The genome editing technique is covered by Directive 2001/18

Comment on Advocate Bobeks Opinion in case C-528/16

Legal analysis by Professor Ludwig Krämer, commissioned by Testbiotech, Germany.

1. The question, whether organisms that were obtained by genome editing are covered by Directive 2001/18[1] or not, is at present the subject of proceedings before the Court of Justice of the European Union (CJEU)[2] . In this case, Advocate General (AG) Bobek has just issued his Opinion[3]. He concluded that plants derived from mutagenesis are exempted from the provisions of the Directive, as the exemption of Article 3(1) of the Directive, read in conjunction with its Annex I B, applied. The application of the precautionary principle does not lead, in his opinion, to a different result. To make a distinction between regulated and non-regulated plants, the AG mostly refers to the criteria whether the technique involves the use of recombinant nucleic acid or not.

2. The Opinion of the AG is not binding for the CJEU. However, it has a considerable weight, as it is the first factual and legal analysis of the case made by someone else than one of the Parties, and as the AG is an eminent lawyer with a rich professional experience and who is in rank equal to a judge at the CJEU.

3. In the following, it will be argued that the Opinion of the AG comes to conclusions which are contrary to the wording and the purpose of Directive 2001/18 and that, genome editing must be understood as being covered by the provisions of that Directive.

4. Directive 2001/18 is process-oriented: it does not consider the genetically modified organism as such, but looks at the process, by which the organism has been altered[4]. One of the ways in which an organism may be altered is the mutagenesis which leads to the mutation of an organism. Mutagenesis involves an alteration of the genome of a living species[5]. When it was attempted to influence the mutation of plants by human intervention, techniques of using

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1 Directive 2001/18 on the deliberate release into the environment of genetically modified organisms and repealing CouncilDirective90/220, OJ2001, l106 p.1.

2 CJEU, case C-528/16 Confédération paysanne a.o. v Premier Ministre, Ministre de l'agriculture , de l'agroalimentaire et de la forêt

3 Advocate General Bobek, Opinion in case C-528/16, ECLI:EU:C:2018:20.

4 see Directive 2001/18 on the deliberate release into the environment of genetically modified organisms, OJ 2001, L 106 p.1, Article 2 no.2: "'genetically modified organism (GMO)' means an organism with the exception of human beings, in which the genetic material has been *altered* in a way that does not occur naturally by mating and/or natural recombinant' (emphasis added)

5 Advocate General (fn.3, above), paragraph 44.

chemicals and/or radiation were developed (random mutagenesis). They were in use worldwide since the 1920s and legislature considered that they did not lead to any concern for human health or the environment .

5. Since 2001, after the adoption of Directive 2001/18, new forms of intervention in the genome were practised; they were essentially characterized by targeted interventions in the genetic material of an organism. The technique consisted in inserting, deleting, modifying or replacing DNA at a specific point in the genome of a living organism. As the intervention is deliberate and takes place at a specific point of the genome, it is conveniently called genome editing.

6. The Advocate General classified organisms which underwent random mutagenesis as well as those which were the subject of genome editing as genetically modified organisms[6]. He concentrated on the question, whether the exemption of Article3(1) and Annex I B (hereafter the mutagenesis exemption) applied to both the random mutagenesis and the genome editing or only to random mutagenesis processes.

7. Article 3(1) of Directive2001/18 reads as follows: "This Directive shall not apply to organisms obtained through the techniques of genetic modification listed in Annex I B". And Annex I B states: "Techniques/methods of genetic modification yielding organisms to be excluded from the Directive, on the condition that they do not involve the use of recombinant nucleic acid and molecules or genetically modified organisms other that those produced by one or more of the techniques/methods listed below are: (1) mutagenesis..."

8. Prior to the adoption of Directive 2001/18 in 2001, there were only conventional or random methods of mutagenesis that were applied to plants or animals; they used chemicals or radiation, in order to reach a mutation. Genome editing as a method was largely unknown, in any case not used in breeding techniques in the EU or worldwide. At best, there were some experiments and products with that technique were not put on the market. These techniques only started to be applied in commercial seed production later.

