 2007. Chaired by Lous van Vloten-Doting, the Biosecurity Committee was given advice by a Focus Group representing science, industry and government.

As the Fouchier case makes clear, biosecurity is not limited to scientific considerations. The Academy hopes its advice will help to bridge the gap between two worlds: the world of researchers in the life sciences and the world of security specialists. The aim is to create interaction between these parties – who now often operate separately from each other – in every phase of research. The Committee therefore proposes establishing a Biosecurity Advisory Committee. This new committee would ideally come under the authority of the Health Council of the Netherlands.

Considering biosecurity aspects at an early stage of research may help avoid delays in publication. It is also crucial for researchers to be aware of potential risks and remain so. This important topic should be considered at length, both in the laboratory and above all in university education programmes. In the Committee's view, then, the importance of the *Code of Conduct for Biosecurity* is undiminished great.

The Academy Board agrees with the Committee's conclusions and recommendations. The Academy is prepared to contribute its expertise in this field, based, among other things, on the work of the Biosecurity Working Group and the present Biosecurity Committee. It will also keep the subject on the national and international agenda, for example in cooperation with its sister academies.

I would like to close by thanking the Van Vloten-Doting Committee for its valuable advice on this subject, whose importance can hardly be overestimated.

Hans Clevers  
President

# SUMMARY

## Background

In September 2011, Dutch virologist Ron Fouchier announced that, based on his group's research findings, the H5N1 (bird flu) virus has the potential to gain airborne transmissibility between mammals. He also identified the biological mutations that the virus must undergo to do so. The US National Science Advisory Board for Biosecurity (NSABB) advised against publishing the full version of the paper. Any data or information that could be used to deliberately develop or spread a mutant H5N1 virus should be left out, it said. The NSABB's advice sparked off heated debate among scientists, politicians and the media. The Dutch government required Fouchier to obtain an export licence before sending the papers out for publication, citing a European Union regulation that puts limits on the export of dual-use technology – in other words, technology that can be used for both scientific and military purposes. After Fouchier was granted the licence, the publication appeared in *Science* (June 2012). Fouchier's employer, Erasmus Medical Centre in Rotterdam, had filed an appeal against the Government's decision to require an export licence, but the competent court rejected that appeal in 2013.

## Request for advice

The H5N1 controversy led the Dutch State Secretary for Education, Culture and Science to ask the Royal Netherlands Academy of Arts and Sciences to advise on how to deal with dual-use research in the life sciences. Specifically, the State Secretary wanted to know:

- *how dual-use research should be assessed,*
- *who should assess dual-use research?*

The Academy Board appointed a Biosecurity Committee and charged it with investigating and answering these questions.

## Security, risk and uncertainty

There is a difference between security (protection against intentional threats) and safety (protection against accident, human failure or threats of nature). The concepts of risk and uncertainty play an important role in security. The Committee agrees with the Scientific Council for Government Policy (WRR) that in issues involving security, the point is to weigh opportunities and threats. That is what it has done with the threats, risks and uncertainties associated with the misuse of biological agents.

## Biosecurity and dual-use research

Biosecurity focuses on preventing the misuse of life sciences research. It is an issue that not only concerns scientists, laboratory technicians and administrators, but also security specialists, politicians, public servants in various ministries and – last but not least – the media. The Biosecurity Committee believes that any definition of dual use involving biological agents should consider both on the technological and biological aspects and on the social and political context. It therefore proposes the following description:

In the context of biosecurity, dual-use research is research

1. that, based on current information, utilises or can reasonably be expected to lead to knowledge, products or technologies that can be misused, and
2. that involves an identifiable threat and a significant risk of misuse, and
3. that can have serious consequences for society (health, safety, agriculture, plants, animals, the environment or property).

## How should dual-use research be assessed?

In line with this definition, the Committee has developed an assessment framework that allows for both biological considerations (the biological agent itself and the nature of the relevant research) and contextual considerations (the social and political context in which the research is being conducted). Researchers should refer – if necessary, repeatedly – to both sets of considerations in the various stages of a research project.

The first question to be considered is *whether* a research project is dual use in nature. The second question is whether this should have consequences. This gives rise to further questions, for example: What constitutes a threat? What sort of threat is it? Who decides? Is the threat serious enough to designate the relevant technology or study (or publication) as dual-use research in accordance with the Committee's definition?

The considerations that apply in the case of research funding or the execution of research may differ from those applying in the case of publication. A threat analysis is therefore relevant when weighing the dual-use aspects of research and of publication.

## Who should assess dual-use research?

In the Committee's opinion, the public should be able to trust researchers and others who engage in knowledge acquisition to assess whether their results can be misused for criminal or terrorist purposes. The responsibility for making that assessment lies mainly with researchers and other parties in the knowledge chain. That is why all such parties must have the opportunity to request specific advice on potential bio-security aspects of their research proposal or research results.

The ability to advise on research with potential dual-use aspects requires knowledge and expertise in multiple areas (the science involved, laboratory security, and national and international threat analyses). The Committee investigated whether any existing arrangements and institutions can serve as an example or act as advisory bodies in potential cases of dual-use research.

In the Committee's view, none of the existing committees or institutions are sufficiently equipped for this task. The Committee therefore proposes establishing a separate Advisory Committee: the **Biosecurity Advisory Committee for Research in the Life Sciences**.

The Committee suggests that the Ministry of Health, Welfare and Sport should install the Advisory Committee and act as coordinator. It also proposes the Advisory Committee should be under the authority of the Health Council. The Committee concludes its advisory report by making a number of proposals for the composition of the Advisory Committee and the duties with which it should be charged.

# 1. BACKGROUND: THE H5N1 CASE

In September 2011, during a conference on Malta, Rotterdam-based virologist Ron Fouchier announced his research group's finding that the H5N1 (bird flu) virus has the potential to gain airborne transmissibility between mammals. The researchers had also identified the biological mutations that the virus must undergo to do so. The announcement caused a considerable stir, certainly in the research community. For the first time, human-to-human transmission of the H5N1 virus seemed plausible, triggering concerns that it could cause an influenza pandemic.

Fouchier submitted the research results to *Science* for publication. At approximately the same time, US-based virologist Yoshihiro Kawaoka (Japan) submitted similar research results to *Nature*. The editorial boards of both journals decided to ask the body that had funded the two studies – the National Institutes of Health (NIH), part of the US Department of Health and Human Services (HHS) – to review the manuscripts. They did so in line with agreements between researchers, science journals and government officials in the United States (and elsewhere) concerning manuscripts whose content could be regarded as dual use. As the term indicates, dual use relates to particular activities or objects which can be used in at least two different ways or for two different purposes. In the life sciences, dual-use research means that the knowledge or technologies acquired through scientific research can be misused for criminal or terrorist purposes or for military reasons. The NIH, in its turn, asked the US National Science Advisory Board for Biosecurity (NSABB) to review the two papers. The editorial boards were following a policy procedure established in 2003 by various key life science journals: "(...) there is information that, although we cannot now capture it with lists or definitions, presents enough risk of use by terrorists that it should not be published. How and by what processes it might be identified will continue to challenge us (...)."<sup>1</sup>

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<sup>1</sup> *Statement on Scientific Publication and Security*, Journal Editors and Authors Group, 15 February 2003

In December 2011, the NSABB recommended curtailing the two manuscripts before publication. Any data or information that could be misused to deliberately develop or spread a mutant H5N1 virus should be left out, it said. When the recommendation was announced, it sparked off heated debate among scientists, politicians and the media. It was the first time that publication (in full) of a scientific article had been advised against for security reasons. The debate spread well beyond the research community. Below is a summary of some of the most important points raised.

- **The nature of the research.** Are the results really so potentially dangerous? Can this knowledge also be obtained in some other manner? The impression was that the mutated virus could lead to a serious or deadly pandemic, but the researchers put matters into context. They argued, for example, that the laboratory animals (ferrets) infected with the virus had only become mildly ill, and that none of the animals had died of the infection.
- **The usefulness of the research.** Why study a mutant H5N1 virus that does not even occur in nature? Although numerous influenza experts claimed that the research results were important to science and to human and animal health, opponents said that the studies were of no use to society. They wanted the researchers and the funding body to explain why these studies had been carried out in the first place.
- **Whether or not to publish the research results .** Even if a study is carried out, is it always necessary or even desirable to make the results available to all?
- **The likelihood of the research being misused, for example by terrorists.** How realistic is the risk that terrorists or others will want to misuse the research results and can actually do so?
- **Academic freedom.** Many of the discussions centred on whether government intervention violates academic freedom. Is it up to the academic community or to government to decide whether a scientific manuscript should be published?

These and related issues were frequent topics of debate in the first six months of 2012. In January, researchers involved in H5N1 research announced a voluntary sixty-day moratorium on their studies. In February, the World Health Organisation (WHO) convened an expert meeting that emphasised the importance of the research (and its publication) while also considering the associated concerns. The meeting proposed extending the voluntary moratorium for an indefinite period until the attendant risks became clearer. The relevant researchers followed up on this recommendation.

A month later, in late March 2012, the NSABB agreed that amended versions of the two papers (Fouchier et al., Kawaoka et al.) could be published in full. Following the NSABB's decision, *Nature* published Kawaoka's manuscript in April 2012. Fouchier's paper remained unpublished, however. The then Ministry of Economic Affairs, Agriculture and Innovation of the Netherlands had required him to apply for an export licence for the manuscript under the terms of the Strategic Goods Decree [*Besluit strategische*

*goederen*]. The Decree implements EU Council Regulation 428/2009, which seeks to prevent the proliferation of nuclear, chemical and biological weapons by controlling exports.<sup>2</sup> The research world was astonished by this: the Regulation itself makes an exception for basic scientific research, and the regime it prescribes had never before been applied to scientific manuscripts in the life sciences. Fouchier's employer, Erasmus Medical Centre in Rotterdam, decided to apply for the licence under protest. The licence was issued at the end of April, allowing the manuscript to be published in *Science*. The relevant issue appeared in June 2012.<sup>3</sup>

This was not the end of the matter, however. The debate continued. Erasmus Medical Centre filed an objection to the compulsory licence. The Dutch Minister for Foreign Trade and Development Cooperation disallowed the objection in December 2012. The case was then submitted to the courts. The District Court of Noord-Holland ruled on 20 September 2013, finding for the Minister.<sup>4</sup> The court considered that non-proliferation was a priority in the Regulation and that exemptions from the licence obligation (for example for reasons of basic scientific research) should be narrowly interpreted. In addition, the court determined that this particular case did not involve basic scientific research because it had a practical purpose (demonstrating the airborne transmissibility of the H5N1 virus).<sup>5</sup>

The interest that the research community and the media took in this ruling shows (once again) that the H5N1 case raises many questions about how to deal with dual-use research in the life sciences. The Biosecurity Committee will address these questions in the present report.

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2 *Council Regulation (EC) No. 428/2009* of 5 May 2009 setting up a Community regime for the control of exports, transfer, brokering and transit of dual-use items

3 Sander Herfst et al., *Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets*, *Science* 336, 1534 (2012)

4 For the text of the ruling see: <http://uitspraken.rechtspraak.nl/inziendocument?id=ECLI:NL:RBNHO:2013:8527>

5 At the time of writing it was not yet known whether Erasmus Medical Centre would appeal the ruling

## 2. REQUEST FOR ADVICE AND ESTABLISHMENT OF THE BIOSECURITY COMMITTEE

In view of the H5N1 debate, the Dutch State Secretary for Education, Culture and Science has asked the Royal Netherlands Academy of Arts and Sciences to advise on the following questions (see Appendix 1):

### Initial questions

- Which statutory frameworks apply and what measures and regulations are available in the Netherlands, and to whom, in connection with dual-use research?
- What impact do these frameworks, measures and regulations have on scientific practice?
- What roles do the individual researcher, the research institution, the research funding body, the authorities, and other stakeholders play in dual-use research, both in the Netherlands and elsewhere?
- What measures are employed elsewhere in Europe and around the world in cases of dual-use research, and what do we know about the impact of those measures?

### Main questions

- How should dual-use research be assessed?
- Who should assess dual-use research?

## 2.1 Establishment and working methods of the Biosecurity Committee

In response to the Minister's request for advice, the Academy Board established the Biosecurity Committee. It was given the task of answering the aforementioned questions (Appendix 2). At the start of its work, the Committee raised a number of points for consideration:

- The Biosecurity Committee emphasises the importance of the modern life sciences for public health and for the prevention and cure of numerous disorders and diseases.
- Legislation divides research into basic research and applied research. The boundary between the two is fluid, however. If there is good reason for further consideration or assessment from the perspective of biosecurity or dual use, then that must apply for both basic and applied research.
- Experience in biosafety matters in the Netherlands shows that broad consensus is important. Such consensus implies that researchers accept the practical restrictions on their research that may result from biosafety regulations.
- The Committee points out that dual-use research is not restricted to virology but can also include other life science domains. One example is the neurosciences, where a growing number of methods are being developed to intervene in human cognition.<sup>6</sup>

The Committee held five plenary meetings. In addition, there were also bilateral meetings and correspondence between members. A Focus Group consisting of researchers working in various scientific disciplines and representatives of professional associations, research institutions, industry and government met twice to review draft versions of the advisory report. The Committee took the Focus Group's comments in account while writing the advisory report. The Focus Group bears no responsibility for the report.

