Ad hoc expert opinion on the judgment of the European Court of Justice in Case C-688/21

presented by

Professor Tade M. Spranger

commissioned by the German Agency for Nature Conservation

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I. Background to the expert opinion

Case C-668/21 *Confédération paysanne and Others*, which follows on directly from the judgment of the European Court of Justice (ECJ) in Case C-528/16 *Confédération paysanne and Others* concerns, in essence, the question whether, in the application of the exemption provided for in Article 3(1) of Directive 2001/18/EC, read in conjunction with point 1 of Annex I B thereto, to techniques/methods of *in vivo* random mutagenesis, it may be presumed that this exemption may be applied also in the case of *in vitro* random mutagenesis. Following the earlier expert opinion dealing specifically with the Opinion of the Advocate General of 27 October 2022 in the case at hand,[1] the present expert opinion addresses the ECJ judgment of 7 February 2023.

II. Continuation of the approach taken in Case C-528/16

Before discussing the details of the judgment at hand, the fact that the ECJ is evidently committed to a rigorous continuation of the approach taken in its pioneering judgment in Case C-528/16 deserves particular mention.

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[1] Spranger, Ad hoc expert opinion on the Opinion of the Advocate General in Case C-688/21, commissioned by the German Federal Agency for Nature Conservation, January 2023.

From the outset, when considering the admissibility of the request, the ECJ observes that even if all the relevant parameters for reaching a decision in the main proceedings were already established or are even expressly included in the judgment in Case C–528/16, further consideration of the present request for a preliminary ruling is both possible and advisable.

"First, even when there is case-law of the Court resolving the point of law at issue, national courts and tribunals retain the broadest power to bring a matter before the Court if they consider it appropriate to do so, and the fact that the provisions whose interpretation is sought have already been interpreted by the Court does not deprive the Court of jurisdiction to give a further ruling …. Second, a national court is in no way prohibited from referring questions to the Court for a preliminary ruling which, in the opinion of one of the parties to the main proceedings, leaves no room for reasonable doubt …"[2]

However, in particular, in reaching its specific answers on the substantive law relevant to the questions referred, it is evident that the ECJ develops its reasoning "step by step" with reference to the judgment in Case C-528/16.[3] By way of these numerous references, the ECJ not only gives additional weight to its statements but also ensures continuity for all the key elements of its substantive findings in the judgment in Case C-528/16.

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[2] Paragraph 36 of the judgment with numerous further references.

[3] See paragraphs 39, 40, 43, 44, 45, 46 and 49 of the judgment.

At the same time, this also makes plain that the ECJ does not wish somehow to modify or qualify its ruling in Case C-528/16 or even to treat that ruling as an "outlier". For this reason, the judgment in Case C-528/16 is now expressly treated as "settled case-law" on the "interpretation of Article 3(1) of Directive 2001/18".[4]

The manner in which the Court lays these foundations has implications for the future development of European genetic engineering law that can hardly be overstated. As a result of the interplay between the ordinary law requirements of Directive 2001/18/EC and, in particular, the precautionary principle under primary law, now emphasised as consistent case-law, clear limits are placed on the possibility to amend even the "ordinary rules" of genetic engineering law. Hence, the ECJ sets out absolute limits – discussed further below – which are unlikely to be exceeded even in the event of a revision of Directive 2001/18/EC. Given that to redraw these limits a revision of Treaty-based and thus "constitutional" rules of primary law, in observance of all consent requirements,[5] would be needed, the likelihood of such a procedure, while theoretically possible, is in practical terms all but excluded.

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[4] Paragraph 39 of the judgment.
[5] For details, see Article 48 TEU.

III. Wording and purpose of the provision as decision-making parameters

The ECJ defines convincingly, from the perspective of legal method, the parameters for resolving the questions referred as follows: "In accordance with settled case-law of the Court, Article 3(1) of Directive 2001/18 must be interpreted as taking account not only of its wording, but also the context in which it occurs and the objectives pursued by the rules of which it is part."[6] Having outlined the roadmap for analysis, the Court then works through it step by step.

