New Genetic Engineering Techniques

Positions of the organic food and farming movement

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Importance of topic for Organic

Definition of Organic Agriculture

"Organic Agriculture is a production system that sustains the health of soils, ecosystems and people. It relies on ecological processes, biodiversity and cycles adapted to local conditions, rather than the use of inputs with adverse effects. Organic Agriculture combines tradition, innovation and science to benefit the shared environment and promote fair relationships and a good quality of life for all involved."

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GMOs not allowed in organic production

- Organic Agriculture is an alternative to conventional and industrial agriculture, legally defined by Regulation (EC) No 834/2007, complemented by private standards. New Regulation (EU) 2018/848 will enter into force in 2021.
- Organic Agriculture is based on a systemic approach, considers the interaction between the plants and their environments, seeks to reduce reliance on external inputs, and is a driver for agronomic innovation.
- The use of GMOs and synthetic pesticides and fertilisers is banned from the organic production process

IFOAM EU's position on new genetic engineering techniques

- IFOAM EU's position adopted in December 2015
- Scope of IFOAM EU's position:
  - Oligonucleotide directed mutagenesis (ODM)
  - Zinc finger nuclease technology types I to III (ZFN-I, ZFN-II, ZFN-III)
  - CRISPR/Cas
  - Meganucleases
  - Cisgenesis
  - Grafting on a transgene rootstock
  - Agro-infiltration
  - RNA-dependent DNA methylation (RdDM)
  - Reverse Breeding
  - Synthetic Genomics

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- There are no legal or technical reasons to exclude new GE techniques from the scope of Directive 2001/18/EC
- IFOAM EU considers that **the use of all GM techniques fall in the scope of the GMO legislation** and **has to remain traceable, labelled, subject to a risk assessment and to the precautionary principle**, even though the GMO might not be the end product, in accordance with the process-based approach laid out in Regulation 1829/2003.

IFOAM Organics International's position on new genetic engineering techniques

- IFOAM Organics International's position adopted in November 2017

- Main objective:

To provide clarity and transparency on the criteria used by the organic sector as to what breeding techniques are compatible with organic systems, which techniques to exclude, and definition on what should be considered as genetic engineering and genetically modified organisms (GMOs)

- **New genetic engineering technologies**:

Techniques such as Oligonucleotide directed mutagenesis (ODM), Zinc finger nuclease technology, CRISPR/Cas, Meganucleases, Cisgenesis, Grafting on a transgene rootstock, Agro-infiltration, RNA-dependent DNA methylation (RdDM), Reverse Breeding, Synthetic Genomics, **are genetic engineering techniques that are not compatible with organic farming and that must not be used in organic breeding or organic production**. The rapid development of these new technologies should entail that clear legal definitions are in place and are regularly updated in order to accurately classify and regulate products derived from such novel techniques.

- Position of IFOAM Organics International is based on:

- the Principles of Organic Agriculture:

The Principle of Health.

The **Principle of Health** in organic agriculture is about serving the wholeness and integrity of living systems (including society) at various levels (immunity, resilience, regeneration, sustainability). The implication for breeding is that useful organisms need to be robust, dynamic, and resilient, able to benefit from interactions with the surrounding biome in which they grow, and to reproduce themselves and to produce high quality, nutritious food.

The Principle of Ecology.

The **Principle of Ecology** in organic agriculture is about contributing to optimally functioning of a diversity of site-specific ecological production systems. This means that breeding needs to develop multilevel approaches, such as decentralized breeding for regional adaptability and enhancing genetic diversity and adapt organism to the environment instead of the environment to the organism.

The Principle of Fairness.

The **Principle of Fairness** in organic agriculture is about serving equity, respect, justice and stewardship of the shared world. It implies the need to develop new socio-economic structures in breeding to ensure free access to genetic resources, no patents of life, breeding approaches that involve all value chain actors, equal benefit sharing among chain partners, and maintenance and accessibility of diversity for future generations.

The Principle of Care.

The **Principle of Care** in organic agriculture is about enhancing efficiency and productivity in a precautionary and responsible manner. We argue that there is plenty of unexplored (and forgotten) knowledge for new multifaceted breeding strategies. It means that organic breeding refrains from breeding techniques that interfere directly at DNA level, including cell fusion and mutation breeding, and stimulates transparent and participatory/collaborative processes.