Five reviewers appointed by the Academy commented on the draft version of the report. They were Prof. Pieter Drenth, Prof. Wiel Hoekstra, Prof. Pauline Meurs, Prof. Annemarie Mol and Prof. Bert Poolman. The reviewers were positive about the report's contents and the Committee's working methods. The Committee addressed various criticisms and incorporated a number of comments concerning the report's contents into the final version. The reviewers bear no responsibility for the report.

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6 The Royal Society, *Neuroscience, Conflict and Security*. RS Policy Document 06/11. Royal Society, London 2012. The document states, among other things: "Neuroscience should be considered as a focal topic in the science and technology review process of the BTWC because of the risks of misuse for hostile purposes in the form of incapacitating weapons"

## 2.2 Initial questions

Which statutory frameworks apply and what measures and regulations are available in the Netherlands, and to whom, in connection with dual-use research?

An appendix to the Government's memorandum to Parliament on biosecurity (dated 26 September 2012) sums up a number of registration obligations in connection with biosecurity (see Appendix 3). In the same memorandum, the Government states that "beyond the statutory biosafety requirements, there are – with a few exceptions – no statutory biosecurity requirements, although many institutions do apply a biosecurity regime."

At the moment, there are no separate rules governing dual-use research. There is, however, a connection with dual-use export control, for example the Strategic Goods Decree [*Besluit strategische goederen*] and the Strategic Services Act [*Wet strategische diensten*]. These were the rules invoked to require a licence for publication of the H5N1 study in *Science*. In its memorandum, the Government announces plans to investigate adding a section on security to existing and new legislation. It is also considering whether it is necessary and possible to draw up statutory security requirements, for example with respect to physical safety and the coaching and training of employees.<sup>7</sup>

The *Code of Conduct for Biosecurity* is a non-statutory instrument drawn up by the Academy in 2007 at the request of the Ministry of Education, Culture and Science (see Appendix 4). It was partly thanks to the Code of Conduct that the researchers in the H5N1 case were well-informed about the dual-use aspects of their research. But the way that case unfolded shows that a code of conduct is not a sufficient basis for a biosecurity policy that is supported by all parties.

What impact do these frameworks, measures and regulations have on scientific practice?

The most important effect of the existing statutory frameworks is that they set the preconditions for research. For example, they define rules on the use of laboratory animals or on research involving genetically modified agents. Strict agreements and rules also apply for research involving human subjects. Researchers engaged in such studies know what licences must be obtained and which assessments must be carried out before they can begin, and what steps they need to take while carrying out the research. The theme and object they have chosen to study is not an issue in this context, nor does it matter whether or not they decide to publish their results.

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<sup>7</sup> Memorandum from the Minister of Security and Justice, the Minister of Health, Welfare and Sport, and the State Secretary for Economic Affairs, Agriculture and Innovation. Session year 2012-2013, 28807, no. 152

## What roles do the individual researcher, the research institution, the research funding body, the authorities, and other stakeholders play in dual-use research, both in the Netherlands and elsewhere?

The Netherlands has not, as yet, introduced any specific rules or procedures for dealing with dual-use research. There is the *Code of Conduct for Biosecurity*, which is mainly aimed at raising awareness and also offers guidelines for dealing with dual-use research. The text of the Code briefly explains to whom each criterion applies and how to deal with that criterion. Responsibility lies with all the stakeholders in the knowledge chain, i.e. researchers, administrators, funding bodies and users. The Code does not make the role of government explicit.

In the context of the Ministry's request, the Committee also looked at the way the Code of Conduct has operated since its introduction. Based on an initial review, the Committee has reached the following, provisional, findings:

- Researchers and other stakeholders consider the Code of Conduct a relevant document for gaining a better understanding and more awareness of the topic of biosecurity. In terms of its content, the Code is satisfactory.
- It appears that experienced researchers and research team leaders are more aware of the Code's existence than younger researchers, for example PhD students.
- A limited survey among potential users also revealed that opinions are divided about the purpose of the Code. Opinions varied from "raising awareness of the dual-use dilemma" to "offering an alternative to statutory regulations".
- There are signs that the Code has only reached a part of its target group. This may be due to the limited number of situations in which the Code is applicable and to its dissemination.

Because the Code continues to be relevant, the Committee argues – in line with the proposals set out later in this report – that it should be an ongoing topic of interest in education, in training researchers, and in applying for research funding. Drawing attention to the Code will raise awareness of possible dilemmas in dual-use research and encourage researchers to be more active and vigilant.

## What measures are employed elsewhere in Europe and around the world in cases of dual-use research, and what do we know about the impact of those measures?

From a global perspective, the Biological and Toxin Weapons Convention (BTWC) would be the obvious institute to regulate dual-use research.<sup>8</sup> However, that is not the case. The Convention prohibits the development of biological weapons, but it does not refer to research (scientific or otherwise) that can lead to such development, intentionally or unintentionally. Because the Convention does not have a verification

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<sup>8</sup> For the Convention text, see: [http://www.unog.ch/80256EDD006B8954/\(httpAssets\)/C4048678A93B6934C1257188004848D0/\\$file/BWC-text-English.pdf](http://www.unog.ch/80256EDD006B8954/(httpAssets)/C4048678A93B6934C1257188004848D0/$file/BWC-text-English.pdf)

*Box 1 Important international rules and conventions*

<b>Convention/rules/organisation</b>	<b>Aim</b>	<b>Participating states</b>	<b>Effect</b>
Biological and Toxin Weapons Convention	Prohibition of development, production and stockpiling of biological weapons	170 states, including the Netherlands	No verification, but confidence-building measures
EU Council Regulation 428/2009	Community regime for the control of exports, transfer, brokering and transit of dual-use items	EU Member States	Mandatory for EU Member States
Australia group	Harmonisation of export controls for biological and chemical agents	39 states, including the Netherlands, and the EU	Voluntary

regime, it does not play an active role in regulating dual-use research, although the subject crops up regularly on its agenda.

Most European Union Member States have few if any specific rules governing biosecurity and dual-use research. Like the Netherlands, they comply with EU Council Regulation 428/2009, which contains a list of biological agents that are potentially dual use in nature (see Appendix 6). Most EU Member States have also joined the Australia Group, an informal community of states that aim to prevent the proliferation of biological and chemical weapons by harmonising their export controls. They do this by drawing up common guidelines and lists of agents.<sup>9</sup> These instructions and rules do not apply specifically to scientific or dual-use research. Most EU Member States are concerned about biosecurity and dual-use research, however, and some are considering more specific regulations and codes of conduct. Europeans – including scientists and research institutes – are following the Dutch H5N1 debate with great interest.

The United States government and research community have been very interested in dual-use research since 9/11 and the subsequent anthrax attacks. In 2004, the US National Research Council published an authoritative report<sup>10</sup> introducing the concept of “experiments of concern”. One of the report’s recommendations led to the founding of the National Science Advisory Board for Biosecurity (NSABB). The NSABB is chartered to have up to 25 voting members who are scientists drawn from a wide range of disciplines, and an outer circle of non-voting members who are employees of government departments and institutions involved in biosecurity matters. The NSABB advises on biosecurity policy, but not on individual projects. Nevertheless, it has been

<sup>9</sup> See: <http://www.australiagroup.net/en/guidelines.html>

<sup>10</sup> National Research Council, *Biotechnology Research in an Age of Terrorism*. Washington DC 2004 (National Academies of Science)

called on to review specific projects on several occasions, the most recent and best-known examples being Fouchier's and Kawaoka's H5N1 studies. Because the NSABB's reviews raised questions and led to considerable discussion, the US Federal Government introduced three new sets of biosecurity guidelines in 2012 and 2013. Two of these guidelines identify the responsibility that the federal government and research institutes bear for oversight of dual-use research.<sup>11</sup> The third is a new framework for research involving "gain of function" (in which the pathogen acquires new traits).<sup>12</sup> Here, the responsibility for oversight lies mainly with the research institution, with oversight being scaled up to federal level if necessary. The relevant procedures are described in the documents concerned.<sup>13</sup>

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11 *United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern*, 31 March 2012; *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, 21 February 2013

12 *A Framework for Guiding U.S. Department of Health and Human Services Funding Decisions about Research Proposals with the Potential for Generating Highly Pathogenic Avian Influenza H5N1 Viruses that are Transmissible among Mammals by Respiratory Droplets*, 21 February 2013

13 These documents only apply to HHS-funded research. They do not cover research carried out by the Department of Defense, for example, or privately funded research

# 3. SECURITY, RISK AND UNCERTAINTY

## 3.1 Security

There is a difference between *security* (protection against intentional threats) and *physical safety* (protection against accident, human failure or natural threats). In the past few decades, the importance of security has been introduced into sectors of society in which it previously played little or no role. Examples involve education and research, healthcare, agriculture, and infrastructure facilities (traffic, energy). These sectors have long been concerned about physical safety, and numerous measures have been introduced to prevent accidents and disasters, ranging from building and clothing regulations to user instructions and compulsory professional qualifications. The more a certain activity poses a risk, the longer the list of safety rules and the more complex they are. A nuclear power plant has to adhere to stricter rules than a doctor's surgery. There is a whole network of inspectorates and review bodies that enforce compliance with the safety rules which are in place.

For a long time, however, security was only a minor concern. The aviation sector was the main exception; it responded to a series of hijackings in the 1970s with a growing list of measures meant to prevent further attacks. In virtually all other sectors of society, accessibility, availability and customer-friendliness outweighed security against intentional threats. Even events such as the train hijackings by Moluccan activists in the Netherlands did not lead to any major change in that respect.

After 11 September 2001, many sectors began to take a closer look at their security arrangements. They had good reason to do so, for the terrorist attacks in New York and Washington DC were followed by others (Madrid in 2004, London in 2005). In the Netherlands, the assassinations of politician Pim Fortuyn and filmmaker Theo van

Gogh had an enormous impact. These and similar events led to the introduction of numerous preventive measures, both in the Netherlands and elsewhere.

Safeguarding security is one of the core tasks of government and it has many different means at its disposal for this purpose: legislation, supervision, screening, injunctions and prohibitions. If all else fails, government can invoke its monopoly on violence. It and it alone is entitled to use violence by deploying the police force or the military. Such use is subject to many conditions and restrictions. This is also true for other measures that government can introduce to safeguard security. Privacy is a good example. The question of how much government can be permitted to infringe on an individual's private life or personal privacy is one that should be subject to democratic control. This has become a hot issue, especially after revelations concerning the US National Security Agency (NSA) and its PRISM project.

### 3.2 Risk and uncertainty

A key question when defining the level of threat is how one goes about the identification of a risk. It is harder to answer that question in security matters than in safety matters, mainly because, alongside the risk factor, uncertainty also plays a role.

This advisory report borrows from the definitions of physical safety and risk applied by the Scientific Council for Government Policy (WRR) in a recent report on risk.<sup>14</sup>

The WRR distinguishes between opportunities and threats, which “refer to potential advantages and disadvantages, i.e. to the effects that may arise”. The WRR uses this terminology in the everyday sense, i.e. “the chance that something will have a favourable or unfavourable impact, and not in the sense of a statistically calculable likelihood”. In cases of risk and uncertainty, the aim is to weigh the opportunities and threats. The purpose of risk and uncertainty management is to prevent or limit incidents and damage or to anticipate them. At its most basic, risk involves the question of when, where and to what extent opportunities and threats will become reality. If there is uncertainty, then a further question is whether the threats will become reality at all.

Risk is a calculable safety problem, provided that the nature and scale of the potential danger, the probability of it occurring and its impact are sufficiently known and undisputed. Risk can be expressed as the function of chance (probability) and consequence (impacts). There are also safety issues related to faulty knowledge and conflicting values. As a result:

- there is a flawed understanding of the relationship between cause and effect (complex);
- threats are conceivable but not indisputable (uncertain);
- the effects are debatable and opinions vary as to what is and is not acceptable in normative terms (controversial).

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14 WRR, *Physical Safety. A Matter of Balancing Responsibilities*. Amsterdam University Press, Amsterdam 2012

The WRR uses the collective term “uncertainty” to refer to such threats. It is important to distinguish between uncertainty and unlikelihood: complex, conceivable, but unproved nor disputed threats are not, by definition, unlikely. In fact, limited knowledge makes it impossible to say anything for certain about likelihood.

In situations of uncertainty potential danger must be understood in the most fundamental sense of the word: threats to physical safety, incidents and harmful impacts are conceivable but not indisputable. Examples include new technologies, new infectious diseases, natural disasters caused by climate change, unprecedented food safety problems, and accidents involving hazardous substances. Terrorist or criminal threats also belong in this category.

It is vital to know the difference between a calculable and an incalculable threat, says the WRR, but at the same time the distinction is a gradual one and the dividing lines are blurred. Investigation, dialogue, experience, and cumulative insight can convert uncertainty into a calculable risk. On the other hand, what may at first appear to be a calculable risk can also become an uncertainty, for example because new parties committed to other values or insights join in the public debate.

The WRR has identified five “reference points” for dealing with risks and uncertainty:

1. intertwine opportunities and threats
2. taking into account the social and psychological properties of danger
3. utilise risk comparisons
4. accept uncertainty
5. organise the way uncertainty is dealt with.

### **3.3 Threats, risks and uncertainties associated with the misuse of biological agents**

How big is the threat that biological agents will actually be misused? The problems that the WRR summarised under the heading “uncertainty” – complex, uncertain and controversial – play a role in answering this question. That is why we can take the WRR’s five reference points as a guideline.

