NUFFIELD COUNCIL ON BIOETHICS

BACKGROUND PAPER

Dual Use in Biology and Biomedicine

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Note
The author was commissioned by the Nuffield Council on Bioethics to write this paper in order to inform the Council's discussions about possible future work on this topic. The paper is intended to provide an overview of key clinical, ethical, social, legal and policy issues, but is not intended to offer any conclusions or recommendations regarding future policy and practice. Any views expressed in the paper are the author's own and not those of the Nuffield Council on Bioethics.

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Background Paper by Filippa Lentzos

The 'dual use' concept

In the field of arms control and disarmament, 'dual use' refers to technologies intended for civilian application that can also be used for military purposes.

The international treaty banning biological weapons, the Biological Weapons Convention, prohibits the development, production and stockpiling of biological weapons, but does not prevent states conducting research activities for peaceful and defensive purposes. However, distinguishing between permitted and prohibited activities is difficult at the level of basic biological research where the same techniques used to gain insight and understanding about fundamental life processes for the benefit of human health and welfare may also be used for the development of biological warfare agents.

There are four frequently cited trends in biology that are complicating this so-called 'dual use dilemma:'[1]

- The increasing pace of change in the life science and related fields.
- The increasing convergence of biology and biomedicine with mathematics, engineering, chemistry, computer science and information theory.
- The increasing diffusion of capacity in biology and biomedicine around the world, particularly in emerging economies such as China and India, and increasing collaborations not only among researchers in scientifically developed countries and between researchers in developed and developing countries, but among regional networks and increasingly among scientists within developing countries.
- The increasing opening up of science with new tools like wikis, blogs and microblogs altering how information is gathered, handled, disseminated and accessed; and amateur communities, scientific outreach and educational toys increasing access to hardware for wetwork in the life sciences.

Dual use 'of concern' (DURC)

The seminal report focusing on the dual use dilemma is the US National Academies of Sciences report *Biotechnology Research in an Age of Terrorism*.[2] Chaired by MIT biologist Gerald Fink, the committee behind the report was set up in response to the growing concern about bioterrorism and the potential for misuse of biotechnology by hostile individuals and states following 9/11 and the 'Amerithrax' attacks (as the FBI code-named the anthrax letters sent to media outlets and the US Senate immediately following 9/11).

The Fink Committee, as it became known, also responded to a set of published scientific experiments in the early 2000s that involved the creation of genetically engineered mousepox and smallpox variants and the artificial

synthesis of poliovirus. These experiments raised policy and public concerns that the scientific papers could be downloaded online by terrorists and used to launch a bioweapons attack.

Biotechnology Research in an Age of Terrorism formed a significant part of the political discourse around dual use in the early 2000s that conflated concerns over cutting edge scientific experiments with the Amerithrax case, and other types of potential bioterrorist events, with little differentiation of the types of factors that might shape each of these distinct threats.

The Committee identified seven classes of experiments that would raise misuse concerns, and that should necessitate further review before they are conducted or published. These include those that: (1) demonstrate how to render a vaccine ineffective; (2) confer resistance to therapeutically useful antibiotics or antiviral agents; (3) enhance the virulence of a pathogen or render a nonpathogen virulent; (4) increase the transmissibility of a pathogen; (5) alter the host range of a pathogen; (6) enable the evasion of diagnostic/detection modalities; (7) enable the weaponization of a biological agent or toxin. The Fink report also recommended the creation of a new National Science Advisory Board for Biosecurity to provide guidance for the review and oversight of such experiments and other dual-use research concerns.

The National Science Advisory Board on Biosecurity (NSABB) was chartered in 2004 by the Executive Office of the President to provide advice to the US government regarding the review and oversight of dual-use research. In the first years of its existence, the NSABB was focused on defining and providing oversight recommendations for dual use research, as well as making recommendations regarding the emerging field of synthetic genomics. At the time, and into the present, the NSABB has been primarily concerned with providing guidance on scientific and technological developments in the life sciences, and how these might lead to biological weapons or bioterrorism threats. In their oversight and evaluation recommendations, the focus of the NSABB has been almost exclusively on the materials and methods sections in scientific papers and also the availability and use of new technologies to produce advanced bioweapons threats.

