Minutes of the European Group on Ethics in Science and New Technologies

Brussels, 16-17 January 2019

1. **Approval of the agenda:** yes

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

3. **List of points discussed:**

DAY 1: 16 January 2019

Introduction & Updates from the members

Christiane Woopen and Jim Dratwa welcomed the members to the meeting and provided updates on recent activities, notably:

- The handover of the Opinion on the 'Future of Work, Future of Society' on 19 December to Commissioners Moedas and Thyssen. The good discussion and strong support shown by both Commissioners on receiving the Opinion was underscored.
- The launch of a call for expression of interest by the World Health Organisation for membership of the forthcoming expert advisory committee on human gene editing. The importance of collaboration between this committee and the EGE was noted and the secretariat informed of on-going contacts and the preparation of a formal letter to this end.

Members informed of recent and forthcoming activities to communicate the work of the EGE across Europe, including presentations of the Opinion on the Future of Work, and on topics including Artificial Intelligence, democracy, the digital citizen, and gene editing. The secretariat requested that Members inform by email of their activities to promote the EGE.

Members also reported on developments in the fields of EGE interest at national level, including:

- The setting up by the Swedish government of a Committee to examine legal aspects of gene editing.
- In the Netherlands, the appointment of advisors on Ethics and AI under the responsibility of the Ministry of Interior.
- In France, INSERM has issued an Opinion on the Chinese experiment of alleged gene editing of twin babies; the adoption of the French Bioethics law adoption is delayed and now due end of 2019; four centres of excellence on AI have been set up in Paris, Lyon, Grenoble and Toulouse.
- In Germany, the Data Ethics Committee (co-chaired by Christiane Woopen) has sent its Guidelines on AI to the German government. The strategy *Ethics in and for design*

was presented to the public in December and a public conference is scheduled for February.

- In the UK, various institutions such as the Ada Lovelace Institute are building their profile on AI governance; the Nuffield working group on gene editing of livestock convened for the first time.
- In Canada, the call for the creation of an observatory on societal aspects of AI launched in December 2018.

Discussion on the next steps for the governance of AI Ethics

The group discussed recent developments in the Commission's strategy towards the governance of AI. It was highlighted that high expectations are now focused on the European Commission anticipating state-of-the-art, internationally recognised, ethical guidelines. Members held an exchange on the draft ethics guidelines released by the AI High Level Group on 18 December 2018. Jim Dratwa answered questions on the context, indicating that the public consultation on those guidelines has been prolonged until 1 February 2019. It was decided, against the background of that consultation and in view of the desire by the Group to provide constructive feedback, to issue a written response focusing on both the content of the guidelines and the process by which they were arrived at.

Hearings I: *Kevin Esvelt, Assistant Professor, Massachusetts Institute of Technology*

Kevin Esvelt explained how the discovery of CRISPR allows scientists to build gene drive systems capable of editing almost any gene in sexually reproducing species and thus altering the traits of wild populations and associated ecosystems. He distinguished between different types of gene drives such as 'self-exhausting' whose spread is limited by certain conditions, and 'local' gene drives whose spread is limited to regional populations. 'Self-propagating' gene drive systems are highly invasive as they are likely to spread to every population of the target species in the world.

He highlighted how gene drives could benefit human health by altering insect populations that currently spread diseases such as malaria, schistosomiasis, dengue, and Lyme so that they can no longer transmit the disease to humans. They could improve the sustainability of agriculture by reducing the need for and toxicity of pesticides and herbicides. They could also aid ecological restoration by removing invasive species and bolstering the defenses of threatened organisms.

Taking into account the potential benefits, he put forward the case for a moral imperative to make use of this technology (e.g. its application to malaria-carrying mosquitos as a means to save the lives of large numbers of people in Africa). He drew attention to Europe's reputation for taking a cautious approach to gene editing and related techniques and its reliance on the

precautionary principle, while arguing that inaction can also prove harmful if it fails to anticipate future challenges and mobilise the means to find a solution.