9. Therefore, the question is, whether the mutagenesis exemption of Article 3 and Annex I B applies to, the random mutagenesis as well as the genome editing, or whether the exemption of mutagenesis only covers the forms of mutagenesis which were known and in use at the moment of adoption of Directive 2001/18.

10. The Advocate General can be understood as being of the opinion that some techniques used the genome editing might be considered as a form of mutagenesis. He did not explain this understanding of the term "mutagenesis". Doubts exist in this regard, as in 2001, the technique of genome editing was unknown. In contrast, the exemption for mutagenesis had already existed in Directive 90/220[7], the directive preceding Directive 2001/18. It had worked

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6 *Ibidem*, paragraphs 60 to 64.

7 Directive 90/220 on the deliberate release into the environment of genetically modified organisms(GMOs), OJ 1990, L 117 p.15.

between 1990 and 2001 without causing any problem in differentiating between genetically modified organisms (plants) and plants where mutations were obtained by subjecting them to the treatment with chemicals or radiation. It is difficult to imagine that the EU, when it adopted Directive 2001/18 had anything else in mind than the random mutagenesis methods which existed at that time. In other words, the term "mutagenesis" in Directive 2001/18 meant to exempt the random mutagenesis methods.

11. This understanding finds support in Recital 17 of Directive 2001/18 which reads: "This Directive should not apply to organisms obtained through certain techniques of genetic modifications which have conventionally been used in a number of applications and have a long safety record". Also this Recital existed already since 1990, as Recital 7 of Directive 90/220.

12. The only technique - apart from some already practiced methods of cell fusion which was also classified as a "traditional breeding method" (Annex I B no.2) - which had been used in a number of applications and had a long safety record - in 1990 as well as in 2001- was the mutagenesis with the help of chemicals or radiation. Thus, if Recital 17 is meant to have any useful effect, it must serve as an interpretation of the exemption of Article3 and annex I B.

13. The Advocate General was of different opinion. He considered the term "mutagenesis"- which is not defined in Directive 2001/18 - as a general term which also might include some techniques used for genome editing. He came to this result by arguing that the use of a specific word - "mutagenesis" - not only included those techniques which came under this term at the time of its insertion into a legislative act, but also all other techniques which were unknown at that time, but which were developed at a later stage. Only such a dynamic interpretation of the term "mutagenesis" was in his opinion compatible with the intention of Directive 2001/18[8].

14. There are several arguments which plead against this understanding. First, the AG has no explanation for the existence of Recital 17. He does not clarify, which techniques would be covered by this Recital. He refers to declarations by the Commission and the Council during the hearing of case C-528/16, according to which Recital 17 was a mere statement and did not intend to differentiate between mutagenesis techniques[9]. Such declarations, though, made at least seventeen years after the insertion of Recital 17 into the Directive, are not very convincing. They leave open the question which techniques were considered by that Recital. The only reasonable answer is that Recital 17 was inserted, in order to further qualify the exemption of mutagenesis, in the sense that only those techniques should be excluded from the scope of application of Directive 2001/18 which had a long safety record and had been used in numerous applications before 2001.

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8 AG (fn.3, above), paragraphs 77 and 107.

9 *Ibidem*, paragraph 95.

15. The AG argued further that the predecessor of Recital 17, Recital 7 of Directive 90/220, was inserted by the Commission in its proposal for a directive which later became Directive 90/220; at that time, the exemption for mutagenesis techniques of Article 3/Annex I B did not exist; it was inserted into Directive 90/220 only at a later stage[10]. This is evidence for the AG that Recital 17 (the earlier Recital 7) and the exemption for mutagenesis are not interdependent.

16. However, this argument is not pertinent: right from the beginning of legislative activities in at the end of the 1980s, it was clear for the Commission, the European Parliament and the Council, that the regulation on genetically modified organisms should not interfere with conventional breeding techniques which had, as it was worded, "a long safety record". This general understanding of delimiting the GMO techniques to conventional techniques was clear for everybody and in Recital 7 of Directive 90/220. This Recital did not need to be changed, when the exemption of "mutagenesis" was added to the text.

17. The history of Recital 7 - which later became Recital 17 - and the exemption of mutagenesis thus leads just to the opposite conclusion of that of the AG: the term "mutagenesis" was used in Directive 90/220 as it was understood and practiced at the time of adoption of Directive 90/220. Had a detailed definition of "mutagenesis" been inserted into the text of Directive 90/220, it would have, without doubt, referred to the use of chemicals and radiation, but not to other techniques such as genome editing, for the simple reason that such techniques were almost entirely unknown.