Current regulatory situation

- Directive 2001/18/EC on the deliberate release of GMOs into the environment
- Regulations 1829/2003 and 1830/2003 on GM food and feed and traceability and labelling of GMOs
- European Court of Justice ruling 25 July 2018:
  - *European Union’s legislation on genetically modified organisms (GMOs) also applies to GMOs resulting from the use of new mutagenesis techniques. It confirmed that only organisms obtained through techniques which have “conventionally been used in a number of applications and have a long safety record“ can be excluded from EU GMO law.*
- Current legislation fit-for purpose -> focus must lie on proper implementation
- However: not consistently applied across all EU member states -> action needed

Why we need regulation of genome editing

- Genome editing (e.g. Crispr/Cas) can result in new genetic combinations -> going far beyond what conventional breeding has done for decades
- New possibilities:
  - simultaneous alteration of multiple DNA sequences on different locations
  - Alteration of protected parts/genetically linked genes
- Genetic engineering processes are not as precise as claimed, and the intended alterations can lead to unwanted side effects

Genome editing: what can go wrong

Sources: ENSSER and TestBiotech

- **Off-target modifications** can occur additionally to the intended alteration of the target site:
  - CRISPR/Cas can induce DNA double strand breaks at non specific and unintended parts of the genome.
  - Problem: predominantly biased detection methods used (PCR sequencing) -> you only find what you are looking for, not enough studies with unbiased detection methods (Whole Genome Sequencing).
- **On-target modifications** can result in unwanted DNA fragments at target site
  - Integration of unwanted DNA fragments at the target sequence or at unintended off-target sites of the genome (e.g. degradation fragments of Cas DNA)
  - Integration errors are under reported or overlooked -> same problem: biased detection methods used
  - Have been reported with ZFN and Crispr/Cas (most used technology)
- **Structurally altered proteins:** An intended alteration at the target site can cause structurally altered proteins (e.g. exon skipping)
- **Restructuring of the genome:** Large genomic deletions and inversions around the target site.
- **Intervention in complex metabolic pathways** -> potential toxic effects might harm protected species and disturb food web mechanisms, e.g.:
  - - influence on the development
  - - alteration of the nutritional composition
  - - altered reaction on stress (herbivory, pathogens, drought, salinity, temperature)
  - - reduced/enhanced fitness
  - - influence on the circadian rhythm
  - - altered flowering induction
- **Gene drive**: ethical issues, and DNA from edited organisms can be incorporated into local population (GM mosquitoes crossed with local populations in Brazil, *Nature*, Evans et al., 2019)

Case study: Genome edited cattle and unexpected outcomes

- Case: Recombinetics
  - Claim: precision breeding to develop hornless cattle
  - However: Unintended addition of DNA from bacteria (including antibiotic resistance gene) from different species during genome-editing process
  - Undetected because the company didn't expect it and did not look for insert
  - Error only detected by government agency (FDA)
- Same error could in principle also occur in plants
- Study: gene-editing errors are under reported and often blind spot for scientists (MIT Technology Review)
- Shows that we need proper risk assessment

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Why we need regulation of genome editing

- specific risks associated with GE techniques need risk assessment procedures
- unexpected outcomes -> risk assessment necessary as errors occur
- Old GM technologies are also used when applying new GM technologies
- Without regulation, unintended effects can go unnoticed

- Are we able to understand the consequences of the intended and unintended changes in complex biological systems, and in complex ecosystems?
- What about gene regulation mechanisms (epigenetics)?

- We need risk assessment :
  - 1. related to the genetic engineering process
  - 2. related to the introduced trait

Why we need traceability and labelling

- GMOs (including plants and animals modified by new genetic engineering techniques) are living organisms able to disseminate and multiply in the environment
- If not traced, organisms from genome editing can enter environment undetected
- How to ensure regulatory oversight and post-market monitoring and how to recall an organism in case a problem is identified?
- Transparency 1st precondition to protect organic markets
- Without labelling and traceability, organic producers unable to guarantee that no GMOs are used in the production process

The high costs of “co-existence”

- Consequences of contamination:
  - loss of organic premium, sell food as feed quality, loss of reputation and markets
  - Example: (Aragon, Spain) contamination of 16 organic farms (2003 -2007); in all cases organic certification was withdrawn, livestock farmers needed to buy in maize feed from other regions.
  - High costs of preventing contamination on farm level -> “co-existence” very costly and in most cases not possible in practice

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Farmers and consumers right to know

- Despite more than 80 GM events authorised for import and use for food and feed at EU level, the whole European food market, conventional and organic, is GMO-free
- Breeders, farmers, processors and consumers have the right to know how their food is produced and to choose GMO-free seeds and products

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Why we need regulation of genome editing

- GMO legislation must be applied to those new techniques that do not have a history of safe use,
- Ensure that products from gene editing go through risk assessment, authorisation, traceability and labelling,
- Safeguard the choice of breeders, farmers, food & feed processors and consumers to opt for GMO-free conventional and organic products,
- GMO legislation gives these actors a legal assurance.