The NSABB proposed a split between two kinds of science. ‘Dual use research’ was used to refer in general to legitimate life sciences research with potential to yield information that could be misused to threaten public health and safety and other aspects of national security. Since nearly all science could be used in this manner, NSABB offered another category: ‘Dual use research of concern’ (DURC). This denoted “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.”[3] Informed by the Fink Committee’s seven classes of experiments, the NSABB identified seven categories of experiments that describe information, products or technologies that if produced from life sciences research mean the research warrants careful consideration for its dual use potential. In contrast to the Fink Committee’s which “illustrated the

types of endeavours or discoveries that would require review and discussion…before they are undertaken, or, if carried out, before they are published in full detail", the NSABB categories, which in some cases were modifications of the Fink Committee categories, were "descriptors of information, products, or technologies that, if produced from life sciences research, might define that research as meeting the criterion for being dual use research of concern."[4]

The NSABB categories are knowledge, products or technologies that could enable any of the following: (1) enhance the harmful consequences of a biological agent or toxin; (2) disrupt immunity or the effectiveness of an immunization without clinical and/or agricultural justification; (3) 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; (4) increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin; (5) alter the host range or tropism of a biological agent or toxin; (6) enhance the susceptibility of a host population; and (7) generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent.

Experiments with high misuse potential

Examples of DURC in biology and biomedicine include those that increase capacity:

- to manipulate the pathogenicity, virulence, host-specificity, transmissibility, resistance to drugs, or ability to overcome host immunity to pathogens;
- to synthesize pathogens and toxins without cultivation of microorganisms or using other natural sources;
- to identify new mechanisms to disrupt the healthy functioning of humans, animals and plants; and
- to develop novel means of delivering biological agents and toxins.

More concretely, there have been a number of high profile experiments over the past few years that have raised significant concern. These have aimed to make mousepox more deadly, synthesize poliovirus from scratch, reconstruct the extinct 1918 flu virus, and make flu viruses more easily able to spread; they are detailed further below. Other research projects that have also raised concerns about their high misuse potential include the development of computer simulations that model the spread of disease, which could also help optimize the impact of a deliberate release; the creation of a chimera virus from the components of an influenza virus and the West Nile Virus; and the identification and characterization of antibiotic resistance to new antibiotics, previously held in reserve for the treatment of multi-drug resistant strains.[5]

More virulent mousepox

In an attempt to create a contraceptive vaccine for mice as a means of pest control, Australian scientists unexpectedly increased the virulence of

mousepox. They inserted interleukin-4 (IL-4), a gene that enhances antibody production, into mousepox and the new virus proved to be highly lethal in infected mice, including those that had been vaccinated against it. After discussion it was decided to pursue publication of the findings.[6]

When the paper was published in the *Journal of Virology* in January 2001,[7] widespread media coverage focused on the potentially dangerous consequences the results could have for public health. Questions were raised about genetic manipulation in general, and there were concerns that similar experiments on orthopoxviruses, such as smallpox, could potentially increase their virulence. Some warned that the paper provided information that could be used to render the smallpox vaccines ineffective.[8]

Synthetic poliovirus

In 2002, researchers demonstrated that it was possible to assemble a synthetic virus by piecing together chemically synthesized oligonucleotides ordered online from commercial DNA synthesizing companies based on openly published polio genomes. The result was a 'live' poliovirus that paralyzed mice. The published paper included a description of methods and materials.

