# Boosting technology transfer and responsible research and innovation (RRI) in plant sciences

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## What is it about?

PlantHUB is a European Industrial Doctoral Programme (EID) funded by the H2020 PROGRAMME Marie Curie Actions – People, Initial Training Networks (H2020-MSCA-ITN-2016). The programme is managed by the Zurich-Basel Plant Science Center. PlantHUB offers training to 10 PhD students in skills and competencies necessary to apply responsible research and innovation (RRI) in the area of plant breeding and production. The programme addresses the demand for RRI leadership in plant science related research and diffusion of innovation.

## Academic – Industry Collaboration

### Academic interface

- ETH Zurich (Switzerland)
- University of Zurich (Switzerland)
- University of Basel (Switzerland)

### Industry interface

- CARLSBERG GROUP, Carlsberg Research Laboratory (Denmark)
- Deutsche Saatveredelung AG (Germany)
- Photon Systems Instruments (Czech Republic)
- BASECLEAR BV (The Netherlands)
- HELIOSPECTRA (Sweden)
- AGROISOLAB GMBH (Germany)

# Public Round Table

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# D22: Public Round Table: What's next after the ECJ judgment on gene editing?, April 11th 2019.

The participants of the TNAM 2019 (Tri-National Arabidopsis Meeting) took a tri-national view (Switzerland, Germany and Austria) of the main issues and potential consequences of the ruling of the European Court of Justice (ECJ) on organisms obtained by mutagenesis.

11 April 2019, 16:00 – 17:30
ETH Zurich, Audimax, Rämistrasse 101, Zürich

**Invited guests**

- Prof. Holger Puchta (Institute of Botany, Karlsruhe Institute of Technology, Germany)[1]
- Franziska Schwab (Swiss Small Farmers Association, Switzerland)[2]
- Prof. Jean-Marc Neuhaus (Institut de Biologie, Université de Neuchâtel, Member of the Swiss Ethics Commission for Non-Human Biotechnology)[3]
- Prof. Matthias Mahlmann (Faculty of Law, University of Zurich, Member of the Swiss Ethics Commission for Non-Human Biotechnology)[4]
- Dr. Ortrun Mittelsten Scheid (Gregor Mendel Institute of Molecular Plant Biology, Austria)[5]

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| **Prof. Holger Puchta** | **Prof. Matthias Mahlmann** | **Franziska Schwab** | **Prof. Jean-Marc Neuhaus** | **Dr. Ortrun Mittelsten Scheid** |

The discussion was chaired by the journalist Mr Andreas Hirstein, *Neue Zürcher Zeitung* (*NZZ*), head of science desk at *NZZ am Sonntag* (NZZ on Sunday). Discussions were held in German. About 80 people attended.

[1] https://www.botanik.kit.edu/molbio/14_146.php
[2] https://www.kleinbauern.ch/verein/Small Farmers Association, Switzerland
[3] https://www.unine.ch/jean-marc.neuhaus
[4] https://www.ius.uzh.ch/en/staff/professorships/alphabetical/mahlmann.html
[5] https://www.oeaw.ac.at/gmi/research/research-groups/ortrun-mittelsten-scheid/

The panel discussion was organized by PlantHUB – a European industrial doctorate program funded by the European Union's Horizon 2020 Research and Innovation Program under the Marie Skłodowska-Curie Grant Agreement No. 722338.

https://www.plantsciences.uzh.ch/en/research/fellowships/PlantHUB.html

https://www.tnam2019.ethz.ch/program/

https://www.tnam2019.ethz.ch/

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The authors have included some background information in italics to enable readers to follow the references in the discussion. The actual discussion and comments from the floor are in upright print.

