

The European Union Court's Advocate General's Opinion and new plant breeding techniques

To the Editor: Rapid progress in new plant breeding techniques (NPBTs) poses challenges for government agencies seeking to apply existing regulatory frameworks to new products. In the European Union (EU), two decisions to come this year will, it is hoped, provide greater clarity as to whether crops generated using NPBTs should be regulated as genetically modified organisms (GMOs)^{1–3}. First, the Court of Justice of the European Union (CJEU) is expected to reach a decision on the ‘mutagenesis exception’⁴ within Directive 2001/18/EC, which legally defines GMOs⁵. Second, the European Commission is expected to issue its much-delayed interpretation of whether NPBTs should fall within the scope of GMO-specific legislation⁶.

Here, we discuss the *Opinion of Advocate General Bobek*⁷, which we believe sheds light on how the EU will likely deal with so-called ‘mutagenic’ NPBTs (e.g., oligonucleotide-directed mutagenesis (ODM), zinc finger endonucleases (ZFNs), transcription-activator-like endonucleases (TALENs) and CRISPR-Cas endonucleases) that do not involve the use of recombinant DNA. If the CJEU follows this Opinion on Directive 2001/18/EC’s ‘mutagenesis exception’, delivered in January by the CJEU’s Advocate General (AG) Michal Bobek, several NPBTs will likely be exempted from the scrutiny of the directive, making room for the EU legislator or member states to regulate mutagenic NPBTs. Expanding on the AG’s Opinion, we go on to discuss four options for how mutagenic NPBTs could be regulated and highlight which path we think is most likely.

According to the AG’s Opinion, any crop obtained through an NPBT that applies recombinant DNA techniques—or other techniques leading to ‘unnatural’ changes—will be considered a GMO within the scope of the directive. Contrary to some observers, the same provisions exempt crops altered only by mutagenesis approaches known when the directive was introduced in 2001, but also to newer approaches introduced since that time⁷.

The AG classifies this exception as ‘minimum harmonization’, meaning that it applies to the directive, but does not preclude member states from adding additional national regulations to mutagenic NPBTs. He also clarifies that it is either the EU’s or member states’ task—not that of the CJEU—to adjust Directive 2001/18/EC to technology advancement. Both notions have important policy implications and put the ball back in the court of policymakers.

Whether this interpretation will also extend to other EU legislation, such as that on GM food and feed⁸, was left open by the AG. Despite some slightly different wording⁷ between Directive 2001/18/EC and the regulations on GM food and feed it is likely that those who drafted the GM food and feed regulations intended that the legal value of the scope of the directive and mutagenesis exemption to be transferred as is to the GM food and feed regulations. The interpretation proposed by the AG would thus apply not only to new crop releases but also to food and feed.

At the same time, the AG’s opinion is non-binding and provides only a proposal for how the CJEU should resolve its case, seeking to clarify which products fall under the directive’s ‘mutagenesis exemption’. The decision of the CJEU will have binding effect only on the interpretation of the directive (and most notably on the GMO definition in art. 2 (2) of the directive and the mutagenesis exception in the annex). Historically, the CJEU has followed most opinions given by AGs⁹.

A key aspect of this CJEU case revolves around the term ‘mutagenesis’, which is not further defined in law. The AG’s Opinion refers to it as “an alteration of the genome of a living species” that does not “entail the insertion of foreign DNA.” New mutagenesis techniques mentioned by the AG include gene-editing techniques, including ODM and site-directed-nuclease-1 (SDN-1)-based techniques (e.g., ZFN, TALENS and CRISPR-Cas endonucleases)⁷. For a gene-edited crop and its derived products not to be regulated as a GMO, it must fulfill one of the two following conditions: first,

if it could have been generated ‘naturally’, then it would fall outside the definition of GMOs and the scope of Directive 2001/18/EC; second, if no recombinant nucleic acids were used to generate it, then that product falls under the “mutagenesis exemption” described above.

Thus, according to the AG’s classification, only those NPBTs that result in mutagenesis would be exempted from Directive 2001/18/EC. The question of who decides which NPBT should qualify as a mutagenesis technique was left open by the AG. We envisage that competent national scientific bodies that conduct risk assessment of GMOs would perform this role. The process would likely involve an initial assessment of the nature and extent of the changes introduced into a plant product, perhaps based on fact sheets provided by developers describing the targeted genome changes that have been introduced and the technique that has been used.

