FARM EUROPE

POLICY BRIEFING

New Plant-Breeding Techniques: What are we talking about?

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Today, the agri-food sectors are more than ever confronted with 3 major demands from our society:

- To provide safe and quality food not only to European citizens but as well to world markets, having in mind the segmentation of these markets, considering both commodities, mid-range and premium markets. Each of them deserves to be considered.
- To keep rural areas lively and viable. This means, first and foremost to maintain and develop a profitable farming activity in all rural areas across the EU. Agriculture is indeed the basis of any possible economic development. Can you build a house without solid foundations? No, indeed. Same story when it comes to economic development of rural areas.
- To optimize the good management of the environment and to fight more effectively against climate change and risks linked to wider and wider spread diseases.

Being able to answer jointly to these three challenges is for sure a challenge itself, but a feasible one, if you accept to make effective use of science and concentrate your efforts on double performance: economic performance and environmental performance.

This is the very basic condition of any success of the EU and the EU agriculture to ensure both growth and job and more environment.

To reach this objective, we need to change our attitude, to live in our time and consider what science tells us, and not what some say that science could tell.
This is true when it comes to precision and smart farming and how policies can incentivize the move of the EU agriculture to a modern, a more eco-environmentally efficient agriculture.

This is true as well when it comes to genetics.

For more than a decade, the global productivity of the EU farming sector has halved. During this decade, the capital productivity of this sector has become negative. According to the EU Commission, this trend would result in a new decrease by 14% of the EU agri incomes in the next 10 years.

Should you accept this simply as a fate? For sure not.

Productivity of EU agriculture has been stagnating for years. It is time now to reinvest in innovation and research, to reinvest in genetics and develop a concrete science-based approach in that respect.

In this framework, objectivity and transparency will be key.

New breeding techniques are said to be promising as modern and faster extension of usual traditional breeding techniques.
But if the aim is to develop sensible policies and orientations based on solid ground, the first question to be answered when it comes to NBTs is: what are we talking about?

- Scientifically, what are NBTs, what does it mean in simple words?
- Economically, what are the expectations and what is already known for sure?
- On Environment, is there any added value?

New Plant-Breeding Techniques in a nutshell

New Plant-Breeding Techniques (NBTs) are methods allowing the development of new plant varieties with desired traits, by modifying the DNA of the seeds and plant cells. They are called ‘new’ because these techniques have only been developed in the last decade and have evolved rapidly in recent years.

Moreover, as these practices are still continuously evolving, there is no limited set of techniques that can be put under the 'umbrella term' of NBTs.[1] Based on assessments of the European Commission, the following plant-breeding techniques can currently be considered as the main NBTs:

1) Site-Directed Nucleases (SDN) (including ZFN-1/2/3 and CRISPR systems);
2) Oligonucleotide Directed Mutagenesis (ODM);
3) Cisgenesis;
4) RNA-dependent DNA methylation (RdDM);
5) Grafting (non-GM scion on GM rootstock);
6) Reverse breeding;
7) Agro-infiltration. [2]

These New Plant-Breeding Techniques, which have emerged as the result of advances in scientific research, enable more precise and faster changes in the plant's genome than conventional plant breeding techniques, which use chemical and radiation processes to alter the genetic characteristics of plants.[3]

As such, they have a significant potential for the plant breeding and agri-food industry, as they entail technical advances, economic savings and the improvement of crop characteristics.

First of all, NBTs have **technical advantages** compared to traditional plant breeding techniques. Some techniques (such as ODM and ZFN) allow site-specific and targeted changes in the genetic material of the plants, and for many of the techniques, the genetically modified code for the desired trait is only present in the first plant, but not in their offspring.

Secondly, NBTs have **economic advantages**, as the use of these techniques reduce the necessary time for plant breeding compared to conventional approaches (for which breeding can take up to 10 years), thus leading to lower production costs.

