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Stakeholder questionnaire on new genomic techniques to contribute to a Commission study requested by the Council

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Questionnaire on new genomic techniques to contribute to the study requested by the Council

Discussed and finalised in the Ad-hoc Stakeholder meeting on 10 February 2020

Background

The Council has requested [1] the Commission to submit, by 30 April 2021, "a study in light of the Court of Justice's judgment in Case C-528/16 regarding the status of novel genomic techniques under Union law" (*i.e.* Directive 2001/18/EC, Regulation (EC) 1829/2003, Regulation (EC) 1830/2003 and Directive 2009/41/EC).

To respond to this Council's request, the Commission is collecting contributions from the stakeholders through the questionnaire below. The study covers all new genomic techniques that have been developed after 2001.

Instructions

For the purpose of the study, the following definition for new genomic techniques (NGTs) is used: techniques that are capable of altering the genetic material of an organism and which have emerged or have been developed since 2001 [2].

Unless specified otherwise, the term "NGT-products" used in the questionnaire covers plants, animals, micro-organisms and derived food and feed products obtained by NGTs for agri-food, medicinal and industrial applications and for research.

Please substantiate your replies with explanations, data and source of information as well as with practical examples, whenever possible. If a reply to a specific question only applies to specific NGTs/organisms, please indicate this in the reply.

Please indicate which information should be treated as confidential in order to protect the commercial

interests of a natural or legal person. Personal data, if any, will be protected pursuant to Regulation (EU) 2018/1725 [3].

[1] Council Decision (EU) 2019/1904, OJ L 293 14.11.2019, p. 103-104, https://eur-lex.europa.eu/eli/dec/2019/1904/oj
[2] Examples of techniques include: 1) Genome editing techniques such as CRISPR, TALEN, Zinc-finger nucleases, mega nucleases techniques, prime editing etc. These techniques can lead to mutagenesis and some of them also to cisgenesis, intragenesis or transgenesis. 2) Mutagenesis techniques such as oligonucleotide directed mutagenesis (ODM). 3) Epigenetic techniques such RdDM. Conversely, techniques already in use prior to 2001, such as Agrobacterium mediated techniques or gene gun, are not considered NGTs.
[3] Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC, OJ L 295, 21.11.2018, p. 39–98

Guidelines

Please note that the survey accepts a maximum of 5000 characters (with spaces) per reply field. You might be able to type more than 5000 characters, but then the text will not be accepted when you submit the questionnaire. You will also receive a warning message in red colour below the affected field.

You have the option to upload supporting documentation in the end of each section. You can upload multiple files, up to the size of 1 MB. However, note that any uploaded document cannot substitute your replies, which must still be given in a complete manner within the reply fields allocated for each question.

You can share the link from the invitation email with another colleague if you want to split the filling-out process or contribute from different locations; however, remember that all contributions feed into the same single questionnaire.

You can save the draft questionnaire and edit it before the final submission.

You can find additional information and help here: https://ec.europa.eu/eusurvey/home/helpparticipants

Participants have until 15 May 2020 (close of business) to submit the questionnaire via EUsurvey.

QUESTIONNAIRE

Please provide the full name and acronym of the EU-level association that you are representing, as well as your Transparency Registry number (if you are registered)

If the name of the association is not in English, please provide an English translation in a parenthesis

Euroseeds 11362308587-10

Please mention the sectors of activity/fields of interest of your association

Euroseeds is the voice of the European seed sector. We therefore represent the interests of those active in research, breeding, production and marketing of seeds of agricultural, horticultural and ornamental plant species. Today, Euroseeds, with more than 34 national member associations from EU Members States and beyond, represents several thousand seed businesses, as well as 67 direct company members, including from seed related industries.

If applicable, please indicate which member associations (national or EU-level), or individual companies /other entities have contributed to this questionnaire

To provide substantiated data to this stakeholder consultation on NGTs Euroseeds conducted a survey within its company membership (in the following referred to as “Euroseeds survey”). The term NGTs in this context was used as described above.

The Euroseeds survey covers three general aspects:
1) Current activities of breeding companies in view of R&D and product development with new breeding methods
2) Future potential of new breeding methods for breeding companies
3) Effect of the ECJ ruling on mutagenesis breeding for breeding companies

Information was collected from Euroseeds Members (direct company members) active in research and breeding. In addition, National Seed Associations were encouraged to collect the same information from their direct company members which are not direct company members of Euroseeds.

With more than 90% replies (completed questionnaires) from Euroseeds direct company members, we can claim that the data are representative for the Euroseeds membership. In addition, replies from company members from national associations were included so that a dataset of replies from in total 62 companies was available for further analysis, these include 10% large companies (> 450 Mio € turnover); 37% medium sized (> 50 Mio up to < 450 Mio € turnover) and 53% small companies (< 50 Mio € turnover)* (Figure 1- attachment file 20.0242). The seed sector is a truly internationally acting sector. 98% of the companies (independent of size) active in NGT related research and development are acting internationally (Figure 3, file 20.0242). The map shown in figure 2 of file 20.0242 indicates the location of the headquarter of companies covered by the Euroseeds survey.

Euroseeds positions as referred to in this consultation were endorsed by the relevant Euroseeds' bodies according to Euroseeds' statutes.

A full list of all Euroseeds' members can be found on our website:
https://www.euroseeds.eu/members/association-members/

If applicable, indicate if all the replies refer to a specific technique or a specific organism

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The term New Genomic Techniques (NGTs) as defined for this study is rather broad. We recognize that NGTs can be used to develop transgenic GMOs as well as to induce targeted changes within the organism's genome. Unless stated differently, the content provided by Euroseeds to this questionnaire relates to applications of NGTs in plants only. Our replies focus on those applications of NGTs that lead to plants that could also have been the result of earlier breeding methods, or might have been obtained from natural processes without human intervention as to the Euroseeds position (1) . This includes plants where
1. there is no novel combination of genetic material (2) (i.e. there is no stable insertion in the plant genome of one or more genes that are part of a designed genetic construct) or
2. the final plant product contains solely the stable insertion of inherited genetic material from sexually compatible plant species or
3. the genetic variation is the result of spontaneous or induced mutagenesis.

All graphics that result from the analysis of the data provided by our members are attached to the questionnaire (filename: 20.0242). Our replies to the stakeholder questionnaire contain references to specific figures of this file as indicated. All references are listed according to the numbering in brackets in our replies and can be found in the attached file 20.0272.

* This categorization is different from the EU definition for SME's as to https://ec.europa.eu/growth/smes/business-friendly-environment/sme-definition_en

A - Implementation and enforcement of the GMO legislation with regard to new genomic techniques (NGTs)

* **1. Are your members developing, using, or planning to use NGTs/NGT-products?**
  - (●) Yes
  - ( ) No
  - ( ) Not applicable

* Please provide details

Euroseeds asked its members in the context of the “Euroseeds survey” about their current research and development (R&D) activities with NGTs, where these activities take place and when companies will most likely bring varieties resulting from new breeding methods to the market (globally).

The share of small seed companies active in R&D with NGTs is close to 50%.
All large companies (100%) and more than 85% of the medium sized companies have R&D activities with NGTs (figure 4 of file 20.0242). The NGT related R&D activities take place in different forms which are independent of the company size. Our data suggest that SMEs rely more strongly on public private partnerships including public funding compared to larger companies (figure 5 of file 20.0242).
While the R&D activities of SMEs are more focused on Europe, larger companies are equally active in the EU as well as outside the EU. This allows more flexibility when it comes to transferring R&D activities including field trials to geographies with enabling regulatory environments (figure 6 of file 20.0242). When it comes to decisions about investments in R&D prohibitive costs, long assessment and approval timelines, labelling requirements and political uncertainty of the EU’s regulatory system regarding decision-making if NGTs would (continue to) be regarded as GMO’s will have a negative effect (figure 14 of file 20.0242).
Around 15% of the companies (independent of size) want to bring products to the market already within the next 5 years (globally). Most of the large companies active in R&D with NGTs plan to bring products to the market within the next 5-10 years while 45% most of the medium sized companies intend to bring products to the market after 10 years only. More than 40% of the smaller companies have not projected the timeline of market releases for NGT products yet (figure 12 of file 20.0242). Around 40% of the companies (independent of size) indicated that intended market releases were delayed due to the current regulatory situation in the EU.
More examples and details on Euroseeds’ members R&D activities with NGTs are provided in our contribution to Question 10.

* **2. Have your members taken or planned to take measures to protect themselves from unintentional use of NGT-products?**

- ○ Yes
- ◉ No
- ○ Not applicable

* Please explain why not

Euroseeds understands the term “unintentional use” in the sense of protecting oneself against the unintended use of products that are regulated as GMO’s in the EU.
To our knowledge, up until now only one product resulting from NGTs is commercially available on the market (US-Calyxt high-oleic soybean (3)). As this soybean is produced, harvested, processed and traded in a closed loop system, no additional specific measures are currently needed.
If there will be more NGT products on the market, the access for seed companies to genetic diversity for further breeding might become restricted in order to prevent unintentional use of NGT-products and to be compliant with the current EU regulatory requirements for GMOs.

Most breeders worldwide make use of the so-called “breeders’ exemption” as provided for in UPOV-based plant variety protection laws. This allows breeders free access to competitor’s commercial germplasm for further breeding and with this to build their breeding efforts on the innovations of other breeders. This breeders’ exemption highly contributes to the innovative strength of the breeding sector (4).

Breeders will be forced to restrict themselves from access to genetic diversity from certain jurisdictions for conventional cross breeding programmes in order to avoid unintentional integration of genetic material from organisms which are qualified as GMOs in the EU (but not necessarily elsewhere). This will lead to two restriction effects: firstly, less access to general genetic diversity by not being able to use commercial germplasm from competitors (breeders exemption) or from research collaborations; secondly, no access to new genetic diversity and interesting traits developed via NGTs in other parts of the world with a more enabling regulatory environment.

The use of germplasm (and with this genetic diversity) which is the basis for all breeding activities will be limited to the germplasm that is either owned by the breeding company itself or to germplasm for which the company can rely on validated information on the origin of the germplasm . This restriction will also have a negative effect on the genetic diversity and with that the innovative capacity of classical breeding in a broad range of crops. This goes against the target of supporting sustainable and climate-proof agriculture with locally adapted varieties, ensuring consumer choice.

* 2 bis. Have you encountered any challenges?

- (●) Yes
- ( ) No

* Please provide details

There are currently no technical measures that allow the detection of plants that are the result of NGTs without prior knowledge of the exact genetic make-up of a particular plant variety (5),(6). This puts EU breeding companies at risk of unintended adventitious presence of respective NGT-germplasm that does not fall under specific regulatory regimes in third countries but would be regarded as regulated GMO in the EU. Given the inherent challenges to identify plants that are the result of NGTs (7);(8), EU breeding companies could find themselves at risk of potential fraud.

In view of transgenic GMOs, the seed sector has a lot of practical hands-on experience with managing and avoiding the adventitious and technically unavoidable presence of such GMOs in conventional seed. The costs of supporting parallel breeding programs are significant and can only be handled by larger companies. This was confirmed by a recent study from Canada (9). Small companies and public breeding institutes chose to strictly avoid regulated GMOs. Developing regulated GMO varieties and conventional varieties simultaneously would need dual phytotrons, greenhouses, laboratories, and land for field trials and would be cost prohibitive. Therefore - and because of the very high regulatory investments for bringing transgenic crops onto the world market - presently, virtually all GMOs are developed by large multinational tech providers involving canola, maize, soybeans, and cotton, while all other commodity varieties are developed at public institutions. In addition, developers of transgenic GMOs have withdrawn almost all cultivation applications from the EU regulatory approval system, and are now focusing product development pipelines on more innovation-friendly parts of the world (10) .

* **3. Are you aware of initiatives in your sector to develop, use, or of plans to use NGTs/NGT-products?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide details

The following non-exhaustive examples list developers working on a broad range of crops and traits that were developed using NGTs.

United States Department of Agriculture (USDA) database of 'Am I regulated'?(11):
As of 6 March 2020, 86 letters of inquiry are published here from both academic institutions and companies to find out whether their applications would result in the organisms in scope of the USDA regulatory oversight. While many of the inquiries concern genome editing in the sense of targeted mutagenesis breeding, there are also cases of other technologies, including RNAi and cisgenesis. Some of these letters date back to 2011. We do not know how many of these 86 applications are close to commercialisation, as some of them may be merely proof of concepts. 17 % of the inquiries concern any of the big four crops of which transgenic varieties are widely grown (maize, soya bean, oilseed rape, cotton). The biggest groups of plants are grasses & cresses, and fruit & vegetables. Developers are mainly medium companies & public research. Only 6 % of the developers are international companies.

The gene editing tracker developed by the Genetic Literacy Project lists many different examples from all over the world (12). The full data are accessible on the respective website.

In addition, scientists from the Julius-Kuehn Institute in Germany created a systemic map with studies on the available evidence for the range of applications of genome-editing as a new tool for plant trait modification (13) which contains 99 different market-oriented applications in 28 different crops leading to plants with improved food and feed quality, agronomic value like growth characteristics or increased yield, tolerance to biotic and abiotic stress, herbicide tolerance or industrial benefits.

Euroseeds as an association is involved in three different EU-funded projects that deal with NGTs:

CropBooster-P (14) brings together some of Europe's most prestigious plant science institutions and stakeholder organizations who will jointly develop the blueprints for the crop varieties of the future. They aim to do this by mapping and assessing current and future strategies, methods and technologies for crop improvement. Also, the consortium will develop a Roadmap for the introduction of these new crop varieties in current agricultural practice by aligning the development of these crops with the needs, concerns, wishes and expectations of society. Euroseeds is involved as a full project partner in different work packages of the project.

CHIC (15) : The CHIC project aims to develop chicory varieties that can be used to produce dietary fibre with enhanced prebiotic effects to promote gut health. At the same time, given its biosynthetic capacity, high yields and low agronomic requirements, chicory has significant potential as a versatile production host in molecular farming for the production of many additional health-related products with benefits for consumers. CHIC also aims to harness this potential for the extraction of other types of health-related compounds (terpenes) as potential lead molecules for drug development. Euroseeds is involved in the stakeholder advisory board of the project.

Cost Action PlantEd (16) : The COST Action PlantEd currently brings together more than 330 experts from 36 European countries and beyond, representing a range of disciplines and sectors all with a focus on plant genome editing. They work together for four years (2019-2023) to advance the technical forefront, assess the impact of the technology, discuss regulatory options, monitor (and potentially influence) public perceptions, and develop a number of outreach and educational activities. The COST Action organises meetings, facilitates researcher mobility and training of young scientists. Euroseeds is the main industry partner.

* **4. Do you know of any initiatives in your sector to guard against unintentional use of NGT-products?**

- ○ Yes
- ◉ No
- ○ Not applicable

* 4 bis. Are you aware of any challenges encountered?

- ◉ Yes
- ○ No

* Please provide details

please check our reply to Question No 2

* **5. Are your members taking specific measures to comply with the GMO legislation as regards organisms obtained by NGTs?**

Please also see question 8 specifically on labelling

- ◉ Yes
- ○ No
- ○ Not applicable

* Please describe the measures and their effectiveness including details on the required financial, human resources and technical expertise

Already during the R&D phase in the EU companies implement measures to ensure that their operations are compliant with existing biosafety and GMO legislation - they maintain authorized contained facilities (labs and greenhouses) and implement stewardship measures to ensure separation of GM and non-GM materials as well as authorization for field trials. Besides the costs for separation (see also our answer to question 2) companies will not be able to provide the information to obtain a so-called “unique identifier”(17) for their NGT plants as required by authorities. As the ENGL-report states (18). “For non-unique DNA alterations affecting one or a few DNA base pairs, an applicant may not be able to develop an event-specific method. Furthermore, under the current regulatory system the event-specific detection method is linked to a specific product application for market authorisation. However, the targeted mutagenesis techniques allow to reconstruct exactly the identical genome-edited product in another plant.”