The primary concern with this research was that it could yield a recipe for reconstructing poliovirus without obtaining a natural virus. There were also concerns that the research could enable the artificial synthesis of smallpox as the smallpox genome had also been published online – though experts pointed out that, due to the much greater complexity of the smallpox virus, it was unlikely that the same approach would be successful in producing a working virus. Critics of the research were also skeptical about the scientific value of the research and the need for its publication,[9] arguing that the techniques used in the experiment were not new and the research did not lead to new knowledge or insights.[10]

Reconstructed 1918 influenza virus

In 2005, researchers successfully re-created the extinct influenza A (H1N1) virus responsible for the 1918 Spanish flu pandemic using gene sequences from archived materials and from lung tissue of an influenza victim who had been buried in permafrost in 1918. Using reverse genetics, the researchers generated the relevant 1918 viral coding sequences and outfitted a relatively avirulent influenza virus with all eight viral segments of the 1918 strain that conferred the unique high-virulence 1918 strain phenotype on the engineered virus. The aim of the research was to increase understanding of the biological properties responsible for the high virulence of the pandemic virus. This knowledge could then be used to devise and evaluate current and future public health interventions should a similar pandemic virus emerge, including strategies to diagnose, treat and prevent the disease. The experiment also indicated that the 1918 virus gene sequences were more closely related to avian (H1N1) viruses than any other mammalian influenza H1N1 strains.

The experiment was published in October 2005 in *Nature*,[11] where the sequences of the final three gene segments of the flu virus genome were published, and in *Science* which published the recreation of the flu virus based on the *Nature* article.[12] While some considered the research to represent a landmark breakthrough, others raised concerns about the risks posed by resurrecting the virus,[13] questioned the safety procedures for handling the virus,[14] and even questioned the scientific value of the experiment, arguing that the research had limited utility.[15] Others questioned whether the research findings should have been published.[16] The NSABB concluded that the scientific benefits of the research far outweighed the biosecurity risks.[17]

More transmissible influenza viruses

An area of virology which creates pathogens that could potentially cause pandemics first attracted attention in 2011. Two leading influenza laboratories, led by Ron Fouchier at the Erasmus Medical Center in the Netherlands and Yoshihiro Kawaoka at the University of Wisconsin-Madison, revealed that they had made versions of the H5N1 avian influenza strain that could now spread between mammals (it could previously only spread between birds). Many scientists worried that if the potent new lab strain was accidentally or deliberately released, it could result in a deadly pandemic. The *New York Times* ran an editorial with the unambiguous headline 'An Engineered Doomsday,' arguing that the modified flu virus could kill tens or hundreds of millions of people if it escaped the lab or was stolen by terrorists. Proponents of gain-of-function research, on the other hand, argued that such studies help us understand influenza transmission and aid public health researchers detect an impending flu pandemic and prepare vaccines.

In January 2012, a group of leading influenza virologists agreed to a voluntary moratorium on these so-called gain-of-function studies. The work resumed in 2013, but new experiments on human-made H5N1 and other dangerous flu strains like H1N1,[18] H7N9[19] and H7N1[20] rekindled concerns—in part because a series of lab accidents and breaches at the Centers for Disease Control and Prevention and the National Institutes of Health had heightened concerns about safety at high-containment labs.[21] In October 2014, the US government stepped in, imposing a federal funding pause on the most dangerous gain-of-function experiments and announcing an extended deliberative process that is still on-going.[22, 23]

Emerging fields with high misuse potential

Emerging fields of research within biology and biomedicine that have raised particular concern include synthetic biology and neurobiology.

Synthetic biology

Synthetic biology is an emerging field that seeks to create a rational framework for manipulating the DNA of living organisms through the application of engineering principles. Although the precise labelling of

synthetic biology and whether it represents a distinctly novel field have been called into question,[24] its key founding principle is to engineer biology, or "to design and engineer biologically based parts, novel devices and systems, as well as redesigning existing, natural biological systems."[25]

The pace of progress in the field has been exceptionally fast. From the first functional virus with 7,500 DNA base pairs synthesized from scratch in 2002 (poliovirus – see case study details above),[26] to 32,000 DNA base pairs synthesized in 2004,[27] to the synthesis of an entire bacterium with over a million DNA base pairs (*Mycoplasma mycoides*) in 2010[28] – a major milestone in the use of DNA synthesis techniques to create more complex and functional products. In 2014, a designer yeast chromosome was constructed[29] – this time a major advance towards building a completely synthetic eukaryotic genome.