It is noteworthy that other jurisdictions have similar procedures for developers. For example, in Argentina, sponsors have the possibility of consulting, at an early stage, with a national scientific advisory body to decide whether crops created using NPBTs fall outside the country’s regulations¹⁰. What’s more, the European Commission has recently proposed a pre-submission procedure for crop developers, although it remains unclear whether this would be used to clarify issues surrounding the categorization of NPBTs¹¹.

If products derived from NPBTs do not fall under Directive 2001/18/EC, how should their development be overseen (at which level, by whom and following which legal framework) in the EU? Taking AG Bobek’s classification of the ‘mutagenesis’ exemption as ‘minimum harmonization’ we envisage at least four options:

Option 1. Member states take action and regulate the use of whole plants and viable materials from plants created with mutagenic NPBTs for release into the environment, such as for field trials and cultivation, under their own laws, which affect only their jurisdiction. In this case, member states have a wide array

of regulatory measures at their disposal, ranging from information obligations to authorization requirements. Within these options, member state practice may also vary. In case of an authorization requirement, some member states may grant approval immediately, whereas others may ask for additional information, restrict cultivation or ban cultivation. Such a framework has been set by Germany in response to a company's submission of a herbicide-tolerant oilseed rape line developed with ODM to the national competent authority for approval¹². Companies may prioritize which jurisdictions they apply in and which they do not. In the case of foods, food ingredients originating from NPBTs will be subject to the EU food law framework, in particular the rules of the General Food Law. Member states' discretion to regulate foods derived from mutagenic NPBTs is narrower in this area, as most provisions of EU food law follow the rules of maximum harmonization¹³.

Option 2. EU institutions take action and introduce legislation to regulate mutagenic NPBTs at the EU-wide level. For example, following a proposal of the European Commission, the EU Parliament and the EU Council would vote on adapting the directive's exemption list to exclude specific mutagenic NPBTs. As a consequence, mutagenic NPBTs would be regulated in a manner comparable to regular GMOs, which require authorization under the directive. Alternatively, the EU could decide to develop parallel EU-wide legislation for NPBTs specifically, with its own requirements and EU-centralized procedures.

Option 3. EU institutions frame member state laws for mutagenic NPBTs. Again, following a proposal of the Commission, the EU Parliament and the EU Council vote on the application of a general legislative framework to govern NPBTs at the EU level, but leave it to the member states to decide how to specifically apply them. In this case EU law could regulate general principles that govern member states' regulatory decisions also for environmental release following, for example, the regulatory technique used in the EU's General Food Law.

Option 4. No action will be taken and mutagenic NPBTs will remain exempt and therefore unregulated in terms of specific GMO law. Nevertheless, companies have to comply with general national regulations, such as the

national seed and environmental laws similar to laws covering non-GM crops, as well as those from the General Food Law, including particularly those for 'novel foods'.

We believe option 4 is unlikely to be taken up EU-wide. Member states most probably will call for specific regulations reflecting their societal and economic needs, as has been seen in parallel cases relating to the cultivation of GM crops in national territories¹⁴. Options 2 and 3 are also unlikely to deliver a well-working framework—past experience has shown that consensus among European policymakers is difficult to find on any type of new legislation concerning bioengineered products¹⁵.

Option 1 may thus be the preferred choice to serve the interests of the public and consumers without stifling innovations in the crop-breeding sector. Within this framework, member states can choose to implement measures, which will likely result in a competitive patchwork of regulations. Some member state regulations will be more demanding than those in other member states. Depending on a host of societal and economic factors¹⁶, the national authorities may dial up or dial down the stringency of their oversight accordingly. Ultimately, as all the different member state frameworks come into line with one another, a more efficient regulatory environment may come into being, resulting in *de facto* harmonization¹⁷.

In summary, we conclude that the AG's opinion creates the opportunity to move away from the current regulation of new crop varieties toward a more scientific, risk-based and decentralized strategy, as outlined above. If the opinion is followed, the possibility opens up of a more transparent case-by-case approach at the member state level. This will not only assure the safety of newly introduced NPBT varieties for consumers and the environment, but also respect differing public opinions and farm business structures across the EU.

COMPETING INTERESTS

The authors declare no competing interests.

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