Detection methods – ways forward

- Adequate detection methods needed to enforce GMO legislation
- ECJ ruling not 'impossible' to implement
- Technical problems can be overcome:
  - (1) Genome-edited products that are already on the market are detectable due to unique patterns, e.g. rapeseed & soybean
  - (2) Unknown genome edited products (and imports) identifiable via off/on target effects and specific modification patterns -> Develop detection methods and strategies based on clear EU mandate and funding
  - (3) National authorities can implement traceability on the basis of documentation

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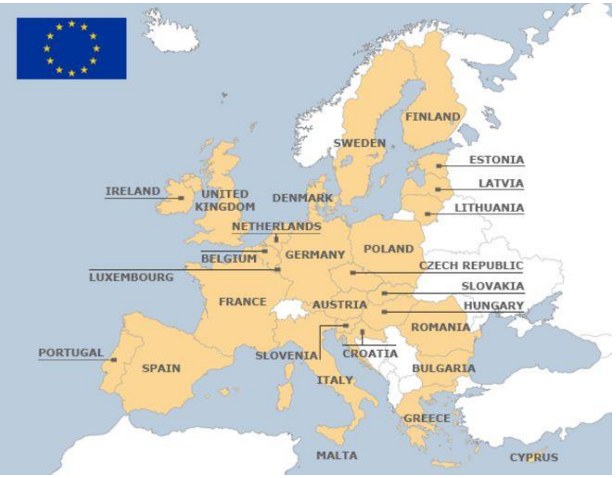
Measures needed on EU level

- After the ECJ decision, there is legal clarity
- No need for new legislation and new studies should not delay action to ensure the EU legal framework is properly implemented
- The EU legislative framework is fit for purpose for the new techniques (although its implementation could be improved)
- EU network of GMO laboratories develop methods and strategies to identify unknown genome edited products, based on a clear EU mandate and funding,
- Imports of rapeseed and soybean from the USA and Canada must be certified as free from new GMOs that are not authorised in the EU,
- No patenting of plants & animals that can be found in nature or obtained by conventional breeding.

Measures needed on national level

- Implementation of GMO legislation + ECJ UE ruling
- Instruct national food authorities to carry out the necessary (import) controls
- Develop national programme to protect organic and conventional farming from contamination



