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Gene-editing of plants – GM through the back door?

Gene-editing techniques may be more precise than 'traditional' genetic engineering in their positioning of the intended alteration to genetic material. However, the newly created organisms can still display unexpected and unpredictable effects, which can have implications for their food, feed or environmental safety. If these new techniques were to be exempted from the EU's regulations for genetically modified organisms (GMOs), there would be no requirement to detect and assess such unintended changes or to assess any potential negative safety effects. Also, there would be no requirement to make the products traceable and label them as GMOs. The GMO regulations in the EU must be interpreted in their intended sense, to encompass all modern biotechnological processes that directly modify genomes. Otherwise, the EU would be failing its citizens.

What is 'gene-editing'?

Gene-editing (or 'genome-editing') techniques allow the direct modification of plant genetic material (usually DNA) at specific locations in the genome. They generally use nucleases, often called 'molecular scissors', which cleave DNA at specific sites and trigger the plant's own repair mechanisms. Techniques involving this molecular scissors include zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), meganucleases (MN) and the clustered regularly interspaced short palindromic repeat (CRISPR/Cas) system. In contrast, oligonucleotide-directed mutagenesis (ODM) is a gene-editing technique that does not use molecular scissors. With ODM, short DNA (or DNA-RNA) fragments (oligonucleotides) are introduced into cells where they trigger the cell to modify its own DNA to match the introduced DNA fragments.

All gene-editing techniques (including ODM) can change, insert or delete one or a few base pairs of DNA[1]. Some applications of these techniques can also insert novel genes into the plant genetic code, similarly to 'traditional' genetic engineering.

Unexpected and unpredictable effects

Just as 'traditional' genetic engineering, gene-editing techniques can induce unintended changes in genetic material even if only one or a few base pairs have been altered[2]. For example, ODM and 'molecular scissors' generally give rise to so-called 'off-target effects' meaning they cut and/alter DNA in places additional to those intended[3].

Both intended and unintended changes can be important in terms of plant protein production and metabolism. Thus, it is possible – and indeed likely – that ODM and other gene-editing techniques can give rise to unexpected and unpredictable effects with implications for food, feed and environmental safety[4].

Different from conventional plant breeding by mutagenesis

It has been suggested that ODM and other gene-editing techniques could be exempt from the EU GMO regulations[5]. One argument given is that the genetic changes would be small when compared to 'traditional' genetic engineering, too small to be classified as recombinant[6]. However, the extent of change to the plant's DNA is irrelevant in determining whether the resulting plant is classified as a GMO under the EU regulations. It does not matter whether only one or two DNA bases have been inserted, changed, deleted or whole novel gene sequences inserted. The DNA remains recombinant in that it has undergone recombination with the plant's DNA. Moreover, the critical question is whether plant genetic material has been directly modified in a way that does not occur naturally. The answer to this is yes.

It has also been argued that gene-editing results in similar changes to the plant genome as mutagenesis[7]. Traditional mutagenesis uses chemicals or radiation to induce random mutations in the plant genome. The plants displaying desired characteristics are then selected for further breeding. Plants developed by this technique are considered as GMOs but exempt from EU regulations.

However, ODM and other gene-editing techniques are wholly different from mutagenesis. They are *in vitro* modern biotechnological techniques. This means that the genetic modification is enacted by heritable material (or material causing a heritable change) that has, for at least part of the procedure, been handled outside the organism by people[8]. In both the EU and Cartagena Protocol, the definitions of a GMO refer to (but not exclusively) the use of such *in vitro* techniques.

Need for risk assessment, detectability and labelling

In addition to the assessment of any novel characteristics of GMOs (e.g. herbicide tolerance), EU regulations require the assessment of any unintended changes and their implications for the safety of the environment, human and animal health. This is essential to achieving the health and environmental protection goals of the EU regulations. These regulations also require that GMO seeds, crops and food/feed products must be detectable and labelled. This allows farmers, consumers and governments to choose whether or not to use the products of genetic modification.

Exemption of plants produced by gene-editing techniques from the EU GMO regulations would mean that there is no requirement to assess any potential effects on food, feed or environmental safety. It would also mean exemption from GMO labelling requirements, restricting the choices available to the clear majority of European consumers that wish to avoid food derived from GMO plants.

The GMO regulations in the EU should be interpreted in their intended sense, to encompass all modern biotechnological processes that directly modify genomes. Otherwise, the EU would be failing its citizens.

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