Minutes of the 14th Plenary meeting of the European Group on Ethics in Science and New Technologies

Brussels, 10-11 April 2019

1. **Approval of the agenda and minutes**

2. **Nature of the meeting:** non-public

3. **List of points discussed:**

- Updates from the Secretariat & the EGE members
- Statement on Ethics
- Gene editing in plants & animals
- Gene editing in humans
- Hearings on gene editing in humans
- Hearings on GE and GM regulation

DAY 1: 10 April 2019

Updates from the Secretariat & the EGE members

- The Group was informed on the latest developments regarding the AI governance in Europe, namely on the recently published EC Communication on AI, and the HLG AI Ethical guidelines on AI issued on the Digital day earlier in the week. The Group appreciated that the revised version of the guidelines takes into account the comments provided by the EGE and duly refers to the EGE, as does the Communication.
- Regarding the future of work, a high-level conference was held on 9 April, following a publication of the report of the High-Level Expert Group on the Impact of the Digital Transformation on EU Labour Markets.
- On 24-26 September 2019, DG RTD will organise Research & Innovation days, in which the participation of an EGE representative is envisaged in the session on gene editing.
- The Group was informed on the upcoming framework program Horizon Europe, namely on its legal basis, the reached agreement in the trilogue and the 'mission' approach, and the role of ethics.
- The EGE members reported on their recent and upcoming participation in a range of conferences (including presentations on topics linked to the EGE's work).

Work in Working Groups

The Group then split in the following two working groups for a breakout session:

- Human germline and somatic gene editing;
- Gene editing in plants, (non-human) animals and non-human primates.

The Working Groups were tasked to identify the key issues under the heading of their group; the key ethical questions at stake; structuring considerations for the Opinion; and issues that link to other areas of the opinion (cross-cutting themes).

Statement on Ethics

The group discussed the conceptual boundaries of the upcoming Statement, as well as the framework in which it will be published and the EGE's role within it. The Statement should, among other objectives, engage with the overstretching of the notion of ethics. The Statement could include the following elements:

- Evolution of ethics in Europe
- Geopolitics of ethics
- Increased need, relevance of ethics (crisis of values)
- Ethics inflation, questions of legitimacy and expertise
- Institutional embedding
- Public engagement and acceptance

The development and launch of the Statement could foresee an event with the participation of prominent experts.

Reporting from the Working Groups

- *Working Group on gene editing in plants and animals*

The Working Group divided its discussion in two parts: first analysing the ethical aspects in plants, then referring to animals.
Regarding gene editing in plants, the main issue is the precision of these technologies in permitting the production of plants more easily, quickly and cheaply than before. It could enable a larger number of different actors (companies, smaller firms) to be involved in the genetic modification of plants.
A set of risks relates to the industrialisation of agriculture. Gene edited plants could reduce agricultural and environmental diversity. Gene editing could also be used to increase diversity, particularly in agriculture, yet there are risks of increasing monocultures.
Gene editing will have an impact on how agriculture is done in Europe, e.g. concerning the size of farms.
Gene editing allows a greater variety, it has a great potential in making products safer, e.g. by removing allergens.
A big question is on the need for regulation – applied to different techniques – GMO, gene editing, biological agriculture.
Another important aspect is patent systems, and the high costs associated with patenting of new techniques. A practical implication is reduced availability of seeds for breeders.
Regarding animals, some other ethical concerns arise, namely, the integrity of animals and a possibility of 'humanising' animals.
It was noted that both for animals and plans, promotion of biological diversity should be prioritisied, and this may imply a role for public institutions (rather than depending on the private sector).

- *Working Group on gene editing in humans*

Most ethical issues in human gene editing are linked with germline, rather than somatic gene editing. In the Opinion, it is important to make a distinction between various techniques / sources for obtaining human embryos, namely: 1) using gametes (allowed in most of the MS); 2) using supernumerous embryos (permitted in some MS); 3) creating embryos for gene editing research (forbidden by Oviedo and in most of the MS). These distinctions involve different regulatory regimes.

It was also pointed out that health is a Member State competency, and needs to be respected when providing recommendations.

