– Preliminary Version –

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Genome editing: Europe needs new genetic engineering legislation

Preliminary remarks

The European Court of Justice's long-awaited ruling of 25 July 2018 has provided clarity: the new technologies blanketed under the term "genome editing" are subject to EU Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms[1]. This means that, in future, all applications of these new technologies will have to go through a very complex, time-consuming and expensive approval procedure, as prescribed by the EU Directive.

However, genetic engineering has evolved dramatically since 2001. The technologies known as genome editing allow the genome to be modified much more quickly and cheaply and in a much more targeted way than was the case with the "old" genetic technology. For example, since it was first described, the CRISPR/Cas9 system has spread throughout the world within only a few years and is now being used in many different fields[2,3,4]. In the meantime, these new technologies have become part of the standard repertoire in research and university education and are also used by many industrial companies.

This situation now poses huge political challenges in Germany and the EU:

- On the one hand, we believe it would be irresponsible to permanently uncouple the EU from a technological development that offers great potential in terms of sustainability and human welfare and that will therefore increasingly shape the bioeconomy in the rest of the world. Even if politicians wanted to, it will not be possible in the longer term to prevent the import of produce produced using genome editing – not least because it is often impossible to detect the use of the technology in the final product.

Only differentiated regulation can do justice to the wide range of potential applications of genome editing.

- On the other hand, the answer cannot be to downplay the risks associated with the rapid spread of these new technologies and opt for complete deregulation. Although there are many applications of genome editing that do not involve a greater ecological risk than traditional breeding methods or randomly occurring mutations, some applications can give rise to increased risks and therefore require more stringent protective regulations.

A differentiated approach to the technology and its applications is therefore called for[5]. Current EU genetic engineering legislation is no longer able to respond adequately to these challenges. Many members of the public instinctively feel that the new technology should be banned on ethical grounds or because of the risks associated with it. However, in reality this would not prevent the spread of genome editing in Europe but would mean that Europe would permanently lag behind the rest of the world, while at the same time having no say in the imperative global regulation of this „biological revolution".

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In order to change this situation, the Bioeconomy Council is calling for a prompt revision of EU legislation on genetic engineering to bring it in line with new technological developments and the latest scientific findings.

This would also honour the original objective of the German Genetic Engineering Act, which, at the beginning of the 1990s, explicitly stated the rationale of promoting and enabling in the "purpose of the Act" and was written with the intention of adapting the regulations to keep pace with technological progress.

The amended genetic engineering legislation should stipulate which applications of genome editing are essentially allowed (without special provisions relating to genetic engineering), which are prohibited and which will only be allowed with a special permit. We must also be aware that some of the risks arising from the use of genome editing cannot sensibly be regulated by genetic engineering legislation but require amendments in other legal fields (for example patent law or agri-environmental law). Therefore these policy fields must also be considered in the equation from the outset, in order to arrive at the best possible overall regulatory solution. In order to promote a substantive debate about the future regulatory procedure for genome editing, the Bioeconomy Council offers the following guiding principles for discussion.

Risk-oriented licensing and approval procedures

Plants

- Breeding is based on crossing and selection. The basis for this is the present genetic diversity. In plant breeding, the mutation rate (mutagenesis) has been artificially increased since the 1960s in order to expand genetic diversity, for example by using chemicals or irradiation[6]. This mutagenesis can now be done in a much more specific way with the aid of genome editing[7]. In terms of future regulation, the legislator could stipulate that no particular provisions would be required under genetic engineering legislation where only a few base pairs (e.g. less than 20) were modified but, in this case, the plants could be released and the tried and tested variety registration regulations applied.

- However, this ruling would mean that the development of a herbicide-tolerant crop would not be subject to genetic engineering legislation where herbicide tolerance was achieved by means of a specific point mutation or modification of only a few base pairs[8]. Arable farming based on herbicide-tolerant crops is contentious from an ecological perspective. However, it is not primarily the modified crops that constitute a potential ecological risk but rather the herbicide that is used or the overall production system associated with it. To this extent, any regulation should not be done under genetic engineering legislation but in other specific areas of legislation (for example, pesticide legislation).