Crop improvements as a result of NBTs include the resistance of plants to diseases and drought tolerance, which can lead to higher yields, as well as higher nutritional qualities and storage or processing qualities.[4]

New Plant Breeding Techniques are currently in an uncertain situation regarding their legal classification, as there is considerable debate on how these practices should be

[1] European Parliamentary Research Service, *New plant-breeding techniques: Applicability of GM rules*, 2016, p. 2.
[2] European Commission, *New plant breeding techniques,* https://ec.europa.eu/food/plant/gmo/legislation/plant_breeding_en.
[3] EPRS, *op.cit.*, pp. 1-2.
[4] Joint Research Centre of the European Commission, er the genetic characteristics of plants-the-art and prospects for commercial development'ev*JRC Scientific and Technical Reports*, 2011.

regulated and whether they (or some of them) should fall within the scope of the EU GMO legislation. [5]

Registration and certification of non-GM and GM seeds in the EU

Seeds, the main focus of New Plant-Breeding Techniques which aim at improving their genetic characteristics, are regulated in the EU by 12 Directives: Directive 2002/53/EC on the common catalogue for varieties of agricultural plant species and 11 sectoral Directives that govern the seeds of specific crop species (for beets, cereals, fodder plants, forest material, fruit plants, oil and fiber plants, ornamental plants, potatoes, vegetables, and wine).

The legislative framework for seeds is based on two elements:

1) **Registration** of the seed varieties;
2) **Certification** of the seed varieties before they can be sold on the EU market.

The general principle is that companies can register their new seed varieties in the national catalogue of one of the EU Member states, which needs to notify the Commission, after which the seed variety will be registered in the Common Catalogue of the EU.

Before registering the variety, the seed needs to be tested for 4 elements:

- **Distinctiveness**: it needs to differ clearly on, at least, one important characteristic from another registered seed variety;

- **Uniformity**: all resulting plants should be identical;

- **Stability**: the plant characteristics should remain in place over generations;

- For agricultural crops, the **'Value for Cultivation and Use'** needs to be proven. [6]

The first three elements are assessed through so-called DUS-tests (Distinctiveness, Uniformity, Stability), while agricultural plant varieties are subjects to additional VCU trials (Value for Cultivation and Use). The DUS-tests allow for the identification and description of varieties, while VCU trials test the agronomic performance of the plants resulting from the seeds, for instance on their yields. In order to be registered in the catalogue, the VCU tests need to show that the seed offers better results in terms of

[5] EPRS, *loc.cit.*
[6] Library of the European Parliament, *Seeds and other plant reproductive material: towards new EU rules*, 2013, pp. 2-3.

cultivation or use than other varieties that are available on the market. **In general, DUS tests are conducted over a period of 2 years, while the VCU trials usually last between 2 and 3 years.**

Before the seeds can be legally sold on the EU market, they also need to undergo a **certification procedure**, through inspections that verify and guarantee their identity, health and quality (for instance in terms of disease resistance). This is applicable to both seeds from inside the EU and seeds coming from outside the EU.

For most varieties, seeds are required to have multiplied over at least two generations (corresponding to around 2 years of control) and need to be sealed, labelled, sampled and tested to ensure that they meet the prescribed minimum standards. Seed certification costs usually account for 1 to 2% of the total production costs, which are mostly shared between the public authorities and the industry

For GM seeds, the legislation also requires the varieties to be authorised in line with the procedures outlined in GMO Directive 2001/18/EC before they can be included in the Common Catalogue and be sold on the European market. If the GM seed will also be used in food and feed, it has to follow the rules of Regulation (EC) 1829/2003 on genetically modified food and feed as well. As a result, the registration of GM seeds requires significant additional costs compared to non-GM seeds.

The authorisation process of "novel foods"

Novel foods are food or food ingredients that have not been consumed significantly within the European Union before 1997, when the first **Regulation 258/97** on novel foods entered into force. It involves food from new sources; food obtained through new technologies (such as nanotechnology) or the use of new substances (for instance plant sterols), as well as food traditionally eaten outside of the EU (for example chia seeds). [7]

A novel food requires a scientific safety assessment and an authorisation before it can be sold on the EU market, and must fulfil the following criteria in order to be authorised:

[7] EFSA, *Novel and traditional food: guidelines finalised*, https://www.efsa.europa.eu/en/press/news/161110.

