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ENSSER Statement

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EU Commission's proposal on new GM plants: no science, no safety

The European Commission's proposal to exempt most 'new' genetically modified (GM) plants from regulation must be rejected as a whole. It is in conflict with science. It puts the population and the environment at risk without informing citizens by labelling and allowing them to make autonomous decisions. It prevents scientists from identifying risks and following up with research because it abolishes traceability and registration of molecular data. Thus, it is an open, shameful attempt to render the precautionary principle inoperative, while the proposal even claims to be in accordance with this principle. New GM plants must remain regulated by the existing EU legislation, which has proven to serve its purpose well.

While we focus our critique in this statement on the major problems of the EC proposal, these are not its only problems. We hope to address all scientific problems of the proposal in a later statement.

European Commission proposal is unscientific

The EC's proposal for a Regulation on NGT plants[1] divides these GM plants into two categories. Category 1 NGT plants have to meet the criteria of Annex I of the Regulation; if this has been "verified" by the competent authority, they can be released and their products placed on the market without any further requirements such as risk assessment, traceability and labelling. Category 2 NGT plants are all other NGT plants; they have to fulfil a reduced portion of the requirements of the existing EU GMO legislation, including a limited risk assessment as well as labelling.

[1] Plants obtained by so-called New Genomic Techniques, including but not limited to CRISPR-Cas. NGT organisms are - as confirmed by the 2018 ruling of the European Court of Justice - genetically modified organisms (GMOs), in this case genetically modified plants.

We expect that virtually all requests for release of NGT plants will be submitted under Category 1 and hardly any under Category 2. So in practice, this proposal will exempt the majority of new GMOs (NGT plants) from EU GMO regulation and its requirements.

In the Treaty on the Functioning of the EU (TFEU), Article 114 § 3 states: "The Commission, in its proposals envisaged in paragraph 1 concerning health, safety, environmental protection and consumer protection, will take as a base a high level of protection, taking account in particular of any new development based on scientific facts."[2]

The proposal disregards many scientific facts. More, it fails the standard of 'science-based', contrary to the EC's claims (EC 2023a, EC 2023b); further, it is in conflict with science, for a number of reasons, including the following ones.

The proposal is not in accordance with science- and evidence-based risk assessment and management best practice, because there is as yet little experience regarding the safety of new genetic engineering techniques in food and in agricultural cultivation. Instead, the proposal provides a list of non-scientific "equivalence criteria" that are overly broad and that simply redefine the vast majority of new GMOs as "equivalent to conventional plants" (Category 1, Annex I). An overarching criterion and a set of five sub-criteria are given, all of which are based on DNA sequences only. However, plants cannot be called biologically equivalent on the basis of their DNA sequences only: a plant is defined by more than just DNA. Moreover, even to call their DNA sequences "equivalent" on the basis of these criteria (e.g. the allowance for any "substitution or insertion of no more than 20 nucleotides", the "deletion of any nucleotides", or the fact that the developer is allowed to do any targeted modification actions up to 20 times in total) is arbitrary. Thus, this postulated equivalence between NGT plants and conventional plants has been artificially manufactured and is just a political classification. Further (see below), there is no validated scientific basis to equate this manufactured "equivalence" to safety.

Lack of protection: concealing the risks behind re-defining "equivalence"

The proposal makes no effort to assess risks or to manage risks from Category 1 GM plants. On the contrary, it intentionally removes all obligations for providing safety data and for undertaking risk assessment and risk monitoring for the majority of new GM plants. It does so by creating the above concept of "equivalence to conventional plants", which is not only unscientific in itself but also bears no relation to the safety of the plants.

