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Genome editing: scientific opportunities, public interests and policy options in the EU

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What is genome editing?

- The deliberate alteration of a selected DNA sequence in a cell, in particular using site-specific nucleases
- Vitally important tool in basic research to help understand biological functions and disease mechanisms
- Opportunities enhanced by CRISPR-Cas9, which is relatively easy to design, produce and use
- Expected wide range of innovative applications in human and animal health, agriculture and food systems, microbial biotechnology and the bioeconomy

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Genome editing evokes enthusiasm but also controversy

- Safety, ethical and other issues have been raised. For example:
  - "Not natural"
  - "Too many gaps in knowledge"
  - "Impacts are uncertain and may be inequitable"
  - "Regulation cannot keep pace with speed of technology innovation"
- What needs to be done to realise the potential of genome editing and take account of societal concerns?

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EASAC Working Group

- Working Group started in early 2016, consensus output peer reviewed in early 2017, endorsed by member academies and published 23 March
- Our purpose:
  - To take a broad perspective on research advances and potential applicability to innovation in different sectors
  - To advise on options to ensure appropriate frameworks for managing innovation
- It is our view that policy considerations should primarily concentrate on sector-specific product regulation and not on the general principles of genome editing as a technology

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How should the applications of genome editing be assessed and regulated?

- We emphasise the importance of ensuring that regulation is evidence-based, takes into account likely benefits as well as hypothetical risks, is proportionate and sufficiently flexible to cope with future advances in science
- Our report covers applications in
  - Plant breeding
  - Animal breeding in agriculture
  - Xenotransplantation
  - Gene drive to modify populations in the wild
  - Micro-organisms
  - Human cell genome editing – building also on the work of FEAM

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Plant breeding in agriculture

- Genome editing brings additional precision in research to increase crop quality, e.g. for improved water and nitrogen use efficiency, better resistance to pests and diseases, reduced allergens
- Novel crops are now appearing, e.g. CRISPR-Cas9-edited mushrooms
- Should such products be considered as GMOs?
  - We ask that regulators confirm that if crops do not contain DNA from an unrelated organism, they do not fall within the scope of GMO legislation
  - The aim should be to regulate the trait/product not the technology

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Animal research and development

- Already subject to stringent regulation of laboratory animal research and to the principles of the 3Rs (replacement, reduction, refinement)
- Significant opportunities for genome editing in livestock and aquaculture – to enhance animal health and welfare as well as increase agricultural production, e.g. protections from porcine reproductive and respiratory syndrome and African swine fever
- We recommend that animal breeding in agriculture should be governed by the same principles as proposed for crop breeding:
  - To regulate the trait not the technology
  - Be open and explicit about what is being done

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Xenotransplantation

- Genome editing is transforming prospects by tackling barriers to transfer of tissues and organs from animals to treat loss or dysfunction in patients – removing endogenous retroviruses and xenoreactive epitopes that trigger rejection
- Also research advances in human-animal (pig) chimeras, e.g. to produce pancreas for transplantation
- Scientific community has important role to assist regulators to prepare for the potential opportunities now coming within range

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Gene drive to modify populations in the wild

- Process of biased inheritance that enables genes to be transmitted from parent to offspring at increased rate
- Opportunities for insect-vector disease control to address public health challenges e.g. malaria, Zika, dengue fever
- "Self-sustaining" efficacy and safety questions including ecological consequences and safeguards to manage risk of escape during research
- EASAC supports recommendations by US NAS for a phased approach to research to enable responsible development and allow sufficient time to consider what amendments are needed to regulatory frameworks

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Micro-organisms and the bioeconomy

- Genome editing in microbes has not raised new issues for regulatory frameworks
- Wide range of potential applications – pharmaceuticals and other high-value chemicals, biofuels, biosensors, bioremediation, and the food chain
- Concerns raised elsewhere about potential for genome editing research to expand outside regulated laboratory settings. We recommended that Global Young Academy should assess issues raised by activities of Do-It-Yourself biology community
- Concerns also raised elsewhere about potential biosecurity implications of misuse (microbes and other species).

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Human cell genome editing: EASAC recommendations

- *Basic research:* intensive research is needed and should proceed subject to appropriate rules and standardised practices
- *Clinical use in somatic gene editing:* should proceed within existing regulatory frameworks (EMA and national agencies)
- *Clinical use in germline interventions:* not acceptable to proceed unless and until scientific, ethical, safety and efficacy issues have been resolved and there is broad societal consensus
- EASAC work draws on previous work by FEAM and International Summit on Gene Editing.

The regulatory situation In Ireland

- 2005 The Donnelly Commission states that a regulatory framework is required to deal with the societal concerns around Assisted Human Reproduction (AHR).
- 2008 The Irish Council of Bioethics echoes the need for regulation of AHR.
- 2009 The Supreme Court expresses criticism of the lack of regulation of AHR
- 2015 The government announces that it is to legislate for AHR and Associated Research including surrogacy, embryo donation, the screening of embryos, gamete donation and stem cell research.
- 2017 A legal regulatory frame work I still not in place.

The Irish Medical Council's code of ethics guidelines ban any experiments on embryos, but it appears that private companies could legally pursue gene-editing of embryos here.

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In conclusion

- In addition to sector-specific elements for assessment and regulation, there are cross-cutting issues for public engagement and for enhancing equity of access to benefits
- EASAC report is on http://www.easac.eu/home/reports-and-statements/detail-view/article/genome-editi.html
- eLife Feature article is on http://www.easac.eu/home/journal-publications/detail-view/article/elife-1.html