- it must not pose a risk to human health
- it must not be less nutritious if it replaces a similar food, and
- it must be labelled to avoid misleading the consumers. [8]

Companies need to submit their applications for the marketing of their novel food to the relevant Member State authority, and are required to present several types of scientific data on the compositional, nutritional, allergenic and toxicological characteristics of the products, as well as information on the production process and the intended use. The authority can allow the marketing of the product if the Commission and other EU Member States do not object, and are also able to ask EFSA for an additional assessment. If a decision of the Commission is needed, it will ask the opinion of the Standing Committee on Plants, Animals, Food and Feed. [9]

The rules applicable to novel foods will be updated in 2018, with the entry into force of **Regulation (EU) 2015/2283**. Within this new regulatory framework, an authorisation procedure can be started by an interested party, a country of by the Commission itself. The Commission will have to possibility to ask EFSA for an opinion on the safety of the novel food and will also need the endorsement of the Standing Committee on Plants, Animals, Food and Feed.

The legislation on novel foods does not cover additives, flavourings, extraction solvents, and most importantly, does not apply to GMOs - which are subject to Regulation EC 1829/2003 on GMOs for food and feed.

So far, there have been around 180 applications for novel foods (7 to 10 applications per year), of which 80 have been authorised for use in the European Union. [10]

The average cost of submitting an application for novel foods is estimated at between €20 000 and €45 000, although based on the fees charged by the national authorities and the data requirements, the expenditures can vary between a few hundred to one million euro. The Novel Food Regulation also foresees the possibility of a simplified procedure for foods similar to existing products, for which the requested fee ranges from €900 to €2000. The average period between the application and the final authorisation is 2 to 4 years. [11]

[8] European Parliamentary Research Service, *Updating rules on novel foods to keep up with scientific advances*, 2015, p. 2.
[9] EFSA, *loc.cit.*
[10] European Commission, *Authorisations*, http://ec.europa.eu/food/safety/novel_food/authorisations_en.
[11] European Parliamentary Research Service, *Updating rules on novel foods to keep up with scientific advances*, 2015, p. 3.

	GMOs	Seeds	Novel foods
Main legislation	- **Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms** - **Regulation (EC) 1829/2003 on genetically modified food and feed**	- **Directive 2002/53/EC on the common catalogue for varieties of agricultural plant species** - **11 sectoral Directives** - **GM seeds also need to follow the GMO legislation: Directive 2001/18/EC and Regulation (EC) 1829/2003**	- **Regulation 258/97, which will be replaced by Regulation (EU) 2015/2283 from 2018 onwards** - **Does NOT apply to GMOs, which are subject to Regulation (EC) 1829/2003 on genetically modified food and feed**
Requirements	- For cultivation: assessments of the environmental risks, monitoring of the GMOs after their release, labelling and registration requirements, and public consultations. - For food and feed: authorisation; supervision; and labelling (if they contain more than 0.9% of GMO components).	- For registration: * DUS tests: identification and description of the seed variety. * VCU trials (for agricultural crops): to test the agronomic performance of the plants resulting from the seeds. - For certification: inspections verifying and guaranteeing the identity, health and quality of the seeds; labelling; and tests of samples.	Safety assessment and authorisation, requiring data on the compositional, nutritional, allergenic and toxicological characteristics of the products, as well as information on the production process and the intended use.
Average costs for approval	- **Registration** fee: up to **€ 90 000** - Total costs of **€6.8 million** on average **for the required data collection** (has varied from €3.8 million to €10.3 million)	**Registration**: - **DUS tests: €90 - €2000 per year *** - **VCU tests: €1000 - €2550 per year *** **Certification: 1% - 2% of total seed production costs *** * mostly shared or even fully paid by the public authorities	**€20 000 - €40 000** (but can vary from a few hundreds to one million euro) For the simplified procedure of novel foods similar to existing products: between €900 and €2000
Average duration for approval	- **For cultivation: 3 years** - **For food and feed: 3 to 4 years**	**Registration:** - **DUS tests: 2 years** - **VCU tests: 2 to 3 years** **Certification: at least 2 years**	**2 to 4 years**

Relevance of "New Techniques" application in EU agriculture

Given the enormous pressure that EU agriculture has to face, such as high population growth, climatic events and shrinking natural resources, the biggest challenge is how to meet increasing food demand (over 9 billion people by 2050), ensuring a high rate of productivity, without impacting the environment.

