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

Frohschammerstraße 14
80807 München
Germany

Phone
0049(0) 15154638040
info@testbiotech.org
www.testbiotech.org

Executive Director:
Dr Christoph Then

EU Transparency Register
ID 151554816791-61

European Commissioner for Health & Food Safety
Ms Stella Kyriakides

CC
Vice-President of the EU Commission
Mr Frans Timmermans

31 March 2023

Criteria for risk assessment of NGT plants

Dear Ms Kyriakides,

The following discussion paper has been brought to our attention: "*Potential criteria to determine whether a plant obtained by targeted mutagenesis or cisgenesis could also occur naturally or be produced by conventional breeding techniques*". It appears to have been authored by the Commission services and distributed to experts in EU Member States.

Please allow us to make a brief comment. In short, the paper suffers from a major misconception: it ostensibly discusses unintended and intended genetic changes caused by NGTs in comparison to previously used breeding methods, but the criteria for comparison have been chosen arbitrarily ('cherry picking') and the conclusions are largely misleading.

The paper initially discusses unintended effects. Criteria chosen in this instance are the type of mutations, e. g. substitutions, insertions and deletions. The number of mutations is also taken into account. Conclusions have thus been drawn that there would be no major differences in the type of mutations - while it is only with NGTs that the number of mutations would be lower.

It goes on to discuss intended changes. The criteria applied in this context are the site of the mutation and the resulting genetic combination. The conclusion drawn here for intended effects is that new genotypes might result from NGT applications that are unlikely to occur with previously used methods, such as random mutagenesis.

The authors have ‘overlooked’ that intended and unintended genetic changes introduced by NGTs (such as ‘CRISPR/Cas’ gene scissors) are caused by the same mechanisms. The same mechanisms that intentionally cause new patterns of genetic change in plants are also a decisive factor for the introduction of unintended genetic changes. Consequently, NGT processes may also cause unintended genetic changes which are different to those which can be expected from conventional breeding (including random mutagenesis):

(1) Gene scissors make the genome available for changes to a much greater extent compared to conventional breeding methods. The likelihood of unintended genetic changes occurring at specific genomic sites is, therefore, higher with NGTs.
(2) Not only the sites of unintended genetic changes, but also the resulting combinations (of unintended genetic alterations) caused by NGTs can be vastly different compared to those resulting from conventional breeding.
(3) NGTs are based on a complex multistep process including old methods of genetic engineering to introduce the DNA for the formation of the gene scissors into the cells. This first step, which is most often applied in plants, can also cause unintended genetic changes (such as unintended insertion of transgenes) that are different to those resulting from conventional breeding.

These findings are explained in detail in the Annex and summarized in the figure below.

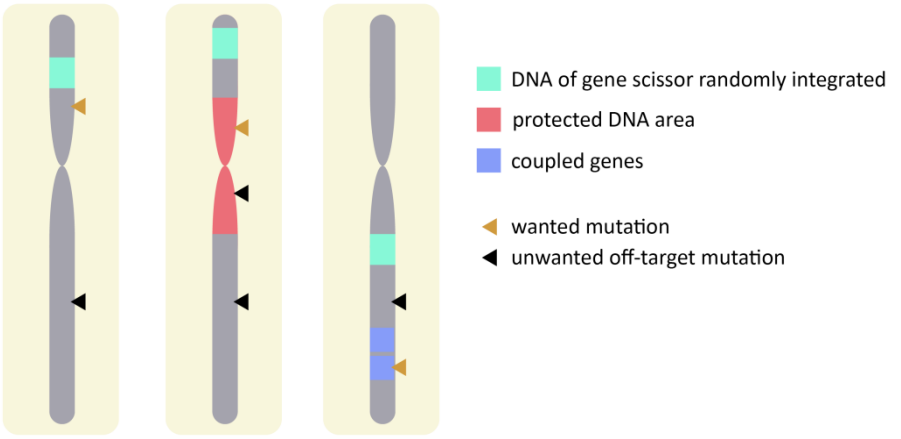

Figure: Unintended genetic changes (mutations) can also occur in conventional breeding. However, NGT methods are accompanied by changes that would not be expected with conventional breeding or random mutations: both the site of mutation and the resulting gene combination can be significantly different to the results of conventional breeding. This is true not only for intended, but also for unintended genetic changes. Some reasons are: NGTs can overcome constraints of natural genome organization used by cells to maintain gene function (such as repair mechanisms, gene duplications, genetic linkages or epigenetic mechanisms). In addition, several different gene loci can be altered simultaneously (multiplexing). The introduction of NGT tools using the untargeted methods of old genetic engineering can also result in unintended genetic changes such as insertions of transgenes in the genome of plants.

As you may conclude from the Annex, EFSA was never asked to examine key questions such as: ‘Which unintended genetic changes are caused by NGT processes that are unlikely to occur with previously used methods (crossing and selection and random mutagenesis)?’ However, unless the EFSA is asked to answer crucial questions, the Commission cannot rely on EFSA answers.

In conclusion: unintended genetic changes caused by NGT processes that are unlikely to result from conventional breeding (including random mutagenesis) are highly relevant to NGT risk assessment. The reason: these changes may trigger adverse effects (direct or indirect, immediate, delayed or accumulated) that were not anticipated and which may go beyond what is known from conventional breeding.

There is, therefore, no scientific basis for fragmenting the current EU GMO regulation. Even in future, all plants derived from processes of genetic engineering should have to undergo risk assessment, as required in Directive 2001/18 and Commission Directive 2018/350. Risk assessment is essential for concluding which genetic irregularities are caused by NGT processes and whether they may have an impact on health and the environment.

It also should be noted that if hazardous unintended genetic changes are overlooked, they may quickly spread within breeding populations and accumulate by further cross breeding. The effects caused by such unintended genetic changes have the potential to put the future of plant and animal breeding at risk, and are, therefore, a risk to the food security of future generations.

With kind regards

Christoph Then, Testbiotech
Executive director
info@testbiotech.org
Tel +49 151 54638040

Annex New Genomic Techniques and unintended genetic changes: EFSA ‘overlooked’ most of the relevant publications, Testbiotech Background, https://www.testbiotech.org/sites/default/files/EFSA%20%E2%80%98overlooked%E2%80%99%20relevant%20publications.pdf