What is Genome Editing?

Genome Editing (also called “gene editing”) is defined as “a group of technologies that give scientists the ability to change an organism’s DNA.”¹ These technologies edit DNA through adding, altering, or removing genetic material at target places inside the human genome. Genome editing is not new—scientists have used various techniques to create genetically modified organisms (GMOs) for decades. Yet the application to humans was limited because the methods were slow, costly, and not considered safe or reliable to deliver the treatment in humans.² The discovery of a system called CRISPR-Cas9³ led to faster, cheaper, and more accurate than existing gene editing systems such as ZFNs and TALENs. CRISPR-Cas9 was adapted from a naturally occurring genome editing system of bacteria used to protect cells from viral infections. CRISPR has been shown to work in human cells by cutting DNA at a predetermined target site, allowing scientists to then insert a different DNA sequence.⁴

Key Benefits and Applications

Genome editing technologies have benefits across several areas of the economy.⁵ The principal implications of genome editing lie in human health and disease. However, genome editing can be used to increase agricultural productivity, food security, and nutritional quality of foods. These technologies can also be used to promote environmental conservation by making species more resistant to disease and climate variations. Additional benefits can also arise from improved industrial bioprocesses and biofuels.

Key Benefits and Applications of Gene Editing Technologies

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<th>Agriculture</th>
<th>Environmental Conservation</th>
<th>Energy &amp; Production</th>
<th>Healthcare</th>
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<td>• Food Security</td>
<td>• Endangered and extinct species</td>
<td>• Improved economic output</td>
<td>• Improved human health</td>
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<td>• Nutrition</td>
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<td>• Increased crop production</td>
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<td>• Climate resistant crops</td>
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<td>• Pest elimination</td>
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¹ National Institutes of Health. “What are genome editing and CRISPR-Cas 9?” Accessible online.
² Ibid.
³ CRISPR is an acronym for “clustered regularly interspaced short palindromic repeats.”
Technological Capabilities and Limitations

Current research on CRISPR has largely focused on animal and laboratory culture models, but is increasingly turning toward human application. The first applications of CRISPR-based therapy in humans will likely be for treatments or “cures” to single-gene diseases such as cystic fibrosis, hemophilia, and sickle-cell anemia. Trials with engineered cells are also underway for immunotherapy in certain types of cancers. In the medium term, CRISPR could be used to reduce the overall risk profile for other diseases where the genetic underpinnings are more complex. Many common diseases—including heart disease, diabetes, neurological conditions, and mental illness—have dozens or hundreds of known genetic risk factors, but also depend on a range of environmental components such as stress, diet, exercise, and toxin exposure to develop. Similarly, simple genetic traits could be among the first that we are able to modify by human genome editing technologies, while those where there are large numbers of genes or less clear genetic underpinnings—such as height or intelligence—would likely come later.

Current Governance and Regulation

The regulatory and governance frameworks around human genome editing are considered in two distinct categories. Germline editing is the modification of human eggs, sperm, or embryos to change the genetic material of a person not yet born, or genetic material that will be passed to future generations. Somatic cell editing is the modification of genetic material of cells that are not passed to future generations such as liver, heart, or brain.

Germline Editing (Eggs, Sperm, Embryos, and heritable genetic changes)

Many countries, including the U.S., have imposed restrictions on access to experimentation on human embryos, which has slowed the pace of research. Since 1979, the US National Institutes of Health's Human Embryo Research Panel has upheld the “14-day rule” to limit research on human embryos to a maximum period of 14 days after their creation or the stage of development that is equivalent to when embryos finish implantation. Most advanced countries have passed laws banning or defunding human germline editing, including Canada, Germany, France, South Korea, and the U.S. 


