TESTBIOTECH Background 13-10-2022

Testbiotech e. V.
Institute for Independent
Impact Assessment in
Biotechnology

Twisted facts and incorrect assumptions about NGT plants

Misleading report published by STOA

Table of Contents

Abstract

In mandating and publishing the “*Genome edited crops and 21st century food systems challenges*” report (EPRS 2022), the Panel for the Future of Science and Technology (STOA) has contravened the basic principles of providing independent and impartial information. The authors of the report and their institute, the Vlaams Instituut voor Biotechnologie (VIB), are well known for their lobbying activities and support for the deregulation of food plants derived from new genomic techniques (NGTs). It has to be assumed that these activities are, at least in part, driven by funding from industry, by patents and the markets. However, the report fails to make this background wholly transparent.

There should be absolutely no doubt that the safety assessments of new and potentially risky technologies or products must be carried out independently of any interests of stakeholders hoping to make a profit. This is also true for the assessment of regulatory issues in the context of NGTs (also called genome editing or New Genetic Engineering). Unless the basic principles of transparency and impartiality are upheld, there can be no way of excluding the promotion of

inadequate or hazardous technologies as ‘solutions’ for, e.g. world hunger, climate change or sustainable agriculture. Ignoring the basic principles of transparency would also mean that the interests behind the marketing of products derived from these technologies would remain hidden from the public.

The fact that these experts were mandated to draw up a report has resulted in the presentation of incomplete and incorrect findings, compounded by misleading statements, messages and conclusions. The main messages in the report can be summarised as: (1) NGT plants offer quick solutions to pressing problems and (2) the genetic changes introduced by NGTs are no different to those resulting from conventional breeding, as long as no transgenes are inserted.

The analysis presented in our backgrounder shows that this kind of reporting is based on assumptions intentionally chosen to diverge from the facts and relevant scientific findings.

Potential benefits:

- The report creates the impression that valuable products are already on the market. However, such claims are not supported by the facts and the report fails to mention important information. In reality, the first plants to be brought to market (soybeans in the US) suffered from low yields and profits, and thus failed to gain any substantial share of the market. The second product (tomatoes in Japan) was supposed to have beneficial health effects which have, however, never been demonstrated.
- The report gives the impression that NGTs dramatically increase efficiency, speed and precision, and thus be superior to conventional breeding. However, existing experience from the last 10 years shows that this might not be the case. In general, NGTs can be used to either generate more extreme versions of already known traits or completely new traits. These traits are often associated with ‘trade-off’ responses (side effects), which can make it necessary to invest a lot more time in the development of a trait compared to conventional breeding.
- The report creates the impression that further plants with valuable new traits derived from NGTs will soon be made available. However, existing experience shows that it is difficult to distinguish real benefits from empty promises. Whatever the case, no reliable conclusions can be drawn without further data and comprehensive technology assessment.

In summary, NGTs, e.g. CRISPR/Cas, have huge potential to alter the genome but this potential does not easily translate into real benefits.

Patents and markets:

The report does warn that the cost of the EU approval process might become an obstacle for smaller companies (SMEs), resulting in further market concentration. It also mentions patents which can hamper or block access to the technology.

However, the report does not explicitly mention that patents currently being granted by the European Patent Office (EPO) not only cover the new technologies, but also hamper, control or block access to biological resources needed by all breeders. As a result, an increasing number of patent monopolies on seeds and plant genes are likely to seriously affect SMEs, and they could lose their freedom to operate. Contrary to what is implied in the report, this development seems to be the main driver of market concentration rather than the costs for the EU approval process.

While patent protection in the US and Canada is similar to that in Europe, there are big differences in GMO regulation in comparison to the EU. Nevertheless, just a few large companies have a dominant market position in regard to transgenic plants. It can, therefore, be concluded that patents are much more relevant to the recent concentration in the seed market than regulatory requirements.

This also shows that comprehensive technology assessment is needed before the technology is introduced into agriculture, so that disruptive effects on the markets and, in particular, breeders can be prevented.

Risk and regulation:

The report gives the impression that, as long as no additional genes are added to the gene pool of a species, the genetic changes introduced by NGTs and their associated risks are equivalent to those resulting from conventional breeding. It is suggested that NGTs should be assumed to be less risky, as the number of the genetic changes caused by NGTs may be limited.

However, our analysis shows that each stage of the process, including (i) insertion of the gene scissor DNA into the cells, (ii) target gene recognition and cleavage and (iii) cellular repair of the genes, can cause intended and unintended genetic changes unlikely to occur as a result of conventional plant breeding, and can be associated with specific risks. The differences between conventional breeding and NGTs can be easily overlooked, but can have serious consequences for health and the environment. Therefore, as required by current EU GMO regulation, in each case, intended and unintended changes have to be assessed as to whether they can have either direct or indirect, immediate or delayed, or cumulative effects on human health and on the environment.