NGT plants and products have no history of safe use. Although most of these techniques have existed for a decade or longer now and cannot be called 'new' anymore, the resulting plants and products have no record of proven safety in the environment, as only very few as yet made it to the market. Nevertheless, these genomic techniques continue to be further developed at a rapid pace, with different techniques yet to come. Neither adaptations of the

[2] https://lexparency.org/eu/TFEU/ART_114/.

techniques nor new ones will necessarily reduce their potential to create an unintended hazard. Where hazard reduction is the outcome for some sources of hazard, it may not be for all. And where hazards may be incrementally reduced, increased efficiency and ease of use will amplify the product line and potentially out-grow the relative benefit of marginally fewer hazards per application. We have seen this with older GM techniques, e.g. applied as Bt plants, which can in the end raise insectide use instead of reducing it. There is no scientifically plausible reason to believe that similar hazard processes may not also occur with the so-called new techniques, e.g. in the form of gene edited insecticidal RNAi plants (see below).

At a minimum, establishing the safety and risk of these new GMOs requires a direct comparison with isogenic, non-modified parental plant lines on a molecular level as well as on a physiological and anatomical level, established from actual evidence. However, the proposal's concept of equivalence has been made so broad and all-encompassing that even highly modified organisms with, for example, altered metabolism and composition escape regulatory oversight. This comes with the risk of plants entering the market containing novel toxins and allergens and reduced nutrient levels. The developer of a Category 1 NGT plant is allowed, for instance, to insert up to 20 base-pairs of any designed sequence and to do so many times (up to 20). Much less than this permitted level of modification would be sufficient, for instance, to create plants that produce insecticides via a mechanism known as RNAi (interfering RNA). By being allowed to remove any genes or DNA sequences and to insert any genes or DNA sequences from a broad “breeders' gene pool”, one can mix and match regulatory on/off switches with gene sequences coding for various proteins and enzymes, and one can make a new GMO that produces special toxins, signalling compounds, hormones or other substances. One can also do so by any other of the “equivalence criteria” steps, as one is allowed to do 20 different interventions that may consist of large genomic alterations (deletions, rearrangements, insertions). This approach equates to a serious risk blindness.

Already, many problems have been documented for NGTs. For example, CRISPR applications have turned out to cause toxicity (Álvarez et al., 2022), mosaicism (Mehravar et al., 2019) and other unintended genomic abnormalities (Höijer et al., 2022; Chu and Agapito-Tenfen, 2022). See also the ENSSER position statement on CRISPR/Cas gene editing (ENSSER, 2023).

Whereas these effects have been observed in organisms intentionally exposed to CRISPR/Cas, its impact and adverse effects on non-target and unintentionally exposed organisms are yet unknown (Schenke and Cai, 2020). Such knowledge is only generated when risk assessments are required and in place and both the impact and the uncertainties are estimated and acknowledged.

Furthermore, no sufficient allowance has been made for the detection and avoidance of inevitable unintentional genetic modifications of the target plants, especially those that arise due to the genetic modification processes used, and that have also been well documented

(e.g. the insertion of genes like the CRISPR-Cas gene, causing thousands of mutations throughout the genome: Wang et al. 2021). Unintended genome-wide mutations numbering in hundreds or thousands are known to arise and accumulate from the plant tissue culture, plant cell transformation as well as the genetic modifying tool (e.g. CRISPR/Cas). This will inevitably lead to unintended alterations in the expression of many genes leading to unpredictable biochemical and compositional changes. We hold that ignoring the risks linked to unintended modifications is negligent and not responsible.

Even Category 2 NGT plants, under the proposal, do not have to fulfil all requirements of risk assessment of GMO Directive 2001/18. This reduction of risk assessment, too, lacks a scientific underpinning and raises the exposure of the environment and the human population to irresponsible levels of risk.

There are two main reasons why NGTs need to remain regulated at least at the current EU level. First, because unintended effects in the environment and to biodiversity conservation are unknown. Second, because risk assessment based on the precautionary principle is case-by-case, since different effects might be observed in different NGT applications and/or species and/or in different receiving environments (CBD, 2016).