For the purposes of detection and identification, applicants are required to develop a unique identifier as defined by regulation EC N° 1830/2003 for each GMO. If NGT derived products are classified as GMOs, this requirement would apply even when the resulting product does not carry a novel combination of genetic material that could be obtained by recombinant DNA technology. Assigning a unique identifier to such products would contradict the regulatory and policy approaches of several countries (including Chile, Brazil and Colombia) to treat certain NGT derived products as conventional breeding products, not covered by their biotech regulations (i. e., no OECD unique identifier needed). The Inclusion of non-transgenic NGT products in the same OECD product database and with the same identification principles as used for transgenic GMOs would disseminate incorrect information about the genetic make-up of these NGT products and create confusion among stakeholders (global regulatory authorities, growers, grain trade, value chain, or consumers). Only if NGTs are used to generate transgenic plants, the unique identifier should be assigned in accordance with established international practices.

* What best practices can you share?

None, see above

* 5 bis. What challenges have you encountered?

To our knowledge, no application for market authorisation of NGT-derived plant varieties has been submitted in the EU, and no NGT-derived plant products are being imported into the EU. Euroseeds member companies generally do not import plant commodities.

The current EU legislation for traceability and labelling of GM crops requires a method to identify and distinguish mutations, which in practice would not always be possible when only one or a few nucleotides have been changed. Therefore, the current EU GMO regulation is not suitable and would mean a ban to bring a genome edited crop on the market (19),(20).

We expect that no applications for authorisation of NGT-derived plants will be submitted in the EU as long as the current EU GMO authorisation system would apply to such products. Moreover, it appears impossible to comply with it when it comes to detection methods (See our answer to question 7 for details).

Subjecting plants obtained by new genomic techniques to the EU GMO authorisation system presents a huge hurdle and disincentive for applicants. The EU's approval system for GMOs is one of the slowest and most unpredictable in the world already when it comes to food and feed import approvals. The regulatory requirements and costs for the applicant have significantly increased over the years and are estimated at EUR 11–16.7 million for an import GMO authorisation. The average time from submission to an EU-wide import authorisation is around 5-6 years (21) . No applications for approvals for cultivation have been submitted for years and remaining applications are stuck in the approval process due to the lack of proper implementation of the respective EU legislation. Costs and delays for such a cultivation application are impossible to estimate, given that only few final authorisations have been granted, and given the decade-long timelines for the few applications which are still pending for cultivation. This situation is a strong disincentive for any company to enter this market. In addition, 17 out of 27 member states plus one region (Wallonie) opted out from GMO cultivation so that a potential market for such authorized GMO varieties would be very limited.

* **6. Has your organisation/your members been adequately supported by national and European authorities to conform to the legislation?**

- ○ Yes
- ◉ No
- ○ Not applicable

* What challenges have you encountered?

At the request of the Competent Authorities under Directive 2001/18/EC, a working group was established already in October 2007 to analyse a non-exhaustive list of techniques for which it is unclear whether they would result in a GMO(22). The final report of the NTWG was not officially published (23). In addition, Commission asked JRC and SAM to come up with reports assessing the State of the art and prospects for commercial development(24) as well as the new technologies in comparison to conventional breeding and transgenic GMOs (25) . The reports were published in 2012 and 2017 respectively. Also, EFSA published a scientific opinion on Cis- and Intragenesis in 2012(26) as well as on the safety assessment of plants developed using Zinc Finger Nuclease 3 and other Site-Directed Nucleases with similar function (27) . Both on request of a Commission mandate.

All these studies provided strong advice to Commission. But contrary to its own repeated announcements the Commission up to today has not come forward with any legal clarification (Guidance) as to the regulatory status of products resulting from NGTs. It was only during the hearing of case C-528/16 at the European Court of Justice (ECJ) that the Commission provided some interpretation of the scope and exemptions of Directive 2001/18 (see quotes from(28) in the footnote). However, contrary to the Commission's and Councils' view, the ECJ interpreted the Directive as meaning that all plants obtained by any form of mutagenesis breeding are GMOs as defined by Article 2(2), and that only plants resulting from mutagenesis breeding methods qualify for the exemption laid down in Annex IB, when they have been used in a number of applications and have a long safety record (according to Recital 17 of the same Directive).

From the Euroseeds survey on NGTs it is obvious that legal uncertainty remains a strong concern. This applies to the lack of international harmonization but also the long period of lack of legal certainty before the ECJ ruling, the continuing lack of legal certainty for NGTs other than targeted mutagenesis as well as the uncertainty when it comes to implementation and enforcement of the current regulatory requirements for NGTs. Furthermore, the uncertainty regarding the timing and the extent of changes to the current regulatory regime are also important factors. This lack of legal certainty continues since 2007 and has had a major negative impact on plant breeding innovation in the EU, discouraging investments. The lack of support by national and EU authorities in clarifying the legal status has led to one of the policy disconnects as noted by EASAC(29).

Please see Q 5 in view of challenges for identification and compliance with regulatory requirements and Q 2 & 4 in view of unintentional use and potential fraud as to the lack of identification measures for like-products.

* **7. Does your sector have experience or knowledge on traceability strategies, which could be used for tracing NGT-products?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please describe the traceability strategy, including details on the required financial, human resources and technical expertise

Our industry has experience with traceability strategies as part of the GMO authorisation process for transgenic GMOs, nevertheless these may not be applicable to NGT products. Methods for detection and identification of the transgenic event need to be provided and consequently validated by the European Union Reference Laboratory for GM Food and Feed. The current detection methods are PCR based and rely on the presence of an introduced DNA sequence which is unique to a certain GMO.
Under the current EU Directive, the procedures for the validation of detection methods as part of the market authorisation application process for NGT plant products will in principle be the same as for the current transgenic GMOs. But as the JRC-/ENGL-Report rightly states, it is questionable if event-specific identification and quantitative detection methods can be developed readily for all NGT plants. For instance, detection methods for those plant products that are characterised by a non-unique DNA alteration (as the NGT products we are referring to in this contribution) will probably lack the specificity required to identify the NGT plant Moreover, accurate quantification may be challenging, for example if only changes of just one or a few base pairs are introduced (30).

Euroseeds members are not aware of any traceability strategies that could be used for identifying certain NGT-products as we refer to them in this contribution and in particular, when such NGT products are part of commodity flows. The JRC further concluded that validation of an event-specific detection method and its implementation for market control is not feasible for NGT plant products carrying a DNA alteration that is not unique. This also corresponds with the conclusions of Euroseeds members.

DNA fingerprint methods using a specific set of molecular markers for certain crop species as discussed within UPOV can be used to distinguish plant varieties but are not suitable to identify the origin of a given genetic variation per se nor are they able to detect NGT derived products in commodity flows. Plant varieties are characterized as “a plant grouping within a single botanical taxon of the lowest known rank, […] which can be defined by the expression of the characteristics resulting from a given genotype or combination of genotypes, distinguished from any other plant grouping by the expression of at least one of the said characteristics and considered as a unit with regard to its suitability for being propagated unchanged”(31). Like human beings can be identified by DNA-marker fingerprints through analyses of a certain marker pattern that is typical for a certain genotype (individuum), DNA-marker fingerprints can also be used to distinguish/identify plant varieties. These fingerprints and the respective genotypic marker pattern do not allow tracing a specific characteristic that might have been created by NGTs since these markers are almost always unrelated to the characteristic in terms of position in the genome and functional linkage. Even if one of the molecular markers used would be specific for a certain genetic change it would not allow the identification of the origin of this change and with that the method that was used to introduce this change into the genome (see JRC/ENGL-report as above). For EU GMO regulation the method is decisive to define the scope of its application. Only if a certain change in the DNA was introduced by a method that is defined as technique of genetic modification according to Directive 2001/18 the resulting plant would be a GMO. If the change cannot be identified as being developed by regulated techniques, it is not possible to enforce the GMO regulation based on such traceability methods.
As long as non-unique changes in the genome which could also occur naturally or through conventional breeding methods are regulated purely on the basis of the method used to create them, it will not be possible to enforce the legislation. It will instead lead to the discriminatory situation in which plants with exactly the same genetic changes, depending on the method they were introduced would require traceability (and labelling) for the one, but not for the other same genetic change.

* **8. Are your members taking specific measures for NGT-products to ensure the compliance with the labelling requirements of the GMO legislation?**

- ○ Yes
- ◉ No

○ Not applicable

* Please describe the measures and their effectiveness including details on the required financial, human resources and technical expertise

none

* What best practices can you share?

none

* Please explain why not

As far as we know there is currently no product resulting from NGTs on the EU market and our members are not active in importing commodities or food products that might require labelling.

* 8 bis. What challenges have you encountered?

In general, labelling would require traceability of NGT products and products derived from NGT products, including proper identification and quantification. In contrast to transgenic GMOs, there are no fool-proof identification methods available for the detection of NGT products that carry genetic alterations that can also spontaneously occur or result from conventional breeding (as referred to in this contribution). This will make traceability and labelling requirements very difficult, if not impossible to enforce (32).
See also our reply to Question 5 and 7. This would be a huge challenge and uncertainty for our members in case those products would be developed for the EU-market.

* **9. Do you have other experience or knowledge that you can share on the application of the GMO legislation, including experimental releases (such as field trials or clinical trials), concerning NGTs/NGT-products ?**

◉ Yes
○ No
○ Not applicable

* Please describe for the:

☑ Agri-food sector
☐ Industrial sector
☐ Medicinal sector

Agri-food sector

In Europe, as far as we know, only five (5!) field trials involving plants altered by genome editing were performed in the last three years(33) . Two field trials in Belgium using maize (at the Vlaams Institute voor Biotechnologie, VIB), one on potato in Sweden from Lyckeby, one on Tobacco in Spain (planned for 2020) and one on Brassica in the UK (at the Rothamsted Institute)(34). In Sweden and Belgium these field trials were performed without GMO permits in 2017 and 2018. This is much lower than in other parts of the world and is mainly explained by the lack of clarity before July 2018.

From what we know, applicants have not been able to provide a detection method for the trials under GMO requirements that can prove with enough certainty that plants that contain a particular mutation were developed by using NGTs. The applicants could only describe the methods used for the molecular characterization of the genetic change which according to the JRC/ENGL report (35) would not allow to undoubtedly identify the origin of a genetic change as a change that is resulting from NGTs when the same change can also be achieved by conventional breeding methods or occur naturally.
In Europe, because of the continuing erosion of GM research, only few Member States still have practical experience with procedures for field trial research. Many national authorities currently lack the understanding to handle field trial permit requests in a timely and appropriate way.

A long history of field trial destructions (e.g. in France) by activist groups and lack of proper protection of the applicant's interests, have led to a continuing decline of field trial research in the EU (36) and transfer of R&D activities to the Americas, e.g.(37).

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527becc8-264d-4b69-8b55-53ef61fcdd0c/20.0272_Euroseeds_References.pdf

B - Information on research on NGTs/NGT-products

* **10. Are your members carrying out NGT-related research in your sector?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please specify including subject, type of research, resources allocated, research location

Euroseeds members were asked in what kind of activities with NGTs their company is involved .
Independent of their size, many companies are involved in different kind of activities with new breeding methods. Some of those activities concentrate on technology development (improvement of existing NGTs as such or development of new or improved enabling technologies), other activities include gene discovery research in which the NGTs are used to better understand the function of genes to be able to use the knowledge in the breeding process. Some SMEs mentioned that they use NGTs for implementation and improvement of existing methods (with the goal to be prepared when a legislative change does allow an economically and technically viable use of products derived from those NGTs). (Figure 7 of file 20.0242)
More than 60% of the companies active in R&D with NGTs also use NGTs for concrete product development or as a breeding tool (Figure 8 of file 20.0242). This refers to the introduction of genetic changes that lead to improved plant characteristics or to improved genetic recombination processes to increase genetic diversity in the breeding process. Since these activities would lead to products regulated as GMOs in the EU, some companies mentioned that their current activities are at different stages of research and product development depending on crop type and region; some companies explicitly excluded product development activities for the EU market.
From the comments provided by companies it becomes clear that a lot of companies are active in R&D only outside EU or for products for the non-EU market since activities would result in a product regulated as GMO in the EU. Since larger companies have a higher share of R&D facilities outside EU, it is easier for them to also benefit from the use of NGTs for concrete product development for non-EU markets (see also figure 13 of file 20.0242).

Euroseeds members were asked in which crops/crop groups their company currently is active in R&D with NGTs. (Figure 9 of file 20.0242)
Independent of company size, current R&D activities occur in a brought range of crops (globally). A reduction in activities due to the regulatory burden would equal a reduction in diversity of applications and opportunities especially for smaller and niche crops.
Companies mentioned that their R&D strategy is dependent upon market size, regulation of NGTs as well as technology readiness for each crop. In particular, the work on trait development is not a priority for vegetables under the current regulatory framework in the EU. Even crops like wheat and rice would in many cases not cover the high costs and considerable investment of time which go along with the regulatory hurdles of a GM authorisation process.
NGTs could be applied relatively easily to most crops (with availability of the tissue culture system to regenerate plants), but regulatory requirements could take this advantage away. This has the consequence of limiting diversity and trait development options for niche crops which could also impact the range of existing agricultural systems.

Euroseeds members were asked which kind of goal/trait their company addresses in R&D with NGTs. (Figure 10 of file 20.0242)
Independent of company size, companies address a wide diversity of characteristics in the different crop species. Agronomic value (yields, plant architecture) as well as resistance against biotic stress (pests and diseases) are most important followed by food quality traits and abiotic stress resistance (drought, heat). Herbicide tolerance as well as industrial applications seem to be of minor interest. Other applications include flavour related traits, shelf-life related traits, digestibility of fodder crops, ornamental value (flower colour) as well as post-harvest quality (e.g. of flowers and vegetables).

The data collected by the Euroseeds survey are comparable to the study of Modrzejewski et al., 2019 (38). Compared to the data from published research studies companies put a stronger focus on biotic and abiotic stress tolerance. This might be due to the requirements of a climate smart and more sustainable agriculture in which farmers as the direct customers of breeders request these characteristics due to climate effects (drought/heat) and the restrictions in use of pesticides (Figure 11 of file 20.0242).

* **11. Are you aware of other NGT-related research in your sector?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please specify

In addition to our input to question number 1, 3 and 10 we are aware of the following activities.

The German JKI analysed NGT related research studies between 1996 and 2018 on a global level (39). Their analysis shows that Asia is leading in relation to applying and publishing genome-editing research in plants (53%) followed by North America (34%) while Europe (13%) is left behind. In total, publications from 33 countries were identified with China in the lead in the number of studies (40%).

A study on CRISPR-Cas9 Application in Canadian Public and Private Plant Breeding (40) asked whether respondents intend to use CRISPR-Cas9 in plant-breeding research over the next 3 years. “Of 88 respondents, 66% stated they anticipate using CRISPR-Cas9 versus 34% not planning to. Of those respondents, 32 from the public and 26 from the private sector anticipated using CRISPR-Cas9 in the near future. This suggests the private sector is more open to future CRISPR-Cas9 use (74%) compared to public breeders (60%).”

