

Institute for Biosafety in Plant Biotechnology

Future Perspectives on Biotechnology Legislation from an Academic Perspective

Joachim Schiemann Thorben Sprink, Frank Hartung

New Breeding Technologies in Plant Sciences

Society for Experimental Biology – SEB Göteborg, July 7-8, 2017

www.julius-kuehn.de

Plant breeding can be considered as a continuum with increasing efficiency and precision. Humans have always been selecting for mutations.



Plant Breeding for a Sustainable and Productive Agriculture addressing Food and Nutritional Security, Climate Change and Human Health

Genetic diversity in the plant kingdom = Genetic resources				
Breeding technologies portfolio				
Conventional	Breeding			
Random undirected genome alterations through crossing or induced mutagenesis Selection based on phenotype or biochemical markers Defined low level regulation, no risk assessment Number of loci affected: half genome (crossing); 1000-5000 (induced mutagenesis)				
Genetical crops with superior o e.g. higher yield, pest resis nutrient use efficien	ly altered chracteristics (traits), tance, drought tolerance, cy, nutritional value			
Genome Editing	Genetic Engineering			
Specific directed genome alterations with or without DNA integration or targeted mutagenesis Selection by molecular markers Regulatory requirements not decided	Specific undirected genome alterations by cisgenic (same gene pool) or transgenic (different gene pool – access to full biodiversity potential) DNA integration			

Number of loci affected: usually 1-4

Selection by molecular markers or phenotype... Defined **high** level regulation including risk assessment Number of loci affected: usually 1-4

To be, or not to be a GMO, that is the question



Source: <u>http://www.thecultureclub.net/wp-</u> content/uploads/2010/10/tennant_hamlet.jpg

"There is no evidence that GM technologies are any riskier than conventional breeding technologies and this has been confirmed by thousands of research projects."

"Finally, we shouldn't forget that there are also other promising novel plant breeding technologies, post-GM, and we shouldn't make the mistake of regulating them to death as we have done with GM."



Anne Glover, former Chief Scientific Adviser to the President of the European Commission

Position of anti-GM NGOs

Open letter to the Commission on new genetic engineering methods

27 January 2015

We call on the Commission to reject any attempt to exclude these new techniques from EU regulation.

In particular, we urge the Commission to ensure that:

- Organisms produced by these new techniques will be regulated as genetically modified organisms under existing EU regulations (Directive 2001/18). This means that they will require a full risk assessment before any approval or authorisation is given.
- Any food, feed and seeds as well as other breeding material produced using such new techniques will be labelled and fully traceable throughout the food and feed supply chain.
- Nothing in the TTIP and CETA negotiations will limit Europe's sovereignty and ability to regulate new genetic engineering methods and products as GMOs.
- Current GM health and environmental safety testing requirements are strengthened in light of the enhanced ability of these new techniques - individually or in combination to alter the genetic code of plants, animals and other organisms.

Jeffrey Wolt: "The process vs. product conundrum"

BVL (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit) Opinion on the legal classification of New Plant Breeding Techniques, in particular ODM and CRISPR-Cas9

http://www.bvl.bund.de/SharedDocs/Downloads/06 Gentechnik/Opinion on the legal classification of New_Plant_Breeding_Techniques.pdf;jsessionid=9A8AE3A96D9EDD1DA8D39B19544B34A9.2_cid32 2?__blob=publicationFile&v=3

VIB (Vlaams Instituut voor Biotechnologie)

When is an organism subject to the provisions of the EU GMO legislation? An indepth analysis

http://www.vib.be/en/about-vib/organization/Documents/rc bvl 2016 00533 GMO definition legal analysis final.pdf

G. Glas & T. Carmeliet: THE EUROPEAN COURT TO RULE ON MILESTONE IN EUROPEAN GMO LEGISLATION. Bio-Science Law Review (BSLR) Vol 16 Issue 2