DAY 2 – 11 April 2019

Hearing with the participation of Professor Pierre JOUANNET

The speaker outlined three kinds of issues related to germline gene editing: technical, medical and ethical.

Technical issues:

1) Primordial germ cells, development from germ cell to zygote to blastocyst, gene editing intervention can take place at various points in this process.
2) Spermatogonia intervention:

The speaker gave an overview of key studies, highlighting the number of embryos (animal) transferred and the number of offspring with successfully genes edited. Despite more successful rates than other techniques, he noted that an important number of transfers were not successful and a significant number of offspring not edited. If we were to apply this research to humans, we could not accept these numbers; we would need 100% of children with successfully edited genes.

In China, University professor He Jiankui announced the birth of twin girls whose DNA had been edited to prevent HIV infection. He said the twins' DNA was modified using CRISPR-Cas9, a technique that allows scientists to remove and replace a strand with pinpoint precision, but the success of the procedure has been called into question.

A solution could be to edit at zygote stage and then test for successful gene editing at the blastocyst stage as it is easier to make an analysis at this stage - less invasive - compared to earlier stages.

However, he underlined that none of the techniques currently available can be used with the required levels of safety and efficacy to modify the genome of germline cells or embryos leading to childbirth. He contended that the absence of clinical applications should not, however, stop basic and preclinical research in this area, including work on human germline cells and embryos. This research should therefore be authorized and supported provided that it is scientifically and medically relevant.

Medical issues:
He explored the medical conditions that may justify the genome editing of human germinal cells and embryos: i.e. to prevent the transmission of a serious monogenic and hereditary disease to the child.
But only when PGD is impossible (e.g. one parent homozygous for a dominant autosomal disease (Huntington's chorea) or both parents homozygous carriers of a recessive autosomal disease (cystic fibrosis). These are very rare cases but they exist. Or when PGD fails (i.e. no unaffected embryos were detected and successfully transferred).

Or to restore fertility (when the origin of the gametogenesis defect is a monogenetic alteration). In countries where sperm donation is not allowed and systematic adoption not practised gene editing offers important prospects.

Ethical issues:
Creating embryos for research is currently not permitted in most EU MS but he contends that research requires creating embryos because researchers cannot obtain embryos carrying a specific gene defect. It is very difficult to do this research with embryos that are created during IVF nor those from PGD processes.

His institute's ethics committee (https://www.inserm.fr/) has proposed renaming embryos created specifically for research 'as embryonic models for scientific purposes'. (https://www.inserm.fr/sites/default/files/media/entity_documents/Inserm_Note_ComiteEthique_GroupeEmbryon_Janvier2019.pdf)

Discussion:

The discussion that followed focused on the following points:

- The distinction between clinical, pre-clinical and basic research. The boundary between pre-clinical and clinical as being linked to the parental project (transfer of the embryo) and enshrined in French law.
- Language and values attached to contested concepts/practices. E.g. re-naming of embryos for research. Embryos considered as part of a parental project as being accorded different status (value of embryo determined by its use?)
- What determines 'safe enough'? What level of risk/uncertainty are we prepared to accept? (IVF example).

Hearings with the participation of Chantal BRUETSCHY (Head of Unit, DG SANTE, E.3), Sirkku HEINIMAA (Deputy Head of Unit), and Ilaria CIABATTI

The speaker presented the current state of play regarding regulation of genetic modification in the EU.

She outlined the three main pieces of EU legislation covering genetically modified organisms:

1) Deliberate release of GMOs (Directive 2001/18/EC)
2) GM food and feed (Regulation (EC) No 1829/2003)
3) Contained use of GMM (Directive 2009/41/EC)

She then presented the background to – and outcome of – the 2018 CJEU ruling on mutagenesis. The key questions addressed by the Court were:

- Are organisms obtained by mutagenesis GMOs within the meaning of Directive 2001/18/EC?
- Are organisms obtained by targeted mutagenesis covered by the mutagenesis exemption?
- Can MSs adopt national legislation on exempted organisms?

The Court ruled that organisms obtained by mutagenesis are GMOs within the meaning of Directive 2001/18/EC. The mutagenesis exemption is only applicable to methods used conventionally in a number of applications and with a long safety record. Organisms obtained by new mutagenesis techniques are subject to the obligations of the GMO Directive. Member States can regulate exempted organisms insofar they comply with EU law and in particular with the rules on the free movement of goods.