The publication “Plant Genome Engineering for Targeted Improvement of Crop Traits” (41) lists in table 1 a number of applications of genome editing tools in different plant species to improve yield, biotic, and abiotic stress resistance, and nutritional quality.

The publication “CRISPR/Cas System: Recent Advances and Future Prospects for Genome Editing”(42) lists in table 2 a number of applications of the CRISPR/Cas9 System in major crops.

The publication “Genome Editing for Crop Improvement – Applications in Clonally Propagated Polyploids With a Focus on Potato (Solanum tuberosum L.) (43) specifically lists in table 1 genome editing case studies in clonally propagated crops and elaborates on the specific challenges for applying NGTs to those crops. A concrete example for genome editing application in potato with an improved starch quality can be found in the attached file 19.0357. Another concrete example from Italy includes fungi-resistant grape vine that drastically could reduce pesticide use in grape vine production (file 20.0275).

Also, for horticultural crops the application of NGTs provides additional opportunities to create new genetic diversity. As Li et al., mention: “Directed breeding of horticultural crops is essential for increasing yield, nutritional content, and consumer-valued characteristics such as shape and colour of the produce. However, limited genetic diversity restricts the amount of crop improvement that can be achieved through conventional breeding approaches. Utilization of CRISPR/Cas editing in crop species can accelerate crop improvement through the introduction of genetic variation in a targeted manner”(44) .

* **12. Has there been any immediate impact on NGT-related research in your sector following the Court of Justice of the EU ruling on mutagenesis?**

Court of Justice ruling: Case C-528/16 http://curia.europa.eu/juris/documents.jsf?num=C-528/16

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please describe

In our Euroseeds survey we asked if R&D activities of Euroseeds members for applying NGTs changed after the 25 July 2018 ECJ ruling on mutagenesis breeding (Figure 13 of file 20.0242).
Around 30% of the SMEs and 20% of the large companies stopped or reduced their activities after the ECJ ruling. Those companies who have major markets outside the EU moved the focus of their product development with NGTs to markets outside the EU. In this context it needs to be recognized that less SMEs are currently involved in the development of NGT products, but for the time being use NGTs specifically for gene discovery research or in development of enabling technology, which is not that much affected by the ruling since it does not result in a regulated product according to Dir. 2001/18.
We assume that the negative impact on volume of R&D activities for commercial product development is actually higher than suggested by the pure number of companies as it is mainly bigger companies with respective big R&D spending that have moved activities outside of the EU. This is confirmed by a study from University of Wageningen scientists who did a survey among Dutch breeding companies that shows that "companies with markets outside the EU intend to reallocate their research"(45).
For the majority of SMEs who have their major market within the EU moving their research or their product focus to non-EU markets is not an option. A lot of company NGT projects were re-evaluated, some were put on hold and activities were modified in specific cases. These include discontinuation of projects, reduction of scope, change of market focus and re-evaluation of timelines. Also, some projects did not start as a consequence of the ECJ decision.
The Dutch study confirms the a strong negative effect of the decision of the CJEU on the investments in CRISPR-Cas technology especially for the vegetable sector (45)45.
The regulatory uncertainty pertaining to products of NGTs is not due to scientific concerns, but rather political interference in the regulatory approval process. Given the highly competitive market for strategic agricultural and food investments, the level of uncertainty that exists within the EU has the potential to divert potential research and development investment away from the EU to markets with more science-based, risk-proportionate, and innovation-supporting regulations (46). Uncertainty and irreversibility have a strong effect on postponing investment in R&D with NGTs (47).
The data of our internal Euroseeds survey confirm this. Around 40% of the companies who want to bring products to the market delayed their intended market release due to regulatory reasons (e.g. GMO regulation in the EU, lack of international harmonization, lack of clarity on how the GMO legislation could be implemented effectively, lack of legal certainty in the EU since 13 years as well as lack of legal certainty for all NGTs except targeted mutagenesis – see our replies to question 6). This shows that the regulatory situation in Europe already has an impact on R&D as well as the innovation capacity and product development also on a global level.
Also, there is uncertainty among young researchers about the impact of the court ruling on the future perspectives in plant sciences in Europe. This is illustrated by the fact that different groups of young researchers have started raising their voices with the goal to enable the use of genome editing for sustainable agriculture and food (48) ,(49), (50). If NGT related research in Europe is negatively affected by the current regulatory situation this also has a negative impact on the seed sector since these young scientists are the future employees of our companies.
The negative effect of disproportionate regulatory requirements on public investment in breeding is also confirmed by a Canadian study which concluded that public breeders have had limited capacity to apply transgenic breeding techniques within their programs due to the additional time and cost required to receive regulatory approval (51).

*** 13. Could NGT-related research bring benefits/opportunities to your sector/field of interest?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide concrete examples/data

In the context of the Euroseeds Survey we asked our members to indicate for which kind of activity and for which crops/traits they see the highest future potential for the application of new breeding methods (Figure 17 of file 20.0242). The results show that independent of their size companies see future opportunities for NGTs in all kind of crops and activities as well as for all kind of traits. These activities include technology development (e.g. new/improved genome editing tools), development of enabling technologies (transformation protocols/ tissue culture/ regeneration), use of NGTs as a breeding tool e.g. to improve recombination frequency and with that genetic diversity or for gene discovery research to better understand the function of genes. In addition, breeders see opportunities to improve agronomic value traits (yield/plant architecture), food/feed quality traits, biotic stress tolerance, abiotic stress tolerance as well as herbicide tolerance or traits in the context of industrial applications of plants like e.g. starch production. Other traits include improvement of nutrient use efficiency to reduce the fertilizer or water input in agriculture. Especially the improvement of biotic stress resistance is driven by the lack of availability of pesticide active substances as well as the intended reduction of pesticide use. A relevant number of companies mention in their comments that the development of herbicide tolerant crops is not an option they are pursuing due to a perceived lack of societal and political acceptance in the EU.
The outcome of the Euroseeds survey is confirmed by a study with Canadian plant breeders. They highlighted different aspects of precision breeding with CRISPR-Cas9. These include precision editing without disruption to the remainder of the genome, the confirmation of genes of interest (which the Euroseeds survey addresses as gene discovery research), cost reduction, and the recent democratization (improved freedom to operate) of CRISPR-Cas9. The study also highlights that precision-breeding capabilities stand out as benefits, allowing plant breeders an increasingly greater ability to target and control the intended mutations. By far, the most significant benefit recognized by 90% of all respondents was that of potentially reduced regulatory oversight of CRISPR-derived varieties, mostly in comparison to transgenic GM breeding technologies (52).

*** 14. Is NGT-related research facing challenges in your sector/field of interest?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please provide concrete examples/data

In the Euroseeds survey, Euroseeds members were asked to indicate the top three factors they see as most significant in limiting the potential of the use of new breeding methods.
These are:

1) Regulatory costs and timelines
2) Legal certainty and future regulatory oversight including timelines for product approvals
3) Public acceptance under GM regulation

These issues are acknowledged also by leading scientists in the field confirming that the high level of regulatory uncertainty and differences between countries represent a bottleneck in harnessing NGTs like CRISPR technology for crop improvement (53).
Access to relevant intellectual property (IP) was mentioned as a potential limiting factor by SMEs while this is not a priority issue raised by large companies.
Some SMEs also mention limited resources when it comes to technology expertise or R&D investments as a hurdle for using NGTs in their companies. For these companies the opportunity to use NGTs in public private partnerships is of importance to enable the use of NGTs. (Figure 14 of file 20.0242)
In addition, companies mentioned that their R&D strategy is dependent upon market size, regulation of NGTs as well as technology readiness for a particular crop. For instance, the work on trait development is not a priority for vegetables under the current regulatory framework in the EU. Even large commodity crops like wheat and rice can in many cases may not recoup the high bring-to-market costs which go along with the regulatory hurdles for GM crops.
NGTs could be applied relatively easily to most crops (a tissue culture system is prerequisite), but GM-regulatory requirements would take away the advantage of shorter development timelines. This has the consequence of limiting diversity and trait development options for niche crops which could also impact the range of existing agricultural systems.
From the comments provided by companies it becomes clear that a lot of companies restrict applications in their R&D activities to regions outside EU or to products for the non-EU market if they result in a GM regulated product in the EU. Since larger companies have a higher share of R&D facilities outside the EU, it is easier for them to also benefit from the use of NGTs for concrete product development outside of the EU market.
In view of the current regulatory situation in the EU especially the lack of GM field trial capacities was mentioned as a bottleneck for the application and optimisation of NGTs. This also negatively affects gene discovery research activities since the effect of the function of genes on the plant phenotype often needs to be checked under field conditions. Additionally, a potential for field destructions of GMO trials by activists, as occurred in the past for field trials of transgenic products would not only mean loss of high value material (limited seed quantities in early breeding phases), but also loss of data and time, plus high effort and resources required for communication and regulatory activities etc..

Other challenges relate to the legal uncertainty regarding the regulatory status of additional NGT applications that were not concretely addressed by the ECJ ruling on mutagenesis breeding. These include approaches like allele replacement, re-introduction of resistance genes from plant genetic resources by cisgenesis approaches (54) or the use of dsRNA to increase genetic diversity by enhancing recombination during cross breeding (55).
Challenges in view of moving or stopping research activities see our answer to Question 12
Challenges of complying with GMO regulation in view of providing a detection method when it comes to field trials for NGT related research see our comments on Question 9.

*** 15. Have you identified any NGT-related research needs/gaps?**

- (●) Yes
- ( ) No
- ( ) Not applicable

* Please specify which needs/gaps, explain the reasoning and how these needs/gaps could be addressed

When asked about opportunities for NGTs in the context of our Euroseeds Survey, companies also commented on research needs and gaps. The following points were addressed:
Especially for smaller and minor crops as well as a broad range of vegetables the development of enabling technology (transformation protocols/ tissue culture/ regeneration) to apply NGTs in these crops is seen as a need for further R&D investments. This is specifically interesting for SMEs since they are more active in breeding of these smaller and niche crops.
Companies mention the need for development of enabling technology to overcome restrictions due to genotype effects or to make modern breeding techniques available for recalcitrant crops; e.g. in vitro regeneration is still a bottleneck for sunflower, pulses or certain cereal species …).
Also, the use of NGTs as a breeding tool to generally improve genetic gain by increasing recombination rate (56) and to increase genetic diversity by overcoming linkage drag is mentioned. For this, gene editing technologies might be used, but also other technologies (e.g. treatment of plants with dsRNA) that do not result in a permanent genetic change in the genome. These products do not show a specific characteristic resulting from the application of an NGT, but a higher general recombination rate during crossing which will result in an increased genetic variability.
The development of multiplex applications which allow addressing several alleles responsible for one characteristic or several characteristics in parallel s is a clear need especially for polyploid species and for crops with long generation times like fruit tree.
The way how NGT tools like CRISPR-Cas are delivered to the plant cell may include an intermediate step including recombinant DNA. Newer developments go into the direction of using DNA-free transformation systems. These have two major problems that also depend on the plant species: (i) Delivery through the plant cell wall and (ii) regeneration of plants from tissue or protoplasts (57). Research needs to also include the development of reliable DNA-free editing systems for diverse crop species.
The further and additional development of new NGT tools like base editor technologies is mentioned as well.
As indicated in our reply on question 1 the R&D activities with NGTs take place in different forms independent of the company size (Figure 5 of file 20.0242). Our data suggest that SMEs more strongly rely on public private partnerships compared to large companies. The above-mentioned needs/gaps need to be addressed by public and private research. Adequate public research funding especially also for public private partnerships will specifically support SMEs in addressing their respective research needs and gaps.
Public support of basic research for NGTs is equally important especially in view of the further development of the NGTs as well as their applicability to a wide range of species. In this context the financial support of genome research including whole genome sequencing of recalcitrant crops is important.
No research activity and public funding will overcome the regulatory hurdles and costs associated with the current GMO regulation and when it comes to the requirements of providing detection and identification methods as soon as plants are supposed to be released for field trials.

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C - Information on potential opportunities and benefits of NGTs/NGT-products

*** 16. Could NGTs/NGT-products bring benefits/opportunities to your sector/field of interest?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Independent of already ongoing activities of companies (see question 1,3 and 10) we asked our company members in the context of the Euroseeds survey if they would invest in product development with new breeding methods for the EU market, if the varieties would not be regulated as GMOs, but as conventional varieties. 100% of the larger companies, 86% of the medium sized and nearly 70% of the small companies would (further) invest in R&D with NGTs if products would not be regulated as GMOs which means that those companies see opportunities. (Figure 15 of file 20.0242)

In the context of the Euroseeds Survey we asked our members to indicate for which kind of activity and for which crops/traits they see the highest future potential for the application of new breeding methods. The results show that independent of their size companies see future opportunities for NGTs in all kind of crops and activities as well as for all kind of traits. (Figure 17 of file 20.0242) These activities include technology development (e.g. new/improved genome editing tools), development of enabling technologies (transformation protocols/ tissue culture/ regeneration), use of NGTs as a breeding tool e.g. for the improvement of recombination and with that genetic diversity or for gene discovery research to better understand the function of genes. In addition, breeders see opportunities to improve agronomic value traits (yield/plant architecture), food/feed quality traits, biotic stress tolerance, abiotic stress tolerance as well as herbicide tolerance or traits in the context of industrial applications of plants like e.g. starch production. Other traits include improvement of nutrient use efficiency to reduce the fertilizer or water input in agriculture. Especially the improvement of biotic stress resistance is driven by the lack of availability of pesticide active substances as well as the intended reduction of pesticide use. A lot of companies mention in their comments that the development of herbicide tolerant crops is not a priority (only ~8%) for them due to a perceived lack of societal and political acceptance.
A survey among Dutch plant breeders confirmed that nearly half of the respondents agree or strongly agree with the statement “The use of CRISPR-Cas technology plays an important role within the development of the products of our company”(58).

* Are these benefits/opportunities specific to NGTs/NGT-products?

- (●) Yes
- ( ) No

* Please explain

NGTs add to the toolbox which allows breeders to more efficiently develop plant varieties that meet rapidly changing needs for farmers, food producers and consumers. Depending on the problem a breeder needs to solve, he or she relies on the tools that are most adequate to solve the problem. Some tools are interchangeable, but each tool has its respective advantage in view of efficiency, speed and precision to solve a problem. Some breeding goals might also be achieved with older breeding tools, but at the expense of speed and precision. Depending on the crop species conventional plant breeding takes around 9-11 years until a new variety can be released to the market (59). NGTs allow reducing this time to market significantly (61). If EU breeders are restricted to use specific tools due to restrictive and disproportionate regulations, they will face a competitive disadvantage in comparison to breeders in other parts of the world with more enabling regulations. Also, certain breeding goals, like e.g. resistances against new and upcoming pests and diseases in the context of changing climate conditions might not be achieved in time. The consequences would directly be imposed onto EU farmers who would need to use more pesticides in order to avoid crop losses. Otherwise, harvests will be reduced and Europe will become even more dependent on food imports. Certain breeding goals are not achievable at all with older breeding tools in terms of costs and timelines (especially in polyploid and vegetatively propagated crops). The consequence would be that EU farmers, consumers and the environment will not benefit from respective varieties or only with undue delay. NGTs allow that “genetic variation in specific characters can be introduced into elite varieties without simultaneously transferring genetically linked DNA or other unwanted DNA. This means that a number of generations of backcrossing to a parental line can be skipped in contrast to what is the case with conventional cross breeding or breeding through random mutagenesis”(60),(61) .