18. The delimitation between conventional breeding techniques and alterations of the genetic material of an organism functioned without the slightest problem throughout the 1990s. Therefore, it did not need a change in the wording of the Directive in 2001.

19. This history also explains why the 2001 insertion, in Annex I B of Directive2001/18, of the use of recombinant nucleic acid molecules does not prove that the legislature of 2001 intended to narrow down the term of "mutagenesis" only by referring to such molecules, but meant, for the rest, to cover all forms of mutagenesis techniques, including those that might be developed in the near or distant future[11]. The mutagenesis techniques which existed in2001 - and which had existed since 1990 and earlier - were exempted: this was already ensured by the joint provisions of Recital 17 and Article 3/Annex I B. No further clarification was necessary.

20. The understanding of Directive 2001/18 cannot leave aside its origins. In the second half of the 1990s, a crisis broke out as regards the deliberate release of GMOs. In a specific case, concerning BT-maize, the Commission had proposed to approve the deliberate release, but was opposed by the majority of Member States which made it impossible to obtain a qualified majority of Member States supporting the Commission proposal. According to the rules applicable at that time, the Commission then submitted its proposal to the Council. In the Council,

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10 *Ibidem*, paragraph 94.

11 In this sense AG, *ibidem*, paragraph 77.

thirteen Member States opposed the Commission proposal, one Member State supported it and one Member State abstained. However, as one Member State sided with the Commission, and the Council needed unanimity in order to deviate from a Commission proposal, no decision was taken by the Council and the file came back to the Commission which authorized the deliberate release[12].

21. This Decision caused an outcry with EU public opinion and Governments of Member States. The Commission and the whole EC were accused of being too receptive to business interests and to neglect the concerns of the public. It was considered inacceptable that a deliberate release could be approved against the opinion of the large majority of the Member States. Five Member States declared publicly that they would not continue with the procedures of authorizing the release of GMOs, until the safety concerns of the Member States were taken more seriously, procedures were changed and the public trust and confidence were restored[13]. No Member State sided in public with the Commission. The whole approval process for GMOs came to a standstill (the so-called de facto moratorium) which had as a consequence that no approval for the release of GMOs was granted[14].

22. Then, the Commission submitted a proposal for amending Directive 90/220[15]. However, the Council was of the opinion that an amendment of Directive 90/220 was not sufficient to restore public confidence in GMO techniques and decided to adopt a completely new text, Directive 2001/18. It introduced the precautionary principle as one of the key principles of the new directive, fixed stricter, more protective conditions for the authorization/approval procedure of GMOs, requested an environmental risk assessment for all applications, provided for the systematic participation of the European Food Safety Authority as a scientific body, gave the public the possibility to be consulted during the decision-making process, provided the possibility of the intervention of a Committee on Ethics, and laid down post-marketing controls.

23. All the provisions which were newly inserted into Directive 2001/18, compared to Directive 90/220, aimed at strengthening the protection of human

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12 Commission Decision 97/98,OJ 1997, L 31 p.69. The full story of this case is reported in European Parliament, Report of the Committee on Environment, Public Health and Consumer Protection of 28 January1999, Opinion of the Committee on Research, Technological Development and Energy of 29 September 1998, document PE 227.836 /A 4-0024/99.

13 The statement of the five Member States- Denmark, Greece, France, Italy and Luxemburg - is published in World Trade Organization (WTO), Dispute Settlement on Approval and Marketing of Biotechnological Products, WT/Ds 291-293, United States, Canada and Argentina v. European Communities, Dispute Panel Report of 29 September 2006, paragraph7474. See also paragraph7484 which reproduced the public statement of seven EU Member States that no authorization for GMOs should be granted, until it was proven that it did not cause safety concerns.

14 This moratorium lasted from 1998 until 2004 or 2005.

15 Commission, COM(1998) 85, OJ 1998,C139 p.1.

health and the environment. There was not one provision where the new Directive relaxed the standards and considered that less protection for humans and the environment should be ensured. In order to ensure a coherent approach and avoid different approaches to GMO releases within the Member States which would have threatened the integrity of the EU internal market, a high level of environmental protection was established in the Directive.