- Even in the amended legal framework, plants in which larger gene segments (e.g. more than 20 base pairs) are modified or gene sequences are transferred across species boundaries would still have to be evaluated and licensed under genetic engineering legislation. With the current procedure, it takes more than 15 years for a genetically modified variety to go through all the tests and be allowed onto the market[9]. We would have to weigh up whether it would be possible to accelerate or simplify the approval process for produce with more complex mutations that could also occur in nature (for example nematode-resistance in sugar beet), accompanied by particularly close scientific monitoring during the first few years of practical use.

Livestock

- There are also relevant applications for genome editing in livestock breeding, for example breeding hornless cattle[10] or specialised laboratory animals for medical research[11]. Unlike in plant breeding, ecological risks (outcrossing into wild species; retrieveability) are hardly relevant in this area. Conversely, however, ethical aspects become more important. Over the last few years, the social debate about modern livestock production has shown that the public are critical of various aspects of livestock farming, e.g. farming methods, regional concentration and also some developments in animal breeding. The Bioeconomy Council believes that a comprehensive livestock strategy is required, in order to arrive at a socially acceptable and sustainable model of livestock production. The Council recommends that guidelines be drawn up for future animal breeding (and hence also for the use of genome editing) and formalised as part of a comprehensive livestock strategy.

- At present, livestock strategies are predominantly being developed on a national level. That is presumably due to the fact that there are varying attitudes to the treatment of livestock in different parts of the EU. Since the Council believes that genetic engineering legislation should be established at EU level, this law must substantially establish a minimum consensus on regulating the use of genetic engineering in animal breeding. To supplement this, the Member States could then be free to implement stricter regulations as part of their national livestock strategies, if they so wished.

Insects

- The genome of insects can also be modified using genome editing, for example to improve the opportunities for biological plant protection, to increase pollination or to influence pest populations. However, these potential benefits are offset by particular ecological risks, since there is no way of retrieving genetically modified insects. Particular care is required if organisms are modified so as to pass on their characteristics as dominant characteristics to the next generation ("gene drive"[12]). The Council recommends exercising a particularly high level of protection in this area and also paying particular attention to the implementation of international transparency rules.

Fish and other aquatic organisms

- Even though fish and aquatic invertebrates can be regarded as livestock in a wider sense, they should nevertheless be covered by special regulations, since the ecological risks are disproportionately greater, due to their high potential for dispersion. The Council recommends that, as with plants, a particularly high level of protection be exercised and particular attention be paid to the implementation of international transparency rules.

Microorganisms

- The Bioeconomy Council suggests following analogous procedure as for plant breeding: if genome editing is used to make point mutations or smaller genome modifications, there is no need to operate a laborious licensing process for this. The reason being that smaller mutations are ever-present in nature and are continuously being generated in biotechnology, even without genetic engineering. Long-standing empirical knowledge in this area tells us that the risks are manifestly low.

- In contrast, greater modifications to the genome or the introduction of genes from a different species (foreign genes) should still be subject to the provisions of the genetic engineering legislation. Here again, as with plants, it would be necessary to weigh up whether the option of an accelerated and simplified approval process might be possible for produce in which more complex mutations can also occur naturally.

Product labelling

Some applications of genome editing are detectable in the end product but some are not. For example, it is possible to detect the transfer of gene segments that are foreign to the species. In contrast, it is not possible to clearly identify techniques used merely to bring about point mutations or specifically install native genes (from the same species), since this could have happened some other way or could have occurred naturally[13].