* **17. Could NGTs/NGT-products bring benefits/opportunities to society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic benefits?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

NGTs allow a more targeted, more efficient, more widespread and quicker introduction of genetic variation into crops for agriculture and food production. A wide range of applications were analysed in a metastudy by Modrzejewski et al. (62) Other examples are listed here (63),(64) ,(65) under question 3 as well as in the references mentioned there. These include, but are not limited to:
- improved resistance against diseases to be able to use less pesticides in a more sustainable agriculture (e. g. mildew resistant wheat, fungal resistant grapevine (file 20.0275), tomato or grapefruit resistant against citrus canker)
- improved resistance against abiotic stress in order to mitigate climate change effects on our food production (e.g. drought tolerant maize or wheat)
- improved agronomic traits in order to boost crop yields, improve productivity, and avoid pre-harvest losses (e.g. wheat with increased grain weight, shatter-resistant oilseed rape, cucumber with female flowers only)
- improvement of quality traits (altered starch composition in potato that allows more environmental friendly and clean starch production(66)) or health related traits (e.g. high-fibre wheat, low-acrylamide potato, low gluten wheat or a high oleic acid soybean, the first NGT product on the US-market) or reduction of antinutrients (e.g. oilseed rape with reduced phytic acid content).

* Under which conditions do you consider this would be the case?

The decision to invest in NGT related R&D for improved plant varieties strongly depends on the regulatory requirements. Undue regulatory burden specifically influences investment decisions of small companies (Figure 16 of file 20.0242). If respective R&D activities are limited to a smaller number of companies and with that a smaller number of crops and traits, society will less benefit from them. An enabling regulatory framework is therefore key.
The role of NGTs to contribute to a sustainable future was highlighted by the World Resources Institute (67). They concluded that fully closing the gaps requires many innovations, these include plant breeding. The report states that “A revolution in molecular biology opens up new opportunities for crop breeding. Progress at the necessary scale requires large increases in R&D funding, and flexible regulations that encourage private industry to develop and market new technologies.”
Also, in view of meeting the sustainable development goals (SDGs) breeding innovations must play a role (68). At the core of the SDGs is global agriculture and it will have to increase the quantity and the quality of food production in order to ensure greater access to healthy diets. As Aerni, 2019 (69) rightly states: “Simultaneously, agriculture must become more sustainable by reducing the use of fertilizer and means of plant protection. The combination of objectives can only be achieved by means of sustainable intensification, which includes the genetic improvement of plants so that they become more tolerant to biotic and abiotic stress factors, make better use of photosynthesis and soil nutrients, and enhance the nutritional value of basic food crops. Conventional plant breeding may still be able to address some of these challenges, but it is time-consuming and cannot be tailored well to local preferences, which results in low adoption rates. New breeding techniques have the potential to address these drawbacks.”
Also, the Swedish Board of Agriculture acknowledged in a report from December 2018 (70) : “The loss of investments in plant breeding due to the ECJ ruling could result in a less climate-adjusted agriculture that cannot persevere in a changing and erratic climate. To be able to meet the challenges that we are facing in the environmental area and with a changing climate, we need varieties with increased resistance to different pests, an improved use of plant nutrients, efficient use of water, tolerance to drought and flooding and adjustments to changes in cultivation systems.”
Euroseeds has further elaborated on the contribution of plant breeding in general and plant breeding innovation specifically to the Commissions ambitions in the context of the Green Deal and its Farm to Fork Strategy (71).
Also the updated EU-Commission Strategy “A sustainable Bioeconomy for Europe: strengthening the connection between economy, society and the environment” acknowledges the role of technological development in breeding for a sustainable Bioeconomy: “Technological development, innovations and digitisation (e.g. precision farming, nature-based solutions, breeding) are significantly improving the potential for higher resource efficiency, decreased environmental and climate impact, increased resilience and decreased costs”(72).

* Are these benefits/opportunities specific to NGTs/NGT-products?

- (●) Yes
- ( ) No

* Please explain

NGTs add to the toolbox which allows breeders to more efficiently develop plant varieties that meet farmers, food producers and consumer's needs. A breeder needs to rely on the tool that is most adequate to solve the given problem. Some tools are interchangeable, but each tool has its respective advantage in view of efficiency, speed and precision to solve a problem. Some breeding goals might also be achieved with older breeding tools, but at the expense of time and precision. CRISPR technology can e.g. accelerate crop domestication. Increasing current crop diversity is one of the most powerful approaches for promoting sustainable agricultural systems, and the domestication of neglected, semi-domesticated or wild crops would increase such diversity (73). If breeders are restricted to use a limited set of tools due to restrictive regulations, they will face a competitive disadvantage in comparison to breeders in other parts of the world with more enabling regulations. Also, certain breeding goals, like e.g. resistances against new and upcoming pests and diseases in the context of changing climate conditions might not be achieved in time. The consequences would be that farmers would need to use more pesticides in order to avoid crop losses or harvests will be reduced and Europe become more dependent on food imports. Certain breeding goals are hardly achievable with older breeding tools. The consequence would be that farmers, consumers and the environment will not benefit from improved varieties.
In view of consumer acceptance, studies indicate that products from specific applications of NGTs (as referred to in our contribution) are more accepted by consumers compared to transgenic products especially if those products provide health or environmental benefits compared to conventional products (74).

* **18. Do you see particular opportunities for SMEs/small scale operators to access markets with their NGTs/NGT-products?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Independent of already ongoing activities of companies (see question 1,3 and 10) we asked our companies in the context of the Euroseeds survey if they would invest in product development with new breeding methods for the EU market, if the varieties would not be regulated as GMO, but as conventional varieties. Nearly 70% of the small and 86% of the medium sized companies would invest in R&D with NGTs if they would not be regulated as GMO's which means that those companies see particular opportunities (Figure 15 of file 20.0242).This shows that an enabling regulatory framework is therefore key.
In the context of the Euroseeds Survey we asked our members to indicate for which kind of activity and for which crops/traits they see the highest future potential for the application of new breeding methods. The results show that independent of their size companies see future opportunities for NGTs in all kind of crops and activities as well as for all kind of traits. See also our reply to Question 17 which is confirmed by the Dutch survey (75) as well as the Canadian study (76). SMEs are generally more active in using NGTs also for minor crop species which would provide specific opportunities for those companies to better address niche markets demands and increase the competitiveness of those crops (see also our reply to question 10). Our Euroseeds survey also shows that any kind of regulatory obligations in addition to regular variety registration influence specifically the decision on SMEs to invest in product development with NGTs. Also, because most SMEs have their major market within the EU, moving R&D activities out of Europe or changing focus of product development to non-EU markets is not an option (Figure 16 of file 20.0242). Analysis of the USDA "Am I regulated?"(77) inquiries in the US and Argentina NGT product consultations shows that over 75% of the applicants were SMEs or public developers (78), meaning that especially SMEs engage in plant breeding with NGTs if the regulatory environment is transparent and enabling.
Whelan et al. analysed the situation for Argentina which does exempt certain non-transgenic NGT products from their biotech regulations and concluded that NGT products seem to follow a much faster development rate from bench to market compared to transgenic GMO's and that this development is driven by a more diverse group of developers, and led mostly by small and medium enterprises (SMEs) and public research institutions (79).

*** 19. Do you see benefits/opportunities from patenting or accessing patented NGTs/NGT-products?**

- (•) Yes
- ( ) No

* Please describe and provide concrete examples/data

Benefits/opportunities from patenting NGTs/products obtained by NGTs:

Yes, patenting creates benefits and opportunities for the patent holder.
New genomic techniques could only be patentable provided they meet the patentability requirements of novelty, inventive step, industrial applicability and enabling disclosure. Under similar conditions, products obtained by new genomic techniques could be patentable. Products can only be patentable if they have not been obtained by an essentially biological processes as outlined in the decision of the EPO's Enlarged Board of Appeal in case G 03/19. Having a patent means having exclusive rights, a benefit, and consequently having strong business opportunities.
Under the sui generis IP system of plant breeder's rights one can protect new plant varieties as such. However, it is not possible to protect innovative breeding techniques under this sui generis IP system, therefore patent protection offers opportunities and benefits for the innovators of these technologies. Patents enable patent holders to recoup R&D and regulatory costs. This further allows patent holders to re-invest in innovation. Patents disclose information on the patented technology which can also provide benefits to others.

Benefits/opportunities from accessing patented NGTs /products obtained by NGTs:

It is rather likely that in the coming years more parties will apply for patents related to NGTs and products obtained by NGTs, but these patents might depend on a limited number of essential patents*.
In case of patents in the field of plant-related inventions, there are certainly benefits from being able to access both the patented technology and the products that might be falling under the patent protection. This is because in plant breeding free access to the widest possible gene pool is key for breeders to be able to continue developing new varieties responding to needs of society and the challenges we face. This principle of free access to and flow of genetic material is enshrined in the so-called breeder's exemption under the UPOV 1991 convention. The UPOV convention is an international convention under the aegis of WIPO which sets out the international standards of plant variety protection, a sui generis IP right for protecting new varieties of plants. Under the breeder's exemption, anybody can use a protected plant variety for the purpose of breeding or developing a new plant variety. This exemption has been largely relied upon by breeders and contributed to the development of the seed industry worldwide.
Therefore, it is of key importance that there is access to the genetic material even if such genetic material is falling under the scope of a patent on an NGT or a product obtained therefrom.

It is important that all other actors of the plant breeding sector can access NGTs because these techniques have a huge potential and can technically also be applied by small companies. Euroseeds, in principle, encourages licensing on fair, reasonable and non-discriminatory (FRAND) terms.
For more complete information, please refer to the Euroseeds Position paper on IP protection for plant-related inventions in Europe (80).

*Essential patents refer to those patents that cover key technology which is a "must-have" for the actors within the sector

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D - Information on potential challenges and concerns on NGTs/NGT-products

* **20. Could NGTs/NGT-products raise challenges/concerns for your sector/field of interest?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Currently, there is no harmonized international approach when it comes to the regulations applicable to products of these new breeding methods including genome editing. However, most countries which already implemented or currently finalise new or updated policies follow the principle approach that only products with a novel combination of genetic material as laid out in the living modified organisms (LMO) definition of the Cartagena protocol (Cartagena Protocol on Biosafety 2000) are in the scope of their biotech regulations. This includes e.g. several South American countries (81).
Already some years ago, the global seed industry started an initiative to encourage countries to agree on a consistent approach to the scope of regulatory oversight for products of the latest plant breeding methods. The first step towards consistency is agreement amongst countries on the criteria that would be used to determine the scope of regulatory oversight (82).
Differing requirements will limit (reduce and slow down) the capacity of the industry to innovate; reduce the diversity of plant genetic resources; have a negative effect on research collaborations; and hinder the movement of germplasm and seed globally. In addition, commodity trade disruption will occur, and agricultural development and food security will be impeded.
Within the WTO the challenge of trading NGT products (commodities and seeds) under the current lack of global harmonization was recognized. In a statement “Agricultural Applications of Precision Biotechnology” countries mention that differing domestic regulatory approaches for products derived from precision biotechnology may result not only in internationally asynchronous approvals, but also in asymmetry of regulatory approaches, and create potential trade issues that could impede innovation. They call upon governments to exercise due consideration to avoid arbitrary and unjustifiable distinctions between end products derived from precision biotechnology and similar end products obtained through other production methods (83) .
In 2017, plant reproductive material of a total value of around 12 bn $ was exported by countries globally (84). This represents around 20% of the value of the global seed market. The lack of global harmonization of regulatory policies regarding products resulting from NGTs in combination with the lack of molecular identification options of NGT products specifically affects the seed industry since in the seed business more than 98% of the European companies active in R&D with NGTs are operating at an international level (Figure 3 of file 20.0242).

* Are these challenges/concerns specific to NGTs/NGT-products?

- (●) Yes
- ( ) No

* Please explain

The lack of global harmonization in regulatory policy approaches specifically concerns NGTs. Transgenic GMOs in all countries require pre-market assessment. While specific regulatory requirements as well as timelines and costs lack harmonization for transgenic GMOs, there is clarity as regards what products fall under these specific requirements. As shown above, there is a growing number of countries worldwide that either have already set or are in the process of setting rules that clearly differentiate between transgenic products (GMOs) and products obtained by NGTs; the only jurisdictions where transgenic GMOs and NGT derived products are clearly subjected to the same GMO rules is the EU and New Zealand.
Also, the challenge to detect and identify NGT products and with this enforce respective regulations (see our replies to questions 2,4,5 and 7) in regions where NGT products require pre-market assessment is a challenge specific to these products.

* **21. Could NGTs/NGT-products raise challenges/concerns for society in general such as for the environment, human, animal and plant health, consumers, animal welfare, as well as social and economic challenges?**

- ○ Yes
- ◉ No

* Please explain why not

Plant breeding has a long history of continuous innovation (see also(85)). Since the discovery of the laws of heredity by Gregor Mendel plant breeders have developed improved breeding methods to make the two major steps in breeding: a) increasing genetic diversity, and b) selecting the best performing plants, more targeted and efficient. Starting with intentional cross breeding at the beginning of the 20th century, the first concepts for hybrid breeding were introduced during the 1920's. One major goal of breeding is to continuously make use of or increase genetic diversity. First attempts to increase genetic diversity by technical means started in the 1930's with using radiation or chemicals to induce random mutations in the plant's genome followed by intense selection procedures to find valuable new traits. New molecular tools of precision breeding help breeders to do their job in an even more precise manner compared to the past. Especially the new tools for genome editing, like CRISPR–Cas provide mechanisms to not only randomly increase genetic variation as it was done by radiation or chemical mutagenesis but also to precisely introduce mutations in genes of known functions to either impair or improve their function. With this, these precision breeding tools can create plants that might also have been produced by conventional breeding methods. These plants would in most cases not be distinguishable with respect to the breeding methods that have been used to create these plants (86). This continuation of innovation towards targeted precision breeding will be essential for economic, social and environmental benefits at large scale and should indeed be considered a highly effective measure for adapting to new and very dynamic settings (87). Regulatory oversight that prevents, slows down or delays the development and marketing of NGT plant varieties will:
prevent farmers in EU to use respective NGT plant varieties, which will put efforts towards more sustainable farming at risk
prevent the use of less pesticides because farmers cannot access more resilient NGT varieties that are resistant against pests and diseases,
put plant health at risk and make farmers less competitive
lead to a situation where certain NGT products with clear consumer benefits (low gluten wheat, low allergenic peanut) might not be available to EU consumers.

Safety considerations are addressed in Q25

By not adopting NGT products, Europe will face challenges to meet its own ambitions to contribute to the numerous SDGs and the targets of the Green Deal Strategy as long as the current process-based regulation continues to be defended by certain European stakeholders in disregard of scientific evidence and being solely motivated by their own business interests(88) .
In view of potential societal/consumer concerns we refer to the Eurobarometer on Food Safety 2019. Only 21% of EU consumers know about gene editing as one of the NGTs and only 4% have specific concerns when it comes to food safety(89) . A recent survey among Norwegian consumers found that "Norwegian consumer attitudes towards the use of gene editing (which was defined as targeted genetic changes without insertion of new DNA) depend on the purpose and what the product is used for (e.g. reducing pesticide use & crop losses, climate adaptation of crop plants, increasing nutrient content, increasing crop plant yields…" (90) . In another international study respondents indicated they would consume both GM and CRISPR food" (91) . Most studies conclude that attitude and acceptance change with knowledge, which shows the need for balanced information and the importance of science as well as risk communication(92) . It is the responsibility of all stakeholders including authorities, to translate science into laymen language and with that facilitate informed decisions of consumers and informed political debate.

