Science and Social Responsibility - Dual Use Research

Biomedical research produces many important benefits for society, but it can also lead to harmful results. Is your research potentially 'dual use'? A quick Dual Use Questionnaire (Attachment 2) will helpyou answer this question.

The term **'dual use'** refers to research that can be used to both good and bad ends and specifically to the risk that: (1) dangerous agents being studied could be stolen or diverted for malevolent purposes, or (2) results, knowledge, or techniques developed in the course of the research could be used to develop new toxins or pathogens. For example, research on bacterial resistance could be used to develop new antibiotics or to make a biological weapon. Research on human genetics could be used to develop treatments for people with genetic diseases or to discriminate against people, based on their genotypes. Among the earliest examples is the research by Fritz Haber and by Albert Einstein (Attachment 1). While scientists often have little control over how their research is applied, used, or interpreted by others, they can regulate the use of shared reagents/data/specimens through Material Transfer Agreements (MTAs) or Cooperative Research and Development Agreements (CRADAs). Most importantly, they have a responsibility to try to anticipate the possible social consequences of their research, maximize the good consequences, and minimize the bad ones. The cases developed for this year's annual Responsible Conduct of Research Training for NIH Intramural Researchers address, in different ways, the social responsibilities of biomedical researchers with respect to dual use research (cases adopted from SERCEB – see below). Dual use research is expected to be very rare.

So far, the misapplication of new biomedical knowledge has not been a significant tactic used by terrorists. But seven years after the 2001 anthrax attacks, a congressionally-ordered study concludes that there is a growing threat of biological terrorism and calls for aggressive defenses on par with those used to prevent a terrorist nuclear detonation. Referring to the fast-growing technologies in DNA synthesis, which offer new capabilities to alter the genes of existing pathogens or to synthesize them artificially, the study warns that future bioterrorists may use the new technology to make synthetic versions of lethal viruses such as Ebola or genetically modified microbes designed to resist ordinary vaccines and antibiotics.

The NIH Dual Use Committee will provide advice on such research – a questionnaire has been developed to help you determine if your research might fall into this category (Attachment 2) and you can email the committee at any time at dualuse@mail.nih.gov. They also review manuscripts ready for submission if the question on dual use is checked on the manuscript clearance form http://www1.od.nih.gov/oir/sourcebook/oversight/pub-clear-form.htm.

This year's cases deal with a topic that many scientists are unfamiliar with, 'dual use' research. We realize that not everyone will feel comfortable presenting these cases to their discussion groups and Dr. Henry Metzger has agreed that he would offer a training session for facilitators interested in that – please contact him at **hm24q@nih.gov**.

We also plan to add a section on **Frequently Asked Questions**. If you and your group have a question you were unable to answer, please send it to **jps@helix.nih.gov** and we will post it on the website along with the answer.

Case 1 – *Streptococcus pneumoniae* Membrane Pump Sequence

Dr. Ann Newby is a third year postdoc working with Dr. Peter Bigshot, a senior researcher of antimicrobial resistance in gram-positive pathogenic bacteria. Ann is studying recently isolated strains of *Streptococcus pneumoniae* that have developed antibiotic resistance and are responsible for significantly increased pneumonia morbidity and mortality. She identified a gene that she believes is responsible for the resistance, one that encodes part of a membrane-bound protein pump that removes materials from bacterial cells, and has created a variant with increased capacity that provides heightened resistance.

Ann and Peter submit a manuscript to a major bacteriology journal describing the bacterial pump gene as well as the implications of its identification for development of new therapeutic approaches. Several days later, Peter receives a call from the journal editor informing him that the paper will undergo special review due to the 'dual use nature' of Ann's research.

When Peter informs Ann of his conversation with the editor, she is understandably very worried that her manuscript may not be accepted for publication as a result of this special review. While the paper is under review, she and Peter reflect on the new dual use review policies being adopted by journals to which they regularly submit. While *S. pneumonia* is not on the **'select agent'** list, provisions of the PATRIOT Act do apply to Ann's work. Dual-use technology and research issues pertain to far more than select agents.