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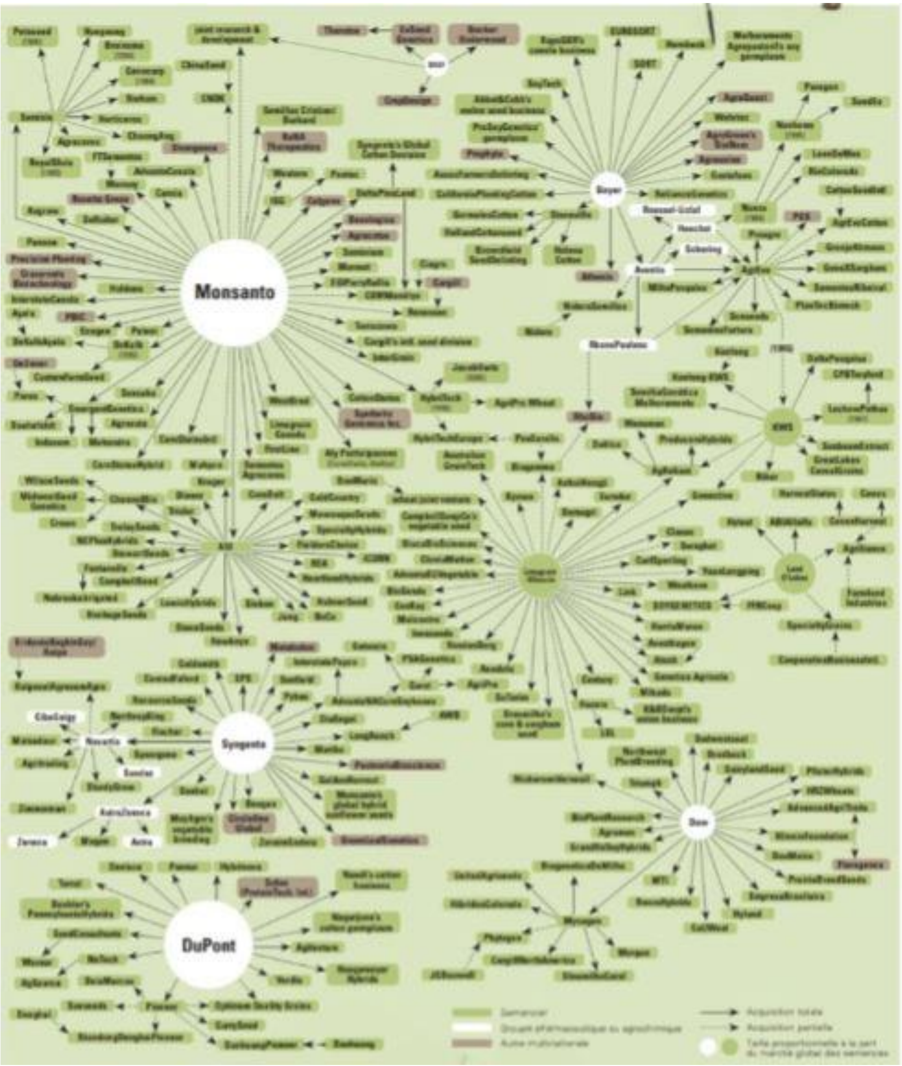
Patents on seeds and animals

- **Intellectual Property Rights (IPR)** are a public policy tool to balance the interests of the inventor with the those of society
- **Patents versus Plant Variety Rights**
- **Patents on seeds hinder innovation in breeding and block the circulation of genetic resources.** Access to genetic biodiversity is essential for creating new varieties and should not be blocked by patents.
- **Patents on seeds** foster market concentration

Market concentration

4 companies controling 60% of the seed market ?



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An increasing number of patents

- Directive 1998/44 on the patentability of biotechnological inventions
- According to NPOS, so far in Europe more than 3000 patents on plants have already been granted, most of them coverning genetic engineering
- In the last 15 years, more than 1500 patents applications on plants derived from conventional breeding have been filed, and more than 200 patents have been granted so far
- Vague description, no distinction between GE and non inventive steps, but very broad claims
- According to NPOS, patents on genetic variations and mutations accounted for 65% of all patents granted on conventionaly bred patents and animals in 2016

A change in the political economy of plant breeding

- Patents on GE have little impact in Europe, but patents on conventional breeding have a far reaching impact
- E.g. the patents granted by the EPO to Rijk Zwaan in 2004 on lettuce derived from conventional breeding with resistance to aphids impacted more than 300 varieties registered in Europe.
- In 2015 the EPO enlarged board of appeal decided in its decision on « broccoli and tomato » that while processes for conventional breeding cannot be patented, plants and animals stemming from these processes are patentable
- Dutch Presidency/EU Commission symposium « Finding the Balance on 18 May 2016 » - IFOAM EU Press Release
- In November 2016: Legal interpretation from the Commission on the exclusion of essentially biological processes
- In June the EPO amended the EPC to exlcude essentially biological processes, but with a narrow interpretation, that still considers selection without crossing or random mutations as patentable

IFOAM EU position

- The scope of the patents should be restricted to the technical process used to produce plants or animals (Patents on processes versus patents on products)
- And plants or animals with similar or identical characteristics obtained by means of essentially biological breeding should not fall within the scope of patents.
- Seeds and genetic traits that can be found in nature and obtained through conventional breeding cannot be patented, **whatever the breeding process described in the patent**. Patents on products, traits or genes derived from genetic engineering breeding techniques should only cover products that contain DNA sequences and traits that cannot be found in nature (including through mutations) or cannot be obtained through conventional breeding methods.
- **The organic movement urges the European Commission to prevent the destruction of the European breeding innovation model and to change Directive 98/44/EC** to render legally binding the exclusion of plants, animals, genes and genetic traits that can be found in nature or obtained through conventional breeding, from patentability.

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Kiitos! Thank you!

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