* **22. Do you see particular challenges for SMEs/small scale operators to access markets with their NGTs /NGT-products?**

- (●) Yes
- ( ) No

* Please explain and provide concrete examples and data

The Euroseeds Survey asked companies to indicate the top three factors they regard as most significant in limiting the potential of the use of new breeding methods.
Regulatory costs and timelines are the most important factors limiting the use of NGTs, independent of company size. Also, company reputation as long as NGTs are regulated under GM legislation is mentioned as an important aspect hindering companies to develop NGT products. (Figure 14 of file 20.0242)
Access to relevant IP is seen as a potential limiting factor by SMEs while this is not a priority issue for larger companies.
Some SMEs mention limited resources when it comes to technology expertise or R&D investments as a hurdle for using NGTs in their companies. For these companies public funding and the opportunity to use NGTs in research collaboration (e.g. public private partnerships) is of importance to enable those companies using NGTs. If public funding is reduced as indicated by some research institutes after the ECJ ruling, SMEs are specifically affected due to their higher level of engagement in pubic private partnerships.
When asked about the effect of the ECJ ruling on their R&D activities, for most SMEs who have their major market within the EU moving R&D activities out of Europe or changing focus of product development to non-EU markets is not an option. In addition, some SMEs replied that all projects were re-evaluated, some projects were put on hold and activities were modified in specific cases. (Figure 13 of file 20.0242) These include discontinuation, reduction of scope, change in market focus and re-evaluation of timelines. Also, some programs did not start as a consequence of the ECJ decision and companies put projects on hold to keep watching the future developments in the EU. The consequence is that especially SMEs lag behind while large companies can continue developing and applying NGTs in other parts of the world with more enabling regulations while under the current regulatory system in Europe they will not be able to bring products to the market.
Also, in view of the international situation with different regulatory policies in place, the challenge for SMEs to comply with these diverse requirements is higher than for large companies. This reduces the competitiveness for EU SMEs (93).
It can be summarized that any additional regulatory requirements to those already applicable to all plant breeding products, including specifically excessive authorisation costs, the time needed for assessment and authorisation are particularly prohibitive for smaller-scale companies.

*** 23. Do you see challenges/concerns from patenting or accessing patented NGTs/NGT-products?**

- (●) Yes
- ( ) No

* Please describe and provide concrete examples/data

Challenges/concerns from patenting/accessing patented NGT-products:

Due to the nature of plant breeding, patentability of plants and/or products derived from NGTs will have a significant negative impact on the free access to genetics for further breeding and improvement since such patents can eventually block others. Regarding NGT-products that may be falling under the scope of patent protection, it is of key importance that access to the genetic material can still be guaranteed since this is what allows breeders to continuously build on each other's inventions and develop ever new and better varieties.
In order to improve accessibility, a limited breeder's exemption would be necessary to be incorporated in national patent laws. (NB: such exemption exists already in a number of national patent laws such as DE, FR, CH, NL, BE). The limited breeder's exemption however still requires that a license is sought from the patent holder if the newly bred variety still contains a patented element. Such licenses should be granted on FRAND terms.
This would be an improvement. However, in order to understand the full problem and see these improvements in perspective, please refer to the Euroseeds Position paper on IP protection for plant-related inventions in Europe (94).

Challenges/concerns from patenting/accessing patented NGTs:

As regards the technology, it is likely that in the coming years more parties will apply for patents related to NGTs but these patents might depend on a limited number of essential patents*.
On the other hand, it is important that all other actors of the plant breeding sector can access NGTs because these techniques have a huge potential and can technically also be applied by small companies. As mentioned before, Euroseeds, in principle, encourages licensing on FRAND terms.
GMO regulation requires the developer of the technology to impose stewardship requirements, which is necessary for ensuring the sustainable and responsible use of the technology but renders the exclusive right stronger and makes licensing more complicated. This poses a challenge on providing access to technology (and to obtained products).
At the same time, the high costs of GMO regulation and the constraints that come with it will imply that no SMEs at all will be able to afford seeking market approval for products developed using NGTs. Consequently, smaller companies will also not have much IP to rely on in licensing negotiations. This renders smaller companies very much dependent on the patented products and on those that can afford the deregulation costs.
As far as the extension of method claims (i.e. claims on NGTs) to the obtained products is concerned, freedom to operate in the field of crossing and selection should be safeguarded and therefore the development of a product with the same characteristics via the use of an essentially biological process and without using the patent holder's material should not be covered by the effect of a patent.
If products resulting from NGTs will continue to be regulated as genetic modification, then the methods and these products will definitely not be available for most breeders as only the large companies can bear the deregulation costs. Further on, GMO regulation of NGTs and resulting products will not only have a consolidation effect at the level of seed companies but also at the level of crops and traits since deregulation costs may be affordable for the largest crops but won't be bearable for smaller crops or traits that are used for smaller markets. Breeding companies might also have as a policy not to become active in regulated crops.

*Essential patents refer to those patents that cover key technology which is a "must-have" for the actors within the sector

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E - Safety of NGTs/NGT-products

*** 24. What is your view on the safety of NGTs/NGT-products? Please substantiate your reply**

As stated in the beginning of this questionnaire, we focus on those applications of NGTs that lead to plants that could also have been the result of earlier breeding methods or might have been obtained from natural processes without human intervention as to the Euroseeds position. In this regard we do not consider that additional safety assessments/testing as done for conventional varieties (see below) are necessary.
Public and private breeders develop varieties and these varieties are propagated through seeds. Today 42.000 varieties are available for farmers in the EU (around 3.500 new varieties each year) and the seeds of these varieties are mostly used to produce feed & food or food components. Breeders, multipliers and seed traders are at the starting point of the agricultural feed & food production chain.
Plant breeding is often said to be a process not (only) of selection, but (foremost) of elimination. Any off-types, unstable lines, or lines showing characteristics such as significant differences in nutrient content, detrimental responses to environmental stresses, diseases, or the presence of other undesirable traits are discarded as soon as they are identified. The generation of genome-wide variation is part and parcel to traditional plant breeding whether by crossing or induced mutation (e.g. with NGTs). This is addressed within well-established practices for crop improvement and by breeders best practices which document relevant phenotypic characteristics (95) . “Therefore, while process-based considerations and characterization of genome level effects may prove somewhat useful in the problem formulation for a given case of genome editing, the nature of the derived product would seem the stronger focus for any subsequent risk/safety assessment which may be conducted” concludes Wolt in his publication on “Current risk assessment approaches for environmental and food and feed safety assessment”(96) .
The environment in which a crop is grown often plays a significant role in affecting plant characteristics, such as the levels of certain anti-nutrients, overall yield and flowering. Therefore, the trialling process occurs over multiple geographies and multiple years in order to observe that potential variability, keeping only those varieties that will meet consumer and grower expectations and show reliable performance under different environmental conditions.
Independent of the breeding technology used, potentially commercial varieties are tested for:
• Geographic and agricultural/horticultural production system adaptation
• Performance characteristics, relative to existing commercial varieties
• Processing characteristics appropriate for that crop, such as milling for wheat, sugar yield for sugar beets, oil quality for canola and sunflower or storage characteristics for fruits and vegetables
• End-user characteristics (as appropriate for that crop), such as protein content or bread-making characteristics for wheat, oil quality for oilseed rape or flavour characteristics for vegetables and fruits
• Regardless of the tools used for breeding, the goal is always the same: To first create genetic diversity in a population of plants and through multiple years of field trials and testing develop new plant varieties that reliably produce safe, nutritious, good tasting food (97).

All partners of the agricultural production chain take their individual responsibilities to contribute to an environmentally safe production of safe feed & food of high quality. Responsibility for product safety is always linked to the specific product developed for marketing. Breeders may thus be considered responsible for varieties with “safe” genetics intended for feed & food production. As described in question 24, a comprehensive regulatory framework for EU-breeders, seed producers, processors et.al. is already in place, including a.o.
• Protocols for DUS and VCU testing
• Common catalogue of varieties of agricultural plant species and marketing of vegetable seed 2002/53-57:
• Seed Marketing Directives (….)
• Plant Health Regulation (EU) 2016/2031
• Seed Treatment Regulation (EC) No 1107/2009
• General Environmental Liability 2004/35/CE
• General Food Law
• Novel Food Regulation (it needs to be noted that a novel food developed from an NGT derived plant could be captured by the EU novel food regulation if it would not result in a GMO)

* **25. Do you have specific safety considerations on NGTs/NGT-products?**

- (●) Yes
- ( ) No

* Please explain

Euroseeds does not have specific concerns regarding the safety of NGTs/NGT-products as referred to in our contribution. But we would like to share specific considerations that lead us to this conclusion:

Technical considerations:
The SAM Note (100) states that conventional breeding and NGTs differ in the extent to which they produce 'unintended effects'. “Unintended effects are, as the term suggests, effects other than those which are desired, resulting from the employment of a technique. ”Unintended effects are caused by unintended mutations, which in conventional breeding result from spontaneous or classical induced mutations (irradiation, chemicals) and can be numerous, occur at random locations, and not possible to control. With genome editing, off-target mutations (mutations in the DNA sequence which is identical or highly similar to the target sequence, located someplace else in the genome) can also occur, however they are much less numerous, and can be mitigated with the proper design of genome editing reagents. As stated in the Note, “The genome editing techniques…may be accompanied by few unintended effects…However, in general the genome editing techniques show a much lower number or complete lack of unintended mutations as compared to organisms obtained via CBT” (Conventional Breeding Techniques).
As stated in our response to Q24, products generated with NGTs that are similar to those that could arise in nature or be produce via conventional breeding techniques are as safe as those conventional products and do not warrant any additional regulatory oversight. As the EFSA scientific opinion on Synthetic biology developments in plants, MC and ERA states for NGTs: “The GMO-panel considers that the analysis of potential off-targets on a regular basis would be of very limited value for the risk analysis”(98).

Regulatory considerations:
As stated by de Jong et al, 2018 (99) “the existing EU regulatory framework, when considered holistically, provides efficient guarantees that every stage of the agri-food supply chain, from lab to fork, is subject to constraints and obligations dictated by harmonised legislations, each providing various degrees of scrutiny, risk management and control, sanctions and remedial action. Comparisons between the existing non-GMO legal framework with the GMO legislation or with any other authorisation regime based on a full pre-market risk assessment are, by definition, of little practical relevance, since such regimes aim to address potentially serious risks, which, as the SAM Note (100) clarifies, ”have not been identified in the case of Non-GMO NBT Products (comment: in their 2017 Note the SAM referred to NGT products as defined in the context of our input/see disclaimer as Non-GMO NBT Products). In the absence of any such concrete, identifiable risk induced by (the use of NBTs for) Non-GMO NBT Products and in view of their non-distinguishability from conventional breeding products, the protection of human/animal/plant health and the environment should thus be considered to be adequately ensured and Non-GMO NBT Products should not be treated differently from products resulting from conventional breeding. The opposite conclusion would not only raise serious concerns under the SPS Agreement but would essentially also mean that all non-GMO plant products on the market today must be considered inadequately regulated.”

Any risk management measure must respect the general EU law principles of proportionality, legal certainty and legitimate expectations, as well as non-discrimination (equal treatment). See also our reply to Q29.

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F - Ethical aspects of NGTs/NGT-products

*** 26. What is your view on ethical aspects related to NGTs/NGT-products? Please substantiate your reply**

During the thousands of years that humans have genetically changed plants, the value of these plants and plant products was assessed by how they looked, smelled, tasted and met human needs. From these interactions, humans learned which plant species are good sources of building materials, medicine and, most importantly, food. They learned which plants are nutritious, have useful phytochemicals, and are safe to eat, and which plants to avoid.
Plant breeding has a history of innovation (see also (101)). Since the discovery of the laws of heredity by Gregory Mendel plant breeders have developed improved breeding methods to make the two major steps in breeding, a) increasing genetic diversity, and b) selecting the best performing plants, more targeted and efficient. Starting with intentional cross breeding beginning of the 20th century, the first concepts for hybrid breeding were introduced during the 1920's. One major goal of breeding is to continuously make use of or increase genetic diversity. First attempts to increase genetic diversity by technical means started in the 1930' s with using radiation or chemicals to induce random mutations in the plant's genome followed by intense selection procedures to find valuable new traits. New molecular tools of precision breeding help breeders to do their job in an even more precise manner compared to the past. Especially the new tools for genome editing, like Crispr–Cas provide mechanisms to not only randomly increase genetic variation as it was done by radiation or chemical mutagenesis but also to precisely introduce mutations in genes of known functions to either impair or improve their function. With this, these precision breeding tools can create plants that might also have been produced by conventional breeding methods like chemical or radiation mutagenesis. These plants would in most cases not be distinguishable with respect to the breeding methods that have been used to develop these plants(102) and with this a true continuation of innovation in conventional breeding which has been and will be essential for economic, social and environmental benefits at large scale and should indeed be considered a highly effective measure for adapting to new and very dynamic settings (103). A regulatory situation that prevents, slows down or delays the development and marketing of NGT plant varieties that do not create specific risks as to the technology by which they were developed as outlined by the SAM (104) is ethically questionable.

For further considerations see our reply to question 27.

*** 27. Do you have specific ethical considerations on NGTs/NGT-products?**

- (●) Yes
- ( ) No

* Please explain

The current regulatory situation leads to a delayed adoption of NGTs in research and breeding as well as respective product development (see also our replies to question 12) and with this to missed opportunities for small innovators as well as developing countries (105). Depriving EU farmers and consumers from the benefits of modern technologies and discriminating them against their counterparts in other parts of the world due to outdated regulations is an ethical problem indeed. We therefore agree with the statement from

EASAC “that the potential costs of not using a new technology, or being slow in adoption, must be acknowledged. There is no time to lose in resolving the problems for food and nutrition security in Europe” (106).

Plant breeding and the adoption of high-yielding varieties played a key role in reducing hunger over the last 100 years. NGTs can help to increase crop diversity, raise yield potentials, provide better resistance to pests and diseases, increase nutrient use efficiency, make crops more resilient to climate shocks, and improve nutritional quality, just to name a few of the types of technologies that plant biotechnologists have already worked on extensively (107).

The role of NGTs to contribute to a sustainable future is highlighted by the World Resources Institute as well as the IPCC special report from 2019 on “Climate Change and Land”. The World Resources Institute concludes that fully closing the gaps (between food demand and supply) requires many innovations, including in crops. The report states that “A revolution in molecular biology opens up new opportunities for crop breeding. Progress at the necessary scale requires large increases in R&D funding, and flexible regulations that encourage private industry to develop and market new technologies”(108). The IPCC report points out that “advances in plant breeding are crucial for enhancing food security under changing climate for a wide variety of crops including fruits and vegetables as well as staples” and that “genetic improvement is needed in order to breed crops and livestock that can both reduce greenhouse gas emissions, increase drought and heat tolerance (e.g., rice), and enhance nutrition and food security”(109).

The issue of non-enabling regulations in view of ethics is also addressed by the Danish ethics Council which concluded in its Statement on GMO AND ETHICS IN A NEW ERA that “it also raises the question of whether it is ethically problematic if the legislation obstructs the development and marketing of GMOs, e.g. those with positive effects, if they are not deemed more risky than similar conventional varieties”(110).