Further observations

There are further observations made in the report concerning the identification of NGT plants and liability issues which need to be corrected and put into context.

- The report gives the impression that if no additional genes are added to the gene pool of a species, the genetic changes introduced by NGTs do not allow NGT-derived plants to be detected or identified. These assumptions are misleading. On the contrary, the specific patterns of genetic change caused by NGTs do typically allow the identification of plants inheriting such changes.

- The report gives the impression that existing regulations on liability are sufficient to cope with any potential damage if NGT organisms were to be deregulated. This statement is misleading: if the precautionary principle, which is currently the basis for GMO regulation, were to be abandoned, liability rules would only apply to damage which has already occurred. However, damage such as the disruption of ecosystems and loss of species cannot be mitigated by payments, and therefore needs to be prevented in advance. Consequently, there is no alternative to upholding the precautionary principle.

Final conclusions

The report provides incomplete and misleading findings, resulting in incorrect statements, messages and conclusions. Its assumptions appear to have been intentionally chosen to diverge from the facts and scientific findings. Therefore, STOA and the Directorate-General for Parliamentary Research Services of the Secretariat of the European Parliament (EPRS) should withdraw this report.

Introduction

According to its own mission statement, the Panel for the Future of Science and Technology (STOA) is a service “*providing committees and other parliamentary bodies in the European Parliament with independent, impartial and accessible information relating to developments in science and technology, including the opportunities they offer alongside the risks and ethical implications*”.[1] New technological developments in biotechnology, such as the CRISPR/Cas gene scissors, are part of its mandate.

On 15 April 2021, STOA held an online conference on the genome editing of plants.[2] Even at that time, concerns were raised that the STOA conference programme might not be sufficiently well-balanced: several members of the international lobby organisation, PRRI, who are known for their advocacy of the biotech industry, were among the speakers. In addition, the keynote speaker was known to have filed patent applications on gene-editing that were licensed exclusively to a biotech company (Corteva/DowDupont).[3]

STOA has once more taken a biased position in mandating and publishing a report on “*Genome edited crops and 21st century food systems challenges*” (EPRS, 2022). The report was authored by experts from the VIB (Vlaams Instituut voor Biotechnologie), which “*in partnership with companies such as Bayer and CropDesign (BASF)*” is testing “*new crops with improved yield and increased stress resistance*”.[4] Cellectis (Calyxt), Bayer and BASF are all research partners of the VIB. Representatives of Bayer and BASF are also members of the General Assembly of the VIB[5], and Bayer is also represented on the Board.[6]

In addition, the VIB plays a leading role in a lobbying platform called the EU-SAGE (European Sustainable Agriculture Through Genome Editing)[7] (for further information see CEO, 2021; Testbiotech 2021). According to the information that was online until February 2022 but has since been deleted[8], Oana Dima holds a position as the ‘Science Policy Manager’, whereas René Custers has a position as ‘Regulatory & Responsible Research Manager’ for EU-SAGE. These two experts are named as the only authors of the STOA report. A third expert from the VIB, Dirk Inzé, is the coordinator of the EU-SAGE network, was a founder of CropDesign (part of BASF until 2021, now part of VIB again)[9] and is also involved in several patent applications for VIB, CropDesign and BASF (Testbiotech, 2021). A recent report published by the Green Group in the EU Parliament on the lobbying activities around New Genomic Techniques (NGT, also genome editing or New Genetic Engineering) also highlights the role of the VIB experts.[10]

It should be accepted as a general principle that the safety of technologies and products must be assessed independently of those stakeholders who may have an interest in making a profit from such technology. This is especially true when it comes to the Panel for the Future of Science and Technology (STOA) and the Directorate-General for Parliamentary Research Services (EPRS) of the Secretariat of the European Parliament which oversees the work of STOA. These services are

---

[1] https://www.europarl.europa.eu/stoa/en/about/history-and-mission

[2] https://www.europarl.europa.eu/stoa/en/events/details/the-challenges-of-genome-editing-in-plan/20210301WKS03261

[3] https://www.testbiotech.org/en/news/what-members-european-parliament-should-consider-when-discussing-new-ge

[4] See https://web.archive.org/web/2020*/http://www.vib.be/en/business-opportunities/Pages/Pipeline.aspx

[5] http://new.vib.be/general-assembly

[6] http://new.vib.be/board-directors

[7] https://www.eu-sage.eu/

[8] https://web.archive.org/web/20220117171459/https://www.eu-sage.eu/contact

[9] https://www.basf.com/global/en/media/news-releases/2021/01/p-21-100.html

[10] https://www.greens-efa.eu/en/article/document/behind-the-smokescreen

meant to inform the members and staff of the European Parliament and provide them with background material to assist in their parliamentary work – they should, therefore, avoid any conflicts of interest when it comes to selecting their experts.