History teaches us that biological weapons were used in three different forms until the start of the twentieth century:

- contamination of food or water with contagious materials or substances;
- use of micro-organisms or toxic substances in weapons systems;
- distribution of infected substances and materials.

The methods were refined during the First World War. Yet, virtually no use was made of biological weapons then, and certainly not on a widespread scale – although the Germans allegedly spread plague in St Petersburg. The Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or other Gases, and of Bacteriological Methods of Warfare, otherwise known as the Geneva Protocol, was signed in 1925. To date, 138 countries have ratified the Geneva Protocol. The United States, the Soviet Union

and other countries continued to research and produce biological weapons, however. As far as we are aware, biological weapons were not used in combat during the Second World War. Japan did perform experiments on Chinese prisoners, while the UK, Canada and the US experimented with the anthrax bacterium on Gruinard Island off the Scottish coast. The island was only declared “safe” again in the 1990s.

The tests continued after 1945, at times with fatal consequences. It is generally accepted that an error made at an anthrax production facility in Sverdlovsk in Russia led to more than seventy deaths in April 1979. The accident occurred after the Biological and Toxin Weapons Convention (BTWC) had entered into force in 1975. The BTWC prohibits experiments with and the production of biological weapons.

Shortly after the 11 September 2001 terrorist attacks in New York and Washington, letters containing anthrax spores went through the US postal system. More than twenty persons developed anthrax infections, eleven of them a life-threatening variety. Five of the victims eventually died. The anthrax letters caused panic worldwide and led to additional security measures. The individual responsible for sending the letters is thought to have been a researcher at a US government biodefence laboratory. These incidents led to serious concerns about the potential of bioterrorism. Until that point, the international community had focused almost exclusively on the use of biological weapons by states. It had consistently overlooked the possibility that terrorists could also produce such weapons even though the tools to do so had always been within easy reach of “ordinary” people, if only by means of “primitive” methods, for example contaminating sources of water with the clothing of people who had died of contagious diseases.

In the Netherlands, the task of threat assessment lies in the hands of the National Coordinator for Security and Counterterrorism (NCTV), the General Intelligence and Security Service (AIVD) and the National Police Force. They estimate the risk of terrorist and other criminal attacks. They also consider the threat associated with the misuse of biological agents. A major attack using biological agents is not thought to be likely, in part because expertise and high-tech equipment are needed to develop and spread pathogens. Although the probability of a successful biological attack is small, the potential consequences of such an incident makes it necessary to properly secure agents and expertise. Smallpox, anthrax or even influenza epidemics could claim many thousands of victims. Agriculture and livestock breeding could also be hard hit, as outbreaks of animal diseases such as swine fever, foot-and-mouth disease and bluetongue disease have demonstrated. Even if the actual impact is relatively small, the political and economic damage can be enormous – just consider the panic that arose after the anthrax attacks in the United States. An ineffectual attack or failed attempt can still cause considerable turmoil. Threats are not constants, and the level of threat therefore fluctuates. Unlike known risks, which are the object of biosafety, terrorist and criminal threats cannot be expressed in hard numbers. Such uncertainties give rise to such questions as: Is there a threat? What sort of threat is it? Who decides on this, and on what grounds? Can a threat simply disappear?

Life scientists cannot answer these or similar questions. They depend on security experts to estimate threats, i.e. intelligence and security agencies, military specialists, and security researchers. Even then, some uncertainty remains. The WRR's reference points, for example accepting uncertainty and organising the way this is dealt with, therefore also apply to both researchers and security experts in the field of biosecurity and dual-use research. These guidelines allow the relevant parties to continue communicating and help steer them away from seeking solutions that create absolute risks or ignore them altogether.

# 4. BIOSECURITY AND DUAL-USE RESEARCH

## 4.1 Biosecurity, biosafety, biorisk

Biosecurity has only recently become a topic of concern. The 2001 anthrax attacks led directly to the introduction of biosecurity rules and guidelines in the life sciences, including in the Netherlands. All the stakeholders are still seeking the best way to deal with this relatively new phenomenon. Even so, a few clear trends have become visible. Biosecurity covers a broader field of operation than biosafety, which focuses mainly on laboratory protocols and rules to prevent accidents and incidents (*to keep bad bugs from the people*). Biosecurity, on the other hand, focuses on preventing individuals from deliberately spreading pathogens in the population (*to keep bad people from the bugs*).<sup>15</sup>

But the two do overlap. Screening, physical safety guidelines, assessment criteria and other measures can be used for both biosafety and biosecurity purposes.

In addition to these two terms, a third term has emerged: biorisk. WHO defines it as “[t]he probability or chance that a particular adverse event, accidental infection or unauthorized access, loss, theft, misuse, diversion or intentional release, possibly leading to harm, will occur”.<sup>16</sup> Biorisk covers various aspects of biosafety and biosecurity, making it a useful concept in public communication. It obviates the need for the

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<sup>15</sup> These “slogans” were used in a presentation during a NSABB conference.

<sup>16</sup> WHO, *Biorisk Management. Laboratory Biosecurity Guidance. Genève 2006* (WHO/CDS/EPR/2006.6)

problematic definition of intentional and unintentional threats.<sup>17</sup>

Biosecurity is mainly concerned with risks outside the laboratory. Such risks are related to the transmissibility of biological agents, the communication of and publicity surrounding research and research results, international agreements and political decisions concerning public health policy. This means that biosecurity not only concerns scientists, laboratory technicians and administrators, but also security specialists, politicians, public servants in various ministries and – last but not least – the media. The H5N1 debate is a pertinent example.

## 4.2 Dual-use research: definition and policy

The concept of dual use is not unique to the life sciences. As the name indicates, dual use relates to activities or objects which can be used in at least two different ways or for two different purposes. That is the case for almost every object ever designed or activity ever developed. A kitchen knife can be used to cut vegetables, but it can also be used as a substitute screwdriver or to wound or kill someone. Palliative medicines are meant to ease pain, but they can also be used to commit suicide. The list is endless. Almost all artefacts and natural products can be used for multiple purposes. Within the context of export control, the EU defines dual-use items as follows: “dual-use items’ shall mean items, including software and technology, which can be used for both civil and military purposes, and shall include all goods which can be used for both non-explosive uses and assisting in any way in the manufacture of nuclear weapons or other nuclear explosive devices”.<sup>18</sup>

The most authoritative definition of the dual use of biological agents can be found in the Fink Report by the US National Research Council. That report narrows the term dual use to “dual use of concern”, by which it means: “Research that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health and safety, agriculture, plants, animals, the environment, or material”.<sup>19</sup> This is the definition adopted by the NSABB, among others. In a further specification, the NSABB draws particular attention to knowledge, products or technologies that:

- enhance the harmful consequences of a biological agent or toxin

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<sup>17</sup> For the sake of completeness: a fourth term has been developed in the US in the context of laboratory security: biosurety. This term refers mainly to the trustworthiness of researchers and other laboratory staff. It became a pressing issue in the US after an investigation into the anthrax attacks in 2001 found that they had almost certainly been sent by a researcher working for a government bio defence laboratory.

<sup>18</sup> *Council Regulation (EC) No. 428/2009* of 5 May 2009 setting up a Community regime for the control of exports, transfer, brokering and transit of dual-use items (Article 2)

<sup>19</sup> National Research Council, *Biotechnology Research in an Age of Terrorism*. Washington DC 2004 (National Academies of Science)

- disrupt immunity or the effectiveness of an immunization without clinical and/or agricultural justification
- confer to a biological agent or toxin, resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitate their ability to evade detection methodologies
- increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin
- alter the host range (i.e. number of hosts) or tropism (target cells and tissues) of a biological agent or toxin
- enhance the susceptibility of a host population
- generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent.

In this definition, which is applied both in the Fink Report and by the NSABB, dual use refers mainly to the possibility that a biological agent (or knowledge of a biological agent) can be used (scientifically, medically, pharmaceutically) *and* misused. It may overlap in a practical sense with dual-use items in export control, but the two definitions are in fact very different.

Dutch biosecurity policy should be based on a generally accepted definition of dual-use research. It is thus essential to arrive at a definition that is satisfactory, acceptable and applicable for all stakeholders, from researchers and research institutions to industry and government. It should be consistent with the definition given in the Fink Report and elsewhere. However, the Fink Report's definition – and the NSABB's more detailed version of it – focuses almost exclusively on the technical or physical properties of a biological agent, and on the nature of the research. If it is to have any relevance for practical biosecurity policy, that definition must be extended and should also refer to contextual aspects, for example threats, intentions and possible consequences. It would then make allowance for the uncertainties inherent to policy-making when defining a biosecurity policy (for example the anticipated threat: scale and nature of possible damage, intentions and consequences).

These considerations have led to the following proposal for a **definition of dual-use research** in the context of biosecurity:

In the context of biosecurity, dual-use research is research

1. that, based on current knowledge, utilises or can be reasonably expected to produce knowledge, products or technologies that can be misused,
2. that involves an identifiable threat and a significant risk of misuse, and
3. that can have serious consequences for society (public health, physical safety, agriculture, plants, animals, the environment or property).

Based on this definition, we identify a framework for assessing dual-use research in the following section.

# 5. HOW SHOULD DUAL-USE RESEARCH BE ASSESSED?

## **From the request for advice:**

There has been broad consensus in recent years about the definition of dual-use research, in line with the Fink Report by the National Research Council. Nevertheless, it often proves difficult in specific cases to arrive at a transparent and authoritative assessment of dual-use research (and research proposals).

It is therefore important to consider how one should arrive at and handle an assessment in which research in the life sciences is qualified as dual-use research. On the one hand, consideration should be given to the object and aim of the research and to identifying the associated risks (both real and potential), both content-related and technical. On the other hand, the social and political context of the research is also important.

If a research proposal is judged as being dual-use in nature, the next step is to determine whether and to what extent the benefits and vested interests (scientific, social) weigh up against the risks to security. That has proved to be a difficult assessment in actual cases. We are therefore asking the Academy to consider how the various interests involved can be weighed up against one another, and hence to develop an “assessment framework” of criteria and considerations to which government and others can refer in decision-making on dual-use research. One particular factor is that, while information is often classified, there is the requirement of verifiability in research (which requires disclosure).

## 5.1 Components of an assessment framework

The debate concerning dual-use research focuses on the potential misuse of technology that is developed for peaceful purposes (healthcare and sickness prevention). The term dual-use research has become particularly common in the life sciences in recent decades but that in itself does not make its application clear to all stakeholders. The task of developing an assessment framework for dual-use research must therefore begin by asking what precisely should be assessed. In line with the definition proposed above, the assessments concern:

- the biological agent that is being studied
- the nature of the research
- the social and political context of the research.

Recent scientific publications propose various ways of arriving at an assessment framework. One such proposal is Jonathan Tucker's "decision framework".<sup>20</sup> The box below lists the considerations that according to Tucker should play a role in the ultimate assessment and decision-making.

### Box 2 Tucker's Decision Framework.

1. Monitor technological developments in academia, government, and private industry with the goal of identifying emerging technologies in the biological and chemical fields that have a potential for misuse;
2. Assess the risk of misuse of an emerging technology according to four parameters: accessibility, ease of misuse, magnitude of potential harm, and imminence of potential misuse;
3. If the aggregate risk of misuse is low, there is no urgent need to devise governance measures, but the technology should continue to be monitored in case its potential for misuse increases over time;
4. If the aggregate risk of misuse is medium or high, go on to assess the governability of the technology, according to five parameters: embodiment, maturity, convergence, rate of advance, and international diffusion;
5. If the aggregate governability of the technology is low, focus on informal governance measures;
6. If the aggregate governability of the technology is medium, consider soft-law governance measures in addition to informal governance measures;
7. If the aggregate governability of the technology is high, consider the full spectrum of governance measures: informal, soft law and hard law;
8. If the risk of misuse associated with the technology appears to be exceptionally grave and imminent, consider more stringent governance measures than the decision framework would lead one to adopt;
9. Based on a cost-benefit analysis, assemble a tailored package of governance measures that reduces the risk of misuse at acceptable cost and in a manner that is acceptable to the major stakeholders.

<sup>20</sup> Jonathan B. Tucker, *Innovation, Dual Use, and Security. Managing the Risks of Emerging Biological and Chemical Technologies*. MIT Cambridge (Ms) 2012, p. 79 ff.

There are a few things that can be said about this model. First, it covers both biological and chemical research. It also refers explicitly to “emerging technologies”, but the component factors can apply equally well to the existing technologies. The underlying assumption of the model is that the assessment will consider both the risk posed by the agent itself and the contextual factors, i.e. governability. The wording of the model is general in nature; it does not, therefore, offer ready-made practical solutions. That makes it different from the models recently developed by the US Government. These models work with a fixed set of “select agents” and a list of “experiments of concern” that appear to lead to a predictable catalogue of “dual-use research of concern”. The danger in this approach is that objects or activities not listed in the catalogue will be overlooked, or that everything that is listed will, by definition, be classified as dual-use research of concern even though that may not always be the case. In Tucker’s model, that danger is much smaller.

On the other hand, subjective or ad hoc considerations can play a bigger role in Tucker’s model, which requires a judgement call on the risk of misuse (is the risk low, medium or high?), and on the magnitude and imminence of the potential harm. Who is to make that call – and how?