Do you know what laws and regulations apply to dual use research? (Attachment 3)

What is a "select agent"? (Attachment 4)

This research has clear potential public health benefits -- do the risks outweigh the benefits? Does Ann's paper pose a level of risk sufficient to prevent its publication?

How can a researcher be held responsible if someone diverts the findings for malevolent purposes?

The interested parties in this case can be identified as ranging from the scientific community as a whole, to the public, potential bioterrorists who would misuse such published information, the journal's editorial board, as well as Peter, Ann, their department, and the entire university in which they are working.

How should scientists (i.e., students, fellows, PIs), administrators, journals, institutions, review boards and the public balance the responsibilities and obligations for new knowledge, public safety, and training? Should trainees, dependent on publications for career progression, work on such projects?

Ann learned that free access to genomic and other scientific databases was being discussed by important scientific bodies, including those that fund research and influence policy. Genome databases were at the very foundation of Ann's research, which began with comparisons of bacterial and associated plasmid genomes across different strains of *S. pneumoniae* and other bacteria to look for sequences altered in resistant- versus non-resistant strains.

Should genomic data for all organisms be freely accessible? If not, is there a logical point at which the line can be drawn on what is and what is not publicly available? How would data not available to the public be accessed? How can researchers balance the need for security with the need for open, international science?
(See National Research Council report *(Executive Summary*
http://books.nap.edu/openbook.php?isbn=0309093058&page=1 **) supporting open access to genome data.)**

Case 2- Pandemic Influenza Genomic Sequence

A senior researcher at the Armed Forces Institute of Pathology (AFIP) sequenced three new genes encoding the polymerase from the 1918 Spanish influenza A virus. This strain caused a pandemic estimated to have resulted in the deaths of 50 million people worldwide. This highly important research both clarified the avian origin of this viral strain and determined the key amino acid changes which, if seen in viruses circulating today, could help identify the more pathogenic human-adapted influenza strains and aid the development of vaccines and antiviral therapies. A manuscript describing these results was submitted to *Nature*.

The Editors at *Nature* recognized the great importance of characterizing the 1918 influenza virus, but *Nature* and most other journals now expect that DNA and amino acid sequences that are described in articles will be submitted to a publicly available database in the field that gives free access to researchers from the date of publication.

What are some of the potential risks of publishing sequence data from novel pathogens?

Could the genetic sequence of the 1918 influenza strain be considered "dual-use" research, carrying the risk that it might be diverted for a harmful use?

The journal's Editor-in-Chief agrees to publish the paper along with the sequence without seeking advice from any government authority or outside advisors.

Did *Nature* overlook an important public health concern by agreeing to publish this sequence?

Nature's Editor-in-Chief felt that the benefits of publishing the sequence clearly outweighed the security and public health risk. In a parallel publication submitted to the journal *Science*, other researchers use reverse genetics to translate the AFIP sequence into a replicating virus. The investigators study the pathogenicity and immune responses to this highly pathogenic strain in infected mice. These studies reveal a number of unusual biological properties and permit the testing of antiviral therapies and vaccines in use against contemporary influenza strains.

Should the risk-benefit assessment of dual-use research differ between *Nature,* that published the sequences, and *Science,* where the studies demonstrated how the actual 1918 influenza virus could be recreated?

Following the two publications, the Department of Health and Human Services (DHHS) established an Interim Final Rule adding to the DHHS select agent list the reconstructed replication-competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments. (http://www.access.gpo.gov/nara/cfr/waisidx_07/42cfr73_07.html)

Does the Federal law change the type of research that may be done with this 1918 influenza strain?

If the rule had been in place prior to the submissions to *Nature* or *Science,* would this have affected publication decisions?