In parallel, he also underscored the serious risks inherent to the use of this technology, should scientists fail to properly anticipate the consequences of their work or should inadequate precautions be taken around this research (e.g. the erroneous release of a genetically modified species that dramatically reshapes the natural world). He worries that there is nothing in the scientific community's current system of regulation that would prevent that from happening.

During the subsequent discussion, the following points were raised:

- Questions of traceability and reversibility: whether it will be possible to distinguish in the future those organisms that have been modified and whether it will be possible to 'reverse' or restore an organism back to its original genetic state (currently this is not possible, only can build a new model to override an unwanted change).
- The use of patent law as a means to govern the use of this technology (and current problematic applications of patenting legislation e.g. 'if human-created, can patent').
- The complexity of moral dilemmas in the context of this technology, e.g. how to determine the 'good', what creates wellbeing, how do we weigh animal suffering with respect to humans (e.g. many support the use of CRISPR-generated gene drive to eradicate malaria-carrying mosquito but should it be used against Screwworm in South America?)
- Who decides what is the 'good'? Esvelt wants to see scientists working more with local communities where their experiments take place. He highlighted that the lack of transparency around scientific research is an obstacle to realising such a public debate (pressures on scientists to be the first to publish on a new discovery, scientists often keep their work secret until the last minute.)

Hearings II: ***Lluis Montoliu, Research Scientist, CSIC, Centro Nacional de Biotecnologia***

Lluis Montoliu, Research Scientist from National Centre of Biotechnology of Spain provided an overview of the latest techniques and developments of CRISPR-CAS technology, including the use of disruptions, deletions, inversions, duplications, point mutations and knock-ins.

He provided his assessment of the current limitations of CRISPR, including issues of on-target uncertainty (many alleles are generated through nonhomologous end-joining; most/all founder edited-organisms are mosaic; etc.) and off-targets issues (similar target sequences can be altered; reaching a significant number of target cells (viral & non-viral delivery systems)).

Referring to the recent (alleged) use of gene editing on embryos of twins to prevent them from contracting HIV, he expressed his concerns that if true, these babies would be 'mosaic', with unpredictable consequences for them and their descendants.

Following the presentation, the discussion focused on a number of points, including:

- Article 13 of the Oviedo Convention and its interpretations (prohibition of gene editing in humans/alteration of the genes of descendants), the fact that not all countries are signatories and whether the current framing is fit for purpose.
- The extreme caution needed around any research on gene editing of humans, including the need for strong controls on such research and for the benefits to have been proven to outweigh the risks.
- The existence of alternative methods (e.g. pre-implantation genetic diagnosis) to address inherited problems without having to resort to gene editing.
- The risks of *in vivo* versus *ex vivo* including the need to apply special precautions to *in vivo* research and limit its application to certain organs, such as the eye.
- The diverse views expressed by the scientific community, including with regard to how to deal with 'rogue research', such as the Chinese twins case (e.g. to ignore or discuss the results?)

Hearings III: ***Diana Herold, DG SANTE; Susanna Louhimies, DG ENV; Dr Mark Prescott and Dr. Romina Aron-Badin, Scientific Committee on Health, Environmental and Emerging Risks (SCHEER)***

Diana Herold provided an overview of the two independent Scientific Committees, the Scientific Committee on Consumer Safety (SCCS) and the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) which provide scientific advice as a basis of policy making for EU policy on public health, consumer safety and the environment.

Susanna Louhimies then provided the legislative background to the recommendation of the SCHEER that "With regard to transgenic techniques (e.g., CRISPR) in Non Human Primates, the SCHEER recommends that the European Commission form a working group to assess the scientific and ethical implications of such research to determine if it should be allowed in the EU and, if so, within what constraints." She introduced Directive 2010/63/EU on the protection of experimental animals, the special consideration accorded to non human primates within Recital 17 of the Directive and the imperative enshrined in the legislation to replace, reduce and refine experiments on animals.

