GUIDELINES FOR RESPONSIBLE CONDUCT IN VETERINARY RESEARCH

IDENTIFYING, ASSESSING AND MANAGING DUAL USE

WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future

MAY 2019

INTRODUCTION

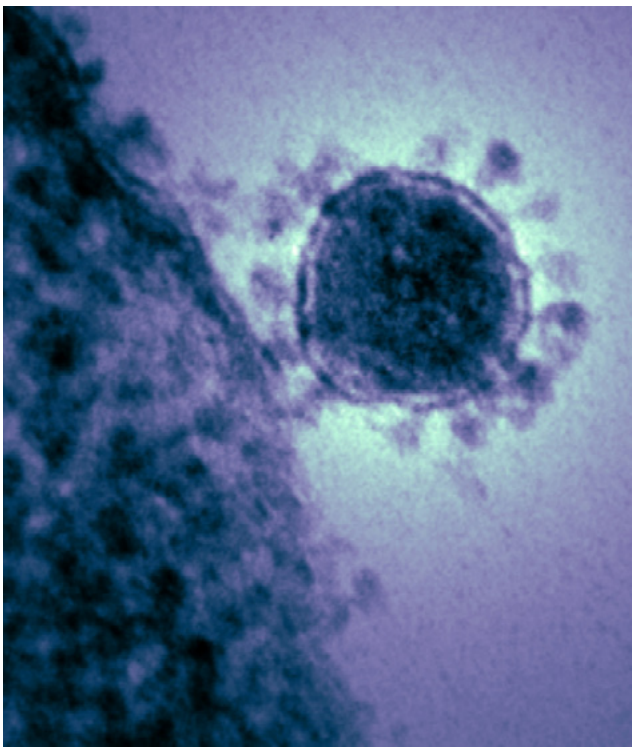
The World Organisation for Animal Health (OIE) has the mandate to improve animal health and welfare worldwide; in line with this mandate the OIE has developed these guidelines with the goal of supporting research by providing information and context on dual-use implications. Life science[1] research is crucial for animal, human, and plant health and is a cornerstone of veterinary medicine, agriculture and public health. An environment that facilitates and encourages research and researchers is of paramount importance for maintaining the benefits already achieved and the continued progress on which sustainable development depends.

Research into animal diseases continues to make major contributions to global food security, the health of livestock, wildlife, working and companion animals, and the ability of countries to safely trade animals and animal products. While the benefits of this research are undeniable, there is a clear recognition that the outputs of all research inherently carry the possibility of unintended consequences and misuse, and therefore have dual-use implications (see Box 1).

BOX 1: WHAT IS DUAL USE?

Knowledge, research, technologies, and materials that can be used for good, can also be misused to harm animals, humans or the environment. This dichotomy is described by the term dual use, which applies to all scientific research that has the potential for both good and bad.

Most things, ideas, materials and technologies can be misused; however, the magnitude of any potential impact varies.



MERS CoV © National Institute of Allergy and Infectious Diseases (NIAID)

1. SCOPE

The OIE has an extensive network of Collaborating Centres and Reference Laboratories, many of which work with pathogens, materials, technologies or knowledge with significant dual-use potential. In addition, numerous other stakeholders similarly engage in activities that could potentially, by accident or malicious intent, result in significant negative effects on animal health or human health. At the same time, their work is instrumental in keeping us safe and improving animal and human health. The history of rinderpest and its eradication is a hallmark example of the successful application of science to save and improve animals and human lives (see Box 2).

The purpose of this guidance is to raise awareness about the dual-use potential of research in veterinary settings, supporting veterinary professionals, researchers and other stakeholders to effectively identify, assess and manage dual-use implications. These guidelines are not prescriptive; they do not provide detailed information on what to do but rather aim at providing thought-provoking impulses and encouraging reflection as countries and institutions work towards implementation of their own dual-use guidelines.

1. Life sciences include all sciences that study living organisms, e.g. animals, humans, plants or microorganisms. Examples in this vast field of research are veterinary medicine, ecology, genetics, immunology or molecular biology

BOX 2: RINDERPEST CASE STUDY

The history of rinderpest and its eradication demonstrates the benefits of research on dangerous pathogens, but also provides an example of how dual-use concerns develop.

Rinderpest virus caused devastating outbreaks in cattle and buffalo over many centuries, leading to famines and deaths in Asia, Europe and Africa. It is estimated that one third of people in Ethiopia and two-thirds of the Maasai population in Tanzania died from starvation as a direct consequence of the 1890s outbreaks in the Horn of Africa and Southern and Eastern Africa. The tremendous impact of rinderpest, in particular an outbreak in Belgium in 1920, was the driver for countries to come together and found the OIE.

Controlling rinderpest required enormous global research efforts which saw the virus widely distributed to laboratories all over the world, and global vaccination campaigns that eventually led to eradication of the disease. Importantly, legitimate vaccine research included the creation of hybrids between rinderpest virus and other morbilliviruses[2]. During this period, the benefits of the research clearly outweighed the risks. However, in the post-eradication era, the creation of such hybrids is strongly discouraged, because the benefits of the research are no longer assessed to outweigh the risks.

Today, even though the disease is eradicated[3], there are still laboratories that have stocks of rinderpest virus and vaccines. Some of these have been, or are applying to be, designated by FAO and OIE to safely hold the virus and vaccine reserves, which involves a strict inspection procedure, while others have chosen to remain outside the FAO and OIE regulation and oversight system. Before rinderpest eradication, there was a clear benefit to having many laboratories holding and working with the virus; but post-eradication the balance has changed, and laboratories have moved from being the engines that drove the eradication, to being the primary risk for re-emergence. So we now face a situation in which to be prepared for a rinderpest outbreak also means creating the opportunity for one to occur. The situation is further complicated by developments in technology that can be used to recreate the virus even if all existing stocks are destroyed, and risk assessments must take this into account, and lead to risk management measures that include holding at least the vaccine strains for the foreseeable future, with plans to rapidly scale up production if required.

2. RISK REVIEW PROCESS

Managing dual-use implications is part of responsible conduct for all scientists, including in the life sciences. Accordingly, researchers and institutions should integrate dual-use risk assessment into their existing standard risk assessment procedures. They should exercise their professional responsibility, performing a continued, detailed and well-informed risk analysis for all stages of the proposed research, from project initiation to data publication (see Fig. 1).

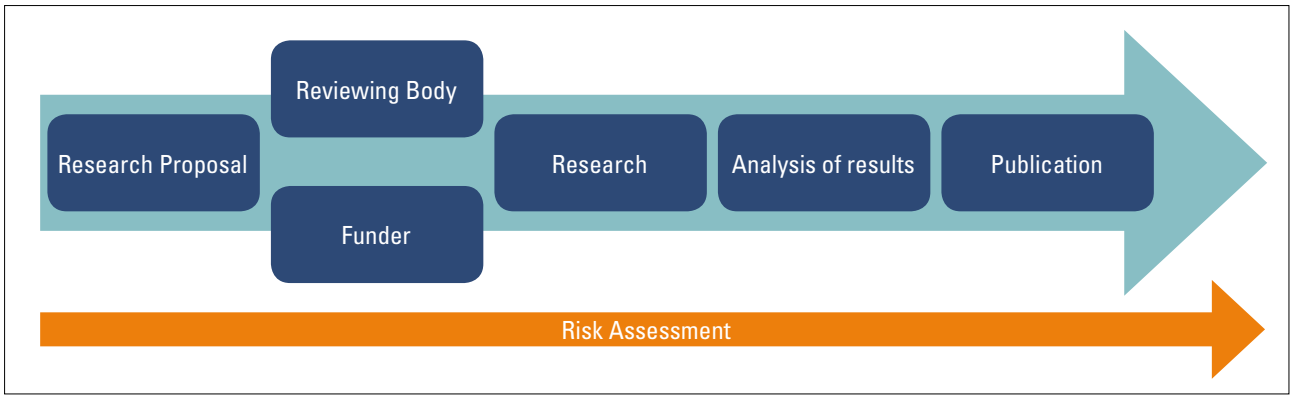
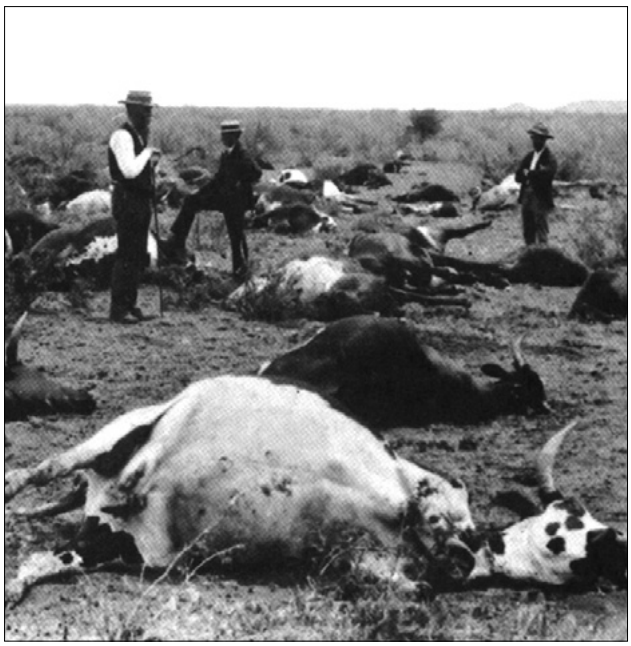


Figure 1
Risk assessment as a continuing process throughout the research life cycle

2. Morbilliviruses belong to the family of paramyxoviruses; different morbillivirus species can infect different hosts, e.g. rinderpest virus (cattle), canine distemper virus (dogs), measles virus (humans)
3. Declaration of global eradication of rinderpest and implementation of follow-up measures to maintain world freedom from rinderpest 2011



https://rinderpestvigilance.com/en/

Researchers should weigh the anticipated benefits against the risks of the research, including identified dual-use implications. Institutions where researchers conduct their work have a responsibility to ensure this risk assessment is done properly and to support researchers accordingly.

The institution should have a review body responsible for oversight of all life science research. Ideally, this review body covers both biosafety and biosecurity considerations, and is the body that should review dual-use implications. Having one review body through which all life science research must pass helps to ensure that all projects are reviewed properly while imposing the least amount of bureaucratic burden on researchers.

2.1
RISK IDENTIFICATION

Research often involves materials or knowledge with significant dual-use potential. This could, among other things, involve dangerous pathogens, experimentally changing important features of pathogens, or new technological developments. Identifying the dual-use implications of research requires careful review – from the design of a research project to conducting an experiment to publishing research results. It is important to note that risks might emerge or change during the experimentation phase, thus it is important to monitor the results with an open mind at all stages of the research life cycle.

No risk identification process can predict all imaginable future possibilities; this is especially true for basic research. Basic research aims at understanding elementary or fundamental problems. Providing this fundamental understanding is a basis for applied research, which aims at solving specific problems. The discovery of the structure of DNA is an example for basic science, which then became the basis of applied research, including identifying and treating genetic diseases, determining paternity or genetic linkages, proving who committed a crime or developing technologies such as genome editing.

While basic research lays the foundation for future developments, the true value will only become apparent in retrospect, as will the risks. Therefore, dual-use risk identification and measures for risk mitigation are more readily applicable to applied research.

2.2
RISK ASSESSMENT

Structured risk assessment should be conducted as early as possible and throughout the research life cycle. Researchers and institutions should take practical steps to evaluate not only the benefits but also the possible risks related to the research. Risk assessment should take into consideration the likelihood and consequences of research results or products being accidentally or intentionally misused but should also consider the consequences of not doing this research. Vaccine research has per se dual-use implications as it deals with pathogens in order to develop vaccines. However, the products of this research are among the most valuable assets we have for defending ourselves or animals against infectious diseases.

Risk assessment can be guided by a variety of criteria (see Box 3) and analytical tools[4]. It is important to keep an open mind, use critical thinking and document the process as well as the conclusions.

2.3
RISK MANAGEMENT

In general, risk management means the process of identifying, selecting and implementing measures that can be applied to reduce the level of risk. In the event that the identified risks are assessed to exceed the potential benefits, consideration should be given to if and how the research could be modified to mitigate the risk, shifting the balance and in some cases whether the research should even proceed. Examples for risk mitigation strategies could involve enhanced engineering controls or substituting a pathogen with a non-pathogenic strain or a related bacteria or virus of lesser pathogenicity for suitable stages of the research.

In addition to sound risk assessment, risk management requires that both the researcher and the institution have the will and authority to take appropriate measures.

4. E.g., this publication: *A qualitative risk assessment methodology for scientific expert panels*

BOX 3:
IMPLICATIONS FOR DUAL USE

There are obvious examples for research activities or consequences which indicate dual-use potential, some are listed below. This list is not exhaustive but rather should trigger critical thinking about intended and potential unintended consequences of research.

- Could the research result in changed or new characteristics of a toxin, biologic or microorganism (e.g. pathogenicity, virulence, transmissibility, stability, host range) with harmful effect?
- Could the research alter the distribution of an animal or plant species in the environment with harmful effect?
- Could the research result in a new or recreated pathogen or toxin?
- Could the research result in reduced host immunity, increased host susceptibility, and/or altered host tropism?
- Could the research promote or induce resistance to therapeutic or prophylactic measures?
- Could the research interfere with detection or diagnosis of a microorganism or toxin?
- Could the research alter the nature of an animal feed or feed plant with harmful effect?
- Could the context or manner in which the research is published or otherwise communicated facilitate misuse?

Further information on risk management in the laboratory setting can be found online[5].

3. RESPONSIBLE CONDUCT

The responsibility for the identification, assessment and management of dual-use implications rests to differing degrees across many stakeholders throughout the research life cycle. Responsible conduct includes considerations related to safety, security and ethics. Recognising the dual-use implications of research is an integral component of being a responsible scientist. Examples of major stakeholders are given below; however, the list cannot be exhaustive. Moreover, public engagement is the responsibility of all stakeholders. Information on the overall benefits of research as well as the elements of the risk review processes should be made available and communicated to the public.

© Nelson Mwangi Muriu, Kenya

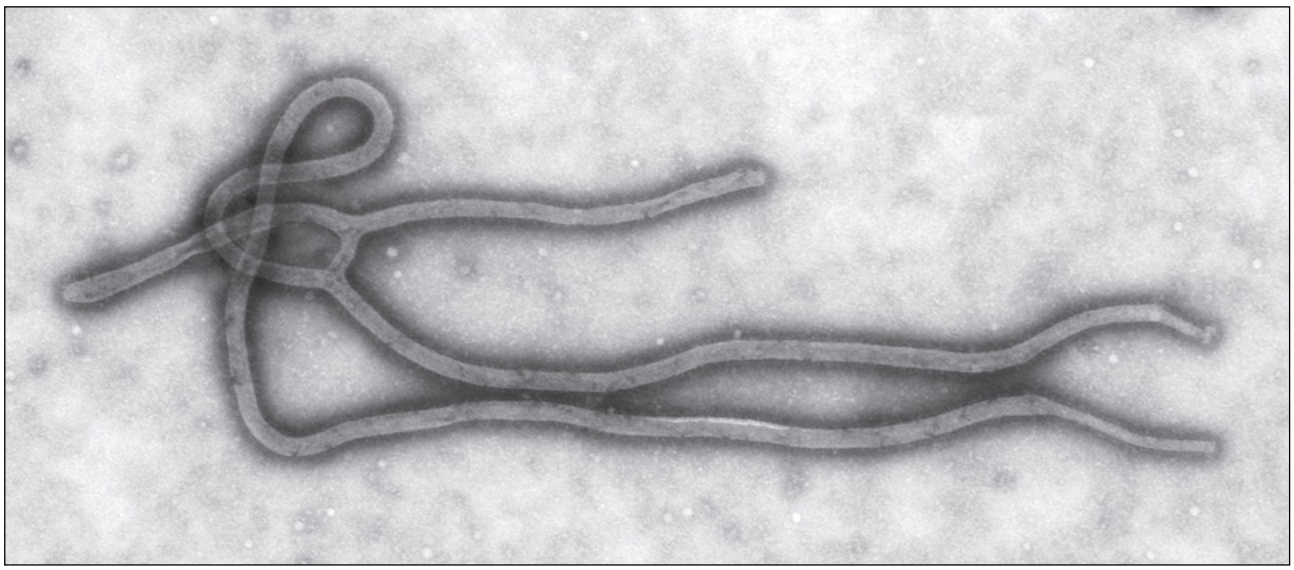
3.1

RESEARCHERS conceive of projects and bear the primary responsibility for the identification, assessment and management of dual-use implications, irrespective of the funding source. They should identify potential risks related to their research and communicate them appropriately within their institution. They should also provide guidance about responsible conduct of research to their staff and trainees. Additionally, they should consider the context and manner in which the research is communicated and published to avoid misuse.

3.2

INSTITUTIONS must be involved and support their researchers in the assessment of risks related to proposed and ongoing research projects. It is the primary responsibility of the institution to assist its researchers in the planning and execution of measures to mitigate these risks and to make sure that all staff are properly trained in recognition of dual-use implications of research. Institutions should engage with the wider community, as both the potential benefits and risks of research ultimately affect the entire society. Mechanisms to include the general public in the consultation process are recommended for selected projects or activities. Institutions should be transparent about the risk review process, while making sure that confidentiality is respected when it comes to specific projects to protect the individual researchers and their intellectual property rights.

5. E.g., www.who.int/ihr/training/biorisk_management/en



© CDC/Cynthia Goldsmith

3.3

GRANT FUNDERS respond to researcher-initiated proposals. They have an important role in assessing the benefits of the research proposal, but may not be best placed to assess dual-use implications. However, as funders they have a responsibility to ensure that the recipients of research funds have appropriate procedures in place to identify, assess and manage potential dual-use implications of the proposed research.

3.4

CONTRACT FUNDERS initiate and commission research and can play a more direct role in study design. These funders, along with researchers and their institutions, share responsibility for identifying, assessing and managing dual-use implications.

3.5

COMPANIES are responsible for the safe, secure and sustainable conduct of research and production beyond their legal and financial liability. Industry has an obligation to protect society from accidental misuse of their products and research. In addition, as part of corporate social responsibility, industry stakeholders should strive for appropriate risk mitigation measures against foreseeable threats of intentional misuse.

3.6

EDUCATORS have a responsibility at all levels, from primary to continuing professional education, to cultivate a sense of responsible conduct with regard to understanding risk in general, including risks related to dual-use implications of research. Educators play a crucial role as they help shape the attitudes, practices and moral compass of young scientists, and should instill responsible conduct as an intrinsic component of the research culture.

3.7

SCIENTIFIC PUBLISHERS should ensure that the peer review process considers dual-use implications in the assessment and presentation of scientific research. In addition to evaluating these implications, scientific publishers should present research in a manner that avoids alarmism and hyperbole.

3.8

OTHER COMMUNICATORS OUTSIDE OF SCIENTIFIC JOURNALS participate in an increasing diversity of forms of dissemination of research. Ultimately, the responsibility for communication of scientific results, and their context, rests with each individual involved in the chain of communication.

3.9

REGULATORY AUTHORITIES often struggle with the fact that scientific advances outpace regulatory frameworks for dealing with research. This can create new safety, security or ethical issues with respect to animal and human health and the environment. Horizon scanning should be an integral part of regulatory frameworks in order to help anticipate new developments and react in a timely manner.

4. GUIDANCE ON IMPLEMENTATION

Beyond the institutional level, reacting wisely to unforeseen and undesirable outcomes of research requires adequate management structures. At the national level, a legal framework is necessary for regulation of the research enterprise to safeguard society from unforeseen and undesirable impacts from research as well as to provide legal clarity for researchers and their institutions. This legal framework should inform and mandate institutional structures that directly oversee safety in the research enterprise. Such a framework is ideally holistic and overarching across all considerations, thus is not specific to potential dual-use implications. Where a legal framework for regulating research enterprises is lacking, countries should seek to develop legislation as soon as possible in order to provide legal clarity and motivate or even enforce the mitigation of negative effects. Without legislation, oversight will be *ad hoc*, unregulated and not harmonised, varying from institution to institution[6] and case to case. Lack of legislation also implies that action is only taken after an incident occurs, and a basis for prosecution may be lacking.

At the institutional level, consideration of dual-use implications should be included in the standard biological risk assessments, which typically involves several stakeholders, including the researcher and the review body (see Box 4). These considerations should be made well in advance of the initiation of the research and should continue throughout the research life cycle. A separate committee for reviewing dual-use implications is neither necessary nor recommended.

The review of dual-use implications should be a component of existing review structures. Dual-use implications should be considered by the standard reviewing body and any appropriate mitigation measures mandated. It is important to note that after committee review, risk assessment does not cease. It is a continuous activity – albeit, between periodic committee reviews, it may involve only the researchers. If unforeseen results are obtained, or developments in the field alter the understanding of the risks, the research should be re-assessed immediately.

BOX 4: REVIEW BODY

Ideally, research institutions should have one review body that considers all biosafety and biosecurity issues, and this should also consider dual-use implications. Having a single dedicated review body, which takes responsibility for the oversight of all life science research, ensures that all projects are considered, and that there are no gaps. For example, consider if dual-use evaluation is delegated to an ethics board but this ethics board only evaluates projects involving human subjects or live animals. In this scenario, dual-use implications of all studies that do not involve human subjects or live animals would be overlooked. Having only one review body (responsible for biosafety and biosecurity, including dual-use implications) also helps avoid the need for multiple and unnecessary committees. As many research projects are relatively straightforward, presenting routine risks, a separate committee for dual-use makes little sense. When a project must pass through multiple committees (e.g. a standard biological risk assessment committee that oversees all life science research, and a separate animal welfare and ethics committee), dual-use implications should be considered by the committee responsible for the oversight of all life science research at the institution. The review body should:

- Include all required expertise. There should be a provision to consult outside experts if the in-house proficiency is not deemed sufficient.
- Have the authority to make decisions that cannot be overruled.
- Have a clear mandate, funds and time to fulfill its tasks.
- Exclude conflicts of interest. There should be an option to invite outside expertise to ensure objective assessment.

6. *Responsible life sciences research for global health security,* WHO 2010, pages 12-17

CONCLUSION

Research on animal health provides undeniable benefits to the health and welfare of animals and people, global food security, and safe trade. Yet all materials, knowledge and technologies can also unintentionally cause harm or be misused to cause harm. The identification of dual-use implications is essential and should not discourage researchers from pursuing the benefits of research. Rather, it should facilitate the assessment and management of risk. Wherever possible, attempts should be made to reduce the risks identified. If, in the final analysis, the risks are assessed to outweigh the benefits it would be inappropriate to proceed with the research.

Irrespective of where activities are being conducted, these guidelines should be taken into consideration and where possible be reflected in national legislation. Ideally, these considerations should also apply to people conducting scientific activities outside of traditional regulated research settings (e.g. citizen science[7] and amateur inventors).

© CDC

These guidelines have been developed to raise awareness about the dual-use implications of research, while strongly encouraging the continued advancement of life science and innovation, which has greatly benefited global safe trade of animals and animal products, food security, public health and animal welfare. By no means are they intended to curb scientific progress; on the contrary, the intent is to encourage research by providing a framework for safe, secure and responsible conduct.

7. Citizen science, do-it-yourself biology (DIY Biology) or biohacking describes a social movement in which biotechnology is used by a broad range of stakeholders, usually outside professional research settings.

FURTHER READING (free pdfs)

- Dual Use Research of Concern in the Life Sciences: Current Issues and Controversies. National Academies of Sciences, Engineering and Medicine, 2017. Link
- A Code of Conduct for Biosecurity. Report by the Biosecurity Working Group. Royal Netherlands Academy of Arts and Sciences, 2008. Link
- Responsible Life Sciences Research for Global Health Security: A Guidance Document. World Health Organization, 2010. Link
- An Efficient and Practical Approach to Biosecurity. Centre for Biosecurity and Biopreparedness, 2015. Link
- Preventing Biological Threats: What You Can Do. Bradford University, 2015. Link

Additional resources to be found on
OIE's Biological Threat Reduction website

WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future

12 rue de Prony • 75017 Paris France • tel. +33 (0)1 44 15 18 88 • fax +33 (0)1 42 67 09 87 • www.oie.int • oie@oie.int

DOI : 10.20506/OIEguidelines.2757