1. Silence of the wording

In relation to the wording of Directive 2001/18/EC, the ECJ holds that for the purposes of differentiating between *in vitro* and *in vivo* contexts at issue in the case, no relevant indicia can be discerned: "In those circumstances, the wording of Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B thereto, does not in itself provide a conclusive indication as to the organisms which the EU legislature intended to exclude from the scope of that directive."[7] Thus, consideration shifts necessarily to the spirit and purpose of the provision viewed in its regulatory context.

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[6] Paragraph 39 of the judgment.
[7] Paragraph 42 of the judgment.

2. Strict interpretation of exemptions

Referring in each instance to the judgment in Case C-528/16, the ECJ emphasises, first, recital 17 and the requirements clearly stated therein for a "history of safe use"[8] and the objective of the directive, set out in Article 1 thereof, and of relevance for interpretation, namely, to protect human health and the environment, in accordance with the precautionary principle, when, first, GMOs are deliberately released into the environment for any purpose other than placing on the market within the European Union, and, second, when GMOs are placed on the market within the European Union as or in products.[9] Taken together, this results ultimately in the need to interpret and apply the exemption for mutagenesis in a strict manner.

"An interpretation of Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B thereto, according to which organisms obtained by means of techniques/methods of mutagenesis would be excluded from the scope of that directive, without any distinctions, would compromise the objective of the protection of human health and the environment pursued by that directive and would fail to respect the precautionary principle which it seeks to implement ….

In the light, in particular, of the foregoing considerations, the Court has held that Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B thereto and in the light of recital 17 thereof,

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[8] Paragraph 43 of the judgment.
[9] Paragraph 44 of the judgment.

must be interpreted as meaning that only organisms obtained by means of techniques/methods of mutagenesis which have conventionally been used in a number of applications and have a long safety record are excluded from the scope of that directive ….

It is important to point out, in that regard, that the limitation of the scope of the exemption provided for in Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B thereto, by reference to the dual criterion of conventional use in a number of applications and with a long safety record, is closely linked to the very objective of that directive, set out in paragraph 44 of the present judgment.

The application of that dual criterion thus makes it possible to ensure that, because of age and the variety of uses of a technique/method of mutagenesis and the information available as to its safety, organisms obtained by that technique/method may be released into the environment or placed on the market within the European Union, without it being necessary, in order to avoid adverse effects on human health and the environment, to subject those organisms to the risk assessment procedures laid down in Part B and Part C respectively of Directive 2001/18.

That application also addresses the requirement of strict interpretation of Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B

thereof, arising from the derogating nature of that provision from the requirement of GMOs to be subject to the obligations laid down in that directive ….”[10]

Thus, for a start, the ECJ is correct to observe, in this regard, that the interpretation of Article 3 of the Directive required in the light of recital 17 thereof also directly facilitates the implementation of the precautionary principle. Likewise, the consequences of the rule-exception relationship emphasised by the ECJ, that is, the widest possible application of the rule, on the one hand, and the strict interpretation that must be given to the exception, on the other hand, are in accordance with general legal methods.[11]

3. Novelty of the nature or the rate of genetic modifications

Starting from its convincing understanding of the rule-exception relationship, the ECJ then proceeds to a finding of pivotal importance. A “technique/method of mutagenesis” that meets the conditions for having a “history of safe use”, and thus is regarded as having a safety record of sufficient duration, may, when combined with other characteristics, result in previously unknown risks.

For this reason, to extend fundamentally the benefit of the exemption from the scope of Directive 2001/18/EC to situations of that kind would not respect the intention of the EU legislature.

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[10] Paragraph 45 et seq. of the judgment.
[11] Spranger, Legal analysis of the applicability of Directive 2001/18/EC on genome editing technologies, commissioned by the German Federal Agency for Nature Conservation, October 2015, p. 25 et seq.

"In that regard, it must be stated that a general extension of the benefit of the exemption provided for in Article 3(1) of Directive 2001/18 to organisms obtained by the application of a technique/method of mutagenesis which is based on the same processes of modification, by the mutagenic agent, of the genetic material of the organism concerned as a technique/method of mutagenesis which has been conventionally used in a number of applications and which has a long safety record, but which combines those processes of modification with other characteristics, distinct from those of that second technique/method of mutagenesis, would not respect the intention of the EU legislature set out in paragraph 48 of the present judgment.