- For this reason, the existing legal obligation to label genetically modified produce can only be maintained if, in future, the use of genome editing for point mutations or a few base pairs ceases to be classified as genetic engineering (see above: proposal for plants and microorganisms). However, if future legislation stipulates that point mutations should also be subject to genetic engineering legislation, the obligation to label should be restricted to larger, foreign genome modifications that are clearly identifiable, as otherwise legal compliance could not be guaranteed in the trade of goods.

- If the labelling obligation were also to relate to organisms with greater genetic modifications (not involving foreign genes from another species), this could give rise to considerable problems in the movement of goods, for trading companies and the inspection authorities in the longer term, since it would no longer be guaranteed that such modifications could be detected in the produce. The more genome editing develops into a standard technology in international plant breeding, the more difficult it will become for European actors to legally check whether there are actually any genetically modified produce contained in imported goods – indeed, what gene sequences should they check for? The State faces the same problem if it wants to check legal compliance.

- This argues in favour of moving away from the general statutory labelling obligation for all types of produce (with or without foreign genes) and opting instead for the voluntary declaration “Not genetically engineered”. Companies who opt to label their produce in this way would then provide certificates throughout the goods chain to prove that no genetically modified organisms have been used in the manufacturing process (similar to the current regulation for the organic food sector).

Registration and monitoring

- Genome editing is not only used by established firms within the biotech sector and in academic research laboratories but also by many private individuals and start-ups. A “Do-it-yourself Biology”movement has emerged from the USA and its adherents conduct CRISPR experiments inter alia[14]. This does not necessarily take place in registered laboratories. The utensils and biochemicals that are required are available anywhere in the world for a few hundred dollars. Releasing the modified organisms is prohibited in Europe but is allowed in the USA for example, so long as it causes no damage to health or the environment. The US assumes that actors develop an adequate degree of self-control and that the fear of being sued for damages enforces sufficiently disciplined user behaviour.

- The Bioeconomy Council takes the view that EU genetic engineering legislation should require anyone who wants to use genome editing to record their use of the technology in an official register (see above for licensing requirements).

- Furthermore, the international community of nations should create a platform for exchanging experiences with different forms of regulation and monitoring of genome editing (see the proposals for a Global Genome Editing Observatory[15, 16]).

Research

Basic Research

- The Bioeconomy Council recommends the funding of basic research in this important future-oriented field of science. State funding should also include training programmes and precompetitive development projects.

- Publicly funded applied research should concentrate on areas that are of relatively little interest to the private commercial sector but of great interest to society as a whole.

Biodiversity research

- There are various hypotheses as to what effect genome editing will have upon biodiversity in agricultural landscapes[17, 18]. On the one hand, it creates better technological opportunities for increasing biodiversity. On the other, use of the technology in free-market competition can also result in the temporary proliferation of superior types of varieties in a particular region, thereby restricting diversity there.

- It is impossible to predict which effect will prevail. It would therefore not be expedient to initiate generally oriented preparatory research on this issue at this stage. Whether or not ex-ante assessments of the effects of genetically modified organisms on biodiversity are necessary can only be decided on a case-by-case basis, since this is not a question of the technology that is used but rather a question of the expected features of the organisms. Should it prove impossible to answer these questions on the basis of theories, models or empirical values, it might be expedient to conduct cultivation trials restricted to model regions, accompanied by close scientific monitoring.

- Independently of the question of whether genetically modified crops are one day used in German agriculture or not, the Bioeconomy Council believes that it is necessary to set up a biodiversity monitoring programme. This is necessary to record the long-term changes in the biodiversity of our agricultural landscapes, so that they can be analysed in terms of possible causes and of controlling policy measures. The Council recommends that genome editing be taken into account from the outset when designing the monitoring programme. The monitoring programme should be capable of identifying changes in the regional range of varieties and their impacts upon biodiversity in agricultural landscapes.