If basic principles of transparency and impartiality are violated, it cannot be excluded that inadequate or hazardous technologies could be promoted as 'solutions' for, e.g. world hunger, climate change and sustainable agriculture. At the same time, the interests in the marketing these products are hidden from the public.

Indeed, the report that STOA published is not consistent with the necessary scientific standards and is hugely influenced by biased interests. It is misleading, partially incorrect, and would need major revision if it is not withdrawn.

The main messages presented in the report can be summarised as: (1) NGT plants offer quick solutions to pressing problems and (2) the genetic changes introduced by NGTs are no different to those resulting from conventional breeding, as long as no transgenes are inserted.

The following section shows that these messages are based on assumptions which have intentionally been chosen to diverge from the facts and relevant scientific findings. It appears that the authors are attempting to pave the way for the deregulation of NGT plants and exempt them from EU GMO regulation.

The potential benefits

There is no doubt that tools such as CRISPR/Cas have a huge potential to introduce genetic changes into the genome of plants. Indeed, NGTs can be used to introduce genetic changes with much greater precision compared to previous techniques of genetic engineering. Consequently, genotypes and biological characteristics can be introduced which are unlikely to be achieved with conventional breeding. In addition, there is also the possibility that conventional breeding outcomes can be 'imitated' or 'repeated' (but at the same time, the expectation for additional benefits may be largely reduced).

The STOA report makes several claims about how this potential will translate into real benefits. There are claims about products already on the market, the speed of development, the benefits of future traits and profits for smaller companies.

Products already on the market

The report names two NGT-derived products that have already been brought to market:
"*There are currently two genome-edited crops on the market. High-oleic soybean in the US and tomato with increased gamma-aminobutyric acid (GABA) levels in Japan. (…) High oleic soybeans contain more oleic and less linolenic fatty acids resulting in higher heat and oxidative stability of the oil (Demorest et al., 2016). GABA is a natural substance that is reported to be effective at reducing blood pressure (Nonaka et al., 2017).*"

As it stands, some crucial information about these products has been omitted from the report:

- The soybean with high-oleic acid oil content was brought to market in the US in 2019. However, the soy failed to produce the desired yields for the farmers and did not meet the expectations of the investors. It appears that the genetic intervention actually resulted in reduced soybean yield. Consequently, the company producing the soybean, Calyxt, exited this line of business in 2020. Sales, earnings and the value of Calyxt stock fell dramatically as a result.[11] It appears to be doubtful whether the soybean is actually still on the market.

- The GABA tomato was approved as the first NGT plant for consumption in Japan in 2021. These tomatoes are meant to have a much higher concentration of a specific plant compound (GABA) compared to conventionally-bred tomatoes. Several previous attempts using conventional breeding to achieve a permanently higher level of GABA in the plants failed. GABA (gamma-aminobutyric acid) is an inhibitory neurotransmitter in the central nervous system which may, amongst others, reduce blood pressure. At the same time, it is known that GABA has a multifunctional role in tomato plants: it influences, for instance, plant growth, resistance to plants pests and diseases as well as several other metabolic reactions (Nonaka et al., 2017). As far as is known, no data are available on the potential benefits or the potentially adverse effects of these fruits.

Conclusion: although the report gives the impression that valuable products have already been brought to market, such claims are not supported by the facts and important information is omitted in the report. Rather, the first plants to be brought to market suffered from low performance in yield and profits, and also failed to gain any relevance on the markets. The second plants, i.e. the tomatoes, were claimed to have beneficial health effects, although these have never been demonstrated.

The speed of development

The report creates the impression that NGTs will increase efficiency as well as speed and precision at the development stage, and thus solve current problems in plant breeding:
"*Each tool has its advantages in terms of efficiency, speed and precision. Some breeding goals may be achieved with older breeding tools as well, but at the expense of speed and precision. Depending on the crop species, conventional breeding takes around nine to eleven years until a new variety can be released to the market (Kaiser et al., 2020). For fruit tree breeding, the time to produce new varieties via conventional breeding is even considerably longer. Genome editing can reduce this time to market considerably (Watson et al., 2018; Wolter et al., 2019). Through genome editing, one can also introduce specific genetic changes into elite plant varieties without simultaneously transferring other undesired genetic changes (Wolter et al., 2019).*"

Again, the report lacks important information in order to put the potential of NGTs into the right context:

- As the example of the soybeans shows and contrary to what was, e.g. claimed in the report, the time between the introduction of the genetic changes and placing the final product on the market cannot be predicted with any accuracy. For example, Calyxt raised the expectation in a presentation to investors[12] that it would take only three to six years to develop a new trait and bring it to the market. The examples of the first NGT-derived food organisms to be deregulated in the US (in 2016), e.g. a non-browning mushroom from Pen University and a waxy maize from Corteva, show that it can take much longer than expected.
- Even if targeted changes to the genome are introduced successfully, there are still several obstacles linked to the process of genetic engineering. In many cases, these changes and new traits will have unintended effects: the Calyxt soybean had a lower yield, the GABA tomatoes could be impacted by their response to environmental stressors. There are further

