Enabling researchers to report concerns about human genome editing research: report for the WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing

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1. Introduction

Concerns have been reported that some researchers, both in China and the United States of America, knew about Dr He Jiankui’s work with human genome editing but that no one reported it before the announcement of the birth of genome-edited babies (1). One explanation is that those researchers indicated that they did not know where and how to report concerns about his research (2).

As a result, the WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing wanted to consider whether and how to encourage and support whistleblowing among the research community in order to prevent a similar occurrence in the future.

The International Commission on the Clinical Use of Human Germline Genome Editing (set up by the United States National Academy of Medicine, the United States National Academy of Sciences and the United Kingdom’s Royal Society) recently called for the establishment of “an international mechanism by which concerns about research or conduct of heritable human genome editing that deviates from established guidelines or recommended standards can be received, transmitted to relevant national authorities, and publicly disclosed” (3).

An article by the Science, Health and Policy-Relevant Ethics in Singapore (SHAPES) initiative, National University of Singapore, also concluded that “an international governance mechanism for reporting unethical germline gene editing is needed”, and that the World Health Organization (WHO) would be well placed to take the lead (4). The authors proposed that the reporting mechanism be attached to the WHO International Clinical Trials Registry Platform.

This paper is intended to inform the Expert Advisory Committee’s discussions. It explores whether there is a need for an international reporting mechanism, what form one might take and where responsibility might rest.

2. Methodology

The Expert Advisory Committee commissioned this work to explore possible mechanisms to encourage and support whistleblowing, with a focus on approaches that could work at national, regional and global scales. Desk-based research and scoping to map the landscape was undertaken to assess approaches used in different sectors, including academic research, health care, aviation, environmental protection and sport. In addition, a stakeholder workshop with whistleblowing experts was held in October 2020 to explore some of the issues raised in further detail.¹

¹ The experts attending the workshop were as follows: C. Fred Alford (Emeritus Professor, University of Maryland, and author of Whistleblowers: broken lives and organizational power); Carl Elliott (Professor in the Center for Bioethics and the Department of Pediatrics, University of Minnesota, currently working on a book about whistleblowing in research on human subjects); Tom Mueller (independent investigative journalist, author
This report looks at the importance of the cultural context, considers the mechanisms that are needed to allow effective reporting, and finally considers options for a possible approach to encourage best practice for research in emerging technologies.

While the starting point for the work was the need for a reporting mechanism in genome editing research, the challenges, barriers and potential mechanisms also apply across other research fields. The scope of the discussion is therefore wide ranging, and it may be more appropriate to consider reporting approaches for emerging technologies more broadly.

3. Context

Terminology

The language used is important (5). The term “whistleblower” – defined as “a person who informs on a person or organization regarded as engaging in an unlawful or immoral activity”2 – while first used with the intent of being supportive (6), can have negative connotations. The equivalent translations in many European languages, for example, are often negative (snitching, betraying, leaking, squealing, dirtying one’s own nest) (7). The term “reporting” may be perceived as more neutral, with no attribution of blame, and is used for example in the aviation sector with the intent of reducing the likelihood of repeat safety incidents. An alternative, and perhaps the most supportive, term is “speaking up”. A number of organizations are introducing “speak up” approaches in order to emphasize an open culture that encourages early warnings.3 This document focuses on “reporting concerns” as a more neutral term.

Barriers to reporting concerns

As a starting point, it is helpful to understand the reasons why people often do not raise concerns about wrongdoing or unethical activity. These appear to be consistent across many sectors, including research (8–11). First, there is the belief that speaking up is futile – nothing will be done. Second, there is concern that those who speak up will experience retaliation – there could be legal, financial and reputational impacts, or implications for their career, if they “put their head above the parapet” and report concerns. And third, there can be practical issues – there is often uncertainty about how, where and to whom to report concerns.

More generally, and perhaps more importantly, there are issues relating to the background cultural context. There is often a culture of silence, a feeling that something is “not my business” and it is better to look the other way. This may be particularly true in a research context, where the “culture is that you respect confidentiality and that when people reveal things in confidence to you, you respect that confidence” (12).

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2 Oxford English Dictionary.

3 See, for example, the National Guardian’s office of the United Kingdom National Health Service (https://www.nationalguardian.org.uk/).
The value of open reporting

Our research suggested that an underlying requirement, if matters of concern are to be actively reported, is a supportive scientific culture. An emphasis on values-based education, with particular attention to research integrity across all training, is essential. This should be demonstrated from the top down, across research institutions, funding bodies and senior leaders in research. Institutions need leadership that upholds the ideals of research integrity, and supports the policies that help implement them.

Implementing appropriate reporting structures is an important part of developing an open culture, because it helps to create a culture where the expectation is that concerns about perceived research misconduct should be openly raised. This should be seen to be about promoting the best possible science, and should be consistent with, rather than opposed to, a culture of scientific challenge and progress.

One sector that has particularly emphasized the need for a culture that encourages the reporting of misconduct is sport. The World Anti-Doping Agency highlights the importance of protecting the integrity of sport, and this is backed up by the provision of a robust mechanism to report wrongdoing (Box 1).

Box 1. World Anti-Doping Agency

The World Anti-Doping Agency (WADA) was established in 1999 to oversee implementation of and compliance with the World Anti-Doping Code, the document harmonizing anti-doping policies in all sports and all countries. The fact that WADA is custodian of a clear anti-doping code means that there is a solid foundation for all its activities. WADA also has a clear statement on gene doping, which is prohibited, and there is expectation that any violation of the prohibition would be reported.

WADA places particular emphasis on improving the culture of sport, with the aim to “create and maintain a zero-tolerance culture for doping” to protect the clean athlete and the integrity of sport, and to stop people “quietly accepting” doping. A wide-ranging education and awareness programme operates internationally. The message is that “speaking out exemplifies the kind of leadership, courage, and character consistent with the spirit of sportsmanship and fair play”.

Reporting mechanism

There is a dedicated Intelligence and Investigations Team, which can instigate rigorous investigations in response to allegations of wrongdoing. There is a clear reporting mechanism, with a dedicated “speak up” website to report concerns about violations. The secure confidential process is open to anyone. A clear whistleblowing policy and process includes details of the procedures for investigation of misconduct and protection for whistleblowers. While operating globally, WADA also collaborates with both national and sport-specific mechanisms to follow up allegations, and works with the Association of National Anti-Doping Organizations.

WADA is funded by both national governments and the Olympic movements. There are significant resource implications in providing an operation on the scale of WADA, though this does also include a widespread testing regime.
4. What mechanisms are needed to report concerns?

There has been an increasing emphasis on mechanisms to report, investigate and sanction wrongdoing and irresponsible behaviour across different sectors, and to support and protect those raising concerns. This is also true within a research context, with an increasing number of national and international codes of conduct and statements on research integrity, for example the Singapore Statement on Research Integrity (Box 2). The emphasis in these codes is mainly on research misconduct, including fabrication and falsification, although “irresponsible research practices that undermine the trustworthiness of research” are also mentioned.

There is currently no single global authority in science that would act as the obvious place to report unethical human genome editing. While WHO has a reporting line, this is intended to be used to raise concerns about WHO or WHO-funded research, rather than any research. While there are some organizations that play a similar role in different sectors, such as WADA, the model would not transfer directly to the research world, not least because of the significant resource implications, the varied national structures, and the lack of appetite to create a dedicated new entity. However, there are elements of best practice that can be drawn from other sectors.

Best practice suggests there are three key requirements for any mechanism:

- a clear reporting mechanism
- a transparent process for investigation
- support and protection for those raising concerns.

### Box 2. Ensuring research integrity

Many countries, academies, professional organizations, and academic research institutions have developed codes of conduct for research integrity that set out principles of research integrity, standards and expectations to ensure best practice and trustworthiness, and the approach that should be taken to address misconduct in research. Examples include:

- All European Academies (ALLEA): [European Code of Conduct for Research Integrity, 2017](13)
- UK Research and Innovation and Universities UK: [Concordat to Support Research Integrity, 2019](14)
- United States National Academies of Sciences, Engineering and Medicine: [Fostering integrity in research, 2017](15)
- Science Council of Japan: [Code of Conduct for Scientists, 2013](16)
- Australian National Health and Medical Research Council: [The Australian Code for the Responsible Conduct of Research, 2018](17)
- WHO: [Code of Conduct for Responsible Research, 2017](18). The list of research wrongdoings specifically includes the failure to adhere to accepted ethical principles for the conduct of
research. An integrity hotline provides an independent service to take reports of wrongdoing confidentially, either by email or through a webpage.

A list of other guides and codes of conduct is available at the Ethics and Integrity portal and in the International Science Council resources.

In addition, there have now been six World Conferences on Research Integrity (WCRI), and the WCRI Foundation was established in July 2017. The second World Conference on Research Integrity in Singapore (2010) focused on national and international structures for promoting integrity and responding to misconduct. The resulting Singapore Statement on Research Integrity included the principle that:

Reporting irresponsible research practices: Researchers should report to the appropriate authorities any suspected research misconduct, including fabrication, falsification or plagiarism, and other irresponsible research practices that undermine the trustworthiness of research.

The third World Conference on Research Integrity in Montreal, 2013, considered research integrity in cross-border research collaborations, and the fifth World Conference on Research Integrity in Amsterdam, 2017, proposed a registry for research on the responsible conduct of research. The Hong Kong Principles for Assessing Researchers, 2019, focused on ways to assess and promote research integrity among researchers.

A clear reporting mechanism

One of the biggest barriers deterring people from reporting concerns is uncertainty about to whom, how and where to report issues. This is particularly true when considering research taking place outside one’s own institution, or in a different country.

There are usually three ways that concerns can be raised.

- **Internally, within an organization or institution.** In a research context, the main responsibility for research misconduct lies with the employer or institution. Best practice is for a research institution to provide a well advertised, safe and confidential mechanism for reporting allegations. Some institutions do clearly advertise how to raise concerns but it is important to recognize that not every institution has such a mechanism, and there are wide variations in the abilities of different institutions and countries to respond appropriately to information received.

- **To an external organization (for example, a regulator, an ombudsperson or a national oversight body).** This has an advantage where there is external enforcement by a responsible agent with teeth. In some contexts, reporting is mandatory and failure to do so can result in penalties for withholding such information. While some sectors have a clear regulator, for example the US Food and Drug Administration (for health) or the UK Civil Aviation Authority (for aviation), this is not always the case in a research context, and there is significant variation between countries.

- **To an investigative journalist.** While this approach is regularly used in some sectors, for example the financial industry, it is less common for scientists to liaise with investigative journalists to report concerns. Pertinent reservations related to this
approach include undermining confidence in science and determining whether the suspicions are sufficiently robust for an investigative journalist to be interested. Researchers may also not know who to contact or trust (4).

In some sectors, all these approaches are used. Aviation, for example, places particular emphasis on the reporting of safety incidents, both to learn from what has happened and to prevent it happening again, not least because of the significant risk of harm where failures happen. Mechanisms include internal safety reports within an organization; occurrence reports to the regulator; reports through dedicated hotlines and whistleblower reports to the regulator; or reports to an independent charity or watchdog. More recently, with concerns about the Boeing 737 crashes, some workers have also reported concerns to journalists.4

The lack of an obvious way to report concerns outside an institution in the research space suggests that there is a need for a new reporting mechanism. This might best be addressed through the establishment of a confidential portal, website or hotline, allowing reporting at any time from anywhere in the world. However, such a mechanism only works if the second element is also in place, namely a transparent mechanism to assess and investigate any reports of wrongdoing.

A transparent process for investigations

It is not enough simply to have a reporting mechanism; there must also be a mechanism to investigate any information provided and to demonstrate that action has been taken where appropriate. People may be deterred from reporting concerns if they believe that nothing will be done or that their action will not make any difference.

There needs to be a robust, transparent process for dealing with allegations, with high standards of integrity, fairness and confidentiality. Best practice is usually to have a two-stage process, beginning with a preliminary enquiry to ensure the concern is valid (that some element of wrongdoing has happened and warrants enquiry, rather than being a “spurious and unfounded accusation”), followed by a more detailed rigorous investigation where warranted (4, 19). The investigation needs to be instigated quickly, and the informant needs to be given regular updates about the process, to provide reassurance that their concerns are being heard.

Such an investigation may either be at an institutional level or undertaken by an external organization at a national level. Within a research context, the Council of Canadian Academies has identified three types of national approach (20): some countries have national legislation and centralized systems with investigatory powers (for example the United States of America5); some countries have no formal legislation, but clear processes to address misconduct, either through an institution or funder (for example, the United Kingdom); while other countries have no national oversight body or compliance mechanism. This final

4 For example, the United States Federal Aviation Administration hotline and AIR21 Whistleblower Protection Program (https://www.faa.gov/about/initiatives/whistleblower/); the European Union Aviation Safety Agency confidential safety reporting; the United Kingdom Civil Aviation Authority safety reporting guidance; and the CHIRP aviation and maritime confidential incident reporting.

5 For example, the United States Office of Research Integrity.
category will need careful thought, and potentially most support when designing an appropriate approach for international reporting and action.

The other two types of stakeholders that may be involved in investigating an allegation are research funders and publishers. Funders will often need to rely on institutions, as the employer, to undertake any investigation, but have a role to set expectations. Publishers now have a code of publication ethics, with mechanisms to ensure that research meets certain conditions before publication (21). They also have clear processes to investigate allegations of misconduct, including fraud or plagiarism, after publication. However, this type of approach is too late to prevent unethical research being conducted in the first instance.

Support and protection for those raising concerns

Reporting concerns across many sectors can be traumatic, and personal costs include retaliation, verbal and physical threats, job loss, legal action and long-term career stigma. Despite attempts to maintain confidentiality, it is often very difficult for whistleblowers to remain anonymous. Those reporting concerns therefore need to be given support and protection to minimize these risks.

There is now legislation in place to protect whistleblowers in at least 30 countries and the number is growing, for example the European Union Whistleblower Protection Directive (2019), which comes into force in 2021, and the United States Whistleblower Protection Act. The focus is often on employees reporting against their own employer, with protection only coming into effect if a person suffers as a result of whistleblowing, but new legislation is increasingly looking at a broader context. There are also a significant number of charities and nongovernmental organizations that exist to help provide support to whistleblowers, although none of these are specific to research.

Ensuring that appropriate mechanisms are in place to minimize the potential harms to a researcher or other person reporting a concern will therefore be crucial. This might require confidential support, mentoring and professional advice (including legal advice) before, during and after the reporting process. This will be particularly important for early career researchers. Studies suggest that young researchers may be particularly vulnerable if they report concerns, but they are also well placed to identify wrongdoing. However, we recognize that it may be particularly difficult to protect early career researchers (22).

5. How can a mechanism for reporting concerns best be delivered?

The findings of this mapping exercise suggest that two things are needed. There needs to be a known, clear mechanism for receiving and investigating concerns, including the provision of support for those who report wrongdoing. This should include a robust and transparent mechanism for ensuring appropriate investigation.

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7 See, for example, Whistleblowing International, National Whistleblower Center, Protect, Government Accountability Project and Transparency International.
These practical measures to make reporting easier would signal the value of research integrity and respect for best practice. Hopefully this should, over time, lead to culture change. While not easy to achieve, changing practices will help to foster a culture whereby reporting concerns is seen as the right thing to do and not a threat to the organization, or to science more generally.

The key question is where should responsibility rest for such an approach? The reporting mechanisms considered above are mainly institutional or national but, given the global nature of the research enterprise, a reporting mechanism needs to be considered at an international level. There is little appetite to create a wholly new entity, so it is important to consider the benefits and risks of other options.

One possibility is for WHO to take on the role. The SHAPES article, for example, recommended that the reporting mechanism might be attached to the WHO International Clinical Trials Registry Platform (4). It could be argued that WHO would be perceived as trustworthy to take on this role and, having set up the registry of trials, has some responsibility. WHO already has a hotline for reporting concerns about WHO, though its remit and resourcing would need to be expanded to take on a broader role. However, while WHO might be well placed to receive the initial report, it would still need to rely on responsible entities in the individual country of interest to conduct a thorough investigation.

Another option might be to work with the InterAcademy Partnership (IAP), a global network consisting of over 140 national and regional member academies of science, engineering and medicine. The IAP, in its report on responsible conduct in global research in 2016, argued that academies and inter-academy organizations need to provide “forceful leadership” to establish and disseminate standards for research integrity (19). The academies are well placed to provide a focus on responsible research, to set standards and particularly to emphasize best practice for human genome editing research. Some have already focused on education and training to promote research integrity. However, there are questions as to whether the IAP and academies are resourced adequately to provide an agile approach to respond to allegations, and there are also concerns about significant conflicts of interest, and a perceived need to protect their profession.

Given there is no clear single entity that can do everything, a third option would be a layered but collaborative approach, with different roles defined for global, national and local institutions. This would reflect the fact that there are currently significant variations in the ability of different countries to respond, and also that there are a number of authoritative players, including regulatory agencies, that have some responsibility and rules already. The first task would be for WHO to identify all the relevant entities and to host a meeting with the IAP, the primary funders and regulators, relevant professional societies (including the European Society of Human Genetics, the International Society for Stem Cell Research, and the American Society of Human Genetics), and key academies.

Stakeholders at the meeting would need to agree:

- the need for a central reporting hotline, to include a web portal and email address, and a decision about where such a hotline should be located;
• the approach by which the central reporting mechanism would link into local mechanisms for detailed enquiries and investigations;

• the protection that would be given to those who reported incidents of concern;

• a clear roadmap, with allocated responsibilities, to promote a culture of research integrity across the sector.

The aim would be to reach consensus about the need for collaboration, and to agree a defined way forward. The risk is that, if there are too many stakeholders involved, it could take a significant length of time to agree an approach, and if no one takes responsibility, the situation will not be addressed rapidly.

Such an approach, linking a global reporting mechanism with regional implementation, appears pragmatic. There are other precedents for linking a global approach with regional implementation, for example to monitor implementation of the International Convention for the Prevention of Pollution from Ships, to oversee compliance with the World Anti-Doping code (see Box 1), or to address concerns about dual use research under the Biological and Toxin Weapons Convention.

Supporting a reporting hotline and ensuring a thorough response, at both global and local levels, will need to be adequately resourced. It may be more feasible and appropriate to look beyond a system set up for human genome editing only, and consider emerging biomedical technologies more broadly. Other areas of emerging technology may also raise concerns, and the need to report wrongdoing will not be unique to human genome editing. Establishing separate mechanisms for each type of research would be unnecessarily duplicative and a waste of resources. It would be more practical to establish a shared approach that can cover any area of emerging technology, including human genome editing. Such an approach would allow the emphasis to be placed on the importance of establishing a culture of research integrity, an essential starting point. The expectation must be that concerns about perceived wrongdoings in research should be openly raised and investigated.

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8 International Maritime Organization.
References


14. The Concordat to Support Research Integrity. United Kingdom Research and Innovation and Universities UK; 2019 (https://www.universitiesuk.ac.uk/policy-and-