The competent authorities in the Member States are implementing the GMO Directive as interpreted by the Court. The Commission and the Member States are discussing relevant issues in particular compliance of products and field trials (ongoing and future).

DG SANTE also informed the group of the recent mandates to EFSA:

- for a scientific opinion on gene drive modified organisms. This includes identifying potential novel hazards of gene drive modified organisms, assessing whether existing guidelines for risk assessment are adequate and sufficient for gene drive modified organisms and identifying possible gaps. Outcome due end-2020.
- for a scientific opinion on synthetic biology (SynBio). This includes assessing whether and which newer sectors/advances should be considered among SynBio developments (agri-food use); identifying potential novel hazards compared to established techniques of genetic modification; and assessing whether existing guidelines for risk assessment are adequate and sufficient for SynBio developments & identify possible gaps. Outcome due end-2020.
- for a scientific opinion on risk assessment of plants modified through SDN-1, SDN-2 and ODM gene editing methods (namely whether methodology and conclusions of previous EFSA opinion on plants modified through SDN-3 are applicable to plants modified through SDN-1, SDN-2 and ODM), due 2020.

Existing opinions (available on the EFSA website) include:

- Scientific opinion on cisgenesis and intragenesis: https://www.efsa.europa.eu/en/efsajournal/pub/2561
- Scientific opinion on SDN3 https://www.efsa.europa.eu/en/efsajournal/pub/2943

Discussion:

The Commission confirmed that there is no intention by the current Commission at the end of its mandate to modify the legislation or existing approach and noted that current legislation is ensuring high level of safety. The group further discussed the following points:

- Regulatory burdens under the existing regime (costs of approval processes, difficulties for small companies to access the technology).
- The need for all the ethical issues at stake to be better clarified and explained including in the agricultural sector.
- The role of public opinion and perception of risk, including the importance of engaging with stakeholders and the public, and the need to address public concerns on new technologies in agriculture.
- Questions of access to technology and justice, including those related to patents.

AOB

- Christiane Woopen provided a de-brief from her presentation at the Representation of the State of Hessen to the European Union on the Opinion on Future of Work, Future of Society. She also reported on the panel on the European AI Strategy at the AI-Summit in Germany the preceding day, where she presented the EGE Statement on AI, Robotics and ´autonomous´ systems.
- Nils-Eric Sahlin and Andreas Kurtz provided a de-brief from their presentation at a DG SANTE & DG RTD jointly organised meeting on gene editing.
- The Secretariat informed that the Round Table and the International Dialogue on Bioethics and Ethics in Science and Technologies are foreseen for October, and members were invited to engage in identifying speakers.

4. Conclusions/recommendations/opinions

- It was agreed that the existing working groups do not define the structure of the upcoming Opinion. Concrete writing should start following the May meeting and each member should then have a short specific text to contribute.

5. Next steps

- Julian Kinderlerer to share his talk on the ethics of patenting of plants.
- Members to begin literature reviews on the topics of their respective working groups.

6. Next meeting

22-23 May 2019, Brussels

7. List of participants

Day 1: Emmanuel Agius, Anne Cambon-Thomsen, Eugenijus Gefenas, Julian Kinderlerer, Andreas Kurtz, Herman Nys, Marcel Jeroen Van den Hoven, Christiane Woopen; Pierre Jouannet; Florence Dose, Jim Dratwa, Louiza Kalokairinou, Johannes Klumpers, Maija Locane, Joanna Parkin.

Day 2: Emmanuel Agius, Anne Cambon-Thomsen, Eugenijus Gefenas, Julian Kinderlerer, Andreas Kurtz, Herman Nys, Nils-Eric Sahlin, Marcel Jeroen Van den Hoven, Christiane Woopen; Florence Dose, Jim Dratwa, Louiza Kalokairinou, Johannes Klumpers, Maija Locane, Joanna Parkin; For the hearings: Chantal Bruetschy, Ilaria Ciabatti, Sirkku Heinimaa, Gerjon Ikink, Sigrid Weiland.