Synthetic biology research has also focused on the creation of a bacterium with the minimal number of genes necessary for the organism to survive. Foundational work on *Mycoplasma genitalium* reduced the bacterium to the minimum 381 genes necessary for keeping it alive, with the aim of using the microbe as a 'chassis' for building new synthetic biological devices able to perform specific tasks.

Advances in synthesis and minimal genome research have been complemented by progress in gene-editing technology, which is enabling deletions and additions in human DNA sequences with greater efficiency, precision and control than ever before. 'CRISPR' (clustered regularly interspaced short palindromic repeats) has become the major technology employed for these purposes and has been used to manipulate the genes of organisms as diverse as yeast, plants, mice and, reported in April 2015, human embryos.[30] The system relies on an enzyme (Cas9) capable of making cuts at any point in a DNA molecule that uses a guide RNA molecule to home in on its target DNA, then edits the DNA to disrupt genes or insert desired sequences. Most of the components can be bought off the shelf; often it is only the RNA fragment that needs to be ordered, with a total cost of as little as $30.[31] Characterised as 'cheap, quick and easy to use', it has been labelled the 'biggest game changer to hit biology since PCR,' the gene-amplification method that revolutionized genetic engineering after its invention in 1985.[32]

Genetic changes in one organism usually take a long time to spread through a population. This is because a mutation carried on one of a pair of chromosomes is inherited by only half the offspring. But 'gene drives' are now allowing a mutation made by CRISPR on one chromosome to copy itself to its partner in every generation, so that nearly all offspring will inherit the change. This means an edited gene can in principle spread through a population exponentially faster than normal.

The dual use discourse around synthetic biology has been focused on the field's potential to create dangerous pathogens from scratch and design radically new pathogens not found in nature. The emphasis has primarily

been on terrorists and non-state actors, with little emphasis on states and military and defence actors.[33]

Trends in synthetic biology research funding indicate a total US investment of $820 million between 2008 and 2014, with a steep upward trajectory.[34] In 2014, two thirds of the $200 million invested came from the Department of Defense and its research agency DARPA.[35]

Funding in other countries is also increasing rapidly. In 2014, the UK and European Commission investment in synthetic biology made up nearly 30 percent of total Euro-American synthetic biology funding.[36] Some of this European funding is also defence-related. In the UK, for instance, which spends twice as much as the European Commission on synthetic biology, the field is one of five emerging technologies identified by the Ministry of Defence to have the most potential for national security.

Neurobiology

The use of novel neurotechnologies by states for either offensive or defensive military purposes in international and domestic conflicts is another emerging area with high misuse potential.[37]

As with synthetic biology, investments in the field are considerable. The European Commission funded Human Brain Project, established in 2013, has an estimated €1,190 million price tag over ten years.[38] The US equivalent, the BRAIN Initiative, was also launched in 2013, as a public-private partnership with an approximate $100 million in the President's Fiscal Year 2014 Budget.[39] Approximately half of the US funding comes from the Department of Defense and DARPA.[40]

Unlike the American programme, the Human Brain Project has an 'ethics and society' component which aims "to explore the project's social, ethical and philosophical implications, promote engagement with decision-makers and the general public, foster responsible research and innovation by raising social and ethical awareness among projects partners, and ensure that the project complies with relevant legal and ethical norms."[41]

The ethics of developments in neurobiology were also considered in the Nuffield Council on Bioethics 2013 report *Novel Neurotechnologies: Intervening in the Brain*. The three main areas in which ethical questions arise were identified as the use of neurodevices in interrogation, the involvement of serving military personnel as participants in research, and the dual use of neurotechnologies developed for therapeutic applications but used for military purposes. In terms of dual use it was highlighted that continuous reflexive evaluation of innovation pathways is an important element of responsible research and innovation in neurotechnologies. It was recommended that, as part of their ethical training, those studying for a higher degree in neuroscience should be alerted to the possible dual-use implications of neurotechnologies.

Responses to dual use risks

Management of DURC-related risks to avoid accidents and potential misuse has been approached in several ways in the UK and US, including through: research oversight mechanisms; policies for funding agencies; policies for journal publishers; institutional and professional codes of conduct and ethics; and awareness-raising and educational initiatives for a range of audiences.