Mark Prescott and Romina Aron-Badin presented the key issues raised by the SCHEER Opinion on the need for non-human primates in biomedical research, production and testing of products and devices, in particular the aspects relating to gene editing of non-human primates. They contended that science in this domain is outpacing any proper consideration of

the ethical and welfare issues and NHPs warrant special consideration given their greater moral status – e.g. capacity for practical reasoning, sense of their own identity, intense social relationships. They highlighted a set of ethical issues including: animal welfare and suffering caused (versus potential benefit); lack of evidence that genetically altered NHPs are significantly more informative about human disease and translate better than GA rodents; the fact that most of the work has been conducted in China and lacks robust regulation; proposals to use CRISPR to insert human genes related to brain development and language into monkeys (issues of inter-species mixing, boundaries of the human).

The discussion that followed highlighted the following points:

- The special considerations accorded to non-human primates (special capacity for suffering or capacity for 'human-like' suffering).
- The extent to which Directive 2010/63/EU is fit-for-purpose; inconsistencies in its implementation and level of scrutiny across the EU.
- The harm-benefit assessment at the heart of Directive 2010/63/EU and the question of whether ethics committees are sufficiently informed and robust to handle these complex issues. How to transmit information about latest techniques as fast as it is being produced? Is there a need to re-think the institutional design of research ethics (greater division of labour and specialised expertise)?
- Issues of animal wastage (producing large numbers of animals for research, only a small number of which can be used).
- Ethical issues invoked by the North/South dimension (prevalence of NHPs in the South, transportation and welfare questions, etc.) including geopolitical, solidarity, and global justice issues (outsourcing/dumping/displacement).

DAY 2 – 17 January 2019

Discussion on AGM

A brief exchange took place on the new system governing financial reimbursements introduced Commission-wide. The Secretariat acknowledged ongoing difficulties with the AGM system. They requested members to keep them informed of any major obstacles encountered so that problems could be flagged to the relevant colleagues.

Discussion on working methods for the Opinion on Gene Editing

A discussion was held on lessons learned and the potential improvements that could be made to the group's working methods. Key questions include how early to begin drafting, how far to advance on clarifying structure and key concepts, the optimum configuration of rapporteurs/working groups, role of the Secretariat, how drafting responsibility should be shared. The following points were underscored:

- The need to develop the structure to a greater extent before forming working groups and beginning work on drafting.
- The preference to move away from the classic 'science', 'law', 'ethics' structure towards an approach that prioritises identifying ethical issues and governance aspects.
- The value of working groups over single rapporteurs as a means to exploit the multi-disciplinarity of the EGE; the possibility of working groups meeting between plenary meetings and in 'breakout' sessions during plenary meetings.
- The need for technical infrastructure to support development of the Opinion, i.e. a common repository for documents and an effective software tool to facilitate parallel working on a document
- The need to clearly identify the role of coordinator/editor of the whole document
- A more developed dissemination/communication strategy, identification of target groups in collaboration with members, development of short summaries and members informed of publication date well in advance.

Hearings IV: *Janusz Bujnicki, member of the Group of Chief Scientific Advisors*

Janusz Bujnicki, member of the Group of Chief Scientific Advisors shortly presented the work of the Group on the topic of gene editing, namely, the Explanatory Note 'New Techniques in Agricultural Biotechnology' (2017), and the Statement 'A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive' (2018). While the Group of Chief Scientific Advisors examined the scientific aspects of these topics, they recognised that they raised serious ethical questions that required further reflection.

The Group's 2018 Statement provides an assessment of the existing regulative framework following the CJEU Ruling of 25 July 2018[1] which ruled that organisms obtained by new techniques of directed mutagenesis fall within the remit of the Directive on GMOs. On the basis of their analysis of the scientific evidence, the group concludes that the GMO Directive is no longer fit for purpose and should be revised to reflect new scientific knowledge. In particular, on the question of safety and unintended effects, the group found that because unintended effects are likely to occur less frequently in gene edited products, these products are potentially safer than the products of random mutagenesis.