Somatic Cell Editing (Non-inheritable genetic changes)

The regulatory process for somatic cell editing falls within the regulatory auspices of medical products and is subject to the clinical trials process. ⁹

International Governance Frameworks

There have been a number of international dialogues around the ethics and regulatory frameworks that should govern human genome editing technologies. During 2016-2018, the OECD’s Director for Science, Technology, and Innovation hosted a series of international meetings around somatic cell genome editing. OECD member state governments, scientists, physicians, bioethicists, civil society, and others mapped current status and stakeholder concerns. The meetings revealed that there is likely to be a broad range of issues that will need to be reconciled among and within member state legislatures and regulatory bodies, including: ¹⁰

- What is the threshold for acceptable risk and benefit for making a specific genome edit?
- What are acceptable applications—for disease prevention, disease treatment, and trait enhancement? Who determines which genes fall into which category? Whose religious or cultural value systems should determine what is acceptable when a society disagrees (i.e., on disability)?
- How should public input be incorporated into the policymaking process in each country?
- How do leaders ensure diverse members of the public have enough genetic literacy to be able to participate?

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Public Purpose Considerations

Genome editing therapies are at the beginning stage of trials in humans. As such, the full extent of feasibility, safety, and impacts is still unknown. A number of critical variables regarding the scientific, policy, commercial, and public responses to genome editing will ultimately determine how the technology is used in the future.\(^\text{11}\) The known variables today include:

- **Technical Feasibility**—whether somatic cell gene editing can effectively mediate health outcomes in adult humans and for which diseases and traits it is effective.

- **Safety**—the rate of “off target” effects and the health outcomes of those impacted as well as immune responses to genome editing.

- **Ownership and Innovation**—whether the technology and techniques are broadly owned and accessible or controlled by a few patent holders who restrict access to other innovators.

- **Affordability and Access**—whether treatments and enhancements are affordable and accessible to all or only a select few; the degree to which this technology is available in advanced versus emerging economies.

- **Control**—whether licenses are required to use the technology or access is open to all; whether “bio-hacking” or self-experimentation is permissible and widespread.

Short-Term Concerns

There are several ethical issues that have immediate implications for ongoing research and clinical trials:

- **Ethics of Human Embryo Experimentation**—The degree to which experimentation on human embryos will proceed will continue to be subjected to much debate across countries. The outcomes are being driven by shifting public opinions toward human genome editing and the effectiveness of stakeholder advocacy/lobbying efforts in each nation.

- **Clinical Trials**—Clinical trials for human genome editing in somatic cells face the same issues of ethics as other forms of medical products, including ensuring patient consent and safety during the process, and in particular the risk-benefit balance of first-in-human trials.

There are also immediate concerns surrounding applications of CRISPR technology for human health that do not involve directly editing human DNA:

• **Biosecurity**—CRISPR technologies can make gene editing of pathogens widely available. However, biosecurity threat assessments have been inconclusive as to whether CRISPR technology adds additional capabilities beyond existing and widely available gene editing techniques for creation of bio-weapons and pathogens.\(^{12}\)

• **Biodiversity**—Some proposed applications of CRISPR—“gene drives”—would target modification of disease-carrying organisms such as mosquitoes that carry malaria, or pests such as mice, rabbits, and insects through inserting faulty genes that would reduce the ability of the species to transmit the pathogen or to reproduce in subsequent generations. Depending on the species, this type of large-scale population loss could have unintended consequences for overall biodiversity, agriculture, food security, and climate stability.\(^{13}\)

### Medium-Term Concerns

Once human genome editing technologies become more advanced and are available for medical treatment and elective consumer uses, additional concerns are likely to arise, including:

• **Pricing and Affordability**—Similar to other forms of breakthrough medical treatments and elective interventions, human genome editing treatments have a risk of price gouging by companies and differential reimbursement rates by national and private insurance companies. This can lead to significant disparities in population health outcomes.

• **Autonomy**—If do-it-yourself kits become available or direct to consumer services are offered, additional concerns may arise around consumer consent and safety for self-administration or experimentation. It is unlikely that DIY kits will have capabilities that are able to deliver safe and effective genome editing for human use at the same level as treatment in a clinic.

