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Opinion

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Proportionate and scientifically sound risk assessment of gene-edited plants

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The recent ruling of the European Court of Justice that gene-edited organisms should be considered—and regulated—as genetically modified organisms (GMOs) has surprised many scientists. First, it departs from the more balanced opinion of the Advocate General published in January, which was seen by many scientists as a good indicator that gene-edited plants would not automatically be considered as GMOs [1]. Second, it contains statements with little scientific basis: for example, when it states that gene editing produces the same effects as the introduction of a foreign gene or that gene editing can produce genetically modified varieties at a rate out of all proportion to those generated by conventional methods of mutagenesis. It is true that gene editing can speed up the process of creating a particular mutant, but random mutagenesis produces mutations at much higher rate. The major concern of many scientists is that this is a rigid judgment that will have a chilling effect on research and development in gene editing in the EU [2]. Here, we analyze the consequences of the ruling and discuss possible options for a scientifically sound and proportionate risk assessment of genetically engineered plants that are compatible with the Court's decision and the present GMO legal framework.

The Court had considered the existing legislation, and in particular the EU Directive 2001/18/EC, which is a modification of the previous Directive 90/220/EEC of 1990. However, this legislation was drafted 28 years ago, and hundreds of millions of hectares have been planted worldwide with GMOs since. We gained much experience in the risk assessment of their derived products, and new techniques have emerged that could be used to solve important questions of Biology and Agriculture. The existing legislation has been criticized as being inappropriate to deal with a new generation of GMOs and, in particular, the gene-edited plants. In particular, critics have maintained that the process-based approach to regulation is outdated in light of new technologies and recommended adopting a product-based risk assessment as is the case in the USA and elsewhere. Many voices from industry and scientists have asked for changing the Directive, and there is a formal proposal from the Netherlands [3]. However, the present European political situation—with divergent political interests and agendas among member states, the European Parliament approaching elections, and the Commission in an apparently weak situation—makes any modification of the Directive very difficult and hazardous.

There is, however, a possible solution: to return to the original spirit of the Directives which stipulates that risk assessment of GMOs should be based on scientific analysis carried out on a case-by-case basis adapted to each genetic modification, the recipient organism, and purpose and scope of the application. As laid down in the EU legislation, the risk assessment has been ascribed to independent scientific committees and, specifically, the EFSA GMO Panel since its establishment in 2002. The European Commission is committed to follow the Panel's advice when member states fail to agree on the approval of any new GMO for food or other uses. Scientists are therefore supposed to play a key role in this process.

The Directive 90/220/EEC was drafted in 1990, only 7 years after the publication of the first gene transfer in plants [4,5] and years before any GMO-derived product was commercialized. At that time, the knowledge on DNA transfer mechanisms and on the potential effects on the genome was limited. However, the mandatory risk analysis, as laid down in the Directive 90/220/EEC, was based on scientific data and scrutiny and it was essentially targeted to each individual GM plant species, the transgene introduced, and the scope of the requested authorization. Thus, the requirement to adapt the risk analysis to the modified plant under assessment taking into account existing knowledge was clear from the very beginning: Annex II of the Directive states "Not all the points included will apply to every case. It is to be expected, therefore, that individual notifications will address only the particular subset of considerations that are appropriate to individual situations". This need for a case-by-case analysis was retained in the EU Directive 2001/18/EC as a key principle.

Moreover, the 1990 Directive allows simplifying the procedure once sufficient experience has gained on the safety of a particular GM product. Its Article 6 states, "If the competent authority considers that sufficient experience has been obtained of releases of certain GMOs, it may submit to the Commission a request for the application of simplified procedures for releases of such types of GMOs". Thus, the original Directives regulating the deliberate release of GMOs in the EU retain ample room for adapting the procedures to each genetically modified organism and derived products. This was the approach followed by the EFSA experts on their opinion on how plants produced by cisgenesis or intragenesis should be evaluated [6], and the working group created by EFSA in 2012 to discuss risk assessment of plants created by site-directed nucleases (SDNs, essentially Zinc

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finger nucleases at that time). Unfortunately, the working group only delivered its opinion of SDN3 uses (targeted introduction of transgenes) [7] and was not asked to discuss gene editing. This decision showed a lack of trust from European authorities in the advice from EFSA and in general in independent scientific opinions.

We have been members of the GMO EFSA Panel since its beginning and we have witnessed a reduction in the flexibility in the scientific procedures, which reflects this decrease of trust in scientists and risk assessors. Over the years, the requirement for a more systematic and routinely applied approach has decreased the latitude of EFSA Panel members and its external advisors to adapt the risk assessment to the type of genetic modification, plant, and scope.

A key moment was the approval of rules such as the Implementing Regulation 503/2013 that imposed a rigid analysis of GM plants and that was the result of political negotiations among EU member states. As a consequence, the present legal framework in the EU imposes a long and costly procedure that greatly limits the commercialization of GMOs and that if applied to the new gene-edited plants and derived products will challenge the commercial use of these new techniques in the EU. Moreover, as gene-edited plants and derived products are difficult to identify and quantify, applying the present GMO legal framework will be challenging, in particular when exporting countries such as the USA will start market varieties that they have already decided not to regulate.

In our opinion, there is an urgent need to strengthen the general trust in science and scientists in the EU and to reinforce the role of scientific advice in issues that have an important scientific basis, such as GMO approval. If we want that policy-makers and society at large trust scientists in controversial issues, the European scientific community needs to renew its commitment to collaborate and to provide quality opinions according to the rules of scientific integrity. Consequently, it would also mean to act independent only of industrial interests but also from eventual interests of the scientific community itself.

It is therefore time to reverse the trend of taking decisions that prevent the use of promising new biotechnologies. That would mean to take into account the experience gained after 28 years of cultivating GMOs and the risk assessments of these and their derived products, thereby acknowledging that no general risk associated with the genetic modification process has been reported after millions of Euros spent in research projects to analyze these plants [8], (www.grace-fp7.eu, www.g-twyst.eu). It would also mean to use the flexibility of the system for case-by-case risk assessments carried out by independent scientists. This was the explicit approach of the first Directive, and it would allow adapting it to the new gene-editing techniques to perform a proportionate and scientifically sound risk analysis while fully complying with the legal framework.

Conflict of interest

The authors have been members of the EFSA GMO Panel (P.P. 2003–2006, J.C. 2006–2012 and 2015–2018). Pere Puigdomènech has been member of the GRACE (2012–2015) and G-TwYST (2014–2018) projects funded by the EU FP7 Program.

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