Analysis of the European Commission report *"Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16*"

1. Introduction

The above referenced European Commission report is produced in response to a request of the Council of the EU in 2019 for a study, in light of the 2018 Court of Justice's judgment in Case C-528/16, regarding the status of new genomic techniques under Union law[1].

The Executive Summary of the report states that *"The study makes it clear that organisms obtained through new genomic techniques are subject to the GMO legislation".*

In the press release that accompanied the report, the Commission sought open debate on new genomic techniques (NGTs).

As a contribution to that open debate, the text below offers an analysis of the report, conducted by the legal and scientific experts listed at the end of this document.

The analysis concludes that the statement *"The study makes it clear that organisms obtained through new genomic techniques are subject to the GMO legislation"* is not substantiated by the report, and that the report leaves crucially important questions unanswered.

2. Observations about the methodology of the European Commission report

An assessment of whether and which organisms obtained through NGTs are subject to the EU GMO legislation requires, as a minimum:

a) an analysis of what constitutes a GMO under Union law along the standard CJEU approach of considering the wording, the general scheme and the spirit of the law; [2]
b) a description of what constitutes NGTs and a specification of the various categories of NGTs,
c) an assessment as to which organisms developed with the specified categories of NGTs are GMOs in the meaning of Union law.

These points are discussed below.

a) Analysis of what constitutes a GMO under Union law

The report contains no analysis of what constitutes a GMO. This is a serious shortcoming from a methodological perspective. It is also surprising, given that the EU GMO definition has been under discussion since 2007, when the European Commission established the Working Group on New Breeding Techniques. As the – never officially published – report of the discussions of that Working Group shows, a main element in the discussions was the phrase of the GMO definition *"altered in a way that does not occur naturally by mating and/or natural recombination".* The main discussion about that phrase was whether it refers to the technique used, to the resulting genetic alterations or to both. What makes it even more surprising that the report does not elaborate on the terms of the GMO definition is that the study itself mentions in subsection 4.2.4 that *"The definition of GMO in*

[1] Reference: SWD(2021) 92 final
[2] See for a detailed analysis of the EU GMO definition for example: VAN DER MEER, P., ANGENON, G., BERGMANS, H., BUHK, H., CALLEBAUT, S., CHAMON, M., . . . ZIMNY, T. (2021). The Status under EU Law of Organisms Developed through Novel Genomic Techniques. European Journal of Risk Regulation, 1-20. doi:10.1017/err.2020.105.

the legislation refers to an alteration of the genetic material, without further defining the term 'alteration'." (underlined emphasis added).

It is essential that the Commission elaborates on the GMO definition and the terms in it.

b) A description of what constitutes NGTs and of the various categories of NGTs

The report describes NGTs as "*techniques that are capable of altering the genetic material of an organism and that have emerged or have been mainly developed since 2001*".

We concur with the approach of starting with a broad description of NGTs, so that the results of the study can be applied to as many current and future NGTs as possible. That said, it would have been helpful to highlight some aspects of the NGT description, such as the fact that this description refers to 'altering' and is not qualified with wording '….alter in a way that….' as in the GMO definition. It would also have been good to clarify whether the term 'genetic material' in this NGT description means genetic material that is capable of continued propagation (as in Annex IA of Directive 2001/18/EC). Finally, it would have been good to elaborate the term 'capable', which means that certain applications may have certain results.[3] (underlined emphasis added).

JRC's technical description of the various categories of NGTs (e.g. SDN technologies and base editing, ODM, cisgenesis/intragenesis, RNA-dependent DNA methylation, reverse breeding and agroinfiltration) is clear and gives a good indication of the variety of NGTs that are available or will be in the foreseeable future. Also, the categorisation of the various NGTs in four groups based on interactions with the genome is helpful in getting a grasp of the overall playing field.

c) An assessment as to which organisms developed with each of the categories of NGTs are GMOs

The section of the report that deals with this question is section 4.2 "*Legal status of organisms developed through NGTs*". See below for a detailed discussion of the subsections of section 4.2. of the report.

As a general observation we note that section 4.2. discusses only a subset of the categories of NGTs described by the JRC earlier in the report. Such a partial discussion cannot serve as a basis for a general conclusion that *"The study makes it clear that organisms obtained through new genomic techniques are subject to the GMO legislation".*

The conclusion of section 4.2 of the report could at most read (depending on the accuracy of the content of the subsections, see below): 'organisms obtained through new genomic techniques specified and discussed in this section are subject to the GMO legislation'.