## Background

*Prof. W. Gruissem, professor of plant biotechnology at ETH Zurich's Institute of Molecular Plant Biology and host of TNAM 2019 gave an introduction to the topic referring to the decision of 25 July 2018 by the European Court of Justice (EJC) that organisms obtained by modern forms of mutagenesis such as CRISPR[6] are not exempt from the EU's GMO legislation. Consequently, genome-edited organisms must comply with the strict conditions of the 2001/2018 EU GMO Directive. European scientists are deeply concerned about the consequences of this ruling. The European Plant Science Organization (EPSO) considers that the ruling of the European Court of Justice (ECJ) on organisms obtained by mutagenesis (case C-528/16) disregards scientific evidence. The ruling subjects plants obtained by recent mutagenesis techniques such as Crispr/Cas-9 mediated genome editing to extensive pre-market risk assessment, whereas plants produced by older, less precise mutagenesis techniques are exempted. In sharp contrast, there is broad scientific consensus that unintended DNA alterations produced by genome editing are of the same type but [of] orders of magnitude less frequent than those produced by older methods such as EMS or radiation mutagenesis.*

*For the EPSO statement (dated 19.2.2019) on the ECJ ruling regarding mutagenesis and GMO see: https://epsoweb.org/library/public/*

*98 leading European science and agriculture institutes have sent a letter and position paper to President Juncker asking for an amendment to this ruling, on the grounds that having to subject genome edited organisms to the same pre-market risk-assessment and authorization processes as transgenic organisms will push genome editing into the hands of a select number of large multinational corporations.*

[6] Clustered Regularly Interspaced Short Palindromic Repeats

**How did Switzerland react to the ECJ judgment?**

*The Federal Council [i.e. Swiss Government] submitted a request to the Federal Offices for Agriculture (FOAG) and for the Environment (FOEN) to revise Swiss law on genetic engineering: to adapt it to new developments, taking account of risks, and observing the precautionary principle. This means that risks and adverse effects arising from organisms produced by new genetic engineering procedures must be identified at an early stage – already before the organisms are applied – and measures must be taken to reduce the risks involved. The federal bodies concerned will clarify how the new genetic engineering procedures and their products are to be classified in line with their inherent risks for humans, animals, and the environment. This is expected to take the form of additional requirements graded according to category; these will also take account of future developments in genetic engineering. A basic ruling on genetic engineering in Switzerland will be issued by the Federal Council by the end of the year.*

*Official memorandum:*
https://www.admin.ch/gov/de/start/dokumentation/medienmitteilungen.msg-id-73173.html

Prof. Matthias Mahlmann, lawyer and member of the Swiss Ethics Commission for Non-Human Biotechnology, explained that the EJC was asked to clarify the scope of GMO regulations and whether these applied to gene editing. The judges decided that plants modified by the new molecular biology techniques such as *Crispr/Cas-9* should be classified as genetically modified organisms and must be labelled as such (mandatory declaration). The ECJ judgment is binding on all EU member states and is a reference point for Switzerland. Switzerland is not bound to this decision but will probably follow the EU. The Swiss Federal Offices for Agriculture (FOAG) and Environment (FOEN) are currently preparing a debate paper on whether the Swiss Gene Technology Act should be revised or not. At the end of the year, the Swiss Federal Council will make a decision on how to regulate gene editing in Switzerland. Prof. Mahlmann emphasized that "**we need a societal discourse in which the political and ethical dimensions of the research in question are explored."** What sort of agricultural system do we want? How are the new technologies to be used? How much do we know? Even if conventional breeding methods are indistinguishable in their effects on the organism from the new mutagenic methods, we still have no long-term studies. We have to gain experience with the new technologies first. How sure are we that we know all we need to know?

Prof. Jean Marc Neuhaus, University of Neuchâtel, backed up Prof. Mahlmann's remarks with the thesis that conventional breeding methods do not differ in their effects on plants from the new mutagenesis methods, but long-term experience is still missing.