• **Licensing and Authorization**—Concerns may arise around unauthorized clinics and providers offering genome editing services and elective treatments to patients who were unable to obtain or afford a service in mainstream healthcare settings. Licensing or other protections will need to be in place to ensure patient safety.

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\(^{12}\) Revill, James. (2017), “Could gene editing tools such as CRISPR be used as a biological weapon?” Accessible online.

\(^{13}\) Prowse, Thomas et al. (2017), “Gene drives could wipe out whole populations of pests in one fell swoop.” Accessible online.
Long-Term Concerns

In the long term, once the technology becomes mature and pervasive, the impacts are more difficult to anticipate. However, in a worst-case scenario, widespread use of human genome editing technologies could have serious societal effects. While these consequences are far in the future, it is important to keep them in mind during the initial stage of technological development.

- **Social Inequalities**—If genome editing becomes widely adopted and accessible to only select groups, the gaps in social inequalities may grow, including health status, education, athletic, and ultimately wealth and income. This could widen economic divides both within nations and between advanced and developing nations.

- **Directed Evolution**—Some states could mandate genome engineering for the purposes of reducing national healthcare and disability expenditures or to conduct eugenics through the pursuit of certain national goals (i.e., population intelligence, racial, or ethnic composition).
APPENDIX A:

Key Questions for Legislation and Regulation of Genome Editing in Somatic Cells in Humans

Many issues pertaining to CRISPR-Cas9 are covered by existing regulatory controls for clinical trials, medical products, and healthcare treatment and insurance regulations. Legislators and regulators will need to consider some important additional issues, including:

1. Scientific and Technical Effectiveness and Safety

   Clinical Standards and Laboratory Safety
   - Do additional standards need to be put in place for laboratories administering genome editing therapies?

   Biosecurity and Bioweapons
   - Do additional controls or safeguards need to be put in place for biosecurity?

2. Commercial Activity and Accessibility

   Pricing and Payer Reimbursement
   - Will there be reimbursement requirements for government and private insurers to cover treatment? For which conditions? At what cost threshold?
   - Will payers reimburse for treatments obtained abroad that are unapproved in the country of origin?

3. Legal and Regulatory Oversight and Control

   Patents, Licensing and Ownership
   - What underlying technologies will be patented?
   - What applications will be able to be patented?
   - What will be done to prevent monopolistic control of genome editing technology?

   Licensing and Controls
   - Will licenses be required for clinics to administer genome editing therapies?
• Will sale of CRISPR DIY kits be legal? For which applications?
• Will self-experimentation be legal?
• What will be the penalty for unauthorized biohacking? What will be the management mechanism?

Product Liability and Damages

• What are the liability and punitive damages for accidents caused to humans or ecological systems? From unauthorized experimentation? How will these cases be managed when damages to an ecosystem occur across international borders?

4. Acceptable Use and Privacy

Acceptable Use

• What is the threshold of evidence required to administer a genome editing therapy for disease prevention or treatment?
• Should elective gene editing be permissible for 1) disease risk reduction; 2) trait modification?
• For germline editing – Should there be a requirement that there are no other solutions (such as using PGD and IVF instead of genome editing) to avoid passing on certain genetic conditions to offspring?

Privacy and Anti-Discrimination

• Under what conditions should a government or private entity have the right to access information on an individual’s genetic profile?
• Do health insurance companies have a right to access information on an individual’s genetic profile?
• Will there be a “tracking mechanism” for which genome edits individuals have received? What entity would maintain it? For what purposes would the information be used?
• Will health insurance companies be allowed to require or incentivize individuals to obtain genome editing therapies as preventative measures for future health risks? If so, for which conditions?
• Under which circumstances will it be legal to use an individual’s genetic profile to inform decisions regarding: 1. Educational opportunities 2. Healthcare 3. Access to financial services 4. Criminal justice 5. Employment opportunities?