The discussion with the EGE focused on the following issues:

- The safety criteria applied to determine the relative safety of techniques; the disparity of safety criteria applied to different techniques (including those techniques excluded

[1] Court of Justice of the European Union. Press Release No 111/18: Retrieved from: https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf

from the scope of the directive such as random mutagenesis) and the emphasis of safety criteria on the safety record of the technology rather than the final product.

- The concept of 'risk' which embodies aspects of uncertainty, and potential harms and hazards. What values underpin the criteria and assumptions we are using to categorise a harm?
- Other factors that bear on risk assessments, including public fear/outrage, as well as the influence of trade policy (e.g. in determining positions of certain member states on GMO imports).
- The feasibility of detecting gene edited organisms. It was highlighted that it is currently not possible to detect all gene editing events, although detectability is expected to improve with time.
- The notion of naturalness, what constitutes 'natural', and what are the boundaries of the natural? Here scientific and societal considerations are at stake.

Discussion on the Opinion on Gene editing

The EGE then resumed the discussion on the Opinion on Gene Editing, outlining potential structures and approaches into the topic. Certain key topics were identified (e.g. Somatic gene editing, germline gene editing, gene drives, GMOs, gene altered animals and non-human primates, and environmental aspects). It was also suggested to use key questions/concepts as a means of framing the Opinion (e.g. use of the naturalness concept as a route into environmental theme and as a means of setting the conditions for assessing impact of technology).

An exchange took place on the notion of risk, risk perception and public opinion. It was decided to frame the February plenary meeting on the two topics of human gene editing and risk. Members proposed potential experts to invite to the next set of hearings.

AOB

- Jim Dratwa informed that the Future of Work Opinion is currently foreseen to be translated into French and German (and possibly Italian and Spanish as well).
- Jim Dratwa informed that the NEC Forum will take place on 4-5 April 2019 in Iași, Romania, following the decision not to organise a NEC Forum in Finland.
- It was agreed that plenary meetings should finish at 16:00 on the second day.

4. Conclusions/recommendations/opinions

- To organise work on the Opinion on the basis of small working groups which will be determined once the overall structure has been developed and clarified.
- To frame the February plenary meeting on the two topics of human gene editing and risk.
- To devise a considered dissemination strategy with the collaboration of the EGE members and the secretariat.

5. Next steps

- The Secretariat will invite/secure two experts, one on human gene editing and one on risk, for hearings in February 2019.
- The Secretariat will prepare a text outlining the proposed video competition for schools foreseen for the public roundtable.

6. Next meeting

19-20 February 2019, Brussels

7. List of participants

Day 1: Emmanuel Agius, Anne Cambon-Thomsen, Ana Sofia Carvalho, Eugenijus Gefenas, Julian Kinderlerer, Andreas Kurtz, Jonathan Montgomery, Siobhán O'Sullivan, Barbara Prainsack, Carlos Maria Romeo Casabona, Nils-Eric Sahlin, Marcel Jeroen Van den Hoven, Christiane Woopen (Chair), Aylin Avcioglu, Wolfgang Burtscher, Jim Dratwa, Louiza Kalokairinou, Johannes Klumpers, Maija Locane, Joanna Parkin.

Day 2: Emmanuel Agius, Anne Cambon-Thomsen, Ana Sofia Carvalho, Eugenijus Gefenas, Julian Kinderlerer, Andreas Kurtz, Jonathan Montgomery, Siobhán O'Sullivan, Laura Palazzani, Barbara Prainsack, Carlos Maria Romeo Casabona, Nils-Eric Sahlin, Marcel Jeroen Van den Hoven, Christiane Woopen (Chair), Aylin Avcioglu, Jim Dratwa, Louiza Kalokairinou, Maija Locane, Joanna Parkin.