Research on rights of ownership and use plus economic consequences

- Genome editing techniques are the subject of patent applications and granted international patents, so that users have to pay to use them commercially. It is debatable to what extent it is possible to patent gene sequences modified by genome editing that produce a certain demonstrable useful feature in the organism. Official patenting practice has evolved in this direction over the last few years, while policy statements often support the basic principle of „you cannot patent nature" or "no patent on life".

- The clarification of such property issues is of fundamental importance for the development of market structures, for the emergence of innovations and the distribution of returns on innovation, for the State's ability to influence economic processes and lastly for social acceptance of new technologies. Controversial opinions and contradictory hypotheses abound in this area of debate; however, as yet there has been no systematic economic analysis of what regulatory options the policymakers might have or what the impact of the various options might be.

- Since genome editing is spreading rapidly and is becoming increasingly important for the global bioeconomy, the Bioeconomy Council believes that there is an urgent need to carry out a systematic economic analysis of the many unanswered questions relating to property rights, "open-source" data and technologies, economic structures and global governance. In order to do this, it is necessary to form interdisciplinary scientific consortia at the interface between biotechnology, natural sciences, social sciences, cultural sciences, economic sciences and legal sciences, with a longer-term focus, to develop proposals for globally sustainable rules and regulations.

Social dialogue research

- The Bioeconomy Council recommends initiating new forms of social dialogue about genome editing. In contrast to many of the methods that have been employed so far, these should not be restricted to an exchange between organised interest groups. In particular, we recommend dialogue-oriented, deliberative processes[19], aimed at public participation and the public at large. These will help to identify the various patterns of perception and interpretation relating to social challenges and potential technological and social solutions and to understand divergent motivations in controversial debates, without at the same time calling for a consensus agreement. In order to be able to use these insights for policy and innovation strategies, various forms of procedure should be developed and trialled, supplemented by accompanying scientific research to determine the efficacy of the different methods[20, 21].

Endnotes

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[4] Doudna, J. A., Charpentier, E. 2014. The new frontier of genome engineering with CRISPR-Cas9. Science, 346(6213), 1258096.

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Scientific reports, 7(1), 482. Verfügbar unter https://www.nature.com/articles/s41598-017-00578-x?WT.feed_name=subjects_plant-biotechnology&error=cookies_not_supported [22.08.2018] *A mildew-resistant tomato was bred by mutagenesis. Such approaches could reduce the use of environmentally harmful pesticides.*

- Washington Post. 2018. The Future of Food – Scientists have found a fast an cheap way to edit your food´s DNA. 11. August 2018. Verfügbar unter https://www.washingtonpost.com/news/business/wp/2018/08/11/feature/the-future-of-food-scientists-have-found-a-fast-and-cheap-way-to-edit-your-edibles dna/?noredirect=on&utm_term=.feba97c5dc03 [22.08.2018] *This article describes the successful breeding of a soy bean with fewer unhealthy transfats.*
- Sánchez-León, S., GilHumanes, J., Ozuna, C. V., Giménez, M. J., Sousa, C., Voytas, D. F., Barro, F. 2018. Low-gluten, nontransgenic wheat engineered with CRISPR/Cas9. Plant Biotechnology Journal, 16(4), 902-910. Verfügbar unter https://www.ncbi.nlm.nih.gov/pubmed/28921815 [22.08.2018] *Since many different genes are responsible for gluten production in wheat, it has not been possible to breed gluten-free wheat using existing methods. However, genome editing makes such targeted breeding possible.*

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[19] Deliberative processes rely on readily available information and good communications between all stakeholders and include debates, organised talks and public discussions.

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About this BÖRMEMO

BÖRMEMOS summarize the Council's appraisal of key aspects of the bioeconomy in a condensed form. They do not claim to provide a comprehensive study of these facts. Rather, they present a focused and generally comprehensible view of each area and its relationship to the bioeconomy. BÖRMEMOS undergo a peer review process. While this process is taking place, they are identified as preliminary. After assessment, they are incorporated in the items of the Council as a whole. They are part of a series of analyses published by the Bioeconomy Council.

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