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G - Consumers' right for information/freedom of choice

*** 28. What is your view on the labelling of NGT-products? Please substantiate your reply**

Labelling requires traceability, an aspect that links to the enforcement of any legislation that distinguishes products based on the plant breeding process, whether conventional, GM, NGTs or another categorisation (111). As mentioned in our reply to question 7, Euroseeds members are not aware of any clear traceability strategies that could be used for identifying NGT-products as referred to in our contribution. The JRC further concluded that validation of an event-specific detection method & its implementation for market control is not feasible for NGT plant products carrying a DNA alteration that is not unique. This also corresponds with the knowledge of Euroseeds members. With that any labelling obligation would require a paper trail system that is potentially vulnerable to fraud if the respective regulated product at no point in time can be clearly identified. An obligatory labelling of NGT-products based on the breeding process only but where the resulting products are indistinguishable from conventional breeding also raises legal concerns regarding the discrimination or stigmatisation of such like-products (112). Specifically also in view of imported products this obligation will not be enforceable when the country of origin does not oblige respective regulatory requirements (113).

Venus et al. conducted a study on the Interaction among the Regulation of New Plant Breeding Techniques, GMO Labelling, & Coexistence & Segregation Costs. Their results indicate that if NGTs are regulated as GM in the European Union, the cultivation of such crops is likely to be unprofitable under the current labelling & coexistence policies (114). In addition, they looked at the gains & losses & came to the conclusion that regulating the NGTs as a non-GM technology generates the largest welfare benefits & would be in line with the requests from many scientists.

We know that the organic sector builds upon a wide range of different process-based labelling systems. But these are voluntary labelling systems that are implemented to differentiate & market products with a price differential to the economic benefit of the respective actors only.

If NGT products would not be regulated as GMOs in the future Euroseeds recognizes the need for information sharing (not labelling!) to
1) enable regulators to control compliance of operators with respective regulations as well as to 2) provide different markets with specific requirements as well as the respective market operators & their customers (consumers) with relevant information.

In view of 1) the Euroseeds members therefore want to assure that information requirements of authorities supporting compliance with existing legislations can be fulfilled. These requirements should be limited to the information that is needed to define the scope of the regulation (e.g. information about the breeding method used, information regarding the verification of the non-transgenic status, or information regarding the molecular characterization of a genetic change). All this information clearly makes sense only if NGT products will be exempted from GMO regulation. This kind of information requirements of authorities also exist in other countries that do not regulate NGTs as GMOs (e.g. several South American countries).

In view of 2) seed companies remain committed to reply to further individual/private information requests from their customers as far as this can be reasonably achieved. Any further information (obligations) on breeding methods used, including on a variety level, that will be shared publicly must be meaningful, scientifically appropriate, & not discriminate innovative companies & products. It should also assure a level playing field between operators – EU-wide, but also internationally - & avoid consumer misinformation & fraud, esp. in view of the international context & the lack of distinguishability regarding like-products. Timetables, practical & harmonized ways of implementation & potential consequences (international movement of material & seed) must also be taken into account.

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H - Final question

*** 29. Do you have other comments you would like to make?**

- (●) Yes
- ( ) No

Please provide your comments here

Outdated Regulation:
The GMO Directive is out-dated & needs to be revised in the light of current knowledge. This is confirmed by EU Science Advice Mechanism Statement (115). Euroseeds suggest a targeted amendment of Directive 2001/18 that excludes products of old & new mutagenesis breeding by NGTs from its definition & adapts Annex IB accordingly. This will align the EU's policy & rules with those established & being developed in the rest of the world; it will also create legal certainty for EU operators by avoiding that Member States adopt individual national rules for products resulting from conventional, random mutagenesis.

Proportionality in regulation &implementation of the precautionary principle:
"The precautionary principle is not an alternative to a risk management approach, or to a scientific risk assessment in the context of the decision-making process, but rather a particular form of risk management. The Commission Communication on the precautionary principle, adopted in 2000 (116), provides the Commission's view & guidelines on the way the precautionary principle should be implemented. There are essentially two conditions necessary to trigger the application of the precautionary principle: (a) the identification of the possibility of harmful effects in the environment or human, animal or plant health (that is, risk); & (b) a scientific evaluation of the risk which, because of the insufficiency of the data, their inconclusive or imprecise nature, makes it impossible to determine with sufficient certainty the risk in question. Pursuant to established case law, the level of protection envisaged by applying the precautionary principle does not necessarily have to be the highest that is technically possible & a purely hypothetical approach to risk or a 'zero risk' approach is not allowed. Concrete risks for human health or the environment must be identified, supported by a minimum amount of serious & independent scientific research.
Any risk management measure must respect the general EU law principles of proportionality, legal certainty & legitimate expectations, as well as non-discrimination (equal treatment). Two indistinguishable varieties obtained by a traditional breeding technique & a NGT respectively cannot be regulated differently.

Avoiding regulatory patchworks between member states –the French Court Case:
The ECJ ruling C-528/18 recognizes the right for the member states to adopt measures regulating those organisms that are exempted from the GMO directive as long as such measures do not conflict with rules on free movement of goods.
The recent French Conseil d´Etat court ruling on mutagenesis (117) raises questions of its further implementation by the French government & may lead to a non-harmonized EU regulatory framework where member states may potentially use their leeway to require additional conditions for placement on the market for products that were so far exempted from the obligations of the GMO Directive 2001/18 with negative implications for the internal market.
Euroseeds calls upon the EU Commission to reflect in its study due by 30th April 2021 how a harmonized regulatory framework for plant varieties derived from NGT´s can be enabled. In view of the definition of conventional breeding techniques to be exempted from gm-regulations we ask the Commission to refer to the EFSA opinion on SDN-3 from 2012 (118) which e.g. considered "mutation breeding" including spontaneous mutations, induced mutations (chemical & physical mutagenesis) & somaclonal variation as a form of in-vitro mutagenesis breeding as conventional breeding.

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Contact

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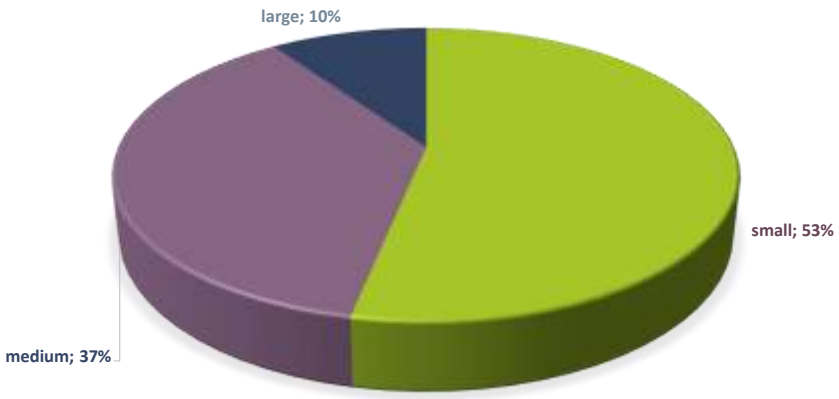
Results Euroseeds Survey

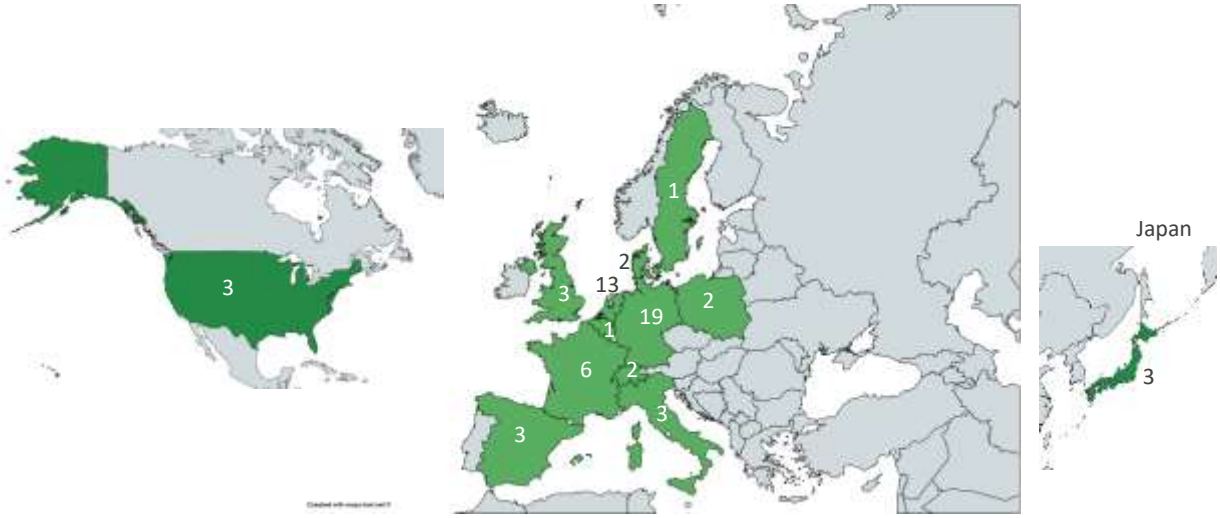
14 May 2020

Figure 1: The Euroseeds Survey covers 62 plant breeding companies of all sizes



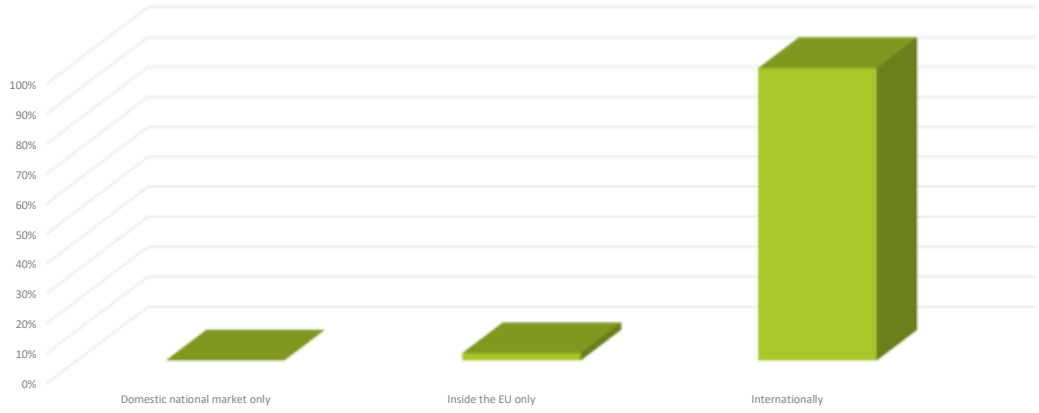
Small: < 50 Mio
Medium> 50 Mio < 450 Mio
Large > 450 Mio
(as to annual turnover)

Figure 2: Geography covered as to the location of the headquarter of companies participating in the Euroseeds Survey



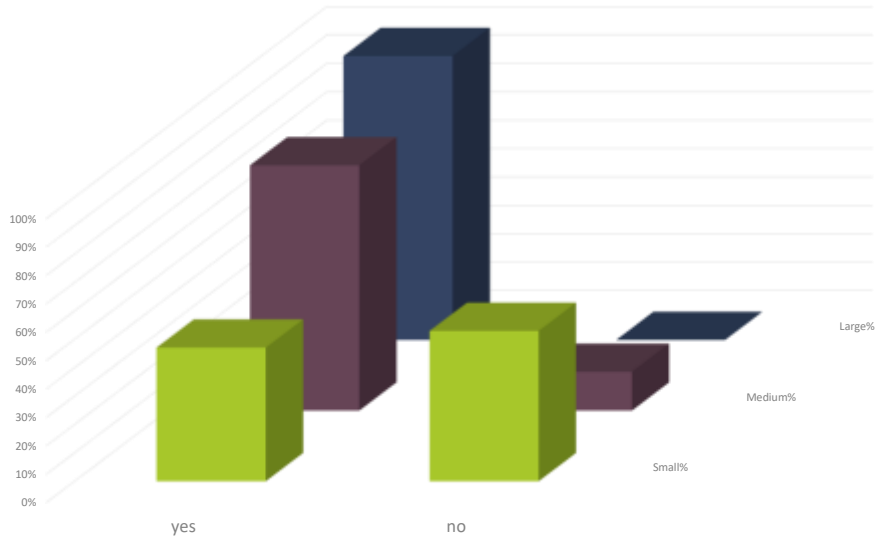
2

Figure 3: Geographies in which companies active in NGT related R&D are generally conducting their R&D, Breeding or Seed Production/Sales



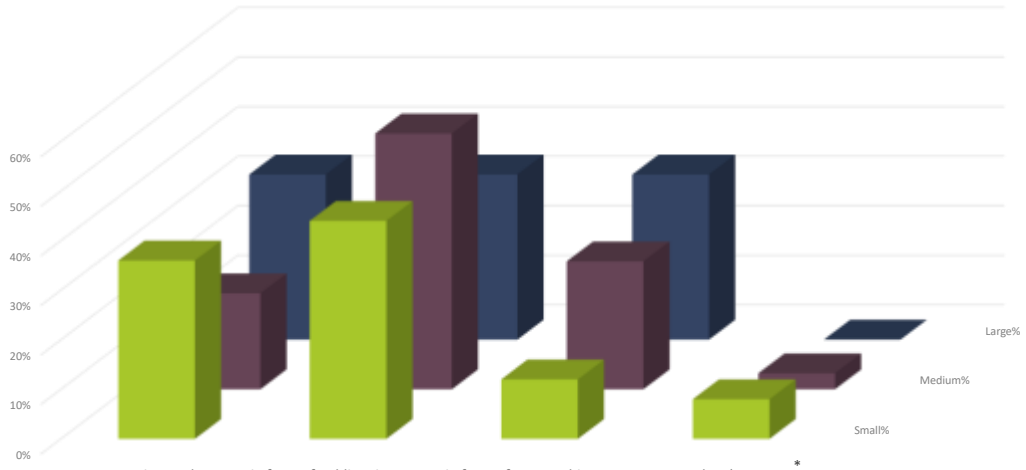
3

FIGURE 4: PERCENTAGE OF COMPANIES CURRENTLY ACTIVE IN NGT RELATED R&D



4

FIGURE 5: KIND OF NGT RELATED R&D ACTIVITIES
(MULTIPLE ANSWERS WERE POSSIBLE)



*
- commissioned,company-funded work at public/independent research organisations authorized for GM work;
- through charitable funding
- funding of PhD project

5

FIGURE 6: GEOPGRAPHIES IN WHICH THE COMPANY'S NGT RELATED R&D ACTIVITIES TAKE PLACE

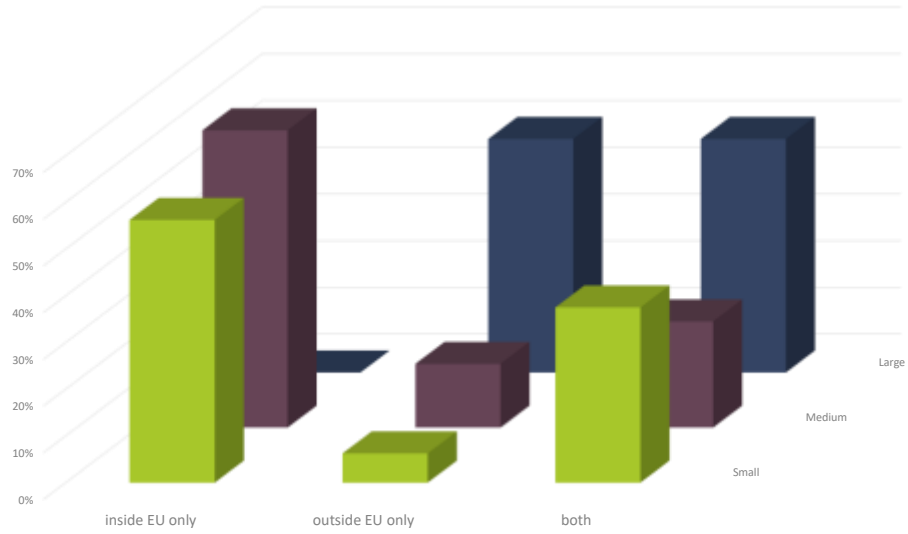


FIGURE 7: KIND OF NGT RELATED R&D ACTIVITIES IN WHICH COMPANIES ARE INVOLVED

(MULTIPLE ANSWERS WERE POSSIBLE)

