Gene Therapy Policies Can Strike An Ethical Balance

By **Ping Wang, John Murray and Angel Wang** (May 3, 2019)

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On July 11, 2018, then-U.S. Food and Drug Administration Commissioner Scott Gottlieb made a public statement about the agency's efforts to advance the development of gene therapies.[1] Gottlieb pointed out that the FDA has approved three separate gene therapy products and the agency has issued six scientific guidance documents intended to serve as building blocks of a modern, comprehensive framework for how the FDA can advance the field of gene therapy.

The FDA's message is clear: Gene therapy is a useful technique in dealing with some of the most serious diseases faced by humans, and the FDA is working toward supporting innovation and maintaining current safety and effectiveness standards for gene therapies.

The FDA defines gene therapy as "a technique that modifies a person's genes to treat or cure disease," which signals that genetic editing of human embryos per se is not currently acceptable.[2] Moreover, the FDA is prohibited from using federal funds to review "research in which a human embryo is intentionally created or modified to include a heritable genetic modification,"[3] which works as a restriction on the creation of genetically edited babies.

Recently, a group of scientists announced the creation of the world's first genetically edited babies. Using CRISPR — a powerful tool to edit genes within organisms — the research focused on a gene called CCR5, which encodes a protein used by the HIV virus as a doorway to infiltrate human cells. The experiment deleted a small section of the CCR5 gene, mimicking a naturally occurring mutation called delta 32; the researchers claimed that this DNA alteration could prevent infection by an HIV virus.

This experiment risks producing increased public and political fear about current gene therapy research and treatments. However, it is important that a natural zeal to prevent the genetic editing of human embryos does not result in legislative measures that could harm the development of potentially life-saving gene therapy technologies.

Policymakers need to understand the fundamental scientific, ethical and legal differences between current gene therapy research and genetically editing babies. To fully appreciate the scientific, ethical and legal implications of genetic editing and its differences from gene therapy treatments as currently approved by the FDA (and many ongoing clinical trials), it is beneficial to understand the basic classifications of human genetic modification.

There are two types of genetic modification: (1) gene therapy, which is aimed at treating a disease, and (2) genetic enhancement, which is aimed at altering normal, nondisease traits beyond levels considered typical of adequate health.[4] Both gene therapy and genetic enhancement can be done to somatic cells, which means the altered DNA is not passed on to the patient's offspring because it does not affect reproductive cells, or to germline cells, which is altering DNA of sperm, eggs or embryos that could intentionally or unintentionally change the genetic makeup of future generations.

Current gene therapy treatments and clinical trials only alter somatic cells and treat serious diseases caused by one or more faulty genes. In contrast, genetic editing of germline cells is heritable, and as a result, any potential benefits and harms could be passed on to future generations.

A United Nations Educational, Scientific and Cultural Organization panel of scientists called for a temporary ban on genetic editing of human germline cells in 2015.[5] The organization's International Bioethics Committee stated that "[i]nterventions on the human genome should be admitted only for preventive, diagnostic or therapeutic reasons and without enacting modifications for descendants," and that the alternative would "jeopardize the inherent and therefore equal dignity of all human beings and renew eugenics."[6]

A particular concern is the potential development of "regulatory havens" — where researchers, medical providers or consumers travel to jurisdictions with less stringent regulations to undertake restricted genetic procedures.

One approach to solve this potential problem could be to create uniform international regulations.[7] As early as 1997, the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, or the Oviedo Convention, established principles under the European Convention on Human Rights in the field of biology and medicine.[8]

For the countries that have signed the treaty,[9] "the genetic constitution of the individual is to be protected against unlawful interventions seeking to modify the germline."[10] Implementation of regulations similar to the Oviedo Convention by countries outside Europe could provide increased public confidence and support for continued development of gene therapy.

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[1] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm613026.htm

[2] https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm573960.htm

[3] Consolidated Appropriations Act of 2016, Public Law 114-113 (adopted December 18, 2015); see also https://law.stanford.edu/2018/12/05/the-first-gene-edited-babies-a-discussion-on-the-legal-and-ethical-questions-with-stanfords-hank-greely/

[4] See https://www.ncbi.nlm.nih.gov/books/NBK447260/

[5] https://en.unesco.org/news/unesco-panel-experts-calls-ban-editing-human-dna-avoid-unethical-tampering-hereditary-traits

[6] https://en.unesco.org/news/unesco-panel-experts-calls-ban-editing-human-dna-avoid-unethical-tampering-hereditary-traits

[7] Charo RA. On the road (to a cure?): Stem-cell tourism and lessons for gene editing. New England Journal of Medicine. 2016a;374(10):901–903.

[8] https://www.coe.int/en/web/bioethics/oviedo-convention

[9] Mostly European countries, see the Chart of Signatures and Ratifications here: https://rm.coe.int/inf-2017-7-rev-etat-sign-ratif-reserves/168077dd22

[10] https://www.ncbi.nlm.nih.gov/books/NBK447261/