Research oversight mechanisms

The US National Academies of Sciences report *Biotechnology Research in an Age of Terrorism* proposed that research identified as falling within the seven classes of experiments of concern (listed above) should be reviewed using the already established system for review of recombinant DNA experiments.[42] It also emphasized the need to educate the scientific community about this issue; to rely on the self-governance of scientists and journals to review research results and decide whether or not to publish; to rely on current legislation and regulation regarding the protection of biological materials; and to harmonize measures at the international level.

The US National Advisory Board for Biosecurity report *Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information* proposed the development of federal guidelines for the oversight of dual use research, local evaluation and review of research with dual use potential by the principal investigator, and institutional review of research where dual use research of concern is identified.[43] The NSABB also emphasized the need for awareness-raising, and ongoing and mandatory education, about dual use research issues and policies.

Following the highly controversial experiments in 2011 to make the H5N1 flu virus more easily able to spread (see case study details above), the US government issued regulations in March 2012 subjecting life science research to increased oversight and security review.[44] The regulations opted for somewhat different criteria for establishing dual use research of concern to that recommended by the National Academies of Sciences and the NSABB. Like the earlier proposed oversight models, the government regulations require a review of research that aims to, or is reasonably anticipated to, produce one or more of seven categories of effects, such as enhancing the harmful consequences of an agent, altering the host range of an agent, or increasing the stability or transmissibility of an agent.[45] However, the government limits the review to research carried out with one of 15 ‘select agents’ deemed to pose the greatest risk of deliberate misuse with most significant potential for mass casualties or for devastating effects to the economy, critical infrastructure or public confidence.[46] (Select agents are similar to ‘Schedule 5’ pathogens of the Anti-terrorism, Crime and Security Act 2001 in the UK.) The review is also limited to public research, i.e. research funded or conducted by the government, and is to be carried out at the institutional level. Institutions are to notify funding departments and agencies,

which in turn report to the Assistant to the President for Homeland Security and Counterterrorism. If any risks posed by the research cannot be adequately mitigated by modifying the design of the project, applying enhanced biosecurity or biosafety measures and the like, then voluntary redaction of publications or communications may be requested, the research may be classified, or the funding may be terminated.[47] A more detailed policy articulating and formalising the roles and responsibilities of institutions and investigators was introduced in September 2014 with effect from September 2015.[48]

No other countries have to date developed guidance or practices like the US to address the potential for terrorist misuse of the knowledge based on biology and biomedical research.

Multilaterally, the Biological Weapons Convention (BWC) is the legal embodiment of a powerful international norm against the use of disease as a weapon and has an important role to play in efforts to manage dual use in the life sciences. BWC member states have reached numerous agreements and understandings related to the management of dual use life science research across a broad range of areas:

- Oversight of science - including guidance on developing national frameworks and the value of harmonizing them, where possible and appropriate;
- Laboratory biorisk management - including understandings on terminology in all official languages of the United Nations and guidance on national arrangements;
- National policies, laws and regulations - including legally and politically binding obligations on the existence of certain national measures; guidance on developing relevant national frameworks as well as their aims and content;
- Codes of conduct - guidance on the content, adoption and promulgation of codes, roles of various stakeholders as well as the relationship of codes with legislation and regulation;
- Education and training activities to raise awareness of the risks associated with the malign use of biology - binding commitments to undertake relevant education and outreach activities as well as guidance on the content and conduct of such efforts.

Funding agencies' policies

In the UK, the three major research funding agencies in biology and biomedicine – the Biotechnology and Biological Sciences Research Council (BBSRC), the Medical Research Council (MRC) and the Wellcome Trust – have issued a joint policy statement on managing risks of misuse associated with grant funding activities.[49] They maintain that a system based on self-governance by the scientific community will be the most effective means of managing the risks of misuse. Their statement also argues that "the community should take active steps to further develop mechanisms of self-governance, and that through doing so the community can ensure that

responsibly conducted research is not unnecessarily obstructed." Leading by example, the three bodies introduced a question on grant applications asking applicants to consider risks of misuse associated with their proposal; explicitly mentioned risks of misuse in guidance to referees as an issue to consider; developed guidance for funding committees and the process for assessing cases where concerns have been raised; and modified organizational guidelines on good practice in research to include specific reference to risks of misuse.