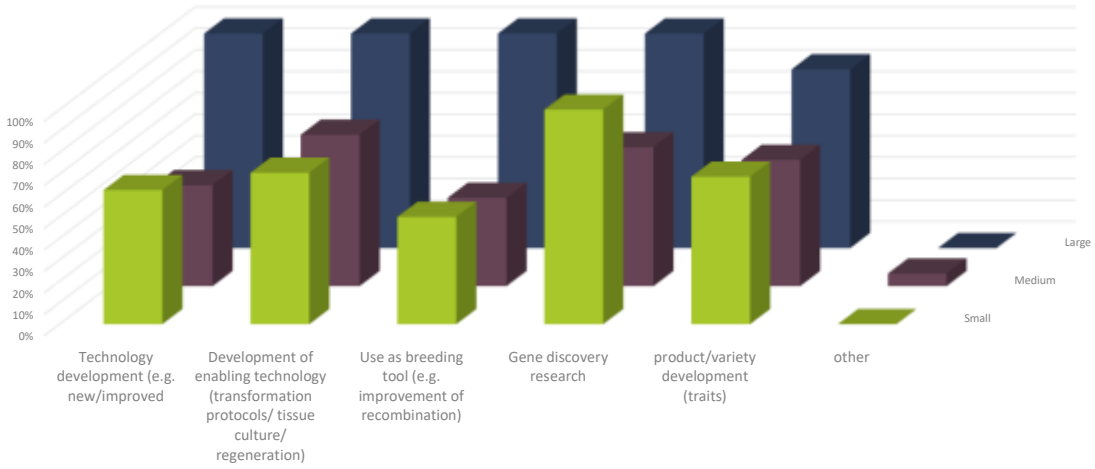
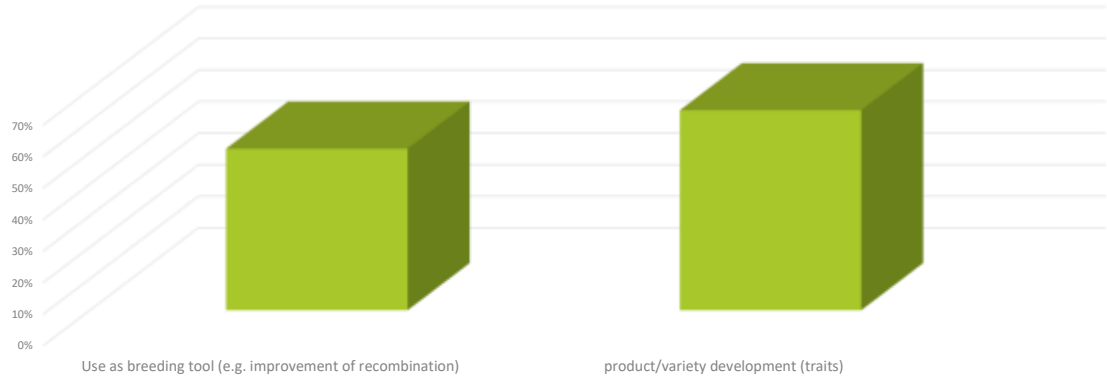


FIGURE 8: PERCENTAGE OF COMPANIES (INDEPENDENT OF SIZE) INVOLVED IN USING NGTS AS BREEDING TOOL* OR FOR PRODUCT DEVELOPMENT*

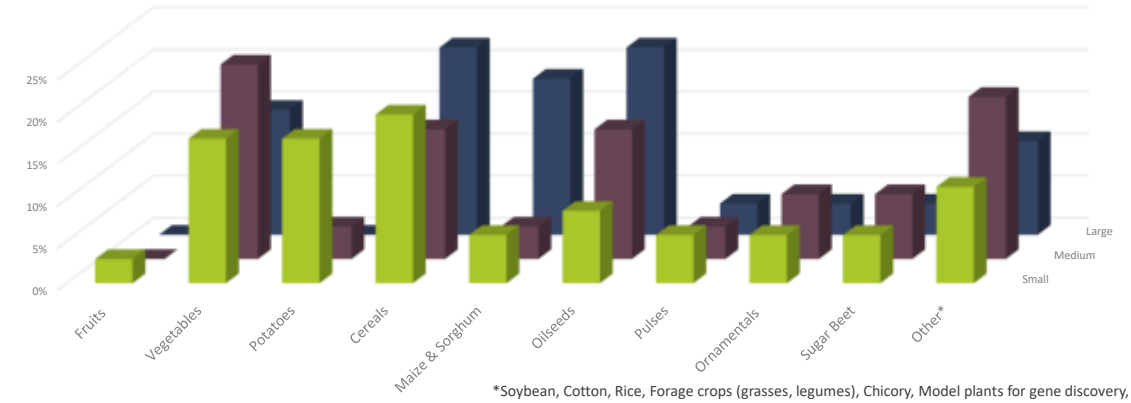


*which would result in a product regulated as GMO in the EU after ECJ ruling on targeted mutagenesis breeding

8

FIGURE 9: CROPS/CROP GROUPS IN WHICH COMPANIES APPLY NGT RELATED R&D

(MULTIPLE ANSWERS WERE POSSIBLE)

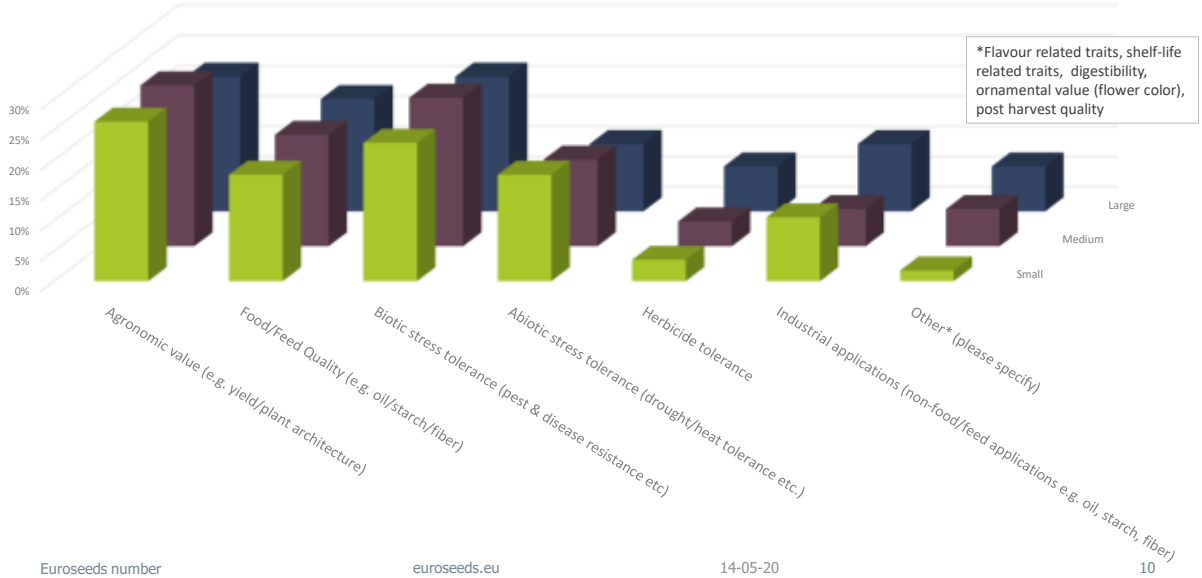


*Soybean, Cotton, Rice, Forage crops (grasses, legumes), Chicory, Model plants for gene discovery, Poppy for pharmaceutical industry, Peanut, Ornamentals as food and medical plants, Hemp, Dandelion, Legumes, Stevia

9

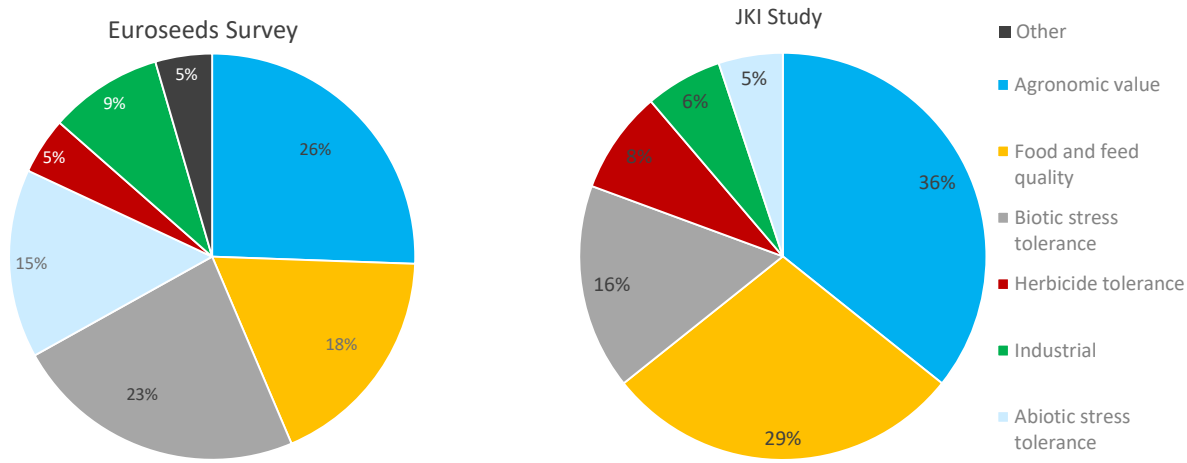
FIGURE 10: BREEDING GOALS THAT COMPANIES CURRENTLY ADDRESS WITH THEIR NGT RELATED R&D ACTIVITIES

(MULTIPLE ANSWERS WERE POSSIBLE)



10

FIGURE 11: COMPARISON EUROSEEDS RESULTS AS TO BREEDING GOALS WITH RESULTS FROM THE JKI STUDY

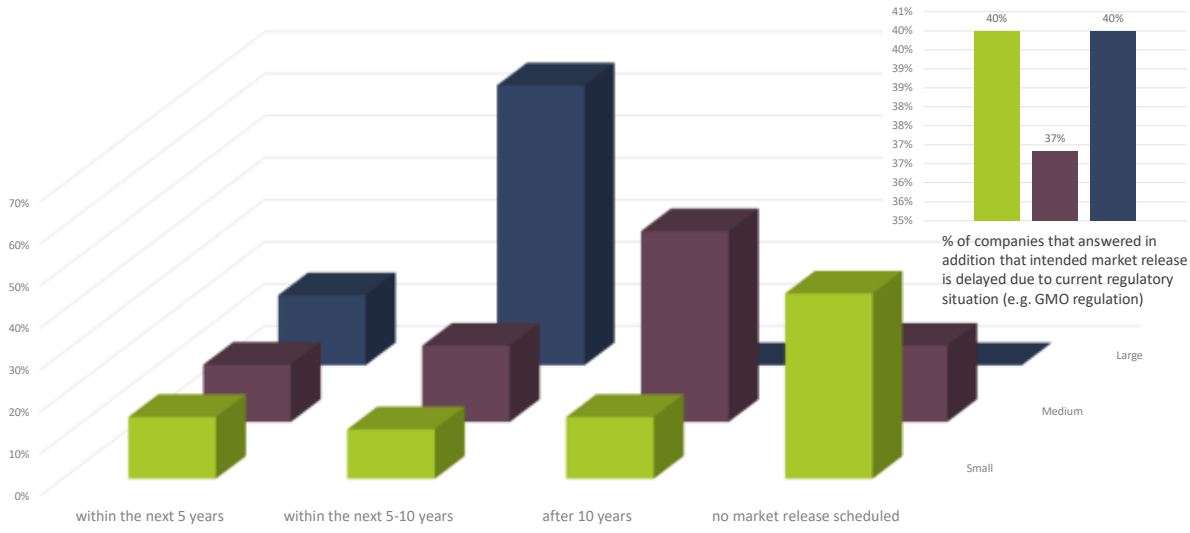


Source: Thorben Sprink/JKI; published in:
Modrzejewski et al. (2018), *Environ Evid* 7 (1), S. 11.
DOI: 10.1186/s13750-018-0130-6.
Modrzejewski et al. (2019), *Environ Evid* 8:27
https://doi.org/10.1186/s13750-019-0171-5

11

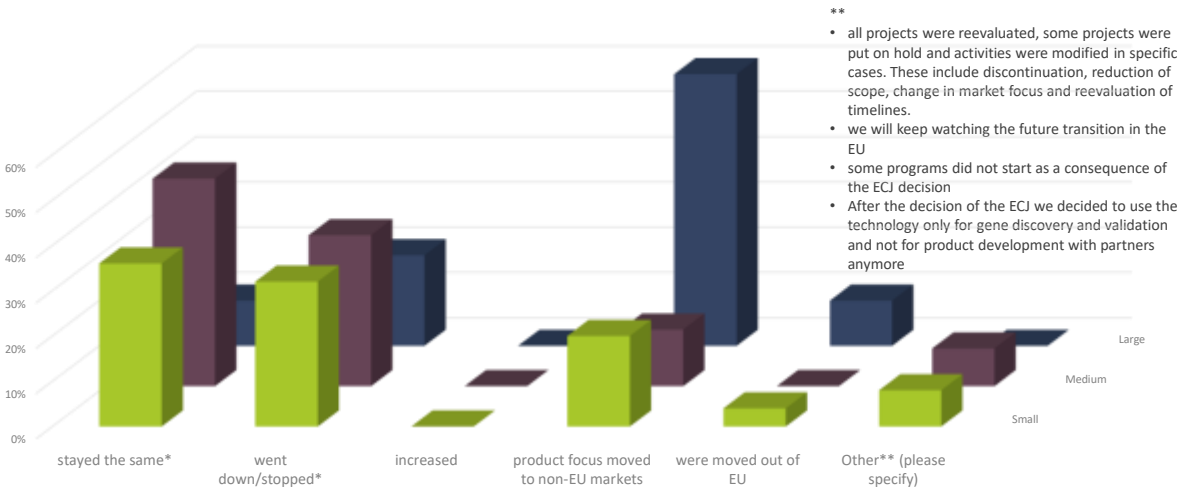
Figure 12: Potential market release (globally) for products resulting from NGT related R&D

(multiple answers were possible)