Kahrmann, J., Bömeke, O., & Leggewie, G. **Aged GMO Legislation Meets New Genome Editing Techniques** Zeitschrift für Europäisches Umwelt- und Planungsrecht

Jahrgang 15, Ausgabe 2 (2017), pp. 176 – 182

http://eurup.lexxion.eu/article/EURUP/2017/2/9

IV. Conclusion

"..., the correct interpretation of the Directive leads to the conclusion that organisms modified by genome editing techniques are not within the scope of the Directive if they could have come into existence naturally by mating, natural recombination and traditional breeding methods including mutagenesis. This is the case for the induction of single point mutations unless foreign DNA is integrated into the target organism's genome. Whether or not the ECJ follows this line of interpretation, more detailed clarification of the European GMO legislation in the long term seems to be inevitable: Due to public demand, politicians certainly will not accept some products of genome editing techniques to be without any specific supervision.

On the other hand, they will not want to burden all products of genome editing techniques with the costly and time consuming authorization procedures of conventional genetic engineering, effectively making this technology inapplicable in Europe."

Main arguments from the documents above:

The EU GMO definition is not purely process-based but refers to the technique used and the characteristics of the end product in a cumulative way.

The EU GMO definition refers to organisms in which the genetic material is altered beyond modifications occurring naturally by mating and/or natural recombination.

Organisms carrying particular groups of edits (especially by SDN-1, SDN-2) do not fall within the legal EU GMO definition since they do not fulfil the end product criteria for GMOs.

Major questions:

- Are these edits beyond modifications occurring naturally by mating and/or natural recombination?
- Can these edits be distinguished on the DNA level from alterations occurring spontaneously in nature or resulting from conventional cross-breeding?

What can we expect from the European Commission?

Timeline of the debate on the legal interpretation of genome editing techniques and resulting crops in the European Union

EU Commissioner Tonio Borg has confirmed that the EU GMO definition refers to both the technique and the end product in response to a European parliamentary question.

Answer of Commissioner Tonio Borg of 17 October 2014 to a parliamentary question (ref. no. E-006525-14) posed by Jan Huitema, Peter van Dalen and Bas Belder

2011-2014 Letter from CIBUS to six Competent Authorities in Europe (Ireland, Finland, Germany, Spain, Sweden, UK)		
July 2014 Letter from CIBUS to BVL	February 2014 Letter from the Finnish Board of Gene Technology to the European Commission	
9 th March Objection by several NGOs 15 th June Letter from the European Commission; clarifying legal opinion announced August	14 th February Legal opinion of the BVL classifying products deriving from RTDS as non-GMO 3 th June BVL rejects the objection	
Letter from the European Commission to EFSA asking for technical assistance September Legal opinion on behalf of NGOs October Legal opinion on behalf of BFN	September Letter from EFSA to European Commission Letter from BVL to European Commission December Legal opinion by BVL	
July 2017		

Legal Interpretation by European Commission still pending

Juncker's SOTEU speech State of the Union Address 2016: Towards a better Europe - a Europe that protects, empowers and defends

Strasbourg, 14 September 2016

A EUROPE THAT TAKES RESPONSIBILITY

... I call on all EU institutions and on all of our Member States to take responsibility. We have to stop with the same old story that success is national, and failure European. Or our common project will not survive. ...

We also have to take responsibility in recognising when some decisions are not for us to take. It is not right that when EU countries cannot decide among themselves whether or not to ban the use of **glyphosate in herbicides**, the Commission is forced by Parliament and Council to take a decision.

So we will change those rules – because that is not democracy.

The Commission has to take responsibility by being political, and not technocratic. A political Commission is one that listens to the European Parliament, listens to all Member States, and listens to the people. ... The Conseil d'Etat has requested the ECJ to rule on four questions regarding new breeding techniques (submitted October 3rd). The starting point was a lawsuit by French NGOs against the French government questioning the transposition of Directive 2001/18/EC into French national law.