Tucker’s model is useful as a guideline when answering the “how” question. It helps to rephrase a number of the component factors of the decision framework as questions:

- Which technological developments in academia and private industry have a potential for misuse?
- What phase of development has the technology reached (ranging from starting phase to “ready for use”)?
- Is there an urgent need for governance measures, or is it enough to monitor developments?
- Is there any reason to focus specifically on the accessibility of the technology?
- Should attention be focused on the publication and dissemination of the relevant knowledge and information?
- Is there any reason to focus specifically on the complexity of potential use or misuse?
- Is there any indication of the magnitude of the potential harm if the technology is misused?
- Is there any indication of the urgency of a potential threat of misuse?
- Is the threat latent or imminent?
- To what extent do international aspects play a role in assessing the threat?

These questions lead us back to the first main question in the request for advice: how should dual-use research be assessed? In line with Tucker’s reasoning and the questions derived from his model, we list a number of factors below that can help us answer that question.

## 5.2 Biological factors

In determining whether a study should be classified as dual use, two different assessment criteria play a role that can be described as “biological” in nature. The first concerns the biological agent that is being studied. Thousands of biological agents have the potential to be misused. Various national governments and international bodies have compiled catalogues listing the specific agents most susceptible to misuse. For example, the Dutch government has issued the Strategic Goods Decree [*Besluit strategische goederen*],<sup>21</sup> based in part on EU Council Regulation 428/2009, which provides an extensive list of dual-use micro-organisms and toxins.<sup>22</sup> The Netherlands is also a member of the Australia Group, an informal community of forty states and the European Union that aims to prevent exports and transport from contributing to the proliferation of biological and chemical weapons. It does this by sharing information on suspect transports and by identifying potentially suspect materials and agents. The Australia Group has compiled lists of agents that should be subject to export control. They include lists of human pathogens, animal pathogens (such as bird flu) and plant pathogens. There is also a list of equipment that can be used to produce biological weapons (e.g. glove boxes, fermenters, and freeze-dryers).<sup>23</sup>

Most lists of dual-use biological agents meant to prevent proliferation were not compiled – at least not in the first instance – with the research community in mind, but rather to monitor and control trade and exports.<sup>24</sup> That is different in the case of the US Government’s list of biological agents for dual-use research. This list consists of 15 “select agents”, a much lower number than EU Council Regulation 428/2009.<sup>25</sup>

It is clear from the many different lists of select agents that diverse approaches and perspectives are possible. On the one hand, no one list is exhaustive; technology continues to evolve, leading time and again to new opportunities for dual use. On the other hand, there are numerous applications of listed select agents in a way that is free, or almost free, of risk.

In the US, the National Research Council (NRC) and, later, the NSABB have focused specifically on the dual-use risk of scientific research. That has led to a second

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21 *Handboek Strategische Goederen en Diensten*, Ministry of Economic Affairs, Agriculture and Innovation, 2012. See also: <http://www.rijksoverheid.nl/onderwerpen/exportcontrole-strategische-goederen>. Under the second Rutte Government, export control has been transferred to the Ministry of Foreign Affairs

22 *Council Regulation (EC) No. 428/2009* of 5 May 2009 setting up a Community regime for the control of exports, transfer, brokering and transit of dual-use items. See: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2009R0428:20120107:EN:PDF>, pp. 88-92 for biological agents and toxins. This list is also included in an appendix to the *Handboek Strategische Goederen en Diensten*

23 [http://www.australiagroup.net/en/biological\\_agents.html](http://www.australiagroup.net/en/biological_agents.html)

24 *Handboek Strategische Goederen en Diensten*, p. 25

25 [http://www.selectagents.gov/resources/List\\_of\\_Select\\_Agents\\_and\\_Toxins\\_2012-12-4-English.pdf](http://www.selectagents.gov/resources/List_of_Select_Agents_and_Toxins_2012-12-4-English.pdf)

“biological” criterion, based on the nature of the research to be performed, specifically the “experiments of concern” referred to earlier.<sup>26</sup> Such experiments have given rise to the term “dual-use research of concern”. In fact, one can say the same thing about these experiments of concern as we indicated above about the lists of select agents: they – although important – just represent specific methods and are therefore only useful tools for assessment. They can never be exhaustive because the relevant lists are neither comprehensive nor complete.

Another question is whether there is a connection between the lists of biological agents and certain categories of research when identifying dual-use research of concern, and, if so, what that connection might be. A recent US Government policy document on “institutional oversight” refers to research in which the two are combined. The document lists 15 select agents and seven experiments of concern.<sup>27</sup>

In line with the above, the Biosecurity Committee believes that research involving a select agent that is not classified as an experiment of concern could nevertheless give rise to dual-use problems (as would an experiment of concern that does not involve a select agent).<sup>28</sup> In other words, the methods described above can never be entirely comprehensive.

In addition, lists and overviews of experiments based on the biological, medical, chemical or other physical properties of an agent or a research outcome do not, by definition, offer information on the social or political context, for example. And it is in that context that misuse occurs.

This has led the Biosecurity Committee to conclude that contextual factors must also be considered when establishing an assessment framework to measure the dual-use nature of a research project.

### 5.3 Contextual factors

If an assessment framework focuses unilaterally on possible biological or physical risks, it may overlook or pay too little attention to human intent (for example the presence or absence of a threat). The social and political context is an important factor

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26 National Research Council, *Biotechnology Research in an Age of Terrorism*. Washington DC 2004 (National Academies of Science), pp. 22-23. See also section 4.2 for the relevant experiments

27 *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, February 2013

28 There are claims that the NSABB equates dual-use research of concern with these “experiments of concern” – contrary to the Fink Report, where the experiments are mainly intended as examples. The reason for this approach is said to be the NSABB’s institutional ties with the NIH, resulting in the number of dual-use research of concern cases being kept to a minimum. (Oral information)

in determining the dual-use nature of a technology or study.<sup>29</sup> Recent history has made that clear. The current interest in dual use in the life sciences can be traced largely to the social and political context that has prevailed since the 2001 terrorist attacks and, more particularly, since the anthrax attacks in the United States.

However, several government institutions were already considering the possible misuse of biological agents before the 11 September attacks. In the Netherlands, for example, the Health Council [*Gezondheidsraad*] published a report on bioterrorism in June 2001 [*Verdediging tegen bioterrorisme*].<sup>30</sup> It did so at the request (submitted in 1999) of the Minister of Health, Welfare and Sport. The report recommended improving coordination of existing control mechanisms and precautionary measures, paying closer attention to the possibility of pathogens being spread deliberately, and developing a counter-bioterrorism plan. After the 9/11 attacks and the anthrax letters, the Health Council produced a supplementary report in which it worked out its recommendations in more detail.<sup>31</sup> In keeping with the Health Council's mission, both reports concentrated on the medical aspects, i.e. prevention, vaccine development, and recognition of symptoms.<sup>32</sup> The social and political aspects of bioterrorism are the responsibility of the General Intelligence and Security Service (AIVD), the Military Intelligence and Security Service (MIVD) and, since 2005, the National Coordinator for Security and Counterterrorism (NCTV). These bodies regularly conduct assessments for various categories of threats, including biological attacks.

It is important to be able to identify a specific threat within its social and political context when drawing up an assessment framework. One question is whether that context can be regarded as more or less static, or as something that is constantly evolving and subject to change. The truth probably lies somewhere in the middle. It is unrealistic to expect the entire political landscape to be mapped out for every dual-use assessment. On the other hand, potential new developments or threats must be considered, including their possible disappearance, because threats come and go, as John Forge so aptly explained.<sup>33</sup> Something that we see as a threat today may no longer be regarded as such tomorrow, owing to a changed political or social context.

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29 That has been confirmed by John Forge: "To classify something as dual use should not simply be the flag that the item *could* have some bad use, that some bad use is in theory possible... for artefacts at least, there has to be some threat to make and use an improvised weapon for it to be dual use." Forge, John, A Note on the Definition of 'Dual Use'. *Science and Engineering Ethics* 16, no. 1 (2009): 111-118

30 Gezondheidsraad. *Verdediging tegen bioterrorisme*. The Hague: Health Council, 2001; publication no. 2001/16

31 Gezondheidsraad. *Bioterrorisme: vervolgadvis*. The Hague: Health Council, 2002; publication no. 2002/11

32 After 2002, the Health Council no longer concerned itself explicitly with bioterrorism. It is unclear whether and to what extent the reports still apply

33 Forge, John A Note on the Definition of 'Dual Use'. *Science and Engineering Ethics* 16, no. 1 (2009) : 111-118

The local, national or regional context is also relevant for an assessment framework. Projects carried out (in part) in turbulent regions will raise other concerns than research conducted in a peaceful setting. If the issue is whether the research results can be published, then location is irrelevant, as the H5N1 debate has shown.

That debate also revealed that dual-use concerns can emerge (or re-emerge) in differing phases of a research project. In the H5N1 study, the dual-use nature of the research only became an issue when the results were submitted for publication. It should be noted, however, that already in the early phases of the study (design, application procedure, funding and actual research), the investigators involved were fully aware of the potential dual-use nature of the research, in part owing to their familiarity with the *Code of Conduct for Biosecurity*. Yet, although the dual-use aspect had thus been considered and assessed at various points, it had not had any consequences until the publication phase.

## 5.4 Biosecurity Assessment Framework

Based on the foregoing, the Committee concludes that when determining whether a study should be regarded as dual use from the perspective of biosecurity, both the biological and the contextual factors must be considered. Both sets of factors play a role in the various stages of a research project. This could lead to reconsideration of the relevant project, or to new assessments in the various phases. The question then is not only *whether* a research project is dual use within the context of biosecurity, but in particular *what consequences* this should have. The main question is: how do we determine what those consequences could or should be, and according to which criteria? Factors relevant in the case of funding or the execution of a study may differ from those relevant to publication of the results, for example.

The H5N1 case is an example of how biosecurity can become a particularly urgent issue in the publication phase. In fact, a new term has emerged in recent debates spurred by the H5N1 case: “informational security”. Researchers would thus be dealing with three levels of security: biosafety, biosecurity and informational security. The implication is that researchers are generally well in control of the first two aspects, which mainly relate to the research phase in the laboratory, but that they may underestimate the possible consequences of publishing dual-use research. Whatever the case may be, this idea confirms that any assessment of security aspects must also consider the specific phase that the study has reached.

# 6. WHO SHOULD ASSESS DUAL-USE RESEARCH?

## **From the request for advice:**

In the *Code of Conduct*, everyone in the research process is considered to bear a share of the responsibility. That will be enough in many cases, but the H5N1 debate has shown that sometimes, more is required than an appeal to the sense of responsibility of parties involved. In cases of high-risk or politically sensitive research, there appears to be a need for an institutional arrangement or perhaps an “organisation” that can advise (similar to the NSABB). Such an organisation should not only have an assigned task but also established working methods. In theory, it should be able to take decisions or even intervene at every stage of the research process and with all the parties involved, from the “greenlight” decision up to and including publication of the results.

## **6.1 Thoughts on rule-making and institutionalisation**

The second main question concerns who or which organisation should assess whether a study is dual use in nature (as defined in the first main question). Here too, it is important to differentiate between the various phases of a research project. The question is: who can or should assess the project, and at what point? It should be noted that not all interests will be equally relevant at every stage of a project. A body charged with oversight of biosecurity and dual use must be able to examine all potential interests, however. It will also have to be independent, so that its assessment is as objective as possible.

The Center for International and Security Studies at the University of Maryland published an authoritative report in which it recommended a system for local, national

and international oversight of the biosecurity issue.<sup>34</sup> The report systematically considers who should assess the dual-use nature of research at each level. Its authors assume that the initiative for assessment should be taken at the local level or by the institute concerned. If necessary, oversight can be scaled up to the national and then to the international level. According to the report, “activities of potential concern” should be dealt with by the institute; “activities of moderate concern” at the national level; and “activities of extreme concern” at the international level.<sup>35</sup> But who decides when and why an activity is of potential, moderate or extreme concern? There is, moreover, an American (Western) bias to this proposal, because it assumes the availability of sufficient institutional and national knowledge and capacity to set up such a system. In reality, only a small number of countries have the necessary institutional or national infrastructure. The international level is another story altogether. The authors advocate establishing an International Pathogens Research Authority. Would it be possible to do this within the context of existing institutions, for example the World Health Organisation or the Biological and Toxin Weapons Convention (BTWC)? International discord on this topic would make decision-making – let alone consensus – extremely difficult, if not impossible. For example, the BTWC has not succeeded in approving a verification regime to monitor compliance with its Convention.<sup>36</sup>

Like the authors of the Maryland report, the US Government also assumes that the research institute should bear primary responsibility for assessment. Government bodies only come into play if the research involves risks and interests that transcend the institutional interests. Here again, there is the question of when and why that should be the case, and who is to make that call.

Experience in the United States shows that a number of matters must become clear before we can answer the “who” question. For example:

- The level of knowledge and expertise concerning the scientific content, laboratory security, and the national and international threat being posed. It should be noted that the various levels identified in the Maryland report – local, national, and international – may not all require these various forms of expertise to the same extent. The necessary type of knowledge or level of expertise may also differ depending on the phase of the study.
- Competence. Who is ultimately responsible? In the US is opted for a federal advisory body, the NSABB, consisting of voting members (scientists) and an outer circle of non-voting members who represent approximately 15 government bodies. The NSABB advises on policy, and not on specific projects. The H5N1 debate has led to new proposals that would allow to assess specific research projects. Industry associations, professional organisations, universities and other academic

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34 *Controlling Dangerous Pathogens, A Prototype Protective Oversight System*. The Center for International and Security Studies University of Maryland 2007

35 *Ibid.*, pp. 37-44.

