AMERICAN SOCIETY of GENE & CELL THERAPY

World Health Organization
Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing

August 16, 2019

Members of the Advisory Committee:

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to submit its views to the World Health Organization (WHO) Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing (the Advisory Committee). ASGCT is a professional membership organization consisting of scientists, physicians, and other professionals working primarily in universities, hospitals, and biotechnology and pharmaceutical companies. The mission of the Society is to advance knowledge, awareness, and education leading to the discovery and clinical application of genetic and cellular therapies to alleviate human disease.

Position on Clinical Application of Gene Editing

We appreciate that the Advisory Committee was established by the WHO to advise and make recommendations on appropriate institutional, national, regional, and global governance mechanisms for human genome editing, including both somatic and germline gene editing. ASGCT recognizes the tremendous potential achievable through the techniques of genome editing and their value for an improved understanding and possible treatment of human disease. Today, there are several ongoing clinical trials throughout the world in which these tools are being used to treat debilitating human diseases through somatic cell gene editing. However, our Society also recognizes that the application of genome editing under some circumstances—specifically germline gene editing combined with the implantation of gene-edited embryos to achieve a pregnancy—are technologies that are not ready for use in humans and pose very serious problems for which there is no scientific or general societal consensus. As such, ASGCT supports a strong ban on clinical germline gene editing unless and until the technical and ethical problems can be solved, broadly and deeply discussed, and societal consensus reached.

From a scientific perspective, too many important questions remain unanswered for human embryo editing to be a safe and acceptable therapeutic application of the technology at this time. The issues that must be addressed before proceeding include, but are not limited to: optimizing the efficiency and precision of on-target modification; defining and minimizing off-target mutations; preventing on- and off-target mutation mosaicism; and understanding how novel on- and off-target mutations might interact with existing human genetic diversity when these new alterations are passed on to future generations.

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In addition, clinical use of germline gene editing poses major ethical concerns, because research subjects would include not only embryos and children, but also future generations of descendants. Before the status quo prohibiting clinical germline gene editing in many nations is revisited, it is vital that extensive engagement occurs among all major stakeholders, including representatives with scientific, medical, patient, caregiver, policy, legal, ethical, and faith perspectives from around the world. These stakeholders need to determine together whether, and under which conditions, clinical germline gene editing should take place in the years ahead. We consider these widely inclusive societal discussions to be essential in developing national, regional, and/or international governance structures to attempt to prevent further irresponsible use of gene editing.

Differentiating Clinical Use of Germline Gene Editing From Somatic Cell Editing

We support international efforts, such as those of the Advisory Committee, to examine and develop recommendations on the scientific and ethical concerns surrounding the clinical use of germline gene editing. However, we believe that these should not inhibit the great scientific advancement represented by gene editing technologies[1] when used on somatic cells, and their potential value for an improved understanding and possible treatment of a variety of diseases. Although clinical trials will be required to demonstrate the safety and efficacy of these approaches, ASGCT views the risks of gene therapy, including somatic cell gene editing, as neither entirely unique nor unpredictable. Thus, clinical trials in the field should fall within existing regulatory frameworks used for other areas of biomedical research for ensuring safety and efficacy in humans. We have confidence that these regulatory entities and their processes, building on decades of work overseeing gene therapy and early gene editing clinical trials, are well positioned to continue such oversight of therapeutic somatic cell gene editing.

ASGCT respectfully expresses its concern regarding the Advisory Committee's first recommendation, which is to request the WHO to immediately start work to develop a registry of all research and development relevant to its mandate.[2] Because the Advisory Committee identified both germline and somatic genome editing to be relevant to its mandate, we are concerned that this registry is under consideration for all genome editing research. ASGCT finds the requirement for registration of somatic cell research to be potentially duplicative of national regulatory requirements, and is concerned that the potential for additional administrative burdens posed by this requirement could delay progress in the development of gene editing treatments. We request the Committee only consider requiring the use of a registry for gene editing research on germline cells and embryos.

The report indicates that the Committee will establish a working group to develop the architecture of the registry, whose task will include agreeing on the types of research that must be included in this registry and the metadata that should be submitted to describe the research in appropriate detail. If the Committee proceeds to establish such a working group, ASGCT respectfully requests WHO consideration of ASGCT participation through representation on the working group.

Call for Reporting

Regarding the Advisory Committee recommendation urging all those conducting or aware of research and development relevant to its mandate, in particular on human germline cells and embryos, to engage with the Committee immediately, we do not view the reporting of research and development of somatic cell editing to be necessary. However, ASGCT appreciates the call for reporting of the clinical use of germline cells and embryos, since the Society supports the development and use of effective and easily accessible mechanisms for reporting potential violations of current societal norms.

Fostering an Inclusive Process

ASGCT appreciates the WHO's emphasis on the importance of inclusivity in the Committee's process. To further facilitate such inclusivity, the Society would encourage additional opportunities for public input throughout the course of the Advisory Committee's work. Moreover, because previous work on these issues has predominantly consisted of input from academic researchers, we encourage a process of genuine public engagement with multiple diverse stakeholders. We consequently urge the WHO Advisory Committee to convene, or obtain input from, all relevant and diverse stakeholders as listed previously.

In addition, ASGCT recommends expanding representation on the Advisory Committee of expert biomedical researchers in gene editing, who may contribute significantly to the analysis of the scientific and regulatory implications of international governance decisions on the therapeutic development of gene editing. The Society would be quite willing to provide or to recommend a member representative to serve on the committee, if so desired. The Society also recommends inclusion on the Advisory Committee of a patient and/or a caregiver for someone with a condition for which gene editing is under current or imminent research.

Summary and Closing Remarks

ASGCT strongly agrees that steps must be taken to prevent further clinical use of germline gene editing at the same time that the efficient development of safe and effective somatic cell gene editing treatments for disease with unmet medical need should be facilitated. As the committee proceeds to explore attributes of effective governance frameworks, ASGCT encourages the identification of a fine balance between the strong international governance required to prevent abuses of gene editing technology and the sufficiently flexible regulatory environment necessary to allow groundbreaking treatments to be developed expeditiously for patients in need of them.

The Society commends the WHO request for reporting of violations of societal norms and encourages the future development of a formal reporting mechanism. Because we place significant value on transparency and true engagement surrounding the clinical use of germline gene editing, ASGCT recommends expanded representation on the Advisory Committee and ongoing collection of broad input from all relevant stakeholders.

Thank you for your consideration of our comments. We look forward to hearing from you regarding next steps for ASGCT to engage in dialogue with you regarding governance mechanisms for human gene editing. Should you have any questions, concerns, or insights you would like to discuss with us, please contact David Barrett, ASGCT Executive Director, at dbarrett@asgct.org, phone 414-278-1341. The Society welcomes the opportunity to provide the Advisory Committee with input from our members on these issues.

Sincerely,

Guangping Gao, Ph.D.
ASGCT President

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[1]Maeder, M. L., & Gersbach, C. A. (2016). Genome-editing technologies for gene and cell therapy. *Molecular Therapy*, *24*(3), 430-446.
[2]Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing (March 18-19, 2019. Geneva). Report of the First Meeting.