---

[11] https://www.bizjournals.com/twincities/news/2022/09/22/calxyt-considering-sale-of-assets-merger.html

[12] http://www.calyxt.com/wp-content/uploads/2018/06/Calyxt-Investor-Presentation_May-2018.pdf

examples to illustrate these problems, e.g. CRISPR wheat with resistance to powdery mildew that was affected by a disruption in plant vitality (Spanu, 2022). Therefore, much more research is needed before NGT plants might become useful in the further breeding process.
- In trees, it is likely that the development of desired traits will take even longer compared to crop plants: perennial growth means it will take several years to grow fruit trees that can really be tested in regard to their intended traits, yield and associated biological effects.

Conclusion: the report gives the impression that NGTs increase efficiency, speed and precision, and thus be superior to conventional breeding. However, existing experience from the last 10 years shows that this is not the case. In general, NGTs enable more extreme versions of already known traits or generate completely new traits. These traits are often associated with 'trade-off' reactions (side effects) that can make it necessary to invest much more time into developing a trait compared to conventional breeding.

Future traits

The report gives the impression that plants with valuable new traits derived from NGTs will be made available soon. It gives the following examples:
"*Improved resistance against diseases to lower the need to use pesticides; improved resistance against abiotic stress in order to mitigate climate change effects on our food production; improved agronomic traits in order to boost crop yields, improve productivity, and avoid preharvest losses; improved quality traits; improved health related traits.*"

Again, further information is needed to put these expectations into context:

- So far, these expectations are mostly based on assumptions, announcements and initial lab experiments. There are no mechanisms in place and no data available to distinguish empty promises from real benefits. Experience gained from the first generation of transgenic crops shows that much more data would be needed to assess the potential benefits. For example, in many cases, the amount of herbicide used on transgenic crops was increased rather than reduced (Benbrook, 2012; Schütte et al., 2017; Schulz et al., 2021, de Lima Seixas et al., 2022), while some authors (such as Klümper & Qaim 2014) claimed major benefits. It appears that there is still a lack of sufficiently defined criteria to assess the overall impact of introducing transgenic plants.
- In order to achieve the 'Green Deal' goals and implement the 'Farm to Fork' strategy, clear and reliable criteria are a prerequisite for making decisions on the hypothetical benefits of each 'event' and the technology as a whole. Without comprehensive technology assessment, NGTs may block systemic options needed to achieve more sustainability, such as further research in agroecology. So far, there are no methods or criteria in place to identify real needs, 'true' benefits or potentially disruptive effects on the economy and/or ecology.[13]
- There is a specific problem with plants that claim health benefits, e.g. the GABA tomato. Assessing their impact on human health would require comprehensive research, especially if several similar products are brought to the market simultaneously, e.g. such as tomatoes enriched with Vitamin D (Li et al., 2022).

Conclusion: the report gives the impression that plants with valuable new traits derived from NGTs will soon be made available. However, existing experience shows that it is difficult to distinguish real benefits from empty promises. Whatever the case, no reliable conclusions can be drawn without further data and comprehensive technology assessment.

[13] See Testbiotech input on consultation by the EU Commission: https://www.testbiotech.org/node/2936

Patents and markets

The report warns that costs incurred for the EU approval process might become an obstacle for smaller companies (SMEs), thus resulting in further market concentration. In addition, it also mentions patents which can hamper or block access to the aforementioned technology. Several statements can be found in the report such as:
"*There is a complex landscape of patents and patent applications on different components of the CRISPR-Cas machinery, derived tools and their applications, amounting to more than 250 published patent families related to the use of CRISPR-Cas in plants (Jefferson et al., 2021). Universities and research institutes are a major contributor in these patent filings. Large players in the agricultural sector such as Bayer, Syngenta, BASF and Corteva have secured exclusive and non-exclusive licences on the IP related to the original CRISPR-Cas inventions from the University of Berkely [sic] and/or the Broad Institute of MIT and Harvard. Corteva has a right to sublicense to international research organisations and other companies (Jefferson et al., 2021). Getting a licence on the necessary IP to use CRISPR-Cas in agricultural crops creates a threshold in the access to the technique.*"

"*Plant characteristics resulting from the application of genome editing can also be protected by a patent, even when the edit could also have occurred naturally. But there must be a clear disclaimer in the patent application that the characteristic has been obtained using a method that is not 'essentially natural'. The use of genome-editing tools in agricultural crops on a wider scale might result in a larger number of agricultural crops that are patent-protected.*"

"*Another factor that fuels the debate is the level of corporate control over the food chain. GMOs are considered a risk factor that may contribute to this as GM crops can only be marketed by a limited number of international corporations. SMEs are not active in this market because they cannot afford the costs and complexities associated with the application of the GMO legislation. It is unlikely that the current GMO legislation will enable SMEs to enter the market of genome-edited crops and contribute to maintain or even expand diversity in the seed market.*"