36 Koos van der Bruggen, Barend ter Haar, *The Future of Biological Weapons revisited. A Concise History of the Biological and Toxin Weapons Convention*. The Hague 2011. See pp. 99-103

institutions have developed various guidelines, instructions and codes of conduct in recent years; some of these are voluntary and some not. What role will these non-governmental organisations play?

- What would be the relationship between such new institutions and existing national and international bodies? Will biosecurity institutions operate alongside existing national or international bodies, or be incorporated into them? If so, into which ones, and why? If not, how do we determine the need for new institutions and procedures, or generate support for them? This question is relevant at national level, and even more so in the international context.

## 6.2 Options for dual-use oversight

In its search for options for oversight of dual-use research, the Committee began by exploring whether any existing rules or institutions can serve as examples. It chose to consider rules and institutions that address issues somewhat similar to those of biosecurity. Wherever possible, the list below indicates whether the relevant rule or institution advises on or assesses specific cases or whether it applies a system-based approach to general policymaking.

## 6.3 Examples of relevant rules and institutions

- Regarding the outbreak management of infectious diseases, the role of the Netherlands' Center for Infectious Disease Control (CIb) (part of the National Institute for Public Health and the Environment, RIVM), which identifies the outbreak and spread of infectious diseases and, where necessary, issues advisory reports after a meeting of the Outbreak Management Team (OMT), is distinct from that of the Dutch Minister of Health, Welfare and Sport, who decides what measures should be taken. The advisory reports are in the public domain. Owing to the public nature of the information and the division of responsibilities, the decision-making process is transparent.

This is a case-specific approach. *The OMT is a group of experts who perform an analysis (the content of which is often broadly accepted) and produce an advisory report based on the outcome. This differs from advising on dual-use research, where the analysis – for example of the security situation – is not, by definition, widely shared.*

- The UK's Defence Notice or D-Notice (now known as the Defence Advisory Notice or DA-Notice) is a voluntary code operating between the government departments responsible for national security and the media. Under this code, the media must report information that could damage national security to the authorities. If that leads to a request not to publish or broadcast the relevant information, the media usually comply. In the UK, the system operates to the satisfaction of the parties involved. For more information, see: <http://www.dnotice.org.uk/index.htm>.

This is a case-specific approach. *The question is whether a similar system would*

work when dealing with dual-use research. It would require further elaboration, and the system would have to be tailored to the specific questions associated with research. For example, the status of an advisory report would need to be clarified: is it binding, or not? The advantage of this system is that it holds the researchers responsible. It is up to them to assess the potential security risks inherent in their research. Conversely, the system is entirely voluntary and – in part owing to the lack of an institutional context – those requesting advice are not under any obligation or pain of penalty to comply.

- The Netherlands National Board for Scientific Integrity (LOWI). The Board was established by the Royal Netherlands Academy of Arts and Sciences, the Netherlands Organisation for Scientific Research (NWO) and the Association of Universities in the Netherlands (VSNU) – in other words, by the research community itself. “It advises the boards of universities, university medical centres, the Sanquin Foundation, the NWO and the Academy regarding violations of norms of research integrity”.<sup>37</sup> LOWI is part of the Academy but operates independently of the Academy Board. It deals solely with complaints submitted to the board of a member institution (for example a university) and about which the board has taken a decision or issued an initial ruling. LOWI’s rulings are not binding and may be disregarded by the board of the relevant institution. In reality, however, the boards always adopt them. For more information, see: <https://www.knaw.nl/en/thematisch/ethiek/landelijk-orgaan-wetenschappelijke-integriteit-lowi>  
This is a case-specific approach. *The difference between LOWI and an organisation that assesses dual-use research is that LOWI virtually always reviews matters of interest only to the research community and of little or no relevance for other issues such as public health or security.*
- Making biosecurity and dual use explicit agenda items during external reviews may persuade researchers to take more responsibility for their actions. External reviews are important and have a huge impact in the scientific community. These factors could be put to good use within the context of biosecurity. Among the questions that an external review committee could pose are the following: Has the research institute reported possible dual-use research? Has such research been registered? Has the *Code of Conduct for Biosecurity* been applied?  
This is a system-based approach. *One possible issue is that assessment would be restricted to the research world. What are the possible social and political consequences, and are they being properly considered? In addition, external reviews are, by definition, ex post facto matters. That means that there will be little or no consideration given to potential dual use while a research project is under way.*
- The Central Committee on Research Involving Human Subjects (CCMO) is the official appeals body for rulings issued by Medical Research Ethics Committees at institutions. It is also the competent authority to take certain decisions, and it can

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37 See: <https://www.knaw.nl/en/thematisch/ethiek/landelijk-orgaan-wetenschappelijke-integriteit-lowi>

impose binding rules. The CCMO further acts as a “liaison” for the political world. It can indicate where, when and why new rules or legislation would be useful or necessary. A CCMO system and public reporting can avoid a situation where those who bear political and official responsibility are excluded. A fitting comparison is the annual public report on euthanasia in the Netherlands. The report does not describe individual cases, of course, but it does provide an overview of how many instances of assisted suicide have been referred to the Public Prosecutions Service. For more information, see: <http://www.ccmo-online.nl/main.asp>

*This is a case-specific and system-based approach. The CCMO's strategy offers interesting guidelines for assessing dual-use research. One important difference concerns the identification of research projects that merit assessment. There is virtually never disagreement about whether and at what point a study involves human subjects. There is bound to be less consensus in the case of dual-use research.*

- The Netherlands Commission on Genetic Modification (COGEM) advises the Dutch Government on the environmental risks of GMOs and raises ethical and societal issues linked to genetic modification. COGEM's aim is to help in making an objective assessment of the environmental risks of genetic modification. It does this by estimating the environmental risks and advising government on suitable safety measures. Based on COGEM's advice, the Ministry of Infrastructure and the Environment issues licences for research involving GMOs. COGEM assesses specific projects and in doing so is helping to build a system of parameters and conditions for licensing. *This is a case-specific and system-based approach. Keeping track of new developments in research and technology and their potential consequences for security and other areas of policy are tasks that could also be very useful in connection with dual-use research. However, the area of application would be more difficult to define. Once again, the key difference is that there is virtually never disagreement about whether a study involves GMOs and at what point. That cannot be said of dual-use research.*
- Regulation of nuclear research at Delft University of Technology.<sup>38</sup> Delft University of Technology is currently not doing research involving proliferation-sensitive material, research in the field of nuclear forensics, and studies investigating methods for monitoring threats and risks arising from nuclear terrorism. The researchers involved could well imagine coming up against restrictions if they attempted to publish results in these areas. It should be noted that there are no rules imposing such restrictions, with the possible exception of the same dual-use rules invoked in the H5N1 case. *This is a system-based approach. Alongside the biological dual-use problem, there is the question of whether the research is in fact dual use in nature. One major difference between nuclear research on the one hand and biological and biomedical research on the other is that the dual-use nature is clearer in nuclear research. Nuclear research has been constrained by extensive security arrangements from the very start. These arrangements cannot simply be transferred to the life sciences without alteration.*

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38 Text based on information provided by Delft University staff.

*Box 3 Relevant oversight models*

	<b>Initiator</b>	<b>Voluntary or non-voluntary</b>	<b>Advice or obligation</b>	<b>Case or system</b>
<b>Outbreak management for infectious diseases</b>	Clb	Non-voluntary	Advice issued to Minister	Case
<b>DA-Notice</b>	Media	Voluntary	Advice issued to board of member institution	Case
<b>LOWI</b>	Board of member institution	Voluntary	Advice to involved party	Case
<b>External review</b>	Statutory rules	Non-voluntary	Obligatory for institution under review	System
<b>CCMO</b>	Statutory rules	Non-voluntary	Obligatory for researcher	Case and System
<b>COGEM</b>	Statutory rules	Non-voluntary	Advice issued to Minister	Case and System
<b>Moratorium on nuclear research</b>	Researchers	Non-voluntary	Obligatory for researcher	System

## 6.4 Biosecurity Advisory Committee for Research in the Life Sciences

### Basic principles

The public should be able to trust researchers who engage in knowledge acquisition – often in an effort to solve certain problems in society – to assess whether their results can be misused for criminal or terrorist purposes, based in part on the *Code of Conduct for Biosecurity*. In the Committee’s view, the responsibility for making that assessment lies mainly with researchers and other parties in the knowledge chain.

We cannot assume, however, that all such stakeholders are sufficiently aware of these risks, or that they are always capable of assessing them properly or willing to do so. A proper assessment is certainly possible to some extent given the expertise and competences present in the knowledge institutions themselves. For example, biosafety officers at institutions are now focusing increasingly on biosecurity aspects. The level of engagement can be improved, but given their competences, it would be difficult

if not impossible for life scientists and the management of research institutions to conduct a contextual threat analysis. Nevertheless, it is incumbent on all stakeholders to ask themselves how to deal with research that has potentially disastrous consequences.

It is vital to set up a transparent structure within which stakeholders can take on the responsibilities identified above. That is why all parties in the knowledge chain must have the opportunity to request specific advice on the potential biosecurity aspects of their research proposal, their findings and publication of those findings. Considering biosecurity aspects at an early stage of research may help avoid delays in the publication phase. Advice concerning dual use should allow for both scientific (specifically life-science) and security-related factors. That option is missing from the models listed in section 6.3. Each one contains elements that would be useful when advising on dual-use research. For example, the Committee believes that biosecurity should become a topic of enquiry in regularly scheduled external reviews of research institutions. Such a system could be undertaken in cooperation with the Biosecurity Office (Bureau Biosecurity), that has as one of its tasks “to create and update a list of organisations that work with high-risk pathogens”.<sup>39</sup>

All things considered, however, the Committee must conclude that existing boards and organisations are not equipped to advise the various parties in the knowledge chain. The Committee is therefore of the opinion that a separate advisory body should be established: the **Biosecurity Advisory Committee for Research in the Life Sciences**.

For practical reasons, the Committee prefers the new Advisory Committee to focus only at The Netherlands for the time being. It is aware of the international and even global nature of the biosecurity issue, but given the diverse practices, experiences and interests involved, it would be difficult to coordinate and arrange matters internationally. The Committee hopes that the Dutch model will serve as an example, and that international – or at least European – rules will be put into place as soon as possible. Further arrangements concerning this topic should be set out in the tasks defined for the new Advisory Committee.

The Committee is further aware that by gearing the rules exclusively to the Dutch situation, it is running a risk: the rules may be stricter in the Netherlands than elsewhere. That could put Dutch researchers at a disadvantage internationally, and throw up barriers to research. The Committee would refer in this regard to the concerns expressed by Danish researchers about Denmark’s relatively stringent rules.<sup>40</sup> However, the Committee trusts that this risk will be kept to a minimum once the new Advisory Committee is installed and gets down to work.

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39 See the Bureau Biosecurity website (in Dutch only): [http://www.bureaubiosecurity.nl/Missie\\_Taken](http://www.bureaubiosecurity.nl/Missie_Taken)

40 See: [http://uk.biosikring.dk/fileadmin/user\\_upload/PDF\\_FILER/Biosikringsdokumenter/en.pdf](http://uk.biosikring.dk/fileadmin/user_upload/PDF_FILER/Biosikringsdokumenter/en.pdf)

## **Establishment, composition, defined tasks**

### ***Establishment of the Advisory Committee***

Biosecurity concerns matters that fall within the remit of government (security, public health, education, and research). That is why the Committee believes it is government's responsibility to establish the Advisory Committee. An apt comparison can be found in the United States, where the Federal Government established the NSABB.<sup>41</sup> Within the Dutch context, comparable situations include CCMO and COGEM, two government-established bodies that advise on significant social and ethical issues.

Biosecurity and dual-use research are topics that relate to a range of different policy domains and, as a result, concern various ministries, civil-society organisations and research institutions. Nevertheless, the Committee believes that a single ministry should be responsible for establishing the Advisory Committee and acting as coordinator. The Committee proposes that the Ministry of Health, Welfare and Sport should inaugurate the Advisory Committee and coordinate matters, possibly on behalf of or in conjunction with other ministries. The Committee's reasoning is that public health and the healthcare system are significant concerns in many dual-use projects and that they would be seriously affected by any misuse of research results. The Ministry is familiar with the task of inaugurating important advisory bodies such as the Health Council and CCMO, and with setting up the necessary administrative frameworks.

The Committee realises that legal arrangements may be needed to structure the Advisory Committee and give it a firmer basis.

### ***Placement of the Advisory Committee***

Both the Committee and the Focus Group have discussed various placement options. The most obvious ones are:

- **National Institute for Public Health and the Environment (RIVM)**

RIVM is part of the Ministry of Health, Welfare and Sport, but operates as a separate implementing agency. RIVM has a great deal of expertise in the areas of public health and healthcare. It also has knowledge in the broader area of environmental research. In addition to RIVM's infrastructure and available knowledge, other important advantages are its relationships with such international bodies as the World Health Organisation (WHO), the US Centers for Disease Control and Prevention (CDC), and the European Centre for Disease Prevention and Control (ECDC). RIVM has an excellent reputation with platforms in which the interests of science and society overlap. A point of consideration is that the Bureau Biosecurity is also part of RIVM. The Committee believes that the two bodies should each have their own responsibilities and duties and that they should remain separate.