[3] See for example the explanatory memorandum to the proposal for Directive 90/220, which elaborates on the meaning and purpose of Annex I Part 1: "this annex is intended to provide, through a periodical update, a clarification of what techniques can make an organism genetically modified within the meaning of this Directive".

3. Observations about section 4.2. "The Legal status of organisms developed through NGTs"

Section 4.2 of the report discusses three types of techniques/applications in subsections:

- subsection 4.2.2: new mutagenesis techniques
- subsection 4.2.3: cisgenesis and intragenesis
- subsection 4.2.4: alteration of genetic material without changes in the nucleic acid sequence

Below we discuss these three subsections of the report.

Subsection 4.2.2. "Application of the EU GMO legislation to new mutagenesis techniques"

This subsection of the report summarises the 2018 CJEU ruling with the following conclusions:

- *The ruling clarifies that organisms obtained by means of new mutagenesis techniques that have appeared or have been mostly developed since the adoption of Directive 2001/18/EC are GMOs subject to the provisions of the Directive.*
- *Therefore, organisms obtained by means of new mutagenesis techniques that have appeared or have been mostly developed since the adoption of Directive 2001/18/EC are GMOs under Regulations (EC) 1829/2003, 1830/2003 and 1946/2003, and subject to their provisions.*

These two conclusions correctly convey the thrust of that part of the 2018 CJEU ruling.

However, this subsection does not address the next two points that are necessary to respond to the 2019 request of the Council:

1. What constitutes 'new mutagenesis techniques' in the sense of EU law and the 2018 ruling?
2. Which NGTs fall under such 'new mutagenesis techniques'?

Since these two points are not addressed in the report, no conclusions can be drawn with regard to what the 2018 CJEU ruling means for organisms obtained by NGTs.

NB: The same applies, *mutatis mutandis*, to the concept of self-cloning as included in Directive 2009/41/EC.

In short, this subsection of the report does not provide substantiation for the statement in the Executive Summary of the report that "*The study makes it clear that organisms obtained through new genomic techniques are subject to the GMO legislation".*

It would be important for the Commission to address the above two questions related to new mutagenesis techniques. NB: With regard to the question what constitutes 'new mutagenesis techniques' in the sense of EU law and the 2018 ruling, due consideration should be given to the fact that – as the CJEU also confirms in its 2018 ruling – mutagenesis in the sense of the GMO Directive results in GMOs. This means that the resulting organism complies with the GMO definition, i.e. the genetic material of the resulting organisms has been altered in a way that does not occur naturally by mating and/or natural recombination. What that means depends on what is meant by the phrase 'altered in a way that…' in the GMO definition.[4]

[4] See for a detailed discussion on this Van der Meer et al, 2021 (see footnote 2).

Subsection 4.2.3. "Application of EU GMO legislation to organisms produced through cisgenesis and intragenesis"

This subsection of the report starts with some comments about the 2018 CJEU ruling on the mutagenesis exemption, and ends with the statement that *"Therefore, since cisgenesis and intragenesis techniques alter the genetic material in a way that does not occur naturally by mating and/or natural recombination, the resulting organisms are GMOs, even if both techniques constitute phenomena that can also occur in nature. Since neither cisgenesis nor intragenesis are listed in Annex IB to the directive, the resulting GMOs are subject to the requirements of the GMO legislation."*

This subsection should first of all have noted that cisgenesis and intragenesis do not refer to any particular technique but are concepts referring to the origin of the genetic material. Second, and more fundamentally, the content of this subsection, which is about mutagenesis, offers no substantiation for the above statement about cisgenesis and intragenesis, because cisgenesis and intragenesis are entirely different concepts than mutagenesis.

The statement in the conclusion that '*cisgenesis and intragenesis techniques alter the genetic material in a way that does not occur naturally by mating and/or natural recombination'* has no basis in the report. This comes back to our earlier observation that the study should, first and foremost, have provided an analysis of the GMO definition and of the phrase "*altered in a way that does not occur naturally by mating and/or natural recombination".* (See also the observations at the next subsection). Subsection 4.2.3 should also have addressed the fact that 'cisgenesis' describes cases where the resulting genetic combination does occur naturally and through mating.