The European Commission also has a system in place to manage submission of research grant applications, where an ethical review panel and a security scrutiny committee can be convened if a research project has ethical or security implications.[50] The Commission has also published a green paper on bio-preparedness, including measures against the potential misuse of research.[51]

Commentators have noted that, in practice, very few research proposals have raised any concerns over the last ten years.[52]

Journal publishers' policies

Following concerns about the publication of several experiments, 32 editors and authors representing some of the most prestigious peer-reviewed journals, including *Nature*, *New England Journal of Medicine* and *Science*, made a joint statement in 2003 on scientific publication and security.[53] The statement made several significant points:

> "We must protect the integrity of the scientific process by publishing manuscripts of high quality, in sufficient detail to permit reproducibility. … We are committed to dealing responsibly and effectively with safety and security issues that may be raised by papers submitted for publication, and to increasing our capacity to identify such issues as they arise. … Scientists and their journals should consider the appropriate level and design of processes to accomplish effective review of papers that raise such security issues. … We recognize that on occasion an editor may conclude that the potential harm of publication outweighs the potential societal benefits. Under such circumstances, the paper should be modified, or not be published. Scientific information is also communicated by other means: seminars, meetings, electronic posting, etc."

Several journal editors have put in place mechanisms for papers that may need additional peer-review because of the potential risks for misuse. The Council of Science Editors, which aims to promote excellence in the communication of scientific information, has published a white paper that includes a section on the responsibilities of editors to the public. This white paper encourages editors to "educate journal boards, reviewers, and authors; establish screening methods to recognize [dual-use research of concern]; obtain reviews of these manuscripts from individuals with technical and security expertise; create an ongoing network to share experience and further refine ways for managing [dual-use research of concern];" and "develop

guidelines and procedures to allow the scientific evaluation as well as evaluation of the possible risk of communicating information with dual use potential."[54]

As with funding applications, commentators have noted that, with the exception of the
controversial 2011 H5N1 flu virus experiments (see case study details above), very few articles have raised any concerns in practice over the last ten years.[55]

Codes of conduct and ethics

Codes of conduct and ethics programmes are two other risk management options that have attracted a great deal of policy attention.

In November 2005, the Interacademy Panel (IAP) issued a statement on biosecurity, which was endorsed by 68 national academies of science. This statement noted: "Scientists have a special responsibility when it comes to problems of 'dual use' and the misuse of science and technology."[56] The statement presented several guiding principles for individual scientists and local scientific communities who wish to develop codes of conduct. These principles include awareness, safety and security in laboratories, education and information, accountability and oversight.

A number of national academies of science have built on the IAP statement, with the Chinese Academy of Sciences, the Royal Netherlands Academy of Arts and Sciences,[57] and the Royal Society[58] all developing codes that either directly make reference to the potential misuse of life sciences research or give more general statements. The International Committee of the Red Cross (ICRC) has been working with scientists in the life sciences to adopt "professional and industrial codes of conduct aimed at preventing the abuse of biological agents."[59]

The American Society for Microbiology has added the following statement to its code of ethics: "ASM members are obligated to discourage any use of microbiology contrary to the welfare of humankind, including the use of microbes as biological weapons and will call to the attention of the public or the appropriate authorities misuses of microbiology or of information derived from microbiology."[60]

Medical associations, including the World Medical Association,[61] the British Medical Association[62] and the American Medical Association's Council on Ethical and Judicial Affairs,[63] have reinforced their existing codes to include issues related to the possibility of accidents or the deliberate misuse of research.