Once the ECJ has registered the case and decided on which questions will be accepted for a ruling, it will take about 15-24 month until a decision/ruling is reached. The outcome of the ruling will certainly have far reaching consequences for the regulation of plants that have been obtained by applying new breeding techniques.

http://www.conseil-etat.fr/Actualites/Communiques/Organismes-obtenus-par-mutagenese

But: are the right questions asked?

Plant Breeding for a Sustainable and Productive Agriculture addressing Food and Nutritional Security, Climate Change and Human Health

Genetic diversity in the plant kingdom = Genetic resources

Breeding technologies portfolio resulting in genetically altered crops with superior characteristics (traits)

Genome Editing			
Group 1: Deletion of any size or a single base pair substitution <u>which could</u> <u>otherwise</u> be obtained through the use of <u>chemical- or</u> <u>radiation-based</u> <u>mutagenesis</u>	Group 2: Introducing only naturally occurring nucleic acid sequences from a sexually compatible relative <u>that could otherwise</u> cross with the recipient organism and produce viable progeny through <u>traditional breeding</u> (including, but not limited to, marker-assisted breeding, as well as tissue culture and protoplast, cell, or embryo	Group 3: " Null segregant" - the progeny of an organism where the only genetic modification was the insertion of donor nucleic acid into the recipient's genome, but the donor nucleic acid is not passed to the recipient organism's progeny and the donor nucleic acid has not altered the DNA sequence of the progeny.	

Genome Editing

Group 4: Introducing any kind of nucleic acid sequence from sexually noncompatible organisms to target the site of introduction ("safe harbor") which could otherwise be obtained less specifically through the use of genetic engineering.

The current legislation is already process- and product-based Case-by-case low level regulation recommended (as conventional breeding) High potential to increase diversity of cultured crops / varieties *→* diverse crops for diverse diets and resilience in changing environments

Conventional Breeding

Consider case-by-case if low level regulation can be applied or not

Scoping paper: New techniques in agricultural biotechnology

SAM HLG is asked in the first instance and by March 2017 to provide an explanatory note on new techniques in agricultural biotechnology including their potential agricultural application in <u>synthetic biology</u> and for <u>gene drive</u>, taking into consideration the most recent developments in the agricultural sector.

In a second phase, SAM may subsequently be asked to supplement this work by describing expected trends in the next decade in agricultural biotechnology for plant and animal breeding, and for microorganisms, and to anticipate forthcoming developments in the agricultural sector.

New techniques in agricultural biotechnology

High Level Group of Scientific Advisors Explanatory Note 02 Brussels, 28 April 2017

> The new techniques are very versatile and can make a number of types of changes to plants, animals and microorganisms. These can include the insertion of genes from the same or other species but also the direct modification of an organism's own genetic sequence in a precise and targeted way, without the addition of DNA to the genome of end-products. Some new techniques do not make changes to genetic sequences at all. > This precision and control over changes made is greater than with the use of conventional breeding or established techniques of genetic modification. As a consequence, these new techniques result in fewer unintended effects. > Assessments of the safety (environmental, health, etc.) of the organisms produced by the new techniques can only be made on a case-by-case basis taking into account, amongst others: the specific mutation; unintended effects; the species into which the mutation is introduced; the environment in which the end product is used; the agricultural practice applied, and its planned use and exposure.

17.12.2015: additional chapter

The European plant science community is following the current debate on the legislative classification of New Plant Breeding Techniques along the lines of European GMO legislation with great interest and concern. Over the years, the EU regulatory framework for GMOs has become increasingly dysfunctional in the sense that:

decisions are often not taken within the legal time frames, and often not on the basis of scientific evidence and risk assessment;

Information requirements and risk assessments have not been differentiated based on gained knowledge, but instead increased and galvanized without scientific justification;

Uncertainty is created about the applicability of the regulatory framework on organisms developed through new crop genetic improvement techniques such as genome editing.