24. In view of this, it cannot be argued, as the AG did, that the mutagenesis exemption of Article3/Annex I B meant to leave the gate open and exempt all future scientific evolutions in gene alterations from the field of application of Directive 2001/18. Rather, the legislature of 2001 had in mind to make sure, as far as any possible, that the public in the EU gained anew confidence in the GMO procedure and could be sure that only such GMO products would be released into the environment that had either a long safety record (Recital 17) or were thoroughly tested according to the environmental risk assessment of Directive2001/18, annex II.

25. This result is also confirmed by the very prominent function which Directive 2001/18 attributed to the precautionary principle. This principle was referred to several times and very prominently, in Recital 8, in Article 1, Article 4 and in the provisions on the environmental risk assessment (Annex II); in particular its mentioning in Article 1, the introductory article of the Directive, needs to be stressed, as this place indicated that the whole drafting and application process should be governed by precautionary considerations. The precautionary principle was given the function to act as a catch-all provision: as soon as there was scientific uncertainty with regard to a GMO, the decision-maker should err on the safe side, in order to protect humans and the environment. Again, this prominent role of the precautionary principle which is found in no other legislative act of the EU, is explained by the loss of trust of the public in the GMO-procedures at European level, the general fear of undesired consequences of a deliberate release of GMOs into the environment and the need to restore this lost confidence.

26. The AG general interpreted the function of the precautionary principle in the context of Directive 2001/18 quite differently. He was of the opinion that the mutagenesis exemption of Article3/Annex I B had nothing to do with Recital 17. Consequently, the term "mutagenesis" had to be interpreted, in his opinion, exclusively on the bases of Annex I B. This excluded the application of the precautionary principle in such an interpretation, as otherwise, this would lead to an interpretation contra legem[16].

27. The AG was certainly correct in stating that the precautionary principle cannot lead to an interpretation of a term *contra legem*. However, the AG's understanding of the term "mutagenesis" was based on the assumption that Recital 17 is irrelevant for the definition of "mutagenesis" in the context of Directive 2001/18. The understanding of this notion here is different: "mutagenesis" in Annex I B is the technique of mutagenesis which has a long safety record and was conventionally used in a number of applications. This is not

16 AG (fn 3, above), paragraph 103.

the case for the "new directed mutagenesis techniques" mentioned in the first question submitted by the French Conseil d'Etat to the CJEU. For this reason, there is no justification, why the precautionary principle should not apply with regard to the question, whether such new techniques come under the field of application of Directive2001/18 or not.

28. This is another aspect which the AG neglected in his analysis: Directive 2001/18 had the declared objective to appease the public in the EU which was concerned about the fact that GMOs were allowed to be released into the environment, though a great majority of Member States considered that their safety had not been proven. For this reason, the legislature did not only amend Directive90/220, as proposed by the Commission, but decided to have a completely new directive drafted. Also, all the supplementary safeguards, mentioned above, had the objective to ensure that human health and environmental safety were not at risk by a release. In view of this, it is completely unlikely that the legislature intended to establish a general derogation for all present and future mutagenesis techniques, knowing that research in biotechnology was ongoing and being aware that with any progress in research such a general exemption would continuously have a wider field of application.

29. With the adoption of Directive 2001/18, the legislature intended to ensure a full harmonization of the provisions of Member States on the release of GMOs into the environment. For this reason, the Directive was based on Article 95 EC (the present Article 114 TFEU) and not on the environmental, consumer protection or another provision of the EC Treaty. And for the same reason, Recital 17 mentioned the "long safety record" as a decisive criterion: it intended to ensure public opinion in Europe that health and environmental safety were the main concern of the new Directive. This corresponds to the fact that Recital 4 warned against risks from GMOs, Recital 5 referred to the protection of human health and the environment, Recital 6 to the principle of preventive action; Recital 7 reaffirmed the need to ensure the "safe" development of GMO products, Recital 8 introduced the precautionary principle as a leading principle stating that it had influenced the drafting of the Directive and would have to be applied in its implementation, and Recital 9 recurred to ethical principles. All these Recitals, which preceded the Recitals that refer to individual provisions of the Directive, underlined the principal objective of the Directive, which was to ensure the maximum amount of safety, when GMOs were released into the environment.