Again, further information is needed to put this information into context:

- It is correct that patents are used to block, hamper and control access to the technology (Testbiotech, 2021). However, the report appears to give the impression that these patents are mostly related to access to the technology. But it is a fact that these patents also block access to biological resources and genetic diversity needed by breeders. For example, patent applications are being filed on the usage of thousands of genetic variations that are needed by all breeders, but which might also be useful for NGTs (e.g. as target sequences). It is incorrect that current European Patent Office practice generally exempts the usage of patented gene sequences in traditional breeding. If, for example, gene sequences are patented, they can no longer be used for the selection of plants that are of interest for further breeding. Therefore, many of these patents overlap and could end the freedom to operate for European breeders (Tippe et al., 2022).
- It also gives the impression that the costs incurred under the EU regulatory system represent an almost insurmountable hurdle for smaller companies entering the market. However, as in the US and Canada, which have similar patent protection but different GMO laws, it is the big companies that dominate the transgenic plant market (Howard, 2015; Clapp 2021). Therefore, it is much more likely that patents are behind the recent concentration in the seed market rather than regulatory requirements. It is also probable that only big companies will

> be able to survive in Europe if NGTs are introduced into the markets on a large scale. As yet, there is no indication that the EU will be able to solve the problems with patent monopolies within the next ten years. On the other hand, it can be assumed that regulatory requirements only have a minor impact on the market as a whole and any negative effects could be easily mitigated if required, even without changing EU GMO regulation or compromising safety.

Conclusion: the current EPO practice of granting patents not only covers the new technologies, but also impacts access to the biological resources needed by all breeders. Therefore, if breeders are pushed into using NGT applications, the current situation will promote further concentration in the seed markets, and thus leave this business in the hands of just a few companies. The ‘seed giants’ are likely to control seed markets and food production systems to an even greater degree than is already the case. SMEs are unlikely to benefit from this development. They will though feel the impact and be at risk of losing their freedom to operate.

Risks and Regulation

The report gives the impression that the genetic changes introduced by NGTs and their associated risks are equivalent to those resulting from conventional breeding, as long as no additional genes are added to the gene pool of a species. There is a suggestion that NGTs should be assumed to be less risky since the number of genetic changes resulting from NGTs may be limited. The report comprises several statements to this effect, such as :
“*The types of alteration introduced using CRISPR-Cas do not differ from the types of alteration (natural or induced) selected by conventional breeding, apart from when used to integrate genetic material that is foreign to the plant's gene pool.*”

“*Whether that property was introduced by a conventional technology or modern genetic technology does not make a difference for the resulting property and its potential to result in harm.*”

“*When CRISPR-Cas is not used to introduce foreign genetic material, the nature of introduced genetic changes, including possible off-target changes, does not differ from genetic changes selected in conventional breeding (spontaneous or induced).*”

“*It is estimated that in a single wheat plant approximately 238 spontaneous genetic alterations occur in each generation (extrapolated from Ossowski et al., 2010), implying that all individual plants in a field slightly differ genetically from each other.*”

“*In conventional cross breeding, for instance, the genetic material undergoes many more changes resulting from crossing. However, a molecular characterisation of the genome-edited plants is required to determine the introduced change with the necessary precision and detail.*”

“Genome editing enables the introduction of those changes in the variety in a direct manner without introducing additional changes, so that, for instance, the Chardonnay characteristics remain fully intact when a characteristic like fungal resistance is added to the grapevine.”

“*In genome-editing the number and frequency of off-target mutations is multitudes lower than in conventional random mutagenesis and during the process of generating a genome-edited crop one has the possibility to select plants that only possess the desired change.*”

These assumptions are mostly incorrect and misleading:

- It is not the number of mutations and the types of alterations, but rather the sites in the genome, the patterns of genetic change and the resulting genotypes that typify the difference between conventional breeding (including random mutations) and NGTs. The reason: compared to natural mutations and methods of conventional breeding (including random mutagenesis), NGTs can overcome the boundaries of natural genome organization that have emerged from evolutionary processes. Relevant factors include repair mechanisms, gene duplications, genetic linkages and further epigenetic mechanisms (see, e.g. Belfield et al., 2018; Filler Hayout et al., 2017; Frigola et al., 2017; Halstead et al., 2020; Huang & Li, 2018; Jones et al., 2017; Lin et al., 2014; Monroe et al., 2022; Wendel et al., 2016), thus making the genome much more extensively available for genetic change (Kawall, 2019; Kawall et al., 2020).
- As a result, only a few changes in the genome might be needed to achieve new genotypes that extend far beyond what can be achieved with conventional breeding, or to generate more extreme versions of already known traits, or new traits which come with ‘trade-offs’ (side effects). These ‘trade-offs’ are the result of interactions in the complex networks of genes, proteins and other biologically active molecules. Such unintended effects can also emerge in cases where the genetic intervention is targeted and precise. There is, therefore, no scientific basis for claiming that a variety such as ‘Chardonnay’, would not show any unintended effects caused by the new trait if it was made resistant to fungal diseases. On the contrary, there are already examples of other plant species which show that resistance to fungal disease is associated with trade-offs in overall plant fitness (see, for example, Spanu, 2022). Therefore, the way in which the Chardonnay example is presented is misleading.
- In addition, the technical potential of tools, such as CRISPR/Cas, is associated with a higher potential for unintended genetic changes that are unlikely to occur naturally. These unintended genetic changes are caused by the multistep process of (1) inserting the gene scissors into the cells and (2) their actions in the genome. The report gives the false impression that all of these unintended changes would very likely also occur with conventional breeding methods (including random mutagenesis). There are, however, no scientific findings to support this claim. While these ‘types’ of genetic alteration might also be observed in conventional breeding, their site, their pattern and their extent can be very different. As is the case with intended traits, unintended effects can also result in genotypes that go far beyond what can be achieved with conventional breeding, and thus result in specific risks. Effects include off-target DNA cleavage, repetitive unit deletion, indels of various sizes, larger structural changes in the targeted genomic region and the unintended insertion of transgenes (for overview see Kawall, 2021). If these unintended effects are overlooked, they may quickly spread within large populations.
- Consequently, there are specific risks inherent to NGTs that may have adverse impacts on the environment, plant or animal health and food safety that go beyond what can be expected from conventional breeding methods. This is also true even if no additional genes are inserted into the genome. Interactions with other NGT organisms and with the environment, including pests, pathogens, climatic conditions, etc. add further huge complexity to these risk scenarios.

Conclusion: at each stage of the process – including (i) insertion of the gene scissor DNA into the cells, (ii) target gene recognition and cleavage and (iii) cellular repair of the genes – both intended and unintended genetic changes can occur which are unlikely to result from conventional plant breeding and which are associated with risks. Therefore, as required by current EU GMO regulation, in each case, intended and unintended changes have to be assessed as to whether they can have either direct or indirect, immediate or delayed, or cumulative effects on human health and on the environment.

Further observations

There are some further observations made in the report on the identification of NGT plants and liability issues which need to be corrected and put into context.

Identification of NGT plants

The report gives the impression that the genetic changes introduced by NGTs do not allow the detection or identification of plants derived from NGTs if no additional genes have been added to the gene pool of a species. The report comprises several statement to this effect:
"*The genetic changes that are introduced by means of the SDN1 and SDN2 types of CRISPR-Cas technology do not differ from changes that can occur naturally or result from conventional breeding. This also means that, without prior knowledge, it is not possible to determine whether the genetic change is the result of genome editing. This means that once genome-edited products are released from the lab it is challenging to trace them through internal markets or across external borders.*"

These assumptions are once again misleading. On the contrary, the specific patterns of genetic change resulting from NGTs do allow the identification of the plants inheriting these changes (Duensing et al., 2018). However, it is, on the other hand, true that it may be challenging to identify the pattern without previous knowledge. Therefore, as foreseen in current EU GMO law, it is necessary to request methods of identification prior to marketing. In addition, an international register should be established, including methods of identifying plants brought to market in other regions.

Liability

The report gives the impression that existing regulation on liability is sufficient to cope with potential damage if NGT organisms were to be deregulated. The report contains the following statement in this regard:
"*Irrespective of the regulatory approach taken, all actors that introduce a genome-edited crop into the EU territory are liable under the Environmental Liability Directive (Directive 2004/35/EC) should that introduction result in damage to protected species and natural habitats, to water or to land.*"

Again this statement is misleading: if the precautionary principle, which is currently the basis for GMO regulation, were to be abandoned, liability rules would only apply to damage which had already occurred. In addition, such damage may only be recognised at a very late stage, and thus lead to irreversible effects on biodiversity or accumulations in the food chain. In general, damage, such as disruption in ecosystems and loss of species, cannot be mitigated by payments and needs to be prevented from the outset. Consequently, there is no alternative to upholding the precautionary principle in face of major uncertainties and risks associated with genetically engineered (genome edited) organisms.

Conclusions

In mandating and publishing the "*Genome edited crops and 21st century food systems challenges*" report, the Panel for the Future of Science and Technology (STOA) has contravened the basic principles of providing independent and impartial information to the members of the EU Parliament.

The analysis provided in this backgrounder shows that assumptions have been made which have been intentionally chosen to diverge from the facts and scientific findings. Consequently, the mandate given to the VIB experts has resulted in a report with incomplete and incorrect findings, compounded by misleading statements, messages and conclusions.

Therefore, STOA and the Directorate-General for Parliamentary Research Services (EPRS) of the Secretariat of the European Parliament should withdraw this report.