In this overall alarming context, the use of some of these **NBTs can play a key role in allowing plant breeders to introduce in an efficient way, very precise, targeted genetic modifications, which have the capacity to fasten the selection speed.** In other words, this translates into: low cost, ease of use and speed up of innovation processes, when compared with conventional plant-breeding techniques. Furthermore, NBTs are not only a valuable option for breeders, but these modern biotechnologies also allow to develop plant varieties that can adapt to climatic changing conditions.

To summarize, NBTs' potential application in agriculture and food systems[12] can be identified in:

- Precise and rapid alteration of crops to boost yields (genetic engineering is more predictable than conventional approach, given the targeted way through which direct modifications of an organism's own genetic sequence are inserted)
- Improved crop & vegetable resource efficiency
- Reduced inputs needs
- Plants with herbicide tolerance
- Plants with pest or insect resistance
- Plants with drought or flood resistance (climate change resilience)
- Enhanced nutritional quality of food crops
- Changes in composition of nutrients in plants (i.e. vitamins or fatty acids)
- Food crops with reduced allergenicity (for example wheat without gluten)
- Increased fruit and vegetable shelf-life

Focusing on the health-safety dimension, as highlighted by the SAM-HLG explanatory note *"an assessment of safety can only realistically be made **on a case-by-case basis** and **depends on features of the end product** including: unintended and intended effects, the species, the environment in which the product is used, **the agricultural practice in question**, the intended use and the exposure".*

[12] European Parliamentary Research Service, *New plant-breeding techniques: Applicability of GM rules*, 2016 p. 2

Accordingly, NBTs should go hand in hand with good agricultural practices. This means that the potential benefits of these new techniques should be further evaluated by considering their complementarity to the conventional farming methods.

Positions of experts, EU institutions and Member States on NBTs

High Level Group of the Commission's Scientific Advice Mechanism (SAM)

In October 2007, upon the request of the EU Member States, the European Commission set up an expert working group composed of nationally appointed scientists, in order to assess whether or which NBTs should be regulated by the GMO legislation. The working group examined the following techniques: ODM, ZFN, cisgenesis and intragenesis, grafting, agro-infiltration, RdDM, reverse breeding and synthetic genomics. [13]

The working group completed its work in 2012, but the final report was never released due to a lack of consensus among the members. While the experts unanimously agreed that plants developed through cisgenesis and intragenesis should fall under Directive 2001/18/EC, opinions were still pending on the regulatory status of the remaining NBTs. [14]

On April 28, 2017 the SAM-HLG released its explanatory Note in response to the request, formulated in the Scoping Paper (adopted by the HLG on 25 November 2016), by the European Commissioners for Health and Food Safety, Vytenis Andriukaitis and for Science, Research and Innovation, Carlos Moedas to provide an up-to-date overview and a comprehensive scientific comparison on *new techniques in agricultural biotechnology***,** including their potential agri applications in both fields of synthetic biology and gene drives, considering the key characteristics of each of these new techniques**.**

The Note underlines, among the other, that:

• *"All living organisms are subject to alterations to their genetic information due to molecular processes which can occur spontaneously and due to exposure to environmental stressors".*

• *"All breeding techniques applicable in agriculture (conventional breeding techniques, CBT; established techniques of genetic modification, ETGM; and new*

[13] European Commission, *loc.cit.*
[14] EPRS, *op.cit.*, p. 4.

breeding techniques, NBT) make use of genetic diversity and change whether naturally occurring or resulting from human intervention, in order to select or generate plants, animals or microorganisms that exhibit preferred characteristics".