30. This intention of the legislature was finally repeated in Article 1 which stated the objectives of harmonizing national laws and ensuring the protection of health and the environment- and Article 4 which laid down the general obligations and started by requesting Member States to take all appropriate measures to avoid adverse effects on human health and the environment. And the precautionary principle obtained the function to serve not only in the drafting of the Directive, but also in its implementation- which necessarily includes the interpretation given to the different terms of the provisions.

31. In contrast to this clearly manifested intention of the legislature, the AG was of the opinion that the use of any new mutagenesis technique would enable the producer of GMOs to escape the provisions of Directive 2001/18 and thus

progressively, with the evolution of science, reduce its field of application. According to the AG, this progressive reduction of the field of application of Directive 2001/18 goes hand in hand with the increased freedom of EU Member States to regulate newly directed mutagenesis techniques[17]. This opinion would have the consequence that on the one hand, the double objectives of Article1 of the Directive - harmonization of national legislation within the EU and a high level of the protection of human health and the environment - would progressively be undermined by the recurrence to new techniques. On the other hand, the public within the EU would more and more be confronted with GMOs that were no longer released on the basis of Directive 2001/18, but on the basis of the legislation of the - in 2001 15, now 28 - Member States. As such national legislation will necessarily be different as regards approaches, intensity of the regulation, the application of the precautionary principle, the intervention of national scientific bodies, the time of introduction of such legislation etc, the public would be confronted with GMOs that offer different degrees of safety. Inevitably, this would lead to controls at the national borders and other barriers to the free circulation of approved GMO products.

32. Such a result is diametrically opposed to the intention of the legislature in 2001 which intended to restore public trust and confidence in GMO techniques and the processes of approving a deliberate release into the environment, and of creating and maintaining an internal market for the release of GMO products.

33. Furthermore, it is by no means unusual that a specific provision which is used in EU law, obtains a different, including a narrower interpretation than originally considered, due to political, economic or scientific evolution. The best-known example concerns the free circulation of goods within the EU. The present Article 34 TFEU - which had existed in the original EEC Treaty since 1958 - prohibited quantitative restrictions on imports and *"all"* measures having equivalent effect between Member States. However, in its famous "Cassis de Dijon" judgment, the CJEU decided that national measures which pursued a legitimate public interest[18] did not constitute measures of equivalent effect and were therefore not prohibited[19]. Later, due to the evolution of environmental law and policy - the environment had not been mentioned in the EEC Treaty of 1958 at all -, it decided that also the proportionate protection of the environment which restricted the free circulation of goods, did not constitute a measure of equivalent effect[20].

34. It follows from this jurisprudence, that a restriction of the term "mutagenesis" to those techniques which were in use in 2001 and had a long safety record, is perfectly compatible with EU law and its interpretation rules.

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17 *Ibidem*, paragraph150.

18 The CJEU mentioned the effectiveness of fiscal supervision, the protection of public health, the fairness of commercial transactions and the defence of consumers.

19 CJEU, case 120/78, Rewe v. Zentralverwaltung, ECLI:EU:C:1979:42.

20 CJEU, case 302/86, Commission v. Denmark, ECLI:EU:C:1988:421.

35. The opinion of the AG that Member States are completely free in regulating or not all techniques used for genome editing and that Directive 2001/18 does not apply to that technique, has other consequences: The absence of EU or of national provisions on genetically modified organisms, where the modification was induced by genome editing, allows GMO producers or importers to bypass the careful and long approval procedure under Directive 2001/18, by using genome editing. This would mean that Directive 2001/18 is obsolete: genetically modified organisms which were modified with the help of genome editing could, in the absence of EU and national provisions, circulate freely within the EU, without environmental risk assessment, assessment by the European Food Safety Authority and the other safeguards which Directive2001/18 had provided for.

Conclusion

36. Genome editing is not a form of mutagenesis as regulated in Article 3(1) and Annex I B of Directive 2001/18. The exemption provided for in those provisions only applies to mutagenesis techniques which have conventionally been used in a number of applications and have a long safety record.

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Ludwig Krämer