Genome Editing for Human Benefit: Ethics, Engagement and Governance

Singapore, 12 – 13 November 2019

Global Forum on Bioethics in Research

Guidance and policy paper: Is prohibition a solution? A reflection on embryo gene editing in the Civil and Commercial Code of Argentina

Ana Palmero, National Ministry of Health, Argentina

Brief description of the context

The new Civil and Commercial Code of Argentina incorporates an explicit prohibition to any practice that produces a genetic modification of the embryo heritable to the descendant, closing the door on research and innovative practice in embryos gene editing for treatment or prevention of disease. The development of CRISPR/Cas9 technology and its potential preventive or therapeutic uses presents challenges on whether a prohibition is the proper legal solution to avoid risks or a precautionary approach that promotes responsible science and respect for persons should prevail.

Commentary

In 2015 the new Civil and Commercial Code of Argentina entered into force. The new Code recognizes human dignity as a fundamental principle which acts as a source for civil rights. In this context, a set of rules related to bioethics issues were incorporated based on the inviolability of the human person. The Article 57 titled *Prohibit practices,* states: *"Any practice designed to produce a genetic alteration of the embryo transmitted to their descendant is prohibited".* Although the original project exceptionally allowed these practices when they were intended to prevent genetic diseases or the predisposition to them, embryos gene editing was finally forbidden based on international global consensus not to allow this practice.[1] The arguments for prohibition were related to:

a. Safety concerns: scientists argued that the current gene editing techniques needed more development for safe uses in clinical reproduction. It was argued as well, that the risk involved in embryos editing for heritable diseases may never be justified due to existing interventions such as preimplantation genetic diagnosis (PGD).[2]
b. Religious objections toward the use of embryos for research. Even though Argentina allows by law in-vitro fertilization (IVF)[3] there is no regulation regarding the use of cryopreserved embryos originally created by IVF in research due to catholics and christians groups pressure to give embryos the same legal status as born human beings. Also, the moral discussion on PGD continues.[4]
c. The inviolability of human genome: it was argued that human genome modification challenges human dignity and human rights.[4]
d. Negative impact in future generations: as germline editing causes genetic changes in descendants, the uncertain risks would affect next generations.[4]
e. Abuse of non-therapeutic interventions for eugenics or enhancements purposes that may exacerbate social inequities. For instance, by improving physical or mental capabilities.[4]

The development of CRISPR/Cas9 technology and its potential to become a more accurate, inexpensive and easy-to-use gene editing than older technologies, opens possibilities for preventive or therapeutic uses of germline editing for serious heritable genetic diseases or predispositions to them.[5] Due to the recent modification of the Code, the use of this technology in the context of assisted reproduction in Argentina is forbidden, closing the door to any possibility of research or innovative practice[6] in embryos gene editing for treatment or prevention of disease.

Given the rapid advance of science in this field, prohibition by law may not be the best solution to avoid future risks. As all progress in science, the potential use of CRISPR in germline editing brings possible benefits, risks, ethical and societal implications as the above mention. These issues must be weighed considering existing ethical standards and respect for human rights and human dignity. Therefore, a precautionary approach would be helpful to discuss CRISPR technology implications and applications.[5] A precautionary approach does not mean prohibition. On the contrary, the precautionary principle was established to give guidance to adopt cautionary measures for emerging technologies in which scientific evidence about human health to present and future generations and environmental damages are still uncertain.[7] The cautionary measures may restrict research. However, according to Kaebnick et al., their purpose is not to stop it but to establish the conditions under which it can be successful.[8]

In this regard, the Report of the Committee on Human Gene Editing of the National Academies of Sciences, Engineering, and Medicine (NASEM)[9] establishes a precautionary approach. The Committee recommends "that germline editing research trials might be permitted, but only after much more research to meet appropriate risk/benefit standards for authorizing clinical trials. Even then, germline editing should only be permitted for compelling reasons and under strict oversight". The committee defines a *set of criteria* that define the conditions under which germline editing would be permissible and successful. These principles permit clinical research trials only for purposes of treating or preventing serious disease or disabilities, in absence of reasonable alternatives, "restricted to editing genes that have been demonstrated to cause or strongly predispose to that disease or condition, and only if there is a stringent oversight system able to limit uses to specified criteria". The committee also recommends that "ongoing reassessment and public participation should precede any heritable germline editing and, for this purpose, public engagement should be incorporated into regulatory oversight". Related to innovative practice, NASEM recognize the possibility of "regulatory havens" that is "jurisdictions with more lenient or non-existent regulations to access the restricted procedures". They highlight both the need for "comprehensive regulation" to curb this possibility and they explicitly recognize that "if it is not possible to satisfy the criteria in the recommendation, the committee's view is that heritable genome editing would not be permissible".[10]

Conclusion and recommendations

The development of CRISPR/CAS9 technique and its potential therapeutic uses has encouraged international debate on whether gene editing for reproductive purposes should be permissible and the conditions under which research must be addressed. This represents a shift from global consensus of prohibition towards permission with strict criteria and prohibition if the criteria cannot be met. In this context, the recent incorporation of embryos gene editing as a prohibit practice in the Civil and Commercial Code may not be the best solution to avoid unintended or uncertain risks. A precautionary approach seems preferable to discuss safety, ethical and societal concerns regarding germline gene editing technologies. The recommendations on the Report of the Committee of NASEM define a precautionary approach that states strict conditions and oversight under which research on heritable germline gene editing should continue. These recommendations could serve as a helpful reference for regulation if the Argentinian Code is ever to be amended to allow the intervention.

To conclude, a key issue to highlight is the incorporation of public engagement in the process of assessing and applying societal values to the risks and benefits of gene editing technologies. Regarding heritable gene editing the committee recommends a broad participation and input by general public.[9] For this purpose, in Argentina public engagement needs to be enhanced to promote public trust in research and scientists. Even though a strict regulation and oversight on clinical trials is in place, general public still have prejudices towards research involving human beings. Also, public engagement would be needed to evaluate if the criteria supported by NASEM could be met in Argentina. Public and policy-makers education is required to encourage public debate and participation. Regulatory authorities could use several approaches to address this gap. For instance, it is not usual that local news media cover research topics, so dissemination of reliable information through mass media and social media would be helpful. Also, research to better understand public views through surveys and interviews with principal stakeholders are

required. The discussion on whether heritable germline gene editing should be permissible or not would be a good opportunity to put in place public engagement strategies that promote valuable public participation and regulatory debate.

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