• "There is heterogeneity within the NBT, and some similarities between some NBT and some CBT and some ETGM, and this is reflected in the variety of end products which can result from the employment of NBT. These similarities and differences relate to 1) molecular mechanisms; 2) the size, location and frequency of the resulting genetic changes (precise and intended vs. imprecise and unintended); 3) the extent to which ETGM are employed in NBT; and 4) the presence or otherwise of exogenous nucleic acids (DNA or RNA) in intermediate and end-products. These factors affect among others the extent to which the genetic changes are detectable".

• "The genome editing subset of NBT can produce precisely located alterations to DNA sequences, ranging from 'point mutations' (changes of one or a few nucleotides, which may be either random or specified) to the insertion of (endogenous or exogenous) genes. Other NBT, such as RNA-dependent DNA methylation (RdDM) make no changes to DNA sequences at all".

• "The end products of NBT may or may not contain exogenous DNA depending largely on the technique(s) employed. The development of an end product that involves the use of NBT may additionally use ETGM in one or more intermediate steps (e.g. in genome editing, RdDM), agro- infiltration, etc.), and as a consequence, exogenous nucleic acids may be present in intermediate products but not necessarily in the end product".

• "This variety and versatility of NBT explains why comparisons between NBT and CBT, and NBT and ETGM, in the Note are only made where relevant, and suggests that grouping techniques together as NBT may not be optimal for scientific or other reasons".

• "Differences between the groups of techniques (CBT, ETGM, and NBT), of relevance to unintended effects and efficiency, depend on the extent to which changes can be targeted, and how precisely they can be made. Changes made with CBT, in particular by mutation breeding in plants, require the screening of a large population in which changes have been randomly induced and the selection of desirable progeny. ETGM and NBT by contrast do not require such extensive screening as pre-defined changes are made to defined genetic sequences or to gene expression".

• "ETGM and NBT differ in the extent to which they produce 'unintended effects'. Unintended mutations do not however always have phenotypic effects, and not all phenotypic effects are detrimental".

• "Random insertion of nucleic acids is characteristic of the employment of ETGM in

plants and animals, and multiple insertion events can also occur at untargeted and therefore uncontrolled genetic locations. By contrast, the NBT of genome editing offer not only the ability to target insertions (resulting in comparatively fewer unintended effects on the expression of other genes or their disruption) but also the ability to make small, precise and specific changes, such as point mutations, which can also be observed in nature. The employment of the NBT of gene editing does not exclude 'off-target' effects, where a precise change is made to a genetic sequence identical or similar to that in which the change is desired, but in another location. By contrast with unintended effects resulting from ETGM and CBT, NBT off-target effects are rare, and in general, the frequency of unintended effects in NBT products is much lower than in products of CBT and ETGM".

• *"The precision available from the employment of NBT and efficiency of their use means that some products can only be realistically obtained with the use of these techniques and not through the use of CBT or ETGM. The issues of unintended effects due to NBT (and in particular, genome editing related off-target effects) are the subject of much research at present as evidenced by the rapidly growing number of publications in the field".*

• *"The Note makes qualitative statements about the relative costs and speed of product development. The speed with which mutations can be introduced using NBT is often higher (in particular when using the CRISPR-Cas genome editing system) than that which can be achieved with ETGM and CBT, mainly due to the reduced need for time-consuming screening procedures and/or back-crossing, with correspondingly lower costs. The time and costs related to subsequent regulatory approval are not within the scope of the Note".*

This independent explanatory note, as also specified in the Scoping Paper, does not take a position; it does not cover legal issues and it does not make policy recommendations to policymakers.

The European Food Safety Authority (EFSA)

The European Food Safety Authority (EFSA) has published opinions on two specific types of NBTs and their safety assessment, namely on plants developed by cisgenesis and intragenesis, and on the Zinc Finger Nuclease 3 technique. EFSA concluded that the existing rules on risk assessments for GMOs are appropriate for cisgenic and intragenic plants, as well as for the ZFN-3 technique.