EPSO has highlighted in an earlier statement that one of the causes of this situation is that in the implementation of the regulatory framework there is a disproportionate focus on the genetic improvement technique used. This has led to the following misinterpretations:

GMOs are merely defined by the use of certain techniques. This is incorrect. Whether or not the resulting organism is a GMO depends entirely on the fact if a novel combination of genetic material has been produced beyond the natural barriers of mating and recombination. This is for example not the case for point mutations obtained by genome editing.

In the present debate on the GMO legislation an increasing number of competent authorities, risk assessment bodies, and stakeholders interpret the EU GMO legislation as both process and product based. EPSO acknowledges this interpretation and considers that this could help to clarify the legal status of the NPBTs.

EASAC Position on NPBTs

The increasing precision now possible in plant breeding represents a big improvement compared with conventional breeding approaches relying on random, uncontrolled chemical- or radiation-induced mutagenesis and on intra- or interspecific crossings with random distribution of genes or alleles. We reaffirm our recommendations from the previous EASAC work on new plant breeding techniques:

- We ask that EU regulators confirm that the products of genome editing, when they do not contain DNA from an unrelated organism, do not fall within the scope of GMO legislation.
- There should be full transparency in disclosing the process used, but the aim in the EU should be to regulate the specific agricultural trait/product rather than the technology by which it is produced. It follows that new technologies would be excluded from regulation if the genetic changes they produce are similar to, or indistinguishable from, the product of conventional breeding and if no novel, product-based risk can be identified.

EASAC Report "Genome editing: scientific opportunities, public interests and policy options in the European Union" published in March 2017



Stimulus for discussion: History of Safe Use / Familiarity

High Level Group of Scientific Advisors Explanatory Note 02

"Assessments of the safety ... of the organisms produced by the new techniques can only be made on a case-by-case basis ..."

PROPORTIONALITY

Does this hold true for any product of plant breeding?

Take care not to misinterpret!

Due to our history of safe use we do not perform an extensive risk assessment for products of conventional breeding including induced mutagenesis. Is the concept of <u>History of Safe Use</u> applicable to genome edited traits in the "historical" range of plant breeding?

Keep in mind: Plants and products thereof resulting from conventional breeding are regulated: e.g. Variety law, Food law

Stimulus for discussion: Genome Editing and Intellectual Property (1)

EPO clarifies practice in the area of plant and animal patents

Press release | 29.6.2017

http://www.epo.org/news-issues/press/releases/archive/2017/20170629.html

The Hague / Munich, 29 June 2017 – On a proposal of the European Patent Office its Administrative Council took a decision to amend the relevant Regulations in order to exclude from patentability plants and animals exclusively obtained by an essentially biological breeding process.

The EU Directive on biotechnological inventions (98/44/EC) was implemented in the EPO's legal framework in 1999. The Directive excludes essentially biological processes from patentability but does not provide for a clear exclusion for plants or animals obtained from such processes.

In its Notice from November 2016 the European Commission clarified that it was the European legislator's intention to exclude not only processes but also products obtained by such processes.

Stimulus for discussion: Genome Editing and Intellectual Property (2)

Plant breeder's rights and patent rights http://www.epsoweb.org/file/2036



In the statement on plant breeder's rights and patent rights EPSO underlines that developing high-performing plant varieties requires substantial investment of skills and technology and that those who develop such varieties are entitled to earn a reward.

On the other hand it is essential to maintain the breeder's exemption, by which breeders can make crosses to the commercial varieties of their competitors, and go on to breed new varieties with novel gene combinations.

The academic exemption for breeding and genetics with commercial varieties should also be maintained.

These exemptions must also apply to varieties generated by New Plant Breeding Technologies [esp. genome editing] including GM. Thank you very much for your attention



Photo: Anke Schiemann

Those who want the world to continue as it is, do not want the world to continue.