*In Nov 2018, the Federal Ethics Committee on Non-Human Biotechnology ECNH published its report: "Precaution in the environmental field. Ethical requirements for the regulation of new biotechnologies." This report invokes the precautionary principle, a tenet of environmental law. Accordingly, treating the new technologies in the same way as genetic engineering procedures is (currently) justifiable under the law, since the use of these new technologies in the environment also involves considerable uncertainty and lack of knowledge.*

***Recommendations**: Improving the reliability of risk assessments in a transparent and understandable manner is the only way to ensure that voters can form free and informed opinions, and hence that risk decisions are reliably made in the course of the political process.*

https://www.ekah.admin.ch/inhalte/ekah-dateien/dokumentation/veranstaltungen/Veranstaltung_7._Mai_2018/EKAH_Broschu__re_Vorsorge_Umweltbereich_e__18_Web_V2.pdf

Franziska Schwab (Swiss Small Farmers Association) pointed out that applied research is currently overrunning fundamental research. New gene editing technologies need not be forbidden but, because of the risk they involve, they must be declared and regulated. For Schwab, gene editing is another form of genetic modification. She argued that precision should not be confused with predictability. Also, the new mutagenesis methods could hit the wrong DNA targets and cause unpredictable changes, compromising crop health and environmental safety. For this reason, environmental campaigners and a number of NGOs argue that GMO regulations must be fully applied to gene-edited crops, and that it is the process, not the organism generated, that determines whether something is a GMO.

*The Schweizer Allianz Gentechfrei SAG (Swiss GMO-Free Alliance), a critical forum on questions of genetic engineering, have welcomed the ECJ decision. They argue that anything produced by genetic engineering is unequivocally a GMO. In a dossier titled Nachweisverfahren (Verification Procedures, published March 2019), they declare that if new genetic engineering procedures also fall under the law on genetic engineering, companies using them must submit relevant information in internationally accessible databases. This information will underpin rapid and reliable tracing of GMOs back to their producer. This is the only way to guarantee freedom of choice for consumers.*

*https://www.gentechfrei.ch/images/stories/pdfs/2018/Factsheet_Nachweisverfahren_NGV_neues_Layout.pdf*

**How do scientists perceive the ECJ decision?**

Dr. Mittelsten Scheid expressed her disappointment about the decision: it was, she said, based on societal pressure rather than scientific knowledge. Products produced by conventional mutagenesis may not be distinguishable from those obtained by gene editing. The ECJ ruling is therefore not scientifically justified: "old" methods are accepted simply because we are used to them; "new," more precise methods remain unfamiliar.

Consequently, the law should be changed so that e.g. crops with small DNA adaptations made through gene editing would follow the regulations for varieties produced through conventional methods such as selective breeding, not those for GM organisms.

Dr. Mittelsten Scheid also argued that the ECJ ruling is likely to squeeze out small biotech companies, as only the big multinationals can afford to go through the long and expensive regulatory process needed to get crops to market.

*In August 2018 the organizers of the International Plant Molecular Biology Congress in Montpellier, France started an online petition calling for a review of the ruling. The petition has now attracted more than 5,500 signatures.[7] It declares that there is "no scientific rationale" for the ruling and that the EU should regulate genetic crop techniques on the basis of science. For example, it says, gene editing does not carry any greater risks to human or animal health than do older, less precise breeding strategies.*

Prof. Holger Puchta (Karlsruhe Institute of Technology, Germany) added that the methods are not new, only their application is new. Nuclease based gene editing has been used for more than 20 years in plants. The public is not aware of what mutations are and that they are natural: there is a great variety of mutations in nature and the natural mutation rate in a crop field is very high: for example, two single plantlets in the same field of barley can differ by 100 mutations. Moreover: How should CRISPR-based gene editing be regulated in practice, as it may leave no footprint in an organism's DNA? So, it is difficult to spot-check crops: a naturally mutated plant or crop might not be distinguishable from a plant mutated with *Crispr/Cas-9* technology. The mutation patterns obtained with the new methods are indistinguishable from natural mutations.

Franziska Schwab (Swiss Small Farmers Association) emphasized that there are also scientists who welcomed the ECJ ruling and that here is no scientific consensus.