In its opinion on cisgenesis and intragenesis, EFSA argued that cisgenic plants have similar risks than plants bred with conventional breeding techniques, but that intragenic (and transgenic) plants can involve additional risks. It notices that all of

these breeding techniques can produce 'variable frequencies and severities of unintended effects', which cannot be predicted beforehand and need to be assessed on a case-by-case basis. In general, however, such unwanted genetic traits can be removed by breeders during the selection and testing phases. EFSA concludes that the risks of these NBTs for human and animal health will depend on factors such as the extent to which the plant is cultivated and consumed. [15]

In its opinion on Zinc Finger Nuclease 3, EFSA found that this technique can minimise the risks of genetic disruption compared to the currently used transgenesis methods, as it allows a more precise insertion of DNA into a defined area of the plant genome. These techniques would also involve less olve less invchanges in the plant genes than most mutagenesis techniques, and when these changes do occur, they would be similar to those produced by conventional breeding techniques. [16]

The Joint Research Centre (JRC)

In 2011, the Joint Research Centre (JRC) of the European Commission published a report on 'New plant breeding techniques: State-of-the-art and prospects for commercial development', which includes an assessment of the intended and unintended changes and effects of NBTs.

The JRC concludes that it is currently impossible to identify the genetic modification for plants bred with the following NBTs: ZFN-1 and 2, ODM, RdDM, grafting, reverse breeding and agro-infiltration. On the condition that information on the introduced DNA is provided, it is however possible to identify the genetic modifications created through ZFN-3 technology, cisgensis/intragenesis and floral dip. Without any prior knowledge on the DNA introduced by the NBT, it is not possible to identify genetic modification in the modified plants.

The European Parliament

On 25 February 2014, the European Parliament issued a resolution on 'Plant breeding: What options to increase quality and yields?', in which it stressed the importance of developing and using NBTs that respond to societal and agricultural demands and being open to the new technologies available. The Parliament also

[15] EFSA, 退 Scientific opinion addressing the safety assessment of plants developed through cisgenesis and intragenesisn*, EFSA Journal,* Vol. 10, No. 2, 2012.
[16] EFSA, 退 Scientific opinion addressing the safety assessment of plants developed using Zinc Finger Nuclease 3 and other Site-Directed Nucleases with similar function'*, EFSA Journal,* Vol. 10, No. 10, 2012.

expressed concerns over the delayed regulatory assessment of NBTs and called on the Commission to clarify their legal status as a matter of urgency. [17]

France

In France, the Environmental Code excludes organisms obtained through mutagenesis from the GMO regulation through Article D.531.2. Nine organisations and trade unions have challenged the legality of this article and requested its repeal to the Prime Minister, who in turn has requested the Council of State (Conseil d'Etat) to repeal the article and pronounce a moratorium on herbicide-tolerant plant varieties obtained through mutagenesis.

On 3 October 2016, **the Council of State referred 4 questions to the European Court of Justice (CJEU)**, related to whether a variety of herbicide-resistant rapeseed obtained through New Plant Breeding Techniques should follow the GMO approval process. These questions especially address the NBTs of ODM (oligonucleotide directed mutagenesis) and SDN (site directed nuclease), and revolve around the following issues:

1) Do organisms obtained through mutagenesis constitute GMOs, and are they therefore subject to the rules of Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms? Or are these organisms, or some of them, exempted from the precautionary measures, impact assessment and traceability requirements included in this Directive?

2) Do varieties obtained through mutagenesis constitute 'genetically modified varieties' subject to the rules laid down by Directive 2002/53/EC on the common catalogue of varieties of agricultural plant species, or are they exempted from the obligations laid down in this Directive?

3) If organisms obtained through mutagenesis are excluded from Directive 2001/18/EC, does this mean that EU Member States are not allowed to subject these organisms to the obligations laid down by the Directive, or do they have a margin of appreciation to define the regime applied to these organisms?