This case is based on two real articles[1] and the issue of publication was reviewed by DHHS and the National Science Advisory Board for Biosecurity (NSABB), a committee chartered by DHHS to advise the Federal government on dual-use research. In an editorial appearing in the same issue of *Science*, however, Nobel laureate and renowned molecular biologist Philip Sharp

[1] Tumpey et al. , *Science*, 310, 71 (2005); Taubenberger et al, *Nature*, 437, 889 (2005)

stated, “I firmly believe that allowing the publication of this information was the correct decision in terms of both national security and public health. It is impossible to forecast how scientific observations might stimulate others to create new treatments or procedures to control future pandemics” [2]. The debate on this particular case and on dual-use research in general will likely continue.

[2] Sharp, P.A. *Science Editorial* vol. 310, 17 (2005)

Case 3 - An Unusual Wrinkle to Translational Research

The bacterium *Clostridium botulinum* produces a toxin that is responsible for about 150 cases of food poisoning a year in the United States. However, bioterrorists could exploit several of its properties, namely that it is accessible, easy to prepare in large quantities, and would be deadly if added to the food or water supply. To counteract the effects of such an attack, Dr. Kim Janda's research team screened a library of compounds predicted to inhibit the activity of botulinum toxin to determine if they could be used therapeutically after the attack.

During the studies - work that was supported by the NIH and The Skaggs Institute for Chemical Biology - Dr. Janda's group found a small molecule scaffold that strongly *enhances* the catalytic activity through an apparent increase in binding affinity. *The compound enhanced the activity of botulinum toxin up to fourteen-fold.*

Publishing a paper that describes how to increase the potency of such a lethal toxin seems irresponsible. **Should these findings be published or should this information be suppressed?**

Dr. Janda and his colleagues reasoned as follows: Thanks to its muscle-relaxing effects, botulium toxin is used in minute doses to treat conditions such as cerebral palsy and spasmodic dysphonia, and even to iron out facial wrinkles. They concluded that "As the importance of the toxin in medicine continues to expand, adaptive immune responses to the toxin must be addressed. The discovery and optimization of small molecule activators may ultimately provide a valuable method for minimizing the dosage, thereby increasing its clinical efficacy." The work was published in J. Am. Chem. Soc. (2006) **128**: 4176.

In connection with an article discussing dual use research, the publication *New Scientist* asked several experts whether they agreed with the decision to publish Janda's findings. They defended it, pointing out that in addition to the possible benefits from enhanced treatment of certain diseases, botulinum toxin is so poisonous already that bioterrorists would have little need to enhance its toxicity.

Do you agree with this reasoning?

Case 4 – Cell-matrix Interaction and Tumor Growth & Metastasis

Dr. Gray is an NIH postdoc interested in cell-matrix interaction and its role in tumor growth and metastasis. She finds that membrane protein X is over-expressed in tumor cells and thinks that it may regulate cell adhesion and invasion. She hypothesizes that the N-terminal domain would make a good dominant-negative inhibitor and discovers that expressing this domain inhibits adhesion and kills tumor cells. To produce pure protein to use as a drug to treat cancer, Dr. Gray and her colleague Dr. White develop a bacterial expression-secretion system and are able to isolate the recombinant N-terminal domain from bacterial culture medium. They are excited to find that it kills tumor cells at remarkably low concentrations (0.1 µg/ml), and they name the recombinant fragment "N-statin." They show that it does not kill normal cells until they use 20-fold higher doses.

They do the following tumor survival study using three doses of N-statin or control buffer administered to mice by intraperitoneal injection:

Low dose (0.2 µg) Medium dose (1 µg) High dose (4 µg)

Days Days Days

The lowest concentration has minimal effect, the medium dose effectively prolongs survival though the mice look lethargic for a week, and the highest dose kills the treated mice.