[7] For current number of signatures see: https://www.change.org/p/ipmb2018-immediate-review-of-the-ecj-ruling-on-plant-genome-editing-9ff3df10-9f7d-44de-b379-8a01a1d71ba2?recruiter=892690431&utm_source=share_petition&utm_medium=twitter&utm_campaign=psf_combo_share_initial.pacific_abi_gmail_send.control.pacific_email_copy_en_gb_1.v0.pacific_email_copy_en_2.v3&utm_term=psf_combo_share_initial.pacific_abi_gmail_send.control.pacific_email_copy_en_2.v2.pacific_email_copy_en_gb_1.v2

**Are the risks rated higher than the opportunities?**

Prof. Neuhaus remarked on the need for sound risk assessment. The precautionary principle means that special care must be taken at the point of uncertainty; however, one cannot 100% exclude the possibility of "something happening."

Dr. Mittelsten Scheid observed that the sense of risk is subjective. We accept far greater risks, for example, if we reject the opportunities offered by the new procedures to meet the globally rising demand for cereals. Who will take on that risk? World cereals production does not meet demand. In the long term, not to use the new technologies is also a risk.

Prof. Puchta pointed out that the use of *Crispr/Cas-9* will reduce global pesticide levels. Of course, the widespread introduction of plants developed with new mutation technology must be regulated. The question is: How much regulation is necessary?

Dr. Mittelsten Scheid added that there is already a legal regulation on the registration, certification and protection of conventionally bred plant varieties that could be applied to the "new plants": a stricter law is not necessary.

Prof. Neuhaus cited the example of the transgenic papaya in Hawaii. This was the only way papaya could be planted again in Hawaii. The government made an exception for the cultivation of transgenic plants because transgenic papaya does not need pesticides.

Prof. Mahlmann commented that normative aspects must be taken seriously. Different interpretations are needed. We, as a society, must face up to and debate the new technologies. It's not a question of prohibition. Regulations create hurdles that obligate scientists to present evidence for the safety of the method. The issue here is the nature of the regulation involved: what it should look like. Scientists must demonstrate that there is no risk involved. So far as the effectiveness of regulation is concerned, all law must live with the fact that it will be broken.

Comments from the floor

- The discussion is strongly marked by a "First World" perspective – risks exceed opportunities. But there are other people who cannot buy large quantities of cereals cheaply, and we have a responsibility toward them, too.
- We are committing a crime against humanity if we only think of ourselves. The world will be overrun by the climate catastrophe.
- There is a disturbing tendency to romanticize where our food comes from. It doesn't come from picture-book farms and farmers. Society must be brought to realize this.

**Why do people fear new technologies?**

Frau Schwab referred to studies showing that animals have been harmed by GMO products:[8] people, she declared, are disturbed by such things. Scientists repeat that there is no risk involved. But can side effects be entirely excluded from genome editing? *Crispr/Cas-9* procedures may harbour as yet unforeseeable dangers to health, for example, and should, therefore, be supervised and regulated with special care. Genome editing produces unwanted mutations – so-called off-target effects – and there is always a residual risk. Risk is not the main problem, but the public should be able to choose. "**Risks must be declared so that one can choose**."

Dr. Mittelsten Scheid supported to provide consumers with a chance to choose, but the information about the product should be factual and not based on non-proven risks.

Comments from the floor

- Rational arguments cannot dispel irrational fears.
- *Crispr/Cas-9* stands for hi-tech and big firms that are overrunning agriculture. That's also a reason why people reject technology.

**What solutions are available for agriculture?**

Frau Schwab emphasized that the solution cannot lie in one technology. No single technology can solve all agricultural problems.

Prof. Mahlmann pointed out that market regulation is already in place: the Swiss Farmers' Union, for example, needs quality products and has a quality strategy.