Further risks of the proposal

The verification procedure for Category 1 NGT plants (art. 6 of the proposal) only refers to Directive 2001/18 (deliberate release of GMOs) and Regulation 178/2002 (General Food Law). But art. 5 of the proposal declares any rules which apply to GMOs in the EU as not applicable to Category 1 plants. So the proposal exempts not only deliberate release of new GM plants from regulatory oversight, but also all intermediate steps in developing these GM plants, such as the initial laboratory stages, which up to now have had to take place in a contained laboratory under Directive 2009/41. Under the proposal, these procedures for making Category 1 plants can be done anywhere without due containment (in principle, even on location outside). Other organisms (e.g. bacteria, fungi, invertebrates) being exposed to the NGT reagents can become unintended hazards. Further, any GM microorganisms made for the purpose of developing either vectors or reagents in the processes for developing Category 1 NGT plants, also seem to be exempted from regulation under the current proposal. The same holds for reagents that are made to use on the plants, such as DNA templates for making guide RNA or nucleases.

The abolishment of the assessment of all these additional risks from the development trajectory of Category 1 plants is another serious oversight of the proposal.

While the plants mostly referred to in the political and public discussions about the proposal are the major annual crops, the exemptions would in fact cover the whole spectrum of plants, including wild plants, forest trees, fruit trees, rare indigenous crops, medical plants,

herbs, etc., with potentially severe impacts on environments, biodiversity, sustainability and health.

Attack on the precautionary principle

There are often situations where the available scientific information about possible harm from human-made innovations gives decision-makers reasonable grounds to suspect possible harm to human health, the environment or biodiversity, but where scientific certainty is lacking. For this reason, the Precautionary Principle (PP) exists and has been enshrined in the Treaty on the Functioning of the EU[3]. The PP lawfully justifies that decision makers take precautionary measures to avoid such harm.

The deregulation of the new Category 1 GM plants amounts to an *a priori* declaration of safety, or in other words, to the risk blindness mentioned above. This is a false claim and a blatant attempt to circumvent the PP, if not an outright attack on it. It is shameful that the EC, in the text of the proposal, claims that it is in accordance with the PP, when the proposal clearly renders the PP inoperative.

The EC has shown no appreciation for the major scientific uncertainties of NGTs (be they known or unknown uncertainties) and even less recognition of the frontiers of science, in biology and genetics in particular. This has been brought to its attention repeatedly in many written expert documents and countless expert presentations. While lawmakers and politicians may not be expected to understand these scientific issues, they are obliged to recognize their lack of understanding and make sure to include and reflect in their policy proposals a diversity of experts' opinions educating and informing them on the matter. However, what we observe is not that uncertainties and the frontiers of knowledge are being embraced, but rather that they are actively excluded by narrowing the space of what is discussed, through taking politically convenient sides, excluding the diversity of scientific opinions and resorting to bias.

Conclusion

The current EU GMO regulations and directives have served a good purpose (environmental safety) and have been successful in doing so for the past twenty years. There are no good reasons for weakening this system, let alone abolishing it for the majority of new GM plants, in particular as these have no history of safe use. Indeed, our advancing knowledge of molecular genetics informs us that the genome of an organism functions as a delicately balanced, integrated network (Gupta et al., 2022; Schaefer et al., 2017), with complex traits being omnigenic in nature having the function of the entire genome at their basis (Boyle et al., 2017; Mathieson, 2021). That genes function as networks, implies that any modification at this level can have major consequences with respect to patterns of gene expression and

[3] https://lexparency.org/eu/TFEU/ART_191/

an organism's biochemistry. Thus, the latest science actually suggests that the law governing genetic modification including NGT should be re-appraised and strengthened rather than weakened. The EC would not only do people a great disservice in weakening GMO legislation, but also expose citizens to unnecessary and unmonitored risks and thus contradict its own treaty. The proposal is to be rejected in toto as its blatant bias makes it unfit even for negotiations; it is beyond repair.

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