4) Does the precautionary principle, guaranteed by Article 191.2 of the TFEU, call into question the validity of Directive 2001/18/EC? Should we take into account the evolution of genetic engineering processes, the emergence of plant varieties obtained through these techniques and the current scientific uncertainties about their impacts and the resulting potential risks for the environment and human and animal health?

[17] European Parliament, *Resolution on iament, ressing the safety assessment of plants developed usin*, 2014, p. 6.

The Council of State will rule on this matter after receiving the opinion of the Court of Justice, which is now foreseen on the 20th of December 2017. [18]

On 29 March 2017, the French Parliamentary Office for evaluation of scientific and technological options (OPECST)[19] - assisted in its work by a Scientific Committee - issued a report on *"the economic, environmental, health and ethical challenges of biotechnology in the light of new research tracks"*, which adopts an holistic perspective on the topic, by examining research in biotechnology, applications of new biotech to human medicine, to the environment, agricultural applications (NBTs), legal and security issues as well as risk assessment and public discussion.

The Report was published after more than a year of study. The overall process gathered a wide variety of actors: from scientists, doctor and academics, to politicians, industries and representatives of civil society.

Having developed this holistic approach, "the rapporteurs support the development of new breeding techniques, which will happen in any case outside Europe".

The rapporteurs call for greater priority to be given to research in this area and decisions to be taken to avoid EU researchers and companies to relocate and so the EU and its Member States to lose ground at global level on this key economic sector.

Regarding the potential role of new breeding techniques applied to agriculture, the rapporteurs, after consultations with scientific experts, concluded that :

- *"New Plant-Breeding techniques should be considered on a case-by-case basis to fully understand the impact of a new genetic trait on the environment";*
- *"Targeted genome modifications techniques could have revolutionary applications in agriculture, as consisting in the very precise introduction of genetic traits, which enable to accelerate the selection speed. Furthermore, they could occur naturally and are virtually undetectable";*
- *"NBTs are complementary to the other agroecology methods. They can be appropriate for both big and small producers"*

[18] Feed Navigator, *France asks ECJ to decide if plants from new breeding techniques are GMOS,* http://www.feednavigator.com/Regulation/France-asks-ECJ-to-decide-if-plants-from-new-breeding-techniques-are-GMOs.

[19] OPECST, which was set up by Act n° 83-609 of July 8, 1983, following a unanimous vote of the French Parliament, aims " *to inform Parliament of scientific and technological options in order, specifically, to make its decisions clear* ". OPECST " *collects information, launches study programmes and carries out assessments".* More details available here: http://www.assemblee-nationale.fr/11/documents/index-oecst-gb.asp

Overall, the rapporteurs specify that "new breeding techniques are not GMOs within the meaning of the EU Directive 2001/18" and that "assessments must be adapted to the risks involved".
With regard to the public opinion dimension, and by recognizing the difficulties that the process would involve, they consider necessary to engage the public in a renewed debate on these new biotechnologies*, "even if they are still at an experimental stage",* by adopting a multidisciplinary approach.

Germany

On Thursday 24 November 2016, Minister of Agriculture Schmidt (CDU/CSU) announced that the Federal Government adopted a draft amendment to the Genetic Engineering Act (18/10459). Under the proposal, organisms obtained through new breeding techniques are not necessarily regarded as GMOs; whether the techniques would fall under the Genetic Engineering Act or not would be assessed on an individual case-by-case basis, and will be both process- and product-related.

The views on NBTs also remain highly divided within the German government. For instance, a legal analysis commissioned by the German Federal Agency for Nature Conservation concludes that the organisms produced by NBTs fall under the scope of Directive 2001/18/EC. The analysis based this judgement on the fact that genetic modifications are carried out purposefully by NBTs and lead to changes in the organisms which do not occur naturally. [20] Meanwhile, the German Federal Office of Consumer Protection and Food Safety argues that certain techniques - ODM and CRISPR-Cas9 - do not constitute GMOs in the sense of the Directive, because the modifications can also be generated through conventional mutagenesis techniques and cannot be distinguished from them. [21]

Other EU Member States

Opinions on the legal status of the various NBTs also differs widely between other Member States and their national government agencies.