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<sup>41</sup> The NSABB advises the US government. It also works to raise awareness among researchers. It is not officially responsible for reviewing project proposals.

- **Royal Netherlands Academy of Arts and Sciences (KNAW)**

The Academy (KNAW) is an independent organisation with an excellent reputation in the scientific world. It is experienced at advising on developments in research and technology, but less so on social issues. The Academy is a member of a widespread international network of science academies and institutes. It has experience in the area of biosecurity, having drafted and distributed the *Code of Conduct for Biosecurity* (2006-2009) and prepared the present advisory report (2012-2013). Because the KNAW is regarded as the most outspoken scientific organisation of the Netherlands, entrusting the Advisory Committee to the Academy's care could create the impression that the interests of science weigh more heavily in its assessments of dual-use research than any potential negative security aspects. Another point of concern is that there is no formal advisory arrangement between the Academy and the national government.

- **Health Council of the Netherlands**

The Health Council's field of operation covers public health and healthcare and the relationship between health, safety, and the environment in the broadest sense. The Health Council was established as an advisory body and designed to operate as such. That makes quick and easy incorporation of new initiatives such as the Advisory Committee possible. The Health Council's main line of approach is to advise on the state of science, but it neither promotes the interests of research nor represents the research community. Its work is, however, supported and carried out mainly by top researchers, many of whom are also members of the KNAW network. The Health Council knows how to get professionals and the public to contribute to its advisory reports and has a good reputation in this respect. It is furthermore part of a large international network. Although the Health Council has not been explicitly involved in biosecurity issues since 2001 and 2002,<sup>42</sup> it consistently considers the potential negative consequences (for security and otherwise) of medical and technological advances in its advisory reports. The Health Council's independent status as an advisory body to the Government (and not only to the Minister of Health, Welfare and Sport) and Parliament is laid down in law. Making the Advisory Committee part of the Health Council may result in its advisory reports being handled in accordance with the Health Council's internal rules and agreements. That would solve the problem of the "administrative peg" for the Advisory Committee.

Box 4 summarises the most important pluses and minuses for placing the Advisory Committee with the above-mentioned institutions.

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<sup>42</sup> Gezondheidsraad. *Verdediging tegen bioterrorisme*. The Hague: Health Council, 2001; publication no. 2001/16. *Bioterrorisme: vervolgadvisie*. The Hague: Health Council, 2002; publication no. 2002/11.

*Box 4 Matrix of possible inaugural organisations*

	<b>Pluses</b>	<b>Minuses</b>
<b>RIVM</b>	<ul style="list-style-type: none"> <li>• Knowledge of public health and environmental issues, incl. biosecurity</li> <li>• Experience working with expert and advisory bodies on science and society</li> <li>• International knowledge and experience</li> <li>• Acknowledged as an authority by the public and political circles</li> </ul>	<ul style="list-style-type: none"> <li>• RIVM is part of the Ministry of Health, Welfare and Sport</li> <li>• Differentiation between Advisory Committee and Bureau Biosecurity KNAW needed</li> </ul>
<b>Academy</b>	<ul style="list-style-type: none"> <li>• Involved in drawing up <i>Code of Conduct</i> and advising on biosecurity</li> <li>• Familiar with advising and assessing</li> <li>• Experience working with expert and advisory bodies</li> <li>• International knowledge and experience</li> <li>• Acknowledged as an authority by scientific and political circles</li> </ul>	<ul style="list-style-type: none"> <li>• Image as advocate of science may undermine authority with politicians and public</li> <li>• Limited experience advising and assessing potential negative effects of research on society</li> <li>• No official relationship with government</li> </ul>
<b>Health Council</b>	<ul style="list-style-type: none"> <li>• Knowledge of public health</li> <li>• Experience working with expert and advisory bodies</li> <li>• International knowledge and experience</li> <li>• Administrative “peg” due to Health Council’s statutory task</li> <li>• Scientific approach and point of view</li> <li>• Experience in assessing possible negative effects of research</li> <li>• Acknowledged as an authority by public, political and scientific circles</li> </ul>	<ul style="list-style-type: none"> <li>• Little recent expertise in biosecurity and dual-use research</li> </ul>

***The Committee’s assessment***

It is important to realise that the quality of the Advisory Committee’s advice will be determined by its members. Whether that advice is accepted and acted on, however, will depend in part on the authority of the organisation to which the Advisory Committee reports. That authority can be broken down into three components: acknowledgement by the public, acknowledgement by political circles, and acknowledgement by the world of science. In the above matrix, the Committee has attempted to paint an objective and transparent picture of the various options for placing the new Advisory Committee.

After weighing up the pluses and minuses summarised above, the Committee concludes that the Advisory Committee would best be placed with the Health Council. Consultations with the Health Council have made clear that it would be able to incorporate this Advisory Committee in a way that matches its own defined tasks and

structure. It is important, however, that the relationship with both researchers and government is crystal clear. One suggestion is for the Health Council and Advisory Committee to work with a “framework request for advice”. The Health Council has already applied this method and it does not require immediate statutory arrangements. The Government can ask the Health Council to establish an Advisory Committee that would inform and advise it on dual-use research. An annual report would be produced describing the Committee’s activities and the current state of affairs in dual-use research. In special cases, the Advisory Committee could produce a separate report addressed to government.<sup>43</sup>

### ***Organisation and Funding***

The Advisory Committee will be restricted in size, consisting of a secretary and, possibly, a small administrative and technical support staff. The secretariat will be housed with the Health Council and come under its management. Funding will be provided from the national budget.

### ***Composition***

The Advisory Committee will have a small number of permanent members (a minimum of five and a maximum of seven), including life scientists and security experts. The permanent members will be appointed by the Health Council. Appointments will not include public servants employed by ministries. This core group can be supplemented by ad hoc experts (Dutch and foreign) in specific areas on a case-by-case basis.

### ***Defined tasks***

The Advisory Committee will have the task of advising all stakeholders in the knowledge chain about the procedures to be followed in potential or actual cases of dual-use research. The researchers and the institutions<sup>44</sup> at which dual-use research may take place, or at which such research may be funded or published, are themselves responsible for complying with the regulations and rules governing biosecurity and dual use. They can contact the Advisory Committee of their own accord. Their responsibility in this regard is similar to the responsibility they bear for the ethical aspects of research involving humans and animals, and for rules pertaining to genetic modification. In those instances, however, researchers are required to notify the relevant committees (DEC, CCMO, COGEM) about their research and, where necessary, apply for licences to carry out some or all of the relevant study. That is not the case here.

The Advisory Committee will adhere to the following basic principles in its advisory work:

- accessible for all stakeholders

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43 The expectation is that the Government and Parliament would already be involved in such cases (as in the H5N1 case).

44 This measure would pertain to all public and private institutions at which dual-use research is conducted.

- independent and transparent weighing up of all relevant interests
- confidentiality
- one-off opportunity to reconsider advice based on the response of the requesting party.

The Advisory Committee's defined tasks can be divided into A. case-specific tasks and B. system-based tasks.

## **A. Case-specific tasks**

### *1. Advising on specific research proposals*

The basic principle is that researchers or institutions must themselves be vigilant about research proposals that may be dual use in nature. That is particularly the case if the study concerned involves a biological agent that appears on a prescribed list of dual-use agents. Researchers and research institutions should be familiar with the relevant legislation and regulations pertaining to dual use and with the associated lists and tables. They should also adhere to such rules. Research proposals that are potentially dual use in nature should be submitted to the Advisory Committee for its opinion. As far as can be determined at this time, the Advisory Committee could recommend one of the following:

- a. The study can be carried out without extra conditions being imposed.* This would be the case if the Committee weighed up all the relevant factors and determined that the risks are very small, and if the study concerned is one that closely resembles research previously assessed.
- b. The study can be carried out if a number of conditions are met.* This would be the case if the benefits of the study were considerable and the risks could be contained. It should be noted that the conditions may differ depending on the phase of the study and the factors involved. The conditions that would apply in the case of laboratory research may differ from those applying in the case of publication.
- c. The study should not be carried out or the findings should not be published (in full).* This would be the case if the risks outweighed the benefits and those risks could not be properly contained.

### *2. Reviewing reports by whistleblowers about projects or researchers*

This will involve developing procedures to deal with such reports in confidentiality and with the necessary scrupulousness and to introduce measures where needed. Appeals and reviews must also be made possible. It may be possible to call on the Advice Centre for Whistleblowers in the Netherlands, founded in 2012 by the Minister of the Interior and Kingdom Relations.

### *3. Reporting*

The tasks described in items 1. and 2. above refer to advisory reports and

recommendations issued by the Advisory Committee for the requesting party. It is up to the requesting party to either follow or ignore that advice. We expect that the Advisory Committee's advice will seldom, if ever, be ignored. In all such cases, the Advisory Committee can suffice by publishing an annual overview. However, the Advisory Committee must also be able to take action (or to let others do so) in cases where the requesting party indicates that it will not follow its advice, or simply does not do so. In the first instance, the requesting party should be allowed to file an objection to the advice. If it persists in objecting even after reconsideration of the advice, the Advisory Committee can address the board or executive committee of the requesting party's organisation and ask them to come to an understanding with this party. If this too does not produce the hoped-for results, then the Advisory Committee should have the option of informing government, as its commissioning body, of its advice. That would only happen if the requesting party and its board/executive committee refuse to follow the Advisory Committee's advice even after repeated consultations. This means that the Advisory Committee would forward both its own advisory reports and opinions and the requesting party's reasons and answer. In such cases, all parties involved (researcher, advisers and government) will be notified no less than two weeks in advance. This option is in line with the national government's final political and administrative responsibility for the relevant issue.

## **B. System-based tasks**

The purpose of the *system-based approach* is to build and maintain trust between parties.

4. *Keeping track of scientific, technological and policy-related trends and developments*  
One of the system-based tasks will be to track trends and developments relevant to biosecurity in science, technology and society, both in the Netherlands and abroad. The Advisory Committee will be able to identify relevant developments or activities in this way and can issue a general advisory report on trends related to aspects of dual-use research.
5. *Maintaining contacts with research institutions*  
Based in part on information collected by RIVM's Bureau Biosecurity, consultations can be scheduled with eligible research institutions, possibly leading to an initiative for a specific advisory report.
6. *Maintaining a network of international contacts*  
The Advisory Committee will consult with relevant international organisations and institutions and consult with them.<sup>45</sup> In particular, it will prioritise the quest for closer cooperation and coordination at European level and, possibly, the eventual

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45 For example, the EU, WHO, BTWC and NSABB.

establishment of EU rules or institutions. The Advisory Committee will also look at broader international developments, for example within the context of WHO or the BTWC.

*7. Public information, communication and accountability*

The Advisory Committee will emphasise communication and accountability to government and society. It will therefore develop a website and publish an annual public report in which it accounts for its actions and provides an overview of its work and advisory reports. Public information and communication will also raise awareness of biosecurity and dual-use issues at research institutions so that they too learn to identify where, when and why action is advised.

## **Evaluation**

It is important for the Advisory Committee to have the opportunity to build knowledge and experience regarding the tasks entrusted to it. A period of at least three years would be desirable. During that time, the Health Council and other relevant organisations and ministries will monitor the Advisory Committee's work closely. At the end of the three-year period, there will be an evaluation that may result in changes being made.

# 7. CONCLUSIONS AND RECOMMENDATIONS

## A. ASSESSMENT FRAMEWORK (HOW)

- An assessment framework for dual-use research involves the complex, multidimensional weighing up of scientific, technological, social and political factors.
- Classification as dual use can lead to measures being taken concerning research funding, execution and publication.
- Such measures should be differentiated based on the various aspects and facets of the study.
- Recommendations to take certain measures should not only be substantiated with reference to the biological or physical properties of the object of research, but also to the potential and foreseeable social and political consequences.

## B. INSTITUTIONAL OVERSIGHT (WHO)

- The primary responsibility for dealing with potential dual-use risks of life science research lies with the researchers and parties in the knowledge chain.
- The *Code of Conduct for Biosecurity* should be an ongoing topic of interest in education and researcher training and for research team heads and funding bodies. Drawing attention to the Code will raise awareness of possible dilemmas in dual-use research and may encourage stakeholders to be more active and vigilant.
- The Biosecurity Advisory Committee for Research in the Life Sciences will be established by the Minister of Health, Welfare and Sport to advise researchers and the knowledge chain. The Committee will report to the Health Council of the Netherlands.
- The Biosecurity Advisory Committee for Research in the Life Sciences will

introduce accessible operational rules and procedures.

- The Advisory Committee will have a small number of permanent members (a minimum of five and a maximum of seven), including life scientists and security experts. The core group can be supplemented by ad hoc experts (Dutch and foreign) in specific areas. There will also be a small support staff.
- The Advisory Committee will have the following tasks:
  - Advising on specific research proposals or publication of results
  - Reviewing reports by whistleblowers about projects or researchers
  - Reporting
  - Keeping track of scientific, technological and policy-related trends and developments
  - Maintaining contacts with research institutions
  - Maintaining a network of international contacts
  - Public information, communication and accountability

# APPENDIX 1

## REQUEST FOR ADVICE BY THE STATE SECRETARY FOR EDUCATION, CULTURE AND SCIENCE

Dear Mr Clevers,

The Biosecurity Code has drawn considerable attention in the past year owing to a debate that arose concerning an H5N1 study (and publication of its results) by Prof. Ron Fouchier's research group at Erasmus Medical Centre. The debate led the researchers to apply – under protest – for an export licence in order to publish their research results. The licence was issued by the Ministry of Economic Affairs, Agriculture and Innovation.