Prof. Neuhaus added that Switzerland is set to vote on the initiative "For a Switzerland without synthetic pesticides."[9] The initiative calls for a ban on synthetic pesticides in agricultural production, imported foodstuffs, and foodstuff production. The implementation of this initiative will require efficient measures to safeguard an adequate harvest. Swiss agriculture will have to make great efforts to meet demand. *Crispr/Cas-9* products may then have a greater chance of acceptance.

Prof. Puchta drew attention to the cost of developing a GMO plant to market launch: €15-30 million. The expensive licensing process in particular is something no small firm can afford. *Crispr/Cas-9* would give small firms a chance. The "Healthy Crops" project (www.healthycrops.org) directed by Prof. Wolf Frommer is a good example of the scope of application this technology presents for small farmers in India. Financed by the Bill & Melinda Gates Foundation, the project is dedicated to the development of blight-resistant rice variants.

[8] Genetically modified soybean in a goat diet: Influence on kid performance
R.Tudisco, S.Calabrò, M.I.Cutrignellia, G.Moniello, M.Grossi, V.Mastellone, P.Lombardi, M.E.Pero, F.Infascelli Link: https://doi.org/10.1016/j.smallrumres.2015.01.023

[9] In February 2019 the initiative "For a Switzerland without synthetic pesticides" collected enough signatures to run a referendum. The Swiss government chose to rejected the initiative, so the initiative will be put to voters in 2020 without the government's support.
https://www.blw.admin.ch/blw/de/home/politik/initiative-sosp.html

Speaking from the floor, Prof. Frommer[10] replied that the ECJ decision again plays into the hands of big companies. Over-regulation of crop seed encourages the development of monopolies

Dr. Mittelsten Scheid added that Europe actually plays a very small role in the global agricultural market. We should also look at what is happening around us. In the long run, Europe cannot go alone. With Europe on one side of the fence and most major non-EU agricultural countries on the other, "**genome-edited plants (and animals) are governed internationally by a number of different, incompatible legal systems."** This means that in a global world with closely interwoven trading channels conflicts are pre-programmed.

Comments from the floor

- Agricultural industrialization generates fear, because people do not know how it works.
- Scientists cannot conduct field experiments to assess risks. Administrative obstacles as well as public opposition (including destructive actions), prevents such experiments. The ECJ ruling increases the difficulties still further.
- Prof. Gruissem presented an example from the floor: In 2016 the wheat harvest in the Canton of Zurich was poor - harvest losses were between 20% and 40%. This was due to the wet months of May and June, which encouraged fungal growth. Scientists have proven that increased plant resistance can be implemented with *Crispr/Cas-9* through targeted point mutation of the corresponding genes: for example, it is possible to prevent mildew disease in wheat by turning off the six copies of the MLO gene simultaneously. So, researchers are currently in a position to use *Crispr/Cas-9* in a concrete instance. But they have to go through a regulation process that costs millions. Technologically, every *Crispr/Cas-9* genome can be sequenced to exclude side effects. However, this is very expensive, and in normal plant breeding is neither demanded nor undertaken. How should this issue be approached legally?

**Has science not been properly communicated?**

Prof. Mahlmann put in a plea for constructive discourse: the discussion must make room for realism. "**Scientific opinion is one opinion among many."** The Gene Technology Act allows a certain margin of interpretation and application. The point is to find a framework within which all parties can live; the political space of debate must be filled. All parties, including scientists, must face up to the need for convincing arguments.

Frau Schwab added that scientists, too, must admit that they do not know, and cannot explain everything.

[10] Prof Wolf Frommer, University of Düsseldorf, Germany. He gave the Keynote talk on 11 April 2019 at the TNAM 2019.

Comments from the floor

- We had this discussion 30 years ago with the introduction of green gene technology. We have learned from the mistakes we made then, that science needs a more powerful lobby organization.
- Science has a credibility problem: How can it regain public trust when people think scientists are lobbying for big industry?
- Scientists have not communicated on a sufficiently broad basis. We now have a better chance to get our messages across. And we are in a position today to offer products that are of higher value to consumers.