In 2015, the Board of Agriculture of Sweden announced, after questions from Swedish researchers, that some Arabidopsis plants that were developed using the CRISPR-Cas9 technology do not fall under the EU definition of a GMO and thus fall outside the scope of the Directive.

[20] German Federal Agency for Nature Conservation, *Legal Analysis of the applicability of Directive 2001/18/EC on genome editing technologies,* 2015.
[21] German Federal Office of Consumer Protection and Food Safety, *Opinion on the legal classification of New Plant Breeding Techniques, in particular ODM and CRISPR-Cas9*, 2016.

In the United Kingdom, the Advisory Committee on Releases to the Environment indicated that only plants obtained through cisgenesis and intragenesis should be recognised as GMOs. On the contrary, the Commission on Genetic Modification (COGEM) of the Netherlands has argued that cisgenic plants should be exempt from the GMO Directive, as this technique only inserts genetic elements from the same or cross-compatible plant species.

Furthermore, the crop development company Cibus has also asked six countries for their opinion on the ODM technique, namely Finland, Germany, Ireland, Spain, Sweden and the United Kingdom. All of these Member States told Cibus that they do not consider the ODM-technique to lead to a GMO as defined by EU legislation.

ANNEX: Short explanations of technical NBT terms

1) Site-Directed Nucleases (SDN)

SDN refers to the general technology of using a DNA-cutting enzyme (nuclease) to generate a targeted break in the DNA. The aim is to take advantage of the DNA break and the plant's natural repair mechanisms to introduce targeted changes in the plant characteristics.

The various applications of SDN are usually called SDN-1, SDN-2 and SDN-3, depending on the specific DNA break and repair process. Examples of SDN techniques include Meganuclease (MN), Zinc Finger Nuclease (ZFN), Transcription Activator-Like Effector Nucleases (TALENs) and Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR).

2) Oligonucleotide Directed Mutagenesis (ODM)

The ODM technology uses a site-specific oligonucleotide (an organic molecule that forms the basic building block of DNA) to cause a specific single-base change to one or only a few bases of the DNA. The oligonucleotide is identical to the DNA sequence in the plant, except for the single base-pair change. The plant cell will repair this 'mismatch' by incorporating it into its own DNA sequence, resulting in a desired specific change in the plant's genome (the oligonucleotide is degraded by the cell after a short period of time).

3) Cisgenesis/Intragenesis

Cisgenesis and intragenesis refer to the introduction of a DNA fragment into a plant that is derived from the same or closely related species, in order to transfer useful genes.

While cisgenesis refers to the introduction of whole unchanged genes, intragenesis uses a new combination of DNA fragments taken from the species itself or from compatible plant species. As such, only cisgenesis can achieve results that are also possible through traditional breeding methods (although in a much shorter time period), while it also entails less risks for unintended effects than intragenesis.

4) RNA-dependent DNA methylation (RdDM)

RdDM uses epigenetic processes to change the activity of targeted genes without changing the DNA itself. As such, it regulates the gene expressions induced by developmental or environmental changes, for instance drought resistance when

plants are exposed to drought conditions. These changes in plants are mediated by small interfering RNA (hence the name RNA-dependent methylation), and may persist for a number of generations, after which the effect will gradually fade away.

5) Grafting (non-GM scion on GM rootstock)

Grafting involves attaching a non-genetically modified scion (the upper part of the plant) onto a genetically modified rootstock. Examples include fruit trees, grapes, tomatoes, cucumbers, and roses.

6) Reverse breeding

Reverse breeding is a method in which the order of events leading to the production of a hybrid plant variety is reversed. The resulting hybrid plant is genetically similar to the original plant and does not contain foreign DNA.

7) Agro-infiltration

Plant parts, mostly leafs, are inserted in the plant through liquid Agrobacterium tumefaciens in order to transfer desired genetics or genetic expressions to the genome of the plant. The response of the plant is monitored to select plants for further breeding. This technique is mainly used to create resistance for crops against diseases.