It cannot be ruled out that the application of a technique/method with such characteristics may lead to genetic modifications of the organism concerned which differ, by their nature or by the rate at which they occur, from those obtained by the application of that second technique/method of mutagenesis.

It follows that the limitation of the examination carried out for the purposes of applying the exemption provided for in Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B thereto, solely to the processes of modification, by the mutagenic agent, of the genetic material of the organism concerned, would present the risk that, under cover of the application of a technique/method of mutagenesis conventionally used in a number of applications and with a long safety record,

organisms may ultimately be obtained whose genetic material is different from those obtained by the application of that technique/method of mutagenesis, whereas it is precisely the experience gained as regards the latter organisms which enables establishing that the dual criterion resulting from that provision is satisfied.

Consequently, the release into the environment or the placing on the market, without having carried out a risk assessment procedure, of organisms obtained by means of a technique/method of mutagenesis with characteristics distinct from those of a technique/method of mutagenesis which has been conventionally used in a number of applications and has a long safety record is likely, in certain cases, to entail negative effects, possibly irreversible and affecting several Member States, on human health and the environment, even where those characteristics do not relate to the processes of modification, by the mutagenic agent, of the genetic material of the organism concerned."[12]

These findings of the Court are, compelling from a methodological perspective and are thoroughly convincing.

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[12] Paragraph 51 et seq. of the judgment.

However, two specific aspects in this connection must be highlighted and are discussed separately below.

a. The possibility and nature of new risks

The first point worthy of mention is the ECJ's express recognition of the possibility of risks that may arise from the application of established technologies with a recognised safety record in new contexts. Combining established "processes of modification of the genetic material of the organism concerned" with "other characteristics"[13] may, in the ECJ's assessment, "lead to genetic modifications of the organism concerned which …, by their nature or by the rate at which they occur," differ from those obtained by the application of the original technique/method.[14]

Thus, for a start, the ECJ holds that even established techniques, in other words, those benefiting from the scope of the exemption from Directive 2001/18/EC may not be regarded "automatically" in every context as sufficiently safe. In reaching this finding, the ECJ also counteracts certain political tendencies that in pursuing a disorderly extension of the exemptions would weaken the regulatory framework provided for in Directive 2001/18/EC and, thus, ultimately, undermine and jeopardise the interests of human health and the environment protected by legislation.

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[13] Paragraph 51 of the judgment.
[14] Paragraph 52 of the judgment.

This analysis by the ECJ is of relevance beyond the limited facts of the case also for the discussions surrounding SDN-1 and SDN-2. Namely, the finding that even established techniques "in new contexts" may lead, among other things, to risks that are of relevance for genetic engineering law is diametrically opposed to the assumption by some stakeholders that new forms of genetic engineering involving only "small modifications" are unproblematic. If even the use of established techniques which, in principle, meet the requirements for a "history of safe use" does not completely eliminate the necessity for a risk assessment under the rules of genetic engineering law,[15] it is certainly not possible to assume that risk assessment procedures can be dispensed with, even as an exception, in the case of new genetic engineering techniques without any "history of safe use".

Finally, in this connection, the ECJ – following on from its judgment in Case C-528/16[16] – also emphasises the existence of different categories of risks. Referring expressly to "the nature" and "the rate" at which "genetic modifications of the organism concerned" occur, it draws attention not only to qualitative but also to quantitative modifications. In addition, the implicit requirement advanced therein for a "holistic" take on risk assessment and analysis is a further rejection of more qualified approaches to interpretation.

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[15] Paragraph 54 of the judgment.

[16] See paragraph 48 of the judgment in Case C-528/16: According to the ECJ, "the development of those new techniques/methods makes it possible to produce genetically modified varieties at a rate and in quantities quite unlike those resulting from the application of conventional methods of random mutagenesis".

b. Unlawful "disguise" of critical forms of genetic engineering

Further, particular mention must be made of the ECJ's express endeavour in the judgment to prevent strategies of regulatory circumvention.

Namely, to base the assessment carried out for the purposes of determining whether the conditions for the application of the exemption apply "solely to the processes of modification, by the mutagenic agent, of the genetic material of the organism concerned, would present the risk that, