Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop in Brief (2019)

DETAILS

10 pages | 8.5 x 11 | PDF
ISBN 978-0-309-48790-0 | DOI 10.17226/25343

CONTRIBUTORS

Steve Olson, Rapporteur; Policy and Global Affairs; National Academies of Sciences, Engineering, and Medicine

SUGGESTED CITATION

National Academies of Sciences, Engineering, and Medicine 2019. *Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop in Brief*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25343.

Proceedings of a Workshop

IN BRIEF

January 2019

Second International Summit on Human Genome Editing: Continuing the Global Discussion

Proceedings of a Workshop—in Brief

On **November 27-29, 2018**, the U.S. National Academy of Sciences and U.S. National Academy of Medicine, the Royal Society of the United Kingdom, and the Academy of Sciences of Hong Kong convened the Second International Summit on Human Genome Editing at the University of Hong Kong (see http://www.nationalacademies.org/gene-editing/2nd_summit/index.htm). The summit brought together more than 500 researchers, ethicists, policymakers, representatives from scientific and medical academies, patient group representatives, and others from around the world. Over the two-and-a-half-day event, topics including the potential benefits and risks of human genome editing, ethical and cultural perspectives, regulatory and policy considerations, and public outreach and engagement efforts were explored. In addition to the hundreds present at the University of Hong Kong, more than 80,000 unique visitors from over 190 countries and jurisdictions viewed the summit's live webcast, and more than 1.8 million viewers watched a special video stream provided by Beijing News.[1, 2]

The second international summit follows the First International Summit on Human Gene Editing, which was held in Washington, DC, on December 1-3, 2015.[3] In a statement released at the end of the 2015 summit, the organizing committee of the 2015 summit observed that intensive basic and preclinical research on genome editing was clearly needed and that such research should be subject to appropriate legal and ethical rules and oversight. The statement said that genome editing of somatic cells—that is, cells whose genomes are not transmitted to the next generation—could be "appropriately and rigorously evaluated within existing and evolving regulatory frameworks for gene therapy, and [that] regulators [...could] weigh risks and potential benefits in approving clinical trials and therapies." However, the 2015 organizing committee stated that genome editing of germline cells, which can be passed on to subsequent generations as part of the human gene pool, would be "irresponsible" until safety issues were resolved and until there was broad consensus that the proposed use of genome editing was appropriate.

The organizing committee for the 2018 summit also released a concluding statement. That statement appears below after a brief summary of summit presentations and discussions. This proceedings, which was prepared by a rapporteur for the U.S. National Academies of Sciences, Engineering, and Medicine, does not represent the conclusions of the organizing committee or of summit participants as a whole. Rather, it highlights important points made during the second summit and provides context for the organizing committee's statement.

[1] Videos of the summit are available at http://www.nationalacademies.org/gene-editing/2nd_summit/second_day/index.htm.

[2] Within a month after the summit concluded, nearly 100,000 additional individuals viewed the archived video of the webcast.

[3] For a summary of the proceedings of the first summit, see National Academies of Sciences, Engineering, and Medicine, *International Summit on Human Gene Editing: A Global Discussion* (Washington, DC: The National Academies Press, 2015).

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Mrs. Carrie Lam, Chief Executive, Hong Kong Special Administrative Region, with Sir John Skehel, Vice President and Biological Secretary, The Royal Society; Dr. David Baltimore, Chair, Summit Organizing Committee; Dr. Lap-Chee Tsui, President, Academy of Sciences of Hong Kong; and Dr. Victor J. Dzau, President, U.S. National Academy of Medicine. Also present are the other members of the summit organizing committee, local dignitaries, and staff.

ANNOUNCEMENT OF HERITABLE GENOME EDITING

On November 25, 2018, shortly before the 2018 summit began, news media reported that a Chinese researcher scheduled to speak at the summit, Jiankui He of the Southern University of Science and Technology, had used genome editing to make genetic alterations in early embryos which were subsequently implanted. A resultant pregnancy reportedly resulted in the birth of twin girls.

The summit organizing committee had invited Dr. He to speak at the summit based upon his earlier work on genome editing, but the committee had not known about Dr. He's effort to use edited embryos to establish a pregnancy. The evening before the summit, the organizing committee met and concluded that, while Dr. He should participate in the summit, he should speak separately from other session speakers to enable full consideration of all speaker presentations. Dr. He's claims about his work have not been independently verified. Statements in this summary about Dr. He's work are based solely upon his presentation at the summit.

Dr. He began his presentation by apologizing that news of the twins' birth had leaked before he could present his research in a peer-reviewed scientific journal. He described how his research team had conducted experiments on embryos from mice and monkeys, human embryonic stem cells, and cultured human embryos to disable a gene known as CCR5, a gene that plays a role in the infection of cells by the human immunodeficiency virus (HIV). After deciding that the procedure used to disable the gene was safe, He and his associates genetically edited fertilized human eggs in an attempt to disable the CCR5 gene. The edited embryos were successfully implanted, and a subsequent pregnancy resulted in the birth of the twin girls, He reported. In response to a question, He said that another pregnancy with a genome-edited embryo is currently in progress.

During the question-and-answer session that followed Dr. He's presentation, summit participants raised many objections to his work. These objections included a lack of oversight and transparency, the inadequacy of the parents' informed consent, the existence of alternatives for preventing HIV infection, the possibility that the genome editing will

cause other health problems, and questions relating to the sources of funding for the research. Following Dr. He's presentation, David Baltimore (California Institute of Technology), Chair of the Summit Organizing Committee, described Dr. He's work as irresponsible. That the work had proceeded, he said, was evidence of "a failure of self-regulation by the scientific community."

In the statement released by the organizing committee at the end of the summit, the committee called for an independent assessment to verify Dr. He's claims. "Even if the modifications are verified, the procedure was irresponsible and failed to conform with international norms," the statement noted. Its flaws included "an inadequate medical indication, a poorly designed study protocol, a failure to meet ethical standards for protecting the welfare of research subjects, and a lack of transparency in the development, review, and conduct of the clinical procedures."

ADVANCES IN THE SCIENCE OF HUMAN GENOME EDITING

As many speakers at the summit observed, the science of genome editing has advanced rapidly since the first summit. The science is based on increasing knowledge of enzymes that interact with DNA, and this has resulted in many potential applications in research, health care, agriculture, and other fields, said Jennifer Doudna (University of California, Berkeley). Continued exploration of the natural diversity of such enzymes is helping to increase the specificity, efficiency, and versatility of genome editing. For example, a new technique known as base editing has made it possible to alter single letters of a DNA sequence without breaking the DNA strand, noted David Liu (Broad Institute). This enables researchers to correct the single nucleotide changes that cause many human diseases. As Feng Zhang (Broad Institute) explained, genome editing is analogous to quickly searching for, finding, and correcting a single misspelled word in a large multivolume text, something that was never before possible. Furthermore, new techniques in genome editing result in far fewer undesired or off-target DNA changes, said Angelo Lombardo (San Raffaele University), further increasing the technique's power and scope.

The development of genome editing is part of a much longer history of scientific advances in genetics and genomics that increasingly have linked the DNA sequences, or genotypes, of cells to the biological characteristics, or phenotypes, of organisms, observed Kathryn Song Eng Cheah (University of Hong Kong). In health care, these new techniques have enabled early diagnosis of genetic diseases, early intervention, enhanced surveillance, targeted therapies, and reproductive confidence for families at risk of such diseases, said John Christodoulou (University of Melbourne). Pak Sham (University of Hong Kong) noted that, even with more common complex diseases that result from a combination of many genetic variants and environmental influences, advances in genetics and genomics have enabled the construction and use of polygenic risk scores that indicate a person's risk of a disease. This knowledge may lead to better ways of treating and preventing such diseases. However, as Dana Carroll (University of Utah) reminded summit participants, greater understanding of genetics and genomics has also revealed the complexity of preventing and treating genetic diseases. While some applications may be forthcoming, many others face significant barriers to preclinical development and clinical use.

APPLICATIONS OF HUMAN GENOME EDITING

Rapid advances in the science of human genome editing have led to discussion of a wide range of potential applications. Several applications were examined in detail at the summit, including potential treatments for blood disorders, immunodeficiency disorders, and Duchenne muscular dystrophy.

Sickle cell disease, beta thalassemia, and related blood disorders are life threatening, painful, lifelong, widespread, and economically costly diseases, explained Merlin Crossley (University of New South Wales) and Sivaprakash Ramalingam (Institute of Genomics and Integrative Biology, Delhi). Blood cells and their progenitor cells are well understood, can be genetically manipulated in culture (i.e., *ex vivo*) and transplanted, and are an obvious target for human genome editing. Many approaches to such editing are being investigated. For example, Matthew Porteus (Stanford University) and his colleagues are exploring a clinical trial that would use hematopoietic stem cells harvested from sickle cell patients that are genetically corrected and then transplanted back into the patient, while Junjiu Huang (Sun Yat-sen University) reported on efforts to edit the gene responsible for beta thalassemia in human embryos in culture. The engagement of patients, family members, and other stakeholders will be critical in such research, said Vence Bonham (National Human Genome Research Institute, National Institutes of Health), when enhancing equity and ensuring that both the patient and research communities benefit as clinical trials and clinical treatments move forward. As Beverley Francis-Gibson (Sickle Cell Disease Association of America) observed, patient organizations can advocate for people affected by blood disorders and raise public consciousness while advancing the search for a universal cure.

In a related clinical area, Adrian Thrasher (University College London) noted that immunodeficiency disorders are favorite targets for gene therapies because the corrected cells often grow more vigorously than uncorrected cells.

Ex vivo somatic gene therapy has become the most effective treatment for certain forms of severe combined immunodeficiency, and clinical trials are under way using gene editing of hemopoietic cells to treat other kinds of diseases.

R. Rodney Howell (University of Miami) and Charles Gersbach (Duke University) discussed the prospects of using human genome editing to treat Duchenne muscular dystrophy (DMD), which is one of the more common eventually fatal genetic diseases. DMD arises from a large number of genetic mutations, requiring that different approaches to gene editing be pursued, some of which are now in clinical trials and in the initial stages of clinical use. However, as Pauline McCormack (Newcastle University) pointed out, the development of gene editing for DMD has been hampered by the great complexity of the disease. This has disappointed both parents and patients.

Several speakers discussed possible applications of genome editing in human embryos. Genome editing is already providing a powerful tool in the exploration of how embryos form, implant, and develop. Among other benefits, such research could assist in increasing low success rates of *in vitro* fertilization, said Kathy Niakan (The Francis Crick Institute).

Germline genome editing of human embryos also could someday provide a way to prevent genetic disease in individuals and disease transmission to future generations, observed Paula Amato (Oregon Health & Science University)—a prospect her group is investigating for several diseases, including hypertrophic cardiomyopathy. Germline genome editing can be carried out in a variety of ways, noted Robin Lovell-Badge (The Francis Crick Institute), including in cells that give rise to egg or sperm cells, in fertilized eggs, and in early embryos. However, before such methods can be used safely and effectively, many scientific questions need to be addressed, including questions about the unique features of the first embryonic cell cycle and the complexities of double-strand break repair described by Maria Jasin (Memorial Sloan Kettering Center Institute). In addition, as several speakers pointed out, procedures such as preimplantation genetic diagnosis or somatic gene editing after birth would be preferable to genome editing of germline cells. Nevertheless, Xingxu Huang (Shanghai Tech University), who detailed his work using base editing, explained that genome editing of human embryos is likely to progress to the point that it could be used, if scientific and social issues were better understood and addressed, to correct pathogenic mutations that affect millions of people worldwide.

PHILOSOPHICAL AND RELIGIOUS PERSPECTIVES

The new ability to alter DNA sequences in cells has raised profound philosophical and religious questions. Mohammed Ghaly (Hamad Bin Khalifa University) said that, from an Islamic perspective, somatic cell therapy is considered acceptable because it is a treatment for disease, has limited scope, and affects only an individual. Germline cell therapy is considered much more controversial in Islamic communities, he continued, because it goes beyond human authority in the universe, has an impact on offspring, and violates the notion that humans are trustees and not owners of their bodies.

In Japan, noted Satoshi Kodama (Kyoto University), human embryos are considered "sprouts of human life" that must be protected to maintain human dignity. A 2016 interim report from an expert panel convened by the Cabinet Office of the government of Japan allowed the use of gene-editing tools on spare embryos for the improvement of assisted reproductive technologies, but it prohibited the creation of human embryos for research, some categories of research on embryos, and clinical applications of germline genome editing.[4]

Margaret Sleeboom-Faulkner (University of Sussex) called attention to the need to broaden the orientation of bioethics to include more expansive notions of health, nature, and embodied knowledge. Harmony with the environment, life as a gift or path, and the cultivation of intuitive or spiritual faculties are all issues that go well beyond defining health in terms of a person's genetic endowment.

Philosophical questions also involve the relationships of human beings with each other. For example, as genome editing progresses, embryos produced in vitro could be immediately examined for genetic defects that could be corrected, said Maurizio Balistreri (Università degli Studi di Torino). Could mothers be required or socially pressured to use reproductive technology based on the belief that they have a duty to perform any act that benefits their offspring? Responsibility toward future generations is important, Balistreri said, but it must be balanced against the interests of others, including women who bear children.

Renzong Qiu (Chinese Academy of Social Sciences) observed that philosophical reflections must be incorporated into governance frameworks for genome editing. This requires, he said, special regulations on applying genome editing in human reproduction, a licensing system, capacity building for review boards, and enhanced review for germline genome modifications. A particular problem with the governance of human genome editing in China, he noted, is the lack of penalties when standards are violated.

[4] Expert Panel on Bioethics, Council for Science, Technology and Innovation (CSTI), *On Research Using Genome Editing Technology on Human Embryos* (Interim Report), April 22, 2016.

REGULATION

A panel specifically on governmental actions and advisory opinions included representatives from China, France, India, Japan, Australia, Singapore, and Hong Kong: Xiaomei Zhai (Chinese Academy of Medical Sciences and Peking Union Medical College), Hervé Chneiweiss (Centre National de la Recherche Scientifique), S. R. Rao (Ministry of Science and Technology), Hidenori Akutsu (National Research Institute for Child Health and Development), Dianne Nicol (University of Tasmania), Tamra Maree Lysaght (National University of Singapore), and Lot Chan (Hong Kong Special Administrative Region). As panel moderator Jennifer Merchant (Université Panthéon-Assas, Paris) observed after the panelists' presentations, all seven jurisdictions, through their own governance procedures, have developed prohibitions against using human germline modification for purposes of reproduction. In China, for example, an extensive regulatory framework governs genome editing, said panelist Xiaomei Zhai. But guidance is needed regarding appropriate oversight and ethically acceptable modes of pursuing this research, she continued, and oversight structures should be in place prior to any attempts to conduct this research for the purposes of human reproduction.

In a related panel on research ethics, five speakers elaborated on some of the ethical considerations underlying genome editing research, and in particular germline genome editing, and the embodiment of those considerations in regulation. Genome editing research invokes three activities, said Jeffrey Kahn (Johns Hopkins University): oversight, approval, and consent. Tetsuya Ishii (Hokkaido University), observed that human germline genome editing has a systemic impact on human rights because of the current uncertainty about outcomes and the inability to obtain consent from someone not yet born.

Bärbel Friedrich (German National Academy of Sciences Leopoldina) pointed to the usefulness of establishing a body that would define a global ethical code of conduct, which could in turn support oversight, approval, and consent. Eben Kirksey (Deakin University) added that ethical considerations are fluid and evolving, especially with new technologies, due to the interplay of responsibility and accountability in relationships. Arriving at ethical conclusions regarding new technologies, said Andy Greenfield (Medical Research Council), requires a very broad conversation with diverse publics using non-technical, substantive, and accessible language.

A CLINICAL PATHWAY FOR GERMLINE GENOME EDITING

George Daley (Harvard Medical School) said that the risks and benefits of germline genome editing are still not so clear as to allow germline genome editing to proceed. He noted, however, that increased scientific understanding and recent reports suggest that it is time to begin considering what a responsible pathway for clinical translation would entail.[5] Establishing such a pathway would require further discussion and consensus building on many difficult issues, but if these issues can be satisfactorily addressed, Daley said, defining a rigorous clinical pathway for germline genome editing could become both morally imperative and essential in precluding irresponsible practices.

Sarah Chan (University of Edinburgh) noted that past reports have laid out principles that would need to be met for germline genome editing to proceed, but those principles will need to be translated into action. Doing so will require that multiple publics and multiple scientific communities be engaged in discussions of ethical issues such as risk, choice, and agency, despite differences in local contexts, values, and opinions. Furthermore, robust governance requires assessing institutions, not just individual experiments and technologies, said J. Benjamin Hurlbut (Arizona State University). Institutions need to be able to listen to and hear multiple voices (including those of religious groups), critically reflect on their actions and policies, and learn from others and from dissent—for example, by inviting the input of those who can provide perspectives not obvious to researchers and clinicians.

Ock-Joo Kim (Seoul National University) supported looking beyond local interests and towards the adoption of universal values when developing human genome editing technology and in applying it in clinical practice. Universal values are important in research, she said, especially given the strong influence of commercial interests and conflicts of interest on this research. Ames Dhai (University of Witwatersrand) cited a 2016 statement by the International Bioethics Committee of UNESCO that called on governments to renounce the possibility of acting alone in relation to engineering the human genome and to establish a shared, global standard for this purpose. She raised the possibility of a United Nations treaty or covenant on the human genome that would globally harmonize the governance of genome editing.[6]

---

[5] National Academies of Sciences, Engineering, and Medicine, *Human Genome Editing: Science, Ethics, and Governance* (Washington, DC: The National Academies Press, 2017) and Nuffield Council on Bioethics, *Genome Editing and Human Reproduction: Social and Ethical Issues* (London: Nuffield Council on Bioethics, 2018).

[6] United Nations Educational, Scientific and Cultural Organization, *Report of the International Bioethics Committee on Updating Its Reflection on the Human Genome and Human Rights*, October 21, 2016.

RESEARCH ETHICS, GLOBAL PERSPECTIVES, AND PRINCIPLES

A panel on global perspectives examined four spheres of ethical governance, as identified by moderator Ayo Wahlberg (University of Copenhagen): (1) ethical deliberations; (2) ethical review; (3) laws, regulations, rules, and guidelines; and (4) ethical interactions. Each can differ between jurisdictions, even if common principles underlie the areas of activity.

Among the distinctive aspects of widespread worldviews in sub-Saharan Africa, said Kevin Behrens (University of Witwatersrand), is the conviction that all entities, including inanimate objects, have a life force that can be diminished or heightened, that the current generation has a duty to husband resources to leave the world in good order for future generations, and that major decisions should be made by consensus rather than majority rule. These principles argue for caution and inclusive decision making in genome editing, but they do not rule it out. Guido de Wert (Maastricht University) pointed out that many of the arguments made against germline genome editing, such as consideration of the autonomy of a child, societal equity, and possible misuse, can be applied as well to other medical technologies, but many jurisdictions have nevertheless permitted those technologies to move forward, so long as they are sufficiently beneficial, safe, and effective. Peter Mills (Nuffield Council on Bioethics) described the reasoning behind the conclusion of the 2018 report *Genome Editing and Human Reproduction: Social and Ethical Issues* from the Nuffield Council on Bioethics: germline genome editing could be morally permissible in certain circumstances but those circumstances do not yet exist anywhere in the world. Yuko Harayama (Tohoku University) outlined the process leading to a 2018 report which called for an enhanced review system for such research, more extensive public consultation, and continued discussion of the issues associated with hereditary diseases, cancer, and the creation of embryos for research.[7]

PUBLIC ENGAGEMENT

A concluding panel explored ways of engaging the public in discussions about human genome editing. Anna Middleton (Wellcome Sanger Institute) summarized results from an international survey on genomics that included such questions as "Are you familiar with DNA, genetics or genomics?" and "Would you donate your anonymous DNA information and medical information for use by for-profit researchers?" Joy Zhang (University of Kent) described the results of the first UK-China multi-stakeholder public engagement training workshop, in which scientists, government regulators, and members of the public spent two days discussing genetically modified organisms, with the one ground rule that they limit their conversation to the empirical process and refrain from making value judgments. The very positive feedback about the workshop from participants shaped the design of resources that can be used to build confidence and capacity much more widely, such as an educational module on public engagement that universities have been incorporating into their curricula.

Megan Munsie (University of Melbourne) discussed work she and her colleagues have done in Australia on engaging the public in discussions of commercial stem cell therapies. By disseminating information and engaging in dialogues, often in partnership with patient groups, they have sought to increase knowledge about these therapies and address the "expectations gap" between what the therapies promise and what can be delivered. Masako Takuma (National Museum of Emerging Science and Innovation) described activities designed to enable participants to become aware of an issue, think about it, listen to others' opinions, and form their own opinions. After one public meeting, a third of participants said that they had changed their opinions about human genome engineering, and the group arrived at a consensus that "the most important thing is to have lots of public discussion on this issue."

In the final session of the summit, the 14-member organizing committee released a concluding statement (see Box 1) and the presidents of the U.S. National Academy of Sciences and U.S. National Academy of Medicine issued a statement in response (see Box 2).

[7] Council for Science, Technology and Innovation (CSTI), *First Report on the Review of the "Basic Principles on the Use of Human Embryos:" Use of Genome Editing Technology for Assisted Reproductive Research Purposes,* March 29, 2018.

BOX 1
ON HUMAN GENOME EDITING II

Statement by the Organizing Committee of the Second International Summit on Human Genome Editing

November 29, 2018

In December 2015, the U.S. National Academy of Sciences and U.S. National Academy of Medicine, the Royal Society of the United Kingdom, and the Chinese Academy of Sciences hosted an international summit in Washington, D.C., to discuss scientific, ethical, and governance issues associated with human genome editing. At its conclusion, the summit organizing committee released a statement identifying areas of research and clinical use that could proceed within current regulatory and governance protocols. The committee also stated that it would be irresponsible to proceed with any clinical use of heritable "germline" editing at that time. Further, it called for continued international discussion of potential benefits, risks, and oversight of this rapidly advancing technology.

As part of their commitment to fostering in-depth and international discussion about human genome editing, the Academy of Sciences of Hong Kong, the Royal Society of the United Kingdom, and the U.S. National Academy of Sciences and U.S. National Academy of Medicine organized the Second International Summit on Human Genome Editing in Hong Kong to assess the evolving scientific landscape, possible clinical applications, and attendant societal reactions to human genome editing. While we, the organizing committee of the second summit, applaud the rapid advance of somatic gene editing into clinical trials, we continue to believe that proceeding with any clinical use of germline editing remains irresponsible at this time.

HUMAN GENOME EDITING RESEARCH

Basic and preclinical research is rapidly advancing the science of somatic and germline genome editing. Better understanding and design of genome editing techniques, including base editing, have produced significant increases in efficiency and precision while greatly reducing off-target events. As was anticipated, somatic genome editing is now being tested in patients.

Making changes in the DNA of embryos or gametes could allow parents who carry disease-causing mutations to have healthy, genetically related children. However, heritable genome editing of either embryos or gametes poses risks that remain difficult to evaluate. Concerns persist that changes may be made in only some cells of early-stage embryos, leaving unedited cells to perpetuate a disease. Germline editing could produce unintended harmful effects for not just an individual but also for that individual's descendants. Changes to a particular trait may have unanticipated effects on other traits that could vary from person to person and in response to environmental influences.

The variability of effects produced by genetic changes makes it difficult to conduct a thorough evaluation of benefits and risks. Nevertheless, germline genome editing could become acceptable in the future if these risks are addressed and if a number of additional criteria are met. These criteria include strict independent oversight, a compelling medical need, an absence of reasonable alternatives, a plan for long-term follow-up, and attention to societal effects. Even so, public acceptability will likely vary among jurisdictions, leading to differing policy responses.

The organizing committee concludes that the scientific understanding and technical requirements for clinical practice remain too uncertain and the risks too great to permit clinical trials of germline editing at this time. Progress over the last three years and the discussions at the current summit, however, suggest that it is time to define a rigorous, responsible translational pathway toward such trials.

A PROPOSED TRANSLATIONAL PATHWAY

A translational pathway to germline editing will require adhering to widely accepted standards for clinical research, including criteria articulated in genome editing guidance documents published in the last three years.[a]

Such a pathway will require establishing standards for preclinical evidence and accuracy of gene modification, assessment of competency for practitioners of clinical trials, enforceable standards of professional behavior, and strong partnerships with patients and patient advocacy groups.