12

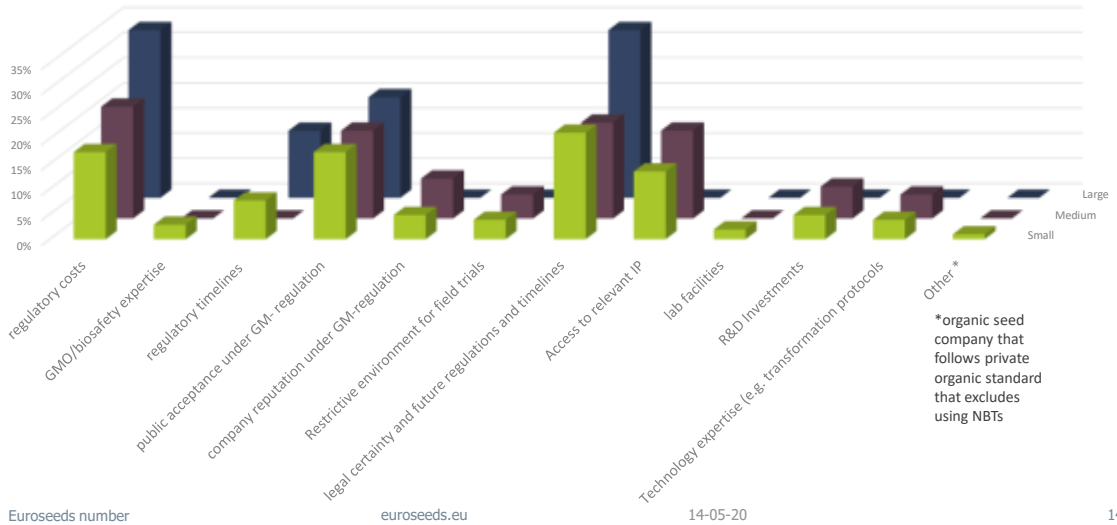
FIGURE 13: EFFECT OF THE ECJ RULING ON NGT RELATED R&D ACTIVITIES OF COMPANIES



13

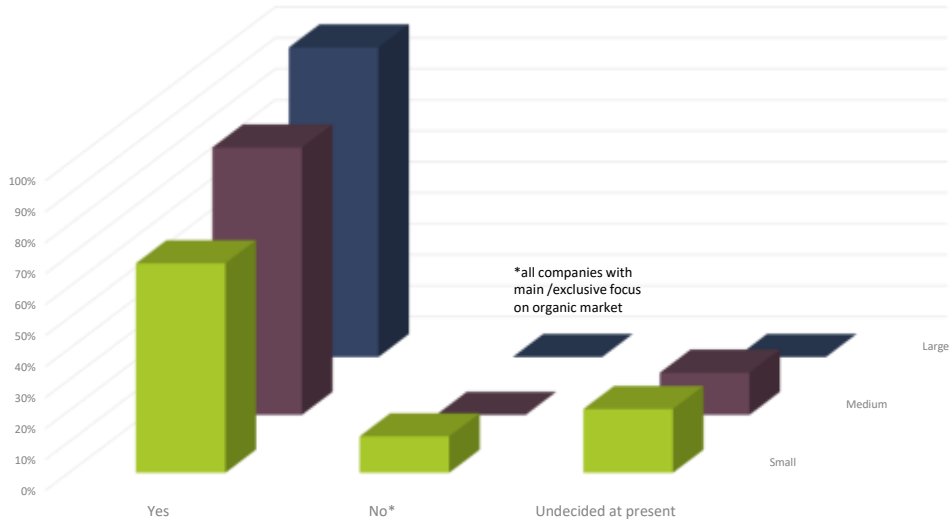
Figure 14: Factors that companies regard as most significant as to negatively influence the potential use of NGTs in their breeding programmes

(3 answers possible)



14

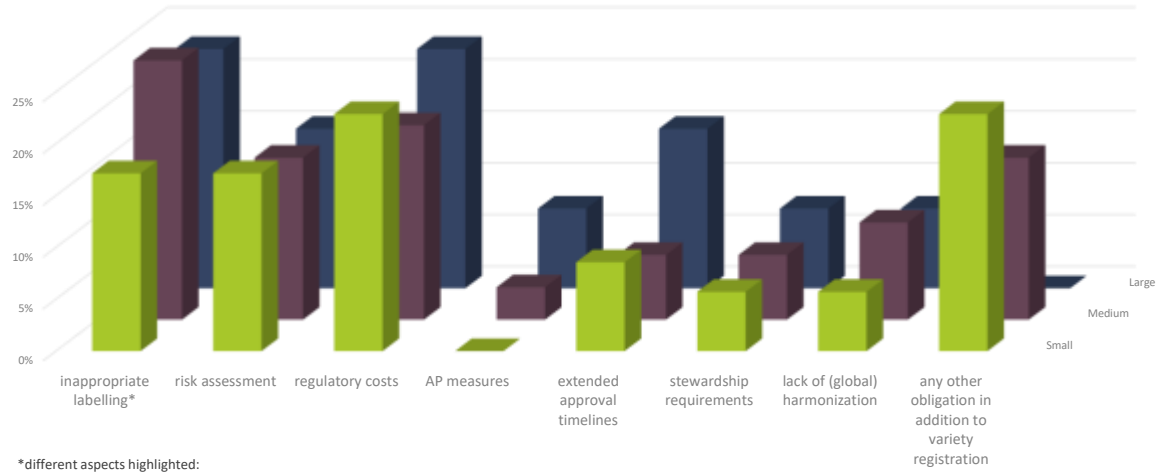
Figure 15: Companies' interest to invest in product development with NGTs for the EU market, if the resulting plants would not be regulated as GMOs, but as conventional varieties



15

Figure 16: Regulatory requirements -in addition to conventional variety testing and registration- that would influence companies' decisions to invest in product development with NGTs in case not regulated as GMOs

(grouping of free comments)

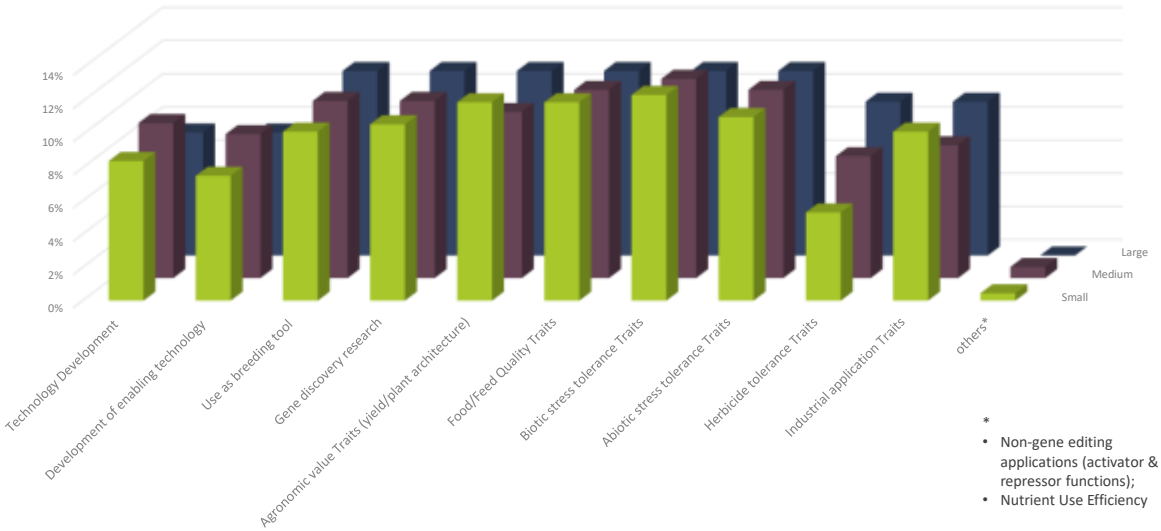


*different aspects highlighted:
Labelling as GMO;
Labelling of indistinguishable "like-products" (see also our comments on Q28 of the NGT consultation);
Labelling of breeding methods required (one organic breeder)

16

Figure 17: Breeding goals for which companies -independent of their current activities- see the highest future potential for the application of NGTs

(multiple answers were possible)



*
- Non-gene editing applications (activator & repressor functions);
- Nutrient Use Efficiency

17

Innovation to preserve **TRADITION**

THE EXAMPLE OF
fungi-resistant grape vine

1 SUSTAINABILITY DUE TO REDUCED FUNGICIDE USE

Grape wine covers only 3% of the EU agricultural area

but is responsible for **60%** ***of fungicide use***

With fungi-resistant grape varieties spraying could be reduced

from 10-20 applications > to 2 or 3 per season.

In addition it saves:

60%-80% ***ECONOMIC COSTS****

40%-60% ***ENERGY COSTS****

60%-75% ***WATER CONSUMPTION***

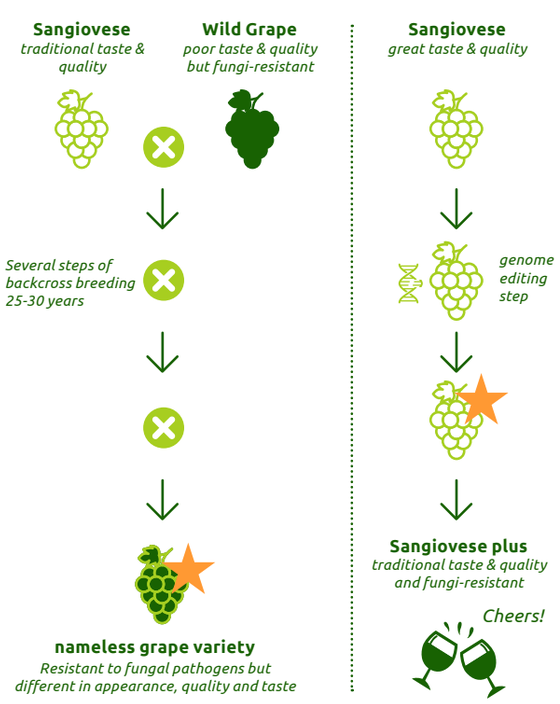
**depending on the region*

2 PRESERVING TRADITION - *Crispr can save our traditional grapes like Sangiovese, Riesling or Merlot*

Growers and producers have optimized their production to certain grape wine varieties and consumers prefer **traditional varieties** from their region. Any cross breeding "destroys" the genetic **identity** of a traditional variety.

Plant breeding innovation, with the latest genome editing techniques, provides opportunities to change single characteristics (e.g. from wild relatives), like resistance to fungi **without destroying the genetic identity of a variety**. A Sangiovese, Riesling or Pinot Noir "plus" can be developed with the typical taste in addition to fungi resistance.

Cross breeding destroys the genetic identity of a traditional variety like Sangiovese – Gene editing can save it!



3 EFFICIENCY OF GRAPE VINE BREEDING

Attempts to **introduce resistance genes by cross-breeding with wild relatives of the modern grape have been successful.**

From seedling to flowering it can take ***3 years***

Taking into account crossbreeding, testing, and certifying, **the whole process of breeding** a new grape variety **can take as long as** ***25 to 30 years.***

This is due to the perennial nature of the grapevine and its long generation time. **Multiple backcrossings are needed to improve the wine quality and selection for good wine-making potential is extremely complex and costly.**

Producing new fungi-resistant grape varieties is therefore two-fold difficult. In addition to being resistant, the grapes also **need to produce a tasty wine that is marketable.**

"With the new genome editing tools we could be able to drink the first glass of wine from the tasty and fungi-resistant Crispr grapes in approximately 10 years time. Cheers!

PROF. MICHELE MORGANTE

#EmbracingNature
www.euroseeds.eu

Euroseeds
Embracing Nature

CONSUMER BENEFITS

Chemically modified starch is used to

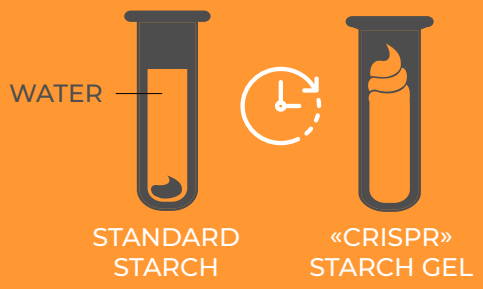
REDUCE FAT WHILE KEEPING THE TEXTURE OF FOOD.

It is IMPORTANT THAT THE STARCH ABSORBS THE WATER AND KEEPS IT OVER TIME,

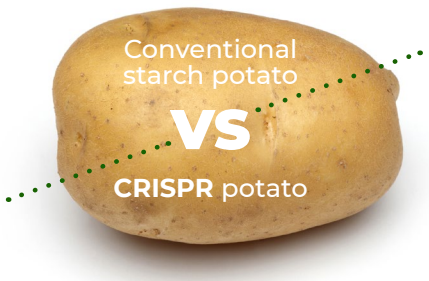
otherwise the product will release water and the storage of the product decreased.

Thanks to **PLANT BREEDING INNOVATION** there is a "CRISPR" - POTATO containing a NATIVE STARCH

that is **STORAGE STABLE** without the need of chemical modification



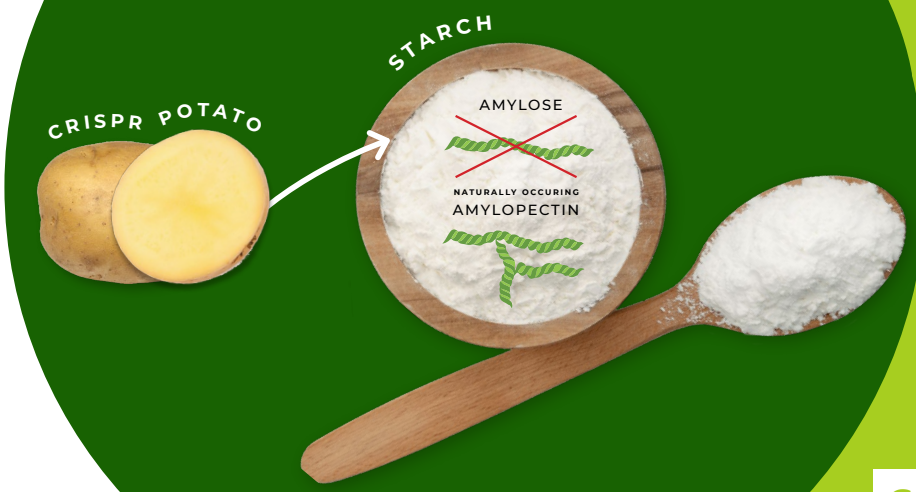
BENEFITS FROM MODERN BREEDING TOOLS



CRISPR IS MORE EFFICIENT than CONVENTIONAL MUTAGENESIS or ANTISENSE RNAI TECHNIQUES

Studies have shown that CRISPR is **A PROMISING ALTERNATIVE TO EFFICIENTLY CREATE TARGETED TRANSGENE FREE MUTATIONS IN POTATOES.**

THE SWEDISH
CRISPR
POTATO STARCH PROJECT



EMBRACING THE POWER OF NATURE

ENVIRONMENTAL BENEFITS

LYCKEBY STARCH COMPANY USES ONLY:

80.000 T OF POTATO = 20.000 T OF STARCH

USING CRISPR POTATO SAVES

4.000-5.000 T OF PROCESS CHEMICALS

EU WIDE 15 TIMES THE AMOUNT

1,2 million T OF POTATO = 300.000 T OF STARCH

SAVING

60.000-75.000 T OF PROCESS CHEMICALS + **7.5 Gwh** PER YEAR

PLANT SCIENCE WOULD MOVE OUT OF EU

IF *EU CONTINUES TO REGULATE THE CRISPR POTATO AS GMO*

ALTHOUGH *IT DOES NOT CONTAIN FOREIGN DNA.*

THIS HAS DIRECT CONSEQUENCES

FOR EU'S COMPETITIVENESS IN SUSTAINABLE FOOD PRODUCTION.

www.plantbreeding.eu

Andersson et al., Physiol. Plant. 2018 doi:10.1111/ppl.12731 supported by Lyckeby Starch AB

#EmbracingNature

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7. ENGL report "Detection of food and feed plant products obtained by new mutagenesis techniques" https://gmo-crl.jrc.ec.europa.eu/doc/JRC116289-GE-report-ENGL.pdf
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