References

Belfield E.J., Ding Z.J., Jamieson F.J.C., Visscher A.M., Zheng S.J., Mithani A., Harberd N.P. (2018) DNA mismatch repair preferentially protects genes from mutation. Genome Res, 28(1): 66-74. https://doi.org/10.1101/gr.219303.116

Benbrook C.M. (2012) Impacts of genetically engineered crops on pesticide use in the U.S. - the first sixteen years. Environ Sci Eur, 24: 24. https://doi.org/10.1186/2190-4715-24-24

CEO (2021) Derailing EU rules on new GMOs - CRISPR-Files expose lobbying tactics to deregulate new GMOs. Corporate Europe Observatory, https://corporateeurope.org/en/2021/03/derailing-eu-rules-new-gmos

Clapp J. (2021) The problem with growing corporate concentration and power in the global food system. Nat Food, 2(6): 404-408. https://doi.org/10.1038/s43016-021-00297-7

Demorest Z.L., Coffman A., Baltes N.J., Stoddard T.J., Clasen B.M., Luo S., Retterath A., Yabandith A., Gamo M.E., Bissen J., Mathis L., Voytas D.F., Zhang F. (2016). Direct stacking of sequence-specific nuclease-induced mutations to produce high oleic and low linolenic soybean oil. BMC Plant Biol, 16(1): 1-8. https://doi.org/10.1186/s12870-016-0906-1

Duensing N., Sprink T., Parrott W.A., Fedorova M., Lema M.A., Wolt J.D., Bartsch D. (2018) Novel features and considerations for ERA and regulation of crops produced by genome editing. Front Bioeng Biotechnol, 6: 79. https://doi.org/10.3389/fbioe.2018.00079

EPRS | European Parliamentary Research Service (2022) Genome-edited crops and 21st century food system, Scientific Foresight Unit (STOA), PE 690.194 – July 2022, https://www.europarl.europa.eu/thinktank/en/document/EPRS_IDA(2022)690194

Filler Hayut S., Melamed Bessudo C., Levy A.A. (2017) Targeted recombination between homologous chromosomes for precise breeding in tomato. Nat Commun 8, 15605. https://doi.org/10.1038/ncomms15605

Frigola J., Sabarinathan R., Mularoni L., Muiños F., Gonzalez-Perez A., López-Bigas N. (2017) Reduced mutation rate in exons due to differential mismatch repair. Nat Genet, 49: 1684-1692. https://doi.org/10.1038/ng.3991

Halstead M.M., Kern C., Saelao P., Wang Y., Chanthavixay G., Medrano J.F., Van Eenennaam A.L., Korf I., Tuggle C.K., Ernst C.W., Zhou H., Ross P.J. (2020) A comparative analysis of chromatin accessibility in cattle, pig, and mouse tissues. BMC Genomics, 21: 698. https://doi.org/10.1186/s12864-020-07078-9

Huang Y. & Li G.-M. (2018) DNA mismatch repair preferentially safeguards actively transcribed genes. DNA Repair, 71: 82-86. https://doi.org/10.1016/j.dnarep.2018.08.010

Howard P.H. (2015) Intellectual property and consolidation in the seed industry. Crop Sci, 55(6): 2489-2495. https://doi.org/10.2135/cropsci2014.09.0669

Jefferson O.A., Lang S., Williams K., Koellhofer D., Ballagh A., Warren B., Schellberg B., Sharma R., Jefferson R. (2021) Mapping CRISPR-Cas9 public and commercial innovation using The Lens institutional toolkit. Transgenic Res, 30(4): 585-599. https://doi.org/10.1007/s11248-021-00237-y

Jones D.M., Wells R., Pullen N., Trick M., Irwin J.A., Morris R.J. (2018) Spatio-temporal expression dynamics differ between homologues of flowering time genes in the allopolyploid *Brassica napus*. Plant J, 96: 103-118. https://doi.org/10.1111/tpj.14020

Kaiser N., Douches D., Dhingra A., Glenn K.C., Herzig P.R., Stowe E.C., Swarup S. (2020) The role of conventional plant breeding in ensuring safe levels of naturally occurring toxins in food crops. Trends Food Sci Technol, 100: 51-66. https://doi.org/10.1016/j.tifs.2020.03.042

Kawall K. (2019) New possibilities on the horizon: genome editing makes the whole genome accessible for changes. Front Plant Sci, 10: 525. https://doi.org/10.3389/fpls.2019.00525

Kawall K., Cotter J., Then C. (2020) Broadening the GMO risk assessment in the EU for genome editing technologies in agriculture. Environ Sci Eur, 32: 106. https://doi.org/10.1186/s12302-020-00361-2

Kawall K. (2021b) The generic risks and the potential of SDN-1 applications in crop plants. Plants, 10(11): 2259. https://doi.org/10.3390/plants10112259

Klümper W., Qaim M. (2014) A meta-analysis of the impacts of genetically modified crops. PloS ONE 9(11): e111629. https://doi.org/10.1371/journal.pone.0111629