After repeating these experiments, the lab rushes to try to publish their exciting results in a prominent journal. They decide to publish the identification of protein X, the purification and characterization of N-statin, and only the medium-dose survival curve (center graph above). In the manuscript, they emphasize that exceptionally low doses are needed, and they decide to leave out the toxicity findings to keep the story simple because they feel that any drug – even aspirin – has side effects at very high doses. They submit the paper immediately after two days of intense writing.

Is this approach acceptable?

While Dr. Gray tries to identify how N-statin works before her fellowship ends in one month, Dr. White wonders if the new drug candidate will work if taken orally. Worried about possible toxicity, he obtains some leftover mice from a neighboring lab and puts N-statin into their drinking water. They all die immediately. Believing that you should "make lemonade if life gives you lemons," he realizes that it might make a good and very cheap rat/mouse poison, because the bacterial expression-secretion system provides an easy source of the material. He is delighted to find that putting just a single drop of the bacterial culture medium on mouse food kills all of another cage of leftover mice. For his own safety with this potent agent, he begins wearing gloves and sometimes even a lab coat – he is complimented by a secretary on his fashionable purple vinyl gloves when he returns some paperwork to the office. He also takes home a flask of bacterial medium after spinning out the cells to be tested by his brother, who runs a pest exterminator business.

What problems do you see with what he has done?

Dr. Gray has to return to her home country, and Dr. Green – the head of the lab – agrees that Dr. Gray can take the plasmids and bacteria with her to continue the work. As she is leaving the U.S. at Dulles airport, vials of these materials are found in her carry-on bag and she is detained by TSA. They ask her about if the contents are non-hazardous and whether they are valuable research materials stolen from the lab she has left.

What could have been done to avoid this problem?

Dr. Gray and Dr. Green manage to talk their way out of the problem with TSA. Dr. Gray returns home, establishes multiple collaborations, and mails her plasmid to a number of colleagues to help her determine N-statin's mechanism of action, with warnings to handle it carefully.

Is there anything wrong with this?

Meanwhile, one reviewer of the submitted paper had been so excited about this powerful new potential drug that he gave a copy of the paper to a grad student in his lab. The student quickly generates an N-statin plasmid by PCR and produces N-statin using the same bacterial expression-secretion system. While purifying the molecule without using gloves, she grabs a quick sandwich at her desk. She is found unconscious and is hospitalized in critical condition – her doctors are baffled.

What went wrong here?

Another reviewer is also impressed by the potency of the biological drug candidate, but wonders in passing whether toxicity might be a concern. The journal returns the paper to the authors for minor revisions. Dr. Green resubmits the paper after adding their toxicity data. After seeing the new results, the Editor begins to worry about the safety of this agent and tells that authors that the journal will probably have to have the paper reviewed further concerning "Dual Use" technology because of the "Patriot Act." Drs. Green, Gray, and White are quite baffled by this action.

What is the editor's concern?

Dr. White tries to continue working with N-statin, but he drops a shaker flask containing N-statin and cuts his foot because he is wearing sandals. He falls unconscious and is hospitalized. Dr. Green cleans up all the mess and puts the materials into MPW waste for disposal.

What should have been done?

Dr. Green goes to bed worried about Dr. White and dreams that he dies, and dreams further that some terrorist thanks him for providing a new tool to kill Americans. The next day, he reads more about the Patriot Act and Dual Use research and realizes that he and his colleagues might even be prosecuted and potentially sent to prison.

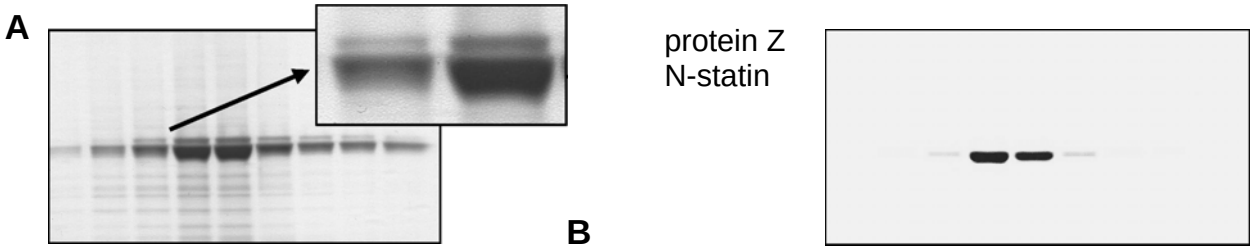
Dr. Gray begins worrying that her paper might not be accepted, that her N-statin might somehow be connected with Dr. White's coma, and that she should have been more careful about distributing her materials. And all just because she wanted to cure cancer!