Awareness-raising and education

Numerous 'bottom-up' initiatives aimed at different scientific audiences have aimed to raise awareness on this topic. These include:

- A study assessing education materials for biosafety, biosecurity and dual-use research at major European Union universities.[64]
- An American Association for the Advancement of Science (AAAS) study examining 14 programmes in the United States that educate graduate or professional students in the biomedical sciences on dual use research issues.[65]
- Educational workshops on dual-use research developed in the United Kingdom and conducted in several regions.[66]
- On-line educational modules developed by: the European think tank the EU Nonproliferation Consortium;[67] Bradford University;[68] the Center for Arms Control and Nonproliferation;[69] the Federation of American Scientists (FAS);[70] the Southeast Regional Center of Excellence for Emerging Infections and Biodefense.[71]

Identification of ethical questions

In the early 21st Century, the dual use discourse focused heavily on high impact 'apocalyptic' bioterrorism attacks from terrorists committed to maximum violence. It focused less on the identities of bioterrorists and their interests in pursuing such attacks, or their capacities to do so. About a decade in, there was a noticeable change in the dual use discourse, led by the WHO and Obama administration. While still focused on high impact bioterrorism attacks, the new discourse emphasized the linkages, particularly in how governments respond, between these sorts of deliberate disease outbreaks on the one hand and naturally occurring disease outbreaks on the other. It promoted the concept of 'catastrophic health events,' coupled the security and health communities more tightly together, and began engaging bioethicists in dual use concerns.

Ethics is at the heart of the biorisk management framework put forward by the WHO (See Figure 1). The WHO maintains: "Questions about the governance of dual use life science research of concern are inherently ethical in nature: What are the responsibilities of various actors; how can the benefits of research, including DURC, be promoted while avoiding harm or minimizing risk; and how can conflicting or divergent priorities be reconciled, i.e. the importance of scientific freedom and progress versus the importance of security."[72]

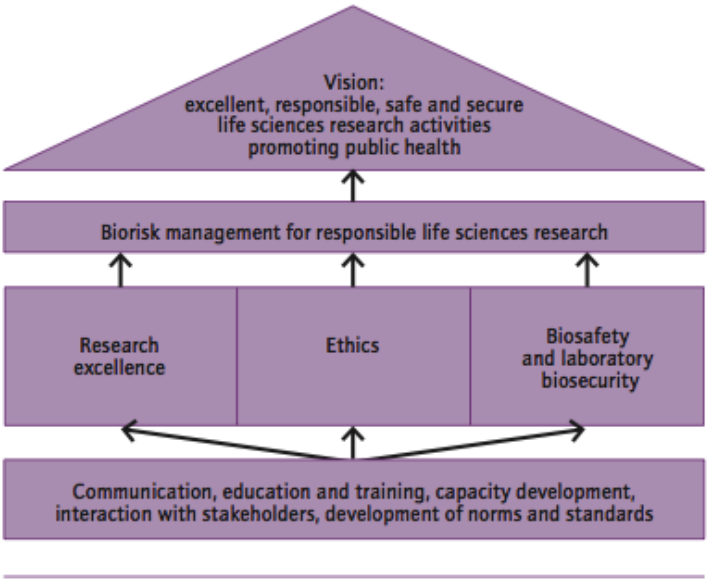

Figure 1: The WHO biorisk management framework for responsible life sciences research.[73]

The critical ethical questions raised by dual use of concern (DURC) revolve around balancing scientific freedom, governance, risk and security, and they cover a broad range of sectors and stakeholders at different hierarchical levels of the governance of science, including:[74]

- individual scientists who must decide what research to conduct and to publish;
- research institutions, which must decide, among other considerations, how to regulate research within their confines, how to educate their researchers, and which laboratory security measures should be in place;
- funding organizations, which must decide how considerations of DURC are incorporated in the application and review processes;
- professional societies, which must make decisions about the development, promulgation and/or enforcement of codes of conduct and education;
- editors and publishers, who must make decisions regarding the review and publication of potentially dangerous papers;
- national governments, which must decide the extent to which important considerations such as review of research and the relevant education of scientists will be mandated, how to bring in the essential stakeholders to formulate sound policies, if/which DURC can be funded, and the extent to which controls should be placed on access to hardware, equipment and tools, or whether the regulatory emphasis should be on people, processes and know-how; and
- international organizations, which must make decisions concerning relevant global policy.

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