The H5N1 case raised a number of questions at various ministries, specifically about its significance for scientific research. Some examples are:

- Which statutory frameworks apply, and what measures and regulations are available in the Netherlands, and to whom, in connection with dual-use research?
- What impact do these frameworks, measures and regulations have on the scientific practice?
- What roles do the individual researcher, the research institution, the research funding body, the authorities and other stakeholders play in dual-use research, both in the Netherlands and elsewhere?
- What measures are employed elsewhere in Europe and around the world in cases of dual-use research, and what do we know about the impact of those measures?

The Netherlands introduced its Biosecurity Code in 2007. Thanks in part to the efforts of the Academy and the Netherlands Organisation for Scientific Research (NWO), the Code has been accepted by the Dutch scientific community. The H5N1 debate has shown, however, that the Code does not offer an unambiguous answer in specific cases. That is hardly surprising, given that it is intended as an awareness-raising tool, and not as a control measure.

Nevertheless, in light of recent events there may be reason to reassess the Code and view it within a broader context, one in which considerations of a scientific nature are

weighed up against the interests of security and, for example, public health. I would therefore ask you to advise me about how to deal effectively with dual-use research. I am not asking you to evaluate the present Code, but I cannot rule out the possibility that my request will result in recommendations to update it.

One of the committees that was closely involved in advising the relevant Minister concerning the H5N1 controversy held a preliminary inter-ministerial meeting concerning the present request for advice. Arrangements will in any event be made for a meeting to be held as soon as possible between the Academy and this interdepartmental committee, so that expectations concerning the request being made to you are clear.

I am hereby asking you (or your designated representatives) to draw up the relevant advisory report, which should address the following key questions:

### **How should dual-use research be assessed?**

There has been broad consensus in recent years about the definition of dual-use research, in line with the Fink Report by the National Research Council.<sup>46</sup> Nevertheless, it often proves difficult in specific cases to arrive at a transparent and authoritative assessment of dual-use research (and research proposals).

It is therefore important to consider **how** one should arrive at and handle an assessment in which research in the life sciences is qualified as dual-use research. On the one hand, consideration should be given to the object and aim of the research and to identifying the associated risks (real and potential), both content-related and technical. On the other hand, the social and political context of the research is also important.

If a research proposal is judged as being dual use in nature, the next step is to determine whether and to what extent the benefits and vested interests (scientific, social) weigh up against the risks to security. That has proved to be a difficult assessment in actual cases. We are therefore asking the Academy to consider how the various interests involved can be weighed up against one another; and hence to develop an “assessment framework” of criteria and considerations to which government and others can refer in decision-making on dual-use research. One particular factor is that, while information is often classified, there is the requirement of verifiability in research (which requires disclosure).

### **Who should make the assessment regarding dual-use research?**

In the Code, everyone in the research process is considered to bear a share of the responsibility. That will be enough in many cases, but the H5N1 debate has shown that sometimes, more is required than an appeal to someone’s sense of responsibility. In

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46 National Research Council, *Biotechnology Research in an Age of Terrorism*. Washington DC 2004 (National Academies of Science)

cases of high-risk or politically sensitive research, there appears to be a need for an institutional arrangement or perhaps an “organisation” that can advise (similar to the NSABB). Such an organisation should not only have an assigned task but also established working methods. In theory, it should be able to take decisions or even intervene at every stage of the research process and with all the parties involved, from the “greenlight” decision up to and including publication of the results.

The point here is therefore to identify who or which organisation should assess the relevant research and apply the criteria referred to above. It is also important to distinguish between the various stages of the research process and to consider at what point in that process an assessment can or should be made and by whom.

The possibility of applying the outcome of such an assessment is determined in part by the legal context (authority, competence, enforceability, assertability). This is all the more urgent because such assessments can have significant international implications. One question, for example, is the regulatory context (nature of research; institution or individual researcher) and the measures involved. In the H5N1 case, one of the key questions was whether and under what circumstances an export rule could be applied to the results of research. It is therefore important to consider both Dutch and European regulations in the advisory report. Another question is whether there are alternatives to full publication.

Finally, I would ask you to look specifically at the following in the advisory report:

- Because not all assessments concerning such research can be left to the individual researcher and there is a need for more comprehensive testing, I ask you to indicate how such testing could be set up and what the role and responsibility of the Academy might be in that context.
- Awareness appears to be a key concept when dealing with dual-use research. How can awareness be optimised, and what role can education and the various training programmes play? In the same connection, I also ask you to publicise your findings after completing the advisory report. This could take the form of a symposium, for example.
- If new institutions or rules are considered necessary, I ask you to describe them in terms of duties, competences, composition, the role of government and science in them, and the involvement and responsibility of various ministries.
- I ask you to indicate explicitly where friction (and, naturally, conflict) might arise between your proposals and existing legislation or customary procedure and to recommend feasible and internationally acceptable solutions.
- Please confirm that you can respond to this request for advice, accompanied by a plan in which you indicate how (composition of advisory committee), within which context, and by which date you expect to complete the report.

Yours sincerely,  
State Secretary for Education, Culture and Science

# APPENDIX 2

## RESOLUTION ESTABLISHING THE BIOSECURITY COMMITTEE

In a letter dated 28 August 2012, the State Secretary for Education, Culture and Science requested the Royal Netherlands Academy of Arts and Sciences to make recommendations on how to deal with “dual-use research” in the life sciences. The Board of the Academy is setting up a Biosecurity Committee to prepare those recommendations.

The Committee’s work will be based on that of the Academy’s Biosecurity Working Group, which drew up a report, *A Code of Conduct for Biosecurity [Een gedragscode voor Biosecurity]*, in 2007.

### Section 1. Task of the Committee

The task of the Committee is to draw up the recommendations requested in the State Secretary’s letter of 28 August 2012 (see the appendix to the present resolution). The Committee will ensure that the draft of its advisory report can be submitted to the Board of the Academy by no later than 22 August 2013 – together with the external peer reviews incorporated by the Committee (see Section 3) – so that the advisory report can basically be provided to the State Secretary in the course of October 2013.

### Section 2. Composition of Committee and Appointment Period

The following persons have been appointed (in their private capacity) to membership of the Committee:

*Chair:*

- Prof. Lous van Vloten-Doting

*Other members:*

- Prof. Roel Coutinho
- Prof. Hans Franken
- Prof. Bob de Graaff
- Prof. André Knottnerus
- Prof. Steven Lamberts
- Prof. Jan Wilschut

The Committee will be assisted by a secretarial department. Mr Jaap Kuiper (Senior Policy Officer, Academy Staff Department) will act as the official secretary to the Committee. The deputy (executive) secretary will be Dr J.J.G. (Koos) van der Bruggen (freelance).

It is assumed (for the time being) that the Committee's term will conclude on 1 November 2013.

### **Section 3. Quality Assurance**

Prior to being appointed, the members of the Committee and the secretarial department have taken note of the Code to Prevent Improper Influence due to Conflicting Interests [*Code ter voorkoming van oneigenlijk beïnvloeding door belangenverstrengeling*] and filled in and returned the Statement of Interests [*Belangenverklaring*] that it contains. The peer review policy is described in the Policy Framework for Quality Assurance in Advisory Reports [*Beleidskader Kwaliteitsborging Adviezen*]. That policy will not be deviated from.

### **Section 4. Follow-up and Communication**

Where necessary and in consultation with the Board of the Academy and the Ministry of Education, Culture and Science, the Committee will follow up and provide for communication concerning its findings.

### **Section 5. Costs and Remuneration**

Pursuant to Section 18(2) of the Regulations governing the Academy, the members of the Committee will receive a travel allowance.

### **Section 6. Confidentiality**

The members of the Committee will observe confidentiality in respect of all information that becomes known to them in the context of the implementation of this resolution and that can be considered to be of a confidential nature.

Adopted in Amsterdam on 15 October 2012 by the Board of the Royal Netherlands Academy of Arts and Sciences.

On behalf of the Board of the Royal Netherlands Academy of Arts and Sciences,

Dr K.H. Chang,  
Director General of the Royal Netherlands Academy of Arts and Sciences

# APPENDIX 3

## EXISTING REGULATIONS<sup>47</sup>

### **A. Registration pursuant to the genetically modified organisms (GMO) regulations (Ministry of Infrastructure and the Environment)**

In order to implement a number of EU directives and regulations, the Genetically Modified Organisms (Environmental Management) Decree [*Besluit genetisch gemodificeerde organismen milieubeheer, Besluit GGO*] (“GMO Decree”) provides that a licence is required in order to work with GMOs. The GMO Bureau [*Bureau GGO*] is the implementing body and holds a full list of companies and institutions engaged in activities involving genetically modified organisms. These may be human, animal, or plant pathogens. The system does not include institutions that work only with wild-type pathogens, i.e. not with GMOs. The system for registering GMOs is current and dynamic.

### **B. Registration pursuant to working conditions regulations (Ministry of Social Affairs Unemployment)**

The Working Conditions Decree [*Arbeidsomstandighedenbesluit*] (Chapter 4, Part 9) sets out the rules that apply in the Netherlands regarding working safely with biological agents. That decree is based on EU Directive 2000/54/EC on the protection of workers from risks related to exposure to biological agents at work. The biological agents concerned are those that are human pathogens and zoonoses; animal and plant pathogens are not included. In order to work with biological agents in categories 2, 3 or 4, written notification must be submitted to the Inspectorate SZW [*Inspectie SZW*] (formerly the Labour Inspectorate [*Arbeidsinspectie*]). Notification does not then need to be given for a subsequent biological agent in category 3, unless it has been categorised provisionally by the employer itself. Notification must be given, however, when working with every subsequent biological agent in category 4. If only diagnostic work is involved, once-only notification is sufficient. In addition, notification must be given again if there have been significant changes in the processes or procedures that may affect the health and safety of employees.

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47 Parliamentary Document [*Kamerstuk*] 28807, no. 152, Appendix. 26 September 2012

### **C. Registration pursuant to the Environmental Licensing (General Provisions) Act (Ministry of Infrastructure and the Environment) and the Activities Decree (Ministry of Economic Affairs, Agriculture and Innovation and Ministry of Infrastructure and the Environment)**

The Environmental Licensing (General Provisions) Act [*Wet Algemene bepalingen omgevingsrecht, Wabo*] (formerly the Environmental Management Act [*Wet milieubeheer*]) and the Activities Decree [*Activiteitenbesluit*] require that notification be submitted for constructing and operating a large number of facilities at which activities take place that may have a negative impact on the environment. Such notification has been required since 1 January 2010 in order to work with a number of animal pathogens in risk categories 1 and 2. This only applies, however, if work is to be carried out with a new animal pathogen or if a new facility is being set up to work with these agents. A random survey of municipalities (which are the competent authority in this context) revealed that they had not so far received any notifications. Prior to amendment of the Activities Decree, there was no obligation to report activities involving wild-type animal pathogens. For some facilities (with a major negative impact on the environment), a licence must be applied for. The competent authority (generally the municipality) deals with the application and in doing so considers what information is necessary in order to issue the licence requested. There is no requirement for centralised registration of notifications or licences.

### **D. Registration pursuant to the Disasters and Crises (Information) Decree (Ministry of Infrastructure and the Environment)**

The purpose of the Disasters and Crises (Information) Decree [*Besluit informatie inzake rampen en crises, BRZO*] is to ensure the provision of information to “security regions” [*veiligheidsregio's*] and local residents (so that they can make the necessary preparations) in the event of disasters. Institutions that intend carrying out large-scale activities involving high-risk microorganisms (more than 10 litres) must notify the management of the security region and the Ministry of Infrastructure and the Environment. Information must also be provided to the security region in the event of accidents and disasters. However, most institutions, for example research laboratories and hospitals, work with smaller volumes than 10 litres of high-risk microorganisms, meaning that their activities do not need to be not registered pursuant to the BRZO.

## **E. Registration pursuant to the quarantine rules for plant pathogens (Ministry of Economic Affairs, Agriculture and Innovation)**

There are two EU directives dealing with quarantine organisms. Directive 2008/61/EC provides, among other things, that Member States must be aware of all activities concerning quarantine organisms. The directive makes it possible (by means of a system of exemptions) to carry out activities that are prohibited under the Plant Health Directive (2000/29/EC), which indicates which organisms present a risk, particularly in the context of exports. These directives have been implemented in Dutch domestic legislation, including in the Plant Diseases Act [*Plantenziektenwet*], the Regulations on the Import and Export of Plants [*Regeling invoer en uitvoer van planten*], and the Decree on the Control of Harmful Organisms [*Besluit bestrijding schadelijke organismen*]. Anyone wishing to carry out work with plant pathogens contained in the quarantine list must apply for a licence from the new Dutch Food and Consumer Product Safety Authority [*Nederlandse Voedsel en Waren Autoriteit*].