After information about what has happened starts to leak out, a number of people besides friends and family members become alarmed or angry at the research team, including the Scientific and Institute Director, safety officers, Chair of the animal care and use committee, the Institute's technology transfer office, the FBI, and Department of Homeland Security.

Why did each react so negatively, and what should have been done instead?

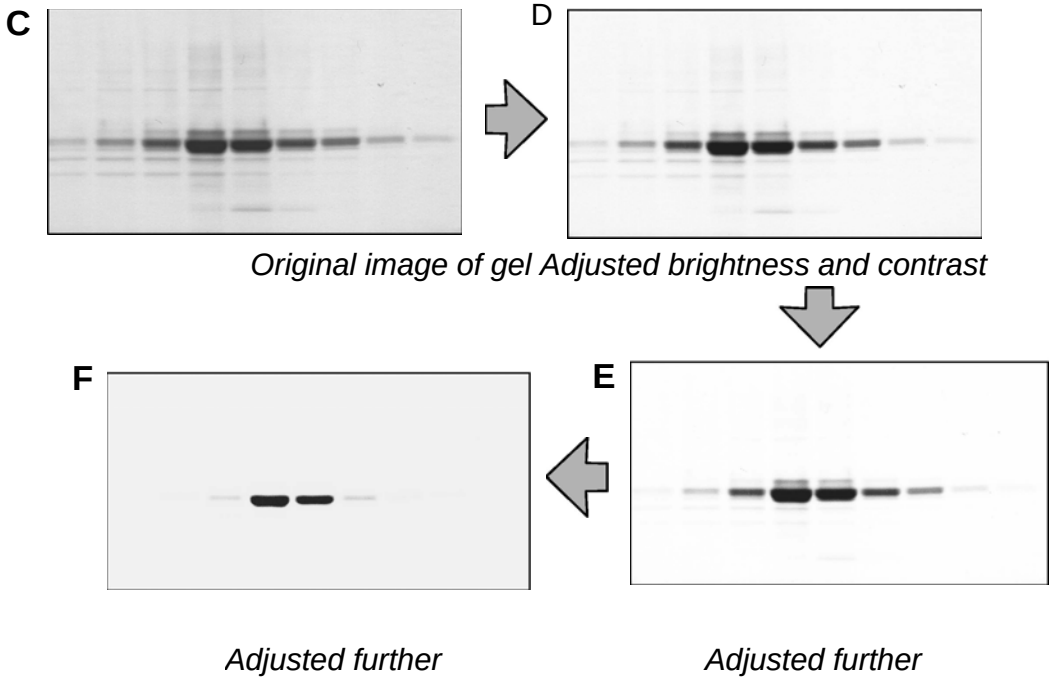
Could you have avoided these problems if N-statin was your discovery?

While the paper is still being evaluated, one of Dr. Gray's collaborators writes to say that he has discovered how N-statin becomes so potent, at least in his own lab: His own preparations contain a second "protein Z" from E. coli (upper band in panel A below) that synergizes with N-statin to kill cells. But he is puzzled because the figure from her paper shows that the same methods produce pure N-statin (panel B).



Dr. Gray sees the same protein Z band in her original gels (***C*** below). But Dr. Green had insisted that she make the gel look prettier by adjusting brightness and contrast, which he felt was "legal" because journals such as Nature allow such adjustments if not selective:

"Processing (such as changing brightness and contrast) is appropriate only when it is applied equally across the entire image and is applied equally to controls."