Finally, this subsection suggests that the 2018 CJEU ruling made observations about changes that can occur also in nature in relation to the scope of the GMO definition. The 2018 CJEU ruling did <u>not</u> do that. The CJEU ruling was about mutagenesis as a technique of genetic modification, and not about other techniques in relation to the GMO definition. Furthermore, the CJEU ruling made no reference to cisgenesis or intragenesis. The CJEU ruling did, however, refer multiple times to 'transgenesis' and 'foreign genes'.

Subsection 4.2.4. "Application of EU GMO legislation to organisms in which the genetic material is altered without changes in the nucleic acid sequence".

This subsection of the report starts with the - pertinent - observation that *"the definition of GMO in the legislation refers to an alteration of the genetic material, without further defining the term 'alteration'.*

Yet, as mentioned earlier, it is striking is that the study makes no attempt to elaborate the terms 'altered' and 'genetic material' in the GMO definition, especially since such elaboration would have touched on the heart of the 2019 Council request.

The only point that the reports makes in relation to the term 'altered' is that "*There are no elements in the legislation supporting a restrictive interpretation of this term as referring only to the alteration of the nucleic acid sequence of the genetic material".*

It should be noted that the text of this subsection leading up to this statement does not reflect:

- the text of the GMO Directive (for example, in Annex IA, which is part of the GMO definition, multiple references are made to "*new <u>combinations</u> of genetic material*"),
- the fact that the EU and its Member States are Parties to the Cartagena Protocol on Biosafety (CPB), which defines in Article 3 the key regulatory term 'living modified organism' as " *Any living organism that possesses a novel <u>combination</u> of genetic material obtained through the use of modern biotechnology*" (underlined emphasis added), and that in the explanatory memorandum to the proposal for Regulation 1946/2003 on the implementation of the CPB, the European Commission stated that "*…the definition of an LMO under the Protocol is largely consistent with the definition of a Genetically Modified Organism (GMO) under Directive 2001/18*".

In summary, the report should have discussed that while there are multiple references in Union law to the fact that 'altered' refers to the nucleic acid sequence of the genetic material, there are no references in the law to aspects such as epigenetic alterations.

4. **Conclusions and recommendation**

Conclusions

An assessment of whether and which organisms obtained through the various new genomic techniques (NGTs) are subject to the EU GMO legislation requires, as a minimum:

- an analysis of what constitutes a GMO under Union law along the standard CJEU approach of considering the wording, the general scheme and the spirit of the law,
- a description of what constitutes NGTs and a specification of the various categories of NGTs,
- an assessment as to which organisms developed with the specified categories of NGTs are GMOs within the meaning of Union law.

The report offers no analysis of what constitutes a GMO. This is a serious shortcoming from a methodological perspective, and it is surprising given that the EU GMO definition has been under discussion since 2007, and given that the report itself recognises that certain terms in the GMO Directive are not defined and/or ambiguous.

The report gives a clear technical description of the various categories of NGTs, which gives a good indication of the variety of NGTs that are available or will be in the foreseeable future.

The does not provide a systematic and comprehensive analysis as to which organisms developed with each of the categories of NGTs are GMOs, because:

- it discusses this question only for a subset of the categories of NGTs described in the report,
- the substantiation given for that subset is insufficient and in part inaccurate

In conclusion, the statement in the Executive Summary of the report that *"The study makes it clear that organisms obtained through new genomic techniques are subject to the GMO legislation."* is not substantiated by the content of the report.

More in general, it is fundamentally impossible to conclude, as the report suggests, that all organisms developed with current and future NGTs are GMOs, because that conclusion would suggest that the qualified definition of GMO (i.e. 'altered in a way that') is fulfilled by an unqualified definition of all current and future NGTs (i.e. 'altered'), which from a legislative perspective would be inappropriate.

In this light it is noteworthy that the report itself recognises that "..*developments in biotechnology, combined with a lack of definitions (or clarity as to the meaning) of key terms, are still giving rise to ambiguity in the interpretation of some concepts, potentially leading to regulatory uncertainty".*

Recommendation

Given the stated potential of New Genomic Techniques to strengthen sustainability in the EU, we urge the European Commission to elaborate on the points raised in our analysis to reduce the ambiguity in the regulatory status of organisms obtained with NGTs.

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