REPORT OF CLINICAL USE OF GERMLINE EDITING

At this summit we heard an unexpected and deeply disturbing claim that human embryos had been edited and implanted, resulting in a pregnancy and the birth of twins. We recommend an independent assessment to verify this claim and to ascertain whether the claimed DNA modifications have occurred. Even if the modifications are verified, the procedure was irresponsible and failed to conform with international norms. Its flaws include an inadequate medical indication, a poorly designed study protocol, a failure to meet ethical standards for protecting the welfare of research subjects, and a lack of transparency in the development, review, and conduct of the clinical procedures.

AN ONGOING INTERNATIONAL FORUM

The organizing committee calls for an ongoing international forum to foster broad public dialogue, develop strategies for increasing equitable access to meet the needs of underserved populations, speed the development of regulatory science, provide a clearinghouse for information about governance options, contribute to the development of common regulatory standards, and enhance coordination of research and clinical applications through an international registry of planned and ongoing experiments.

In addition to the establishment of an international forum, the organizing committee calls upon national academies and learned societies of science and medicine around the world to continue the practice of holding international summits to review clinical uses of genome editing, to gather diverse perspectives, to inform decisions by policymakers, to formulate recommendations and guidelines, and to promote coordination among nations and jurisdictions.

[a] See, for example, National Academies of Sciences, Engineering, and Medicine, *Human Genome Editing: Science, Ethics, and Governance* (Washington, DC: The National Academies Press, 2017) and Nuffield Council on Bioethics, *Genome Editing and Human Reproduction: Social and Ethical Issues* (London: Nuffield Council on Bioethics, 2018).

BOX 2
Statement By

Marcia McNutt, President, U.S. National Academy of Sciences
Victor J. Dzau, President, U.S. National Academy of Medicine

November 29, 2018

We thank the organizing committee of the Second International Summit on Human Genome Editing, held this week in Hong Kong, for planning an important and timely conference on a rapidly advancing area of science and medicine. We support the committee's concluding statement, which reiterates the need for the global scientific and medical communities to continue to work together to further define responsible approaches to human genome editing research and clinical use.This is especially true given the unexpected announcement this week from a researcher in China claiming to have edited the embryonic genomes of newborn twins. The summit addressed this troubling revelation and underscored guidance that was provided in a 2017 report from the U.S. National Academy of Sciences and National Academy of Medicine. That report outlined criteria under which clinical trials and applications of germline editing might be permitted, but only when there is compelling medical need with a clear understanding of risks versus benefits, and only under stringent oversight, with sufficient transparency and public input. Not following these guidelines would be an irresponsible act.

The summit heard the claim by the researcher and discussed its potentially profound implications. We share the organizing committee's deep concerns that the researcher did not follow guidelines such as those recommended in the 2017 National Academies report, or other international norms of responsible scientific conduct.

We are committed to continuing to provide leadership on the responsible pursuit of human genome editing research and applications, and to work together with our colleagues at other Academies around the world to host additional forums and to develop future guidelines. The events in Hong Kong this week clearly demonstrate the need for us to develop more specific standards and principles that can be agreed upon by the international scientific community. We look forward to joining others on the path forward called for by the organizing committee.

DISCLAIMER: This Proceedings of a Workshop—in Brief has been prepared by **Steve Olson** as a factual summary of what occurred at the meeting. The organizing committee's role was limited to planning the meeting. The statements made are those of the author or individual meeting participants and do not necessarily represent the views of all meeting participants, the organizing committee, U.S. National Academy of Sciences and U.S. National Academy of Medicine, the Royal Society of the United Kingdom, and the Academy of Sciences of Hong Kong.

REVIEWERS: To ensure that it meets institutional standards for quality and objectivity, this Proceedings of a Workshop—in Brief was reviewed by **Hank Greely**, Stanford University; **Richard Hynes**, Massachusetts Institute of Technology; and **Pilar Ossorio**, University of Wisconsin. **Marilyn Baker,** National Academies of Sciences, Engineering, and Medicine, served as the review coordinator.

SPONSORS: The workshop was supported by the National Institutes of Health, the Wellcome Trust, and the Burroughs Wellcome Fund.

For more information, visit http://www.nationalacademies.org/gene-editing/2nd_summit/index.htm.

Suggested citation: National Academies of Sciences, Engineering, and Medicine. 2019. *Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop—in Brief.* Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/25343.

Policy and Global Affairs

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

The nation turns to the National Academies of Sciences, Engineering, and Medicine for independent, objective advice on issues that affect people's lives worldwide.
www.national-academies.org