Was this adjustment ethically "legal"?

Besides potentially misleading readers, what was the other effect?

What should Dr. Gray and Dr. Green do about the paper under review?

Points to Consider

- Research that can be classified as dual use will be very rare but the issue of social responsibility with regards to one's research applies to everyone

- Dual research is expected to be rare but all NIH scientists should review the Dual Use Questionnaire (Attachment 2) to determine whether any research projects they are currently carrying out might fall into the dual use category. If you are not sure, contact dualuse@mail.nih.gov

- It will be preferable to determine if your research has the potential to be considered dual use when you start the project rather than at the point that you are ready to submit a manuscript for publication

- Some scientific journals have established specific policies and procedures regarding publications of this type of research

- This is an evolving policy area and the status of specific research topics may change to dual use or conversely, be removed from these lists, with time

Attachment 1

Fritz Haber and Albert Einstein

The dilemma of what the social responsibilities of scientists are for research that has moral as well as scientific implications is not a new issue. In the first half of the twentieth century, Fritz Haber, a chemist and Albert Einstein, a physicist both performed research that had potential applications beyond the initial problem they were studying. However, their views about the responsibility of the scientist with regard to other uses of his research differed greatly.

Fritz Haber determined how to fix nitrogen to produce ammonia, a necessary component of fertilizer, thereby averting a population crisis. However, ammonia is also used to produce explosives, and the ability of Germany to generate nitrogen for ammunitions prolonged World War I. Haber was not troubled by the ramifications of his research, saying that his only concern was the scientific discovery—"The interest of a wider circle has its source in the recognition that ammonia synthesis on a large scale represents a useful...way to satisfy an economic need. This practical usefulness was not the preconceived goal of my experiments". His outlook changed during World War I when Haber developed chemical warfare, becoming so involved in the process that he was on the front lines to aid with gas release. This involvement in chemical warfare almost cost him the Nobel Prize in chemistry.

Albert Einstein's famous formulation, $E = mc^2$, indicating that a large amount of energy could be released from a small amount of matter, also derived from a purely scientific question. While this knowledge was eventually used in the development of the atomic bomb, Einstein's involvement was also political, as he had become very influential in the United States. Although he was a pacifist, Einstein wrote a letter to President Roosevelt to convince him to develop an atomic bomb before Germany did. Einstein regretted writing the letter to FDR, and he subsequently worked with other scientists to prevent further use of the atomic bomb. However, he realized the significance of dual use research, noting that "The release of atomic energy has not created a new problem. It has merely made more urgent the necessity of solving an existing one."

Attachment 2

Dual Use Questionnaire

	Yes	No
1. Will an intermediate or final product of your research make a vaccine less effective or ineffective?		
2. Will the final or intermediate product of your research confer resistance to antibiotics or antivirals?		
3. Will your work enhance the virulence of a pathogen or render a non-pathogen virulent?		
4. Will the results of your work increase the transmissibility of any pathogen?		
5. Will your research result in alteration of the host range of a pathogen?		
6. Will your research result in a product or intermediate that that may prevent or interfere with diagnosis of infection or disease?		
7. Does your research enable “weaponization” of an agent or toxin?		
8. Even though your research did not involve ***any*** of the aforementioned seven criteria, and recognizing that your work product or results of your research could conceivably be misused, is there the potential for your results/product to be ***readily*** utilized to cause public harm?		

For consultation on these questions, please contact **dualuse@mail.nih.gov**

Attachment 3

RELEVANT FEDERAL LAWS

Two major U.S. federal laws relevant to life sciences research were passed by the U.S. Congress in 2001 and 2002:

1 United and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 or Patriot Act was passed after the 9/11 attacks:

- Makes it a felony to possess a type or quantity of a biological agent that cannot be justified for prophylactic, protective, or peaceful purposes.
- Makes it a federal crime for convicted felons, illegal aliens or fugitives to possess or transport biological agents or toxins, in any quantity and for any reason.
- Defines biological agents as microorganisms, or any recombinant or synthesized component thereof, capable of: causing death, disease, or other biological malfunction in a human, animal, plant or other living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment.(Public Law 107-56 2001).
- Among the biological agents referenced by the Patriot Act is a subset of Select Agents that the Centers for Disease Control or U.S. Department of Agriculture deem most likely to be used as biological weapons. A revised list of such agents went into effect in early 2003, and the rules governing their use, transfer, and registration were finalized in 2005.

2 In 2002, Congress enacted the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, also known as the Bioterrorism Preparedness Act.

- Adds new requirements for the USDA and HHS to consider when determining what should be listed as a Select Agent.
- Requires that Federal agencies must be informed of research, possession, and transport of Select Agents.
- Requires FBI background checks on anyone accessing, transporting, or receiving these agents; and
- Requires that facilities in which these agents are used and stored must be secured in specific ways.(Public Law 107-88 2002)

Attachment 4

Select Agent – a biological agent or toxin that has the potential to pose a severe threat to public health and safety

These include:

Abrin
Cercopithecine herpesvirus 1 (Herpes B virus)
Coccidioides posadasii
Conotoxins
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Ebola viruses
Lassa fever virus
Marburg virus
Monkeypox virus
Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments.
Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Saxitoxin
Shiga-like ribosome inactivating proteins
South American Haemorrhagic Fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)
Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses (Central European Tick-borne encephalitis, Far Eastern Tick-borne encephalitis [Russian Spring and Summer encephalitis, Kyasanur Forest disease, Omsk Hemorrhagic Fever])
Variola major virus (Smallpox virus) and Variola minor virus (Alastrim)
Yersinia pestis

(c) Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms:

(1) Nucleic acids that can produce infectious forms of any of the select agent viruses listed in list above

(2) Recombinant nucleic acids that encode for the functional form(s) of any of the toxins listed above if they:

(i) Can be expressed *in vivo* or *in vitro*, or

(ii) Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro.*

(3) HHS select agents and toxins listed above that have been genetically modified.

(d) HHS select agents or toxins that meet any of the following criteria are excluded from the requirements of this part:

(1) Any HHS select agent or toxin that is in its naturally occurring environment, provided the select agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.

(2) Non-viable HHS select agents or nonfunctional HHS toxins.

(3) HHS toxins under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor, if the aggregate amount does not, at any time, exceed the following amounts: 100 mg of Abrin; 100 mg of Conotoxins; 1,000 mg of Diacetoxyscirpenol; 100 mg of Ricin; 100 mg of Saxitoxin; 100 mg of Shiga-like ribosome inactivating proteins; or 100 mg of Tetrodotoxin.

(e) An attenuated strain of a HHS select agent or toxin may be excluded from the requirements of this part based upon a determination that the attenuated strain does not pose a severe threat to public health and safety.

From: Title 42--Public Health PART 73--SELECT AGENTS AND TOXINS
http://www.access.gpo.gov/nara/cfr/waisidx_07/42cfr73_07.html

Weighing the Risks and Benefits of Dual Use Research

What is Dual Use Research?

Dual use research is typically conducted for positive purposes by legitimate scientists, but it also has the potential for misuse as, for example, in the case of nuclear technology research. The dilemma is how to permit free accessibility to scientific data while minimizing national security risk. As a life science professional either working in a laboratory or overseeing a laboratory that works with materials with the potential for dual use, such as infectious agents, it is your responsibility to know the most current laws and rules. Those relevant to the research projects with which you are involved should be incorporated into your lab's rules and the decisions you make as a researcher, a research administrator, or a member of your research community.

WHAT TYPES OF RESEARCH MAY CAUSE DUAL USE CONCERNS? RECOMMENDATIONS FROM THE SCIENTIFIC COMMUNITY, 2004

The HHS Secretary chartered the National Science Advisory Board for Biosecurity (NSABB) to advise the federal government on policies related to dual use research. NSABB drew from the National Academy of Sciences' report called *Biotechnology Research in an Age of Terrorism* to develop their list of 7 research categories of concern which they recommended to the HHS Secretary in June 2007:

- **Enhance the harmful consequences of a biological agent or toxin;**
- **Disrupt the immunity or the effectiveness of an immunization without clinical and/or agricultural justification;**
- **Confer resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against a biological 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 or tropism of a biological agent or toxin;**
- **Enhance the susceptibility of a host population; or**
- **Generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent.**

In addition to making recommendations on the definition and criteria of dual use research of concern, the NSABB also made recommendations on oversight and communication strategies for the responsible conduct.

Select Agents

The National Select Agent Registry Program oversees the activities of possession of biological agents and toxins that have the potential to pose a severe threat to public, animal or plant health, or to animal or plant products. On this website you will be able to view current regulations regarding select agents, and access additional resource information, as well as download application packages and submit forms electronically http://www.selectagents.gov/index.html.

***RULES AND LAWS GOVERNING LIFE SCIENCE RESEARCH*:**

As illustrated in the figure below, there are layers of rules and governance that dictate all research practices, from decisions made on an individual level to institutional rules and finally federal and even international standards.

PUBLICATION POLICIES

The select agent regulations (42 CFR 73, 9 CFR 121, and 7 CFR 331) place no specific restrictions on the publication of select agent research findings. However, any records or information systems that could allow an individual to gain access to the select agents or toxins should be safeguarded to prevent unauthorized access, theft, loss, or release of these materials. APHIS and CDC strongly encourage entities to refrain from publishing detailed information about select agent and toxin locations, quantities on site, or researchers. APHIS and CDC consider all information provided to the Select Agent Programs in APHIS/CDC Forms 1, 2, 3, 4, and 5 to be "Sensitive but Unclassified (SBU)." Publication of SBU information could compromise the security and safety of the regulated community, public, animals, plants, and homeland security. APHIS and CDC do not release site-specific or identifying information associated with the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121) to the public.

Publication policies must be determined on a case by case basis but some journals have published guidance regarding the use of microbial information. The American Society of Microbiology (ASM), publisher of several journals[3], as the following policy statement on the "Use of Microbiological Information":

> The Council Policy Committee (CPC) of the American Society for Microbiology affirms the long-standing position of the Society that microbiologists will work for the proper and beneficent application of science and will call to the attention of the public or the appropriate authorities' misuses of microbiology or of information derived from microbiology. ASM members are obligated to discourage any use of microbiology contrary to the welfare of humankind, including the use of microbes as biological weapons. Bioterrorism violates the fundamental principles expressed in the Code of Ethics of the Society and is abhorrent to ASM and its members.
>
> ASM recognizes that there are valid concerns regarding the publication of information in scientific journals that could be put to inappropriate use as described in the CPC resolution mentioned above. Members of the ASM Publications Board will evaluate the rare manuscript that might raise such issues during the review process. However, as indicated elsewhere in these Instructions, research articles must contain sufficient detail, and material/information must be made available, to permit the work to be repeated by

[2] ASM publications include: Antimicrobial Agents and Chemotherapy, Applied and Environmental Microbiology Clinical and Vaccine Immunology, Clinical Microbiology Reviews, Eukaryotic Cell, Infection and Immunity, Journal of Bacteriology, Journal of Clinical Microbiology, Journal of Virology, Microbiology and Molecular Biology Reviews, Molecular and Cellular Biology

others. Supply of materials should be in accordance with laws and regulations governing the shipment, transfer, possession, and use of biological materials and must be for legitimate, bona fide research needs. Links to, and information regarding, these laws and regulations can be found at http://www.asm.org/.