# APPENDIX 4

## CODE OF CONDUCT FOR BIOSECURITY

### Background

At the request of the Dutch Minister of Education, Culture and Science, the Royal Netherlands Academy of Arts and Sciences set up a Working Group in 2006 to formulate a *Code of Conduct for Biosecurity*. The Working Group decided to do this, as far as possible, in the context of a dialogue with the relevant institutions, organisations, and researchers. As part of that approach, a broadly based liaison group was set up. The latter generated comparable responses to those that had already arisen at workshops held in other countries: relative unfamiliarity with the risks – for most of those involved, this was something new – and concern that any measures taken might have a negative effect on the progress of research and freedom to publish.

According to the Academy's Biosecurity Working Group, a code of conduct on biosecurity is not a goal in itself. "There is no point in having a document that simply disappears into a desk drawer or a filing cabinet. Raising awareness is the most important objective of a code of conduct on biosecurity, which is why the code of conduct presented here was developed in dialogue with practitioners and with stakeholders from the world of science, the business community and government. After all, the content of the code of conduct must reflect relevant scientific, social and political developments and, equally importantly, the day-to-day practice of individuals and organisations working in the field."<sup>48</sup>

### Text of the *Code of Conduct for Biosecurity*

#### Basic principles

The aim of this code of conduct is to prevent life sciences research or its application from directly or indirectly contributing to the development, production or stockpiling of biological weapons, as described in the Biological and Toxin Weapons Convention

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48 KNAW, *A Code of Conduct for Biosecurity*. Amsterdam 2007, p. 26

(BTWC), or to any other misuse of biological agents and toxins.

## **Target group**

The *Code of Conduct for Biosecurity* is intended for:

- professionals engaged in the performance of biological, biomedical, biotechnological and other life sciences research;
- organisations, institutions and companies that conduct life sciences research;
- organisations, institutions and companies that provide education and training in life sciences;
- organisations and institutions that issue permits for life sciences research or which subsidise, facilitate and monitor or evaluate that research;
- scientific organisations, professional associations and organisations of employers and employees in the field of life sciences;
- organisations, institutions and companies where relevant biological materials or toxins are managed, stored, stockpiled or shipped;
- authors, editors and publishers of life sciences publications and administrators of websites dedicated to life sciences.

## **Rules of conduct**

### ***Raising awareness***

- Devote specific attention in the education and further training of professionals in the life sciences to the risks of misuse of biological, biomedical, biotechnological and other life sciences research and the constraints imposed by the BTWC and other regulations in that context.
- Devote regular attention to the theme of biosecurity in professional journals and on websites.

### ***Research and publication policy***

- Screen for possible dual-use aspects during the application and assessment procedure and during the execution of research projects.
- Weigh the anticipated results against the risks of the research if possible dual-use aspects are identified.
- Reduce the risk that the publication of the results of potential dual-use life sciences research in scientific publications will unintentionally contribute to misuse of that knowledge.

### ***Accountability and oversight***

- Report any finding or suspicion of misuse of dual-use technology directly to the competent persons or commissions.
- Take whistleblowers seriously and ensure that they do not suffer any adverse effects from their actions.

### ***Internal and external communication***

- Provide (additional) security for internal and external e-mails, post, telephone calls and data storage concerning information about potential dual-use research or potential dual-use materials.

### ***Accessibility***

- Carry out (additional) screening with attention to biosecurity aspects of staff and visitors to institutions and companies where potential dual-use life sciences research is performed or potential dual-use biological materials are stored.

### ***Shipment and transport***

- Carry out (additional) screening with attention to biosecurity aspects of transporters and recipients of potential dual-use biological materials.

# APPENDIX 5

## BIOLOGICAL WEAPONS

What are biological weapons? The Biological and Toxin Weapons Convention gives the following definition:<sup>49</sup>

1. Microbial or other biological agents, or toxins,<sup>50</sup> whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes;
2. Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.

Biological weapons can be described more generally as means of delivering pathogenic organisms or poisons of biological origin in order to kill or harm people, animals or plants. Virtually all pathogenic organisms – for example bacteria, viruses or fungi – can be used in biological weapons. In the past, these have included the biological agents anthrax, foot and mouth disease, plague and smallpox. In order to increase their effect, these agents are delivered in enhanced or concentrated form. Missiles, bombs or hand grenades can be used, as well as injections or dispersion across agricultural land.

Even before the Second World War there was the 1925 Geneva Protocol “for the Prohibition of the Use of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare.”<sup>51</sup> The protocol was therefore directed only against the use of biological weapons. However, the United States, the Soviet Union and other countries continued to research and produce biological weapons, which was formally permitted. As far as we are aware, biological weapons were not used during the Second World War. Japan did perform experiments on Chinese prisoners, while the United Kingdom, Canada, and the United States experimented with the anthrax bacterium on Gruinard Island off the Scottish coast. The island was only declared “safe” again in the 1990s. Experiments continued after the war, at times with fatal consequences. It is generally accepted that an error at an anthrax production facility in the Russian city of Sverdlovsk (now known by its previous name of Yekaterinburg) led in April 1979 to an anthrax outbreak in which more than seventy people died.

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49 Text of the Convention available at <http://www.opbw.org/convention/conv.html>

50 A toxin is a potent, complex organic compound of biological origin. There are mineral, vegetable, bacterial, and animal toxins

51 Text available at <http://www.icrc.org/applic/ihl/ihl.nsf/Article.xsp?action=openDocument&documentId=58A096110540867AC12563CD005187B9>

## Biological and Toxin Weapons Convention (BTWC)

The incident in Sverdlovsk occurred after the Biological and Toxin Weapons Convention (BTWC) had already come into force. Unlike the Geneva Protocol, the BTWC prohibits not only the use of biological weapons but also the development, production, and stockpiling of bacteriological (biological) and toxin weapons. The BTWC also dictates that existing stockpiles should be destroyed. The Sverdlovsk incident illustrates the weaknesses of the BTWC: it does not provide for any means of enforcing compliance, for example on-site inspections. In recent years, however, agreement has been reached on:

- national measures (including in criminal law) to implement the prohibition provisions in the BTWC;
- national measures regarding the security and supervision of pathogenic organisms;
- more international means for responding with research and action to the potential use of biological weapons or suspicious outbreaks of disease;
- strengthening and broadening of international cooperation on identifying, preventing and combating infectious diseases;
- development and distribution of codes of conduct for scientists.

These are all measures that the BTWC signatory states can implement on a voluntary basis. Doing so contributes to creating a situation of greater mutual goodwill and understanding. There has definitely been progress in a number of fields, for example the development of codes of conduct for scientists. Partly as a result of this, considerable encouragement has been given to contributions by scientific and other experts.

# APPENDIX 6

## LIST OF BIOLOGICAL AGENTS IN EU REGULATION 428/2009

### Human pathogens, zoonoses and “toxins”,

a) Viruses, whether natural, enhanced or modified, either in the form of “isolated live cultures” or as material including living material which has been deliberately inoculated or contaminated with such cultures, as follows:

1. Andes virus;
2. Chapare virus;
3. Chikungunya virus;
4. Choclo virus;
5. Congo-Crimean haemorrhagic fever virus;
6. Dengue fever virus;
7. Dobrava-Belgrade virus;
8. Eastern equine encephalitis virus;
9. Ebola virus;
10. Guanarito virus;
11. Hantaan virus;
12. Hendra virus (Equine morbillivirus);
13. Japanese encephalitis virus;
14. Junin virus;
15. Kyasanur Forest virus;
16. Laguna Negra virus;
17. Lassa fever virus;
18. Louping ill virus;
19. Lujo virus;
20. Lymphocytic choriomeningitis virus;
21. Machupo virus;
22. Marburg virus;
23. Monkey pox virus;
24. Murray Valley encephalitis virus;
25. Nipah virus;
26. Omsk haemorrhagic fever virus;
27. Oropouche virus;
28. Powassan virus;
29. Rift Valley fever virus;
30. Rocio virus;
31. Sabia virus;
32. Seoul virus;
33. Sin nombre virus;
34. St Louis encephalitis virus;
35. Tick-borne encephalitis virus (Russian Spring-Summer encephalitis virus);
36. Variola virus;
37. Venezuelan equine encephalitis virus;
38. Western equine encephalitis virus;
39. Yellow fever virus

b) Rickettsiae, whether natural, enhanced or modified, either in the form of “isolated live cultures” or as material including living material which has been deliberately inoculated or contaminated with such cultures, as follows:

1. *Coxiella burnetii*;
2. *Bartonella quintana* (*Rochalimaea quintana*, *Rickettsia quintana*);
3. *Rickettsia prowasecki*;
4. *Rickettsia rickettsii*.

c) Bacteria, whether natural, enhanced or modified, either in the form of “isolated live cultures” or as material including living material which has been deliberately 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 dysenteriae*;
12. *Vibrio cholerae*;
13. *Yersinia pestis*;
14. *Clostridium perfringens* epsilon toxin producing types;
15. Enterohaemorrhagic *Escherichia coli*, serotype O157 and other verotoxin producing serotypes.

d) “Toxins”, as follows, and “sub-unit of toxins” thereof:

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 inactivating proteins;
10. Microcystin (Cyanoginosin);
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).

e) Fungi, whether natural, enhanced or modified, either in the form of “isolated live cultures” or as material including living material which has been deliberately inoculated or contaminated with such cultures, as follows:

1. *Coccidioides immitis*;
2. *Coccidioides posadasii*.

## **Animal pathogens,**

a) Viruses, whether natural, enhanced or modified, either in the form of “isolated live cultures” or as material including living material which has been deliberately inoculated or contaminated with such cultures, as follows:

1. African swine fever virus;
2. Avian influenza virus;
3. Bluetongue virus;
4. Foot and mouth disease virus;
5. Goat pox virus;
6. Porcine herpes virus (Aujeszky’s disease);
7. Swine fever virus (Hog cholera virus);
8. Lyssa virus;
9. Newcastle disease virus;
10. Peste des petits ruminants virus;
11. Porcine enterovirus type 9 (swine vesicular disease virus);
12. Rinderpest virus;
13. Sheep pox virus;
14. Teschen disease virus;
15. Vesicular stomatitis virus;
16. Lumpy skin disease virus;
17. African horse sickness virus.

b) Mycoplasmas, whether natural, enhanced or modified, either in the form of “isolated live cultures” or as material including living material which has been deliberately inoculated or contaminated with such cultures, as follows:

1. *Mycoplasma mycoides* subtype *mycoides* SC (small colony);
2. *Mycoplasma capricolum* subtype *capripneumoniae*.

# APPENDIX 7

## COMPOSITION OF BIOSECURITY FOCUS GROUP

- S. Banus**, National Institute for Public Health and the Environment (RIVM), Bureau Biosecurity
- P. Bertens**, Nefarma, Association for Innovative Medicines in The Netherlands
- M. van den Biggelaar**, Ministry of Health, Welfare and Sport
- S. Brul**, Swammerdam Institute for Life Sciences, University of Amsterdam
- R. Busker**, TNO (Innovation for Life), Rijswijk
- H. de Cock**, Faculty of Science, Department of Biology, Microbiology, Utrecht University
- Ph. van Dalen**, Ministry of Health, Welfare and Sport
- R. Dekker**, Ministry of Infrastructure and the Environment
- F. Delemarre**, Biosafety Officer, Crucell Leiden
- R. Duba**, Ministry of Infrastructure and the Environment
- B. Ent** (from 1 April 2013), Ministry of Economic Affairs
- Q. Eijkman**, Centre for Terrorism and Counterterrorism, Leiden University, The Hague Campus
- R. Fouchier**, Faculty of Medicine, Department of Virology, Erasmus MC Rotterdam
- R. Geurts**, Laboratory for Molecular Biology, Wageningen University and Research Centre
- R.J. de Groot**, Faculty of Veterinary Medicine, Department of Infectious Diseases and Immunology, Department of Virology, Utrecht University
- S. Hamelink**, Ministry of Security and Justice
- J. Heesterbeek**, Faculty of Veterinary Medicine, Chair of Theoretical Epidemiology, Utrecht University
- I. Helsloot**, Professor in the Politics of Safety and Security, Nijmegen School of Management, Radboud University Nijmegen
- V. Hendriks** (until 1 April 2013), Ministry of Economic Affairs
- K. de Jong**, Ministry of Foreign Affairs, Security Policy Department
- E. Kampert**, Biosafety officer BSL 3/4, National Institute for Public Health and the Environment, Bilthoven
- J. van Kasteren**, Chair, Association of Science Journalists in the Netherlands (VWN)
- E.J. Koops**, Tilburg Institute for Law, Technology, and Society (TILT), Tilburg University
- C. Laane**, Netherlands Genomics Initiative, The Hague
- M. Levi**, Executive Board, Academic Medical Centre, Amsterdam
- J.W.M. van der Meer**, Emeritus Professor of General Internal Medicine, Radboud University Medical Centre, Nijmegen
- F. Meerts**, Ministry of Security and Justice
- F. Miedema**, Executive Board, Utrecht University Medical Centre
- E.R. Muller**, Dutch Safety Board, The Hague

**L. van den Oever**, Netherlands Institute for Biology (NIBI), Utrecht  
**J. Rokx**, Ministry of Education, Culture and Science  
**K.J. Steenhoek**, Ministry of Foreign Affairs (Export Control)  
**D. Stemerding**, Rathenau Institute, The Hague  
**P.P. Verbeek**, Professor of Philosophy and Technology, Faculty of Behavioural Sciences,  
University of Twente, Enschede  
**G. van Willigen**, Biosafety Officer, Leiden University Medical Centre, Leiden  
**J. Wisse**, Netherlands Biotech Industry Association (NIABA), The Hague