Li J., Scarano A., Gonzalez N.M., D'Orso F., Yue Y., Nemeth K., Saalbach G., Hill L., de Oliveira Martins C., Moran R., Santino A. Martin C. (2022) Biofortified tomatoes provide a new route to vitamin D sufficiency. Nat Plants, 8: 611-616. https://doi.org/10.1038/s41477-022-01154-6

de Lima Seixas R.N., da Silveira J.M.F.J., Ferrari, V E. (2022) Assessing environmental impact of genetically modified seeds in Brazilian agriculture. Front Bioeng Biotechnol, 10: 977793. https://doi.org/10.3389/fbioe.2022.977793

Lin T., Zhu, G., Zhang J., Xu X., Yu Q., Zheng Z., Zhang Z., Lun Y., Li S., Wang, X., Huang Z., Li J., Zhang C., Wang T., Zhang Y., Wang A., Zhang Y., Lin K., Li C., Xiong G., Xue Y., Mazzucato

A., Causse M., Fei Z., Huang S.(2014) Genomic analyses provide insights into the history of tomato breeding. Nat Genet, 46: 1220-1226. https://doi.org/10.1038/ng.3117

Monroe G., Srikant T., Carbonell-Bejerano P., Becker C., Lensink M., Exposito-Alonso M., Klein M., Hildebrandt J., Neumann N., Kliebenstein D., Weng M.-L., Imbert E., Ågren J., Rutter M.T., Fenster C.B., Weigel D. (2022) Mutation bias reflects natural selection in *Arabidopsis thaliana*. Nature, 602: 101-105. https://doi.org/10.1038/s41586-021-04269-6

Nonaka S., Arai C., Takayama M., Matsukura C., Ezura H. (2017) Efficient increase of ɣ-aminobutyric acid (GABA) content in tomato fruits by targeted mutagenesis. Sci Rep, 7: 7057. https://doi.org/10.1038/s41598-017-06400-y

Ossowski S., Schneeberger K., Lucas-Lledó J.I., Warthmann N., Clark R.M., Shaw R.G., Weigel D., Lynch M. (2010) The rate and molecular spectrum of spontaneous mutations in *Arabidopsis thaliana*. Science, 327(5961): 92-94. https://doi.org/10.1126/science.1180677

Schütte G., Eckerstorfer M., Rastelli V., Reichenbecher W., Restrepo-Vassalli S., Ruohonen-Lehto M., Wuest Saucy A.G., Mertens M. (2017) Herbicide resistance and biodiversity: agronomic and environmental aspects of genetically modified herbicide-resistant plants. Environ Sci Eur, 29: 5. https://doi.org/10.1186/s12302-016-0100-y

Schulz R., Bub S., Petschick L.L., Stehle S., Wolfram J. (2021) Applied pesticide toxicity shifts toward plants and invertebrates, even in GM crops. Science, 372(6537): 81-84. https://doi.org/10.1126/science.abe1148

Spanu P.D. (2022) Slicing the cost of bread. Nat Plants, 8: 200-201. https://doi.org/10.1038/s41477-022-01115-z

Testbiotech (2021) What Members of the European Parliament should consider when discussing New Genetic Engineering (New GE) with STOA. https://www.testbiotech.org/content/stoa-backgrounder

Tippe R., Moy, A-C., Eckhardt J., Meienberg F., Then C. (2022) Patents on genes and genetic variations block access to biological diversity for plant breeding: patent research conducted in 2021 shows how industry is trying to patent genes, plants, seeds and food. No Patents on Seeds!, https://www.no-patents-on-seeds.org/en/report2022

Watson A., Ghosh S., Williams M.J., Cuddy W.S., Simmonds J., Rey M.D., Hatta M.A., Hinchliffe A., Steed A., Reynolds D., Adamski N.M., Breakspear A., Korolev A., Rayner T., Dixon L.E., Riaz A., Martin W., Ryan M., Edwards D., Batley J., Raman H., Carter J., Rogers C., Domoney C., Moore G., Harwood W., Nicholson P., Dieters M.J., DeLacy I.H., Zhou J., Uauy C., Boden S.A., Park R.F., Wulff B.B.H., Hickey, L.T. (2018) Speed breeding is a powerful tool to accelerate crop research and breeding. Nat Plants, 4(1): 23-29. https://doi.org/10.1038/s41477-017-0083-8

Wendel J.F., Jackson S.A., Meyers B.C., Wing R.A. (2016) Evolution of plant genome architecture. Genome Biol, 17: 37. https://doi.org/10.1186/s13059-016-0908-1

Wolter F., Schindele P., Puchta H. (2019) Plant breeding at the speed of light: the power of CRISPR/Cas to generate directed genetic diversity at multiple sites. BMC Plant Biol, 19(1): 176. https://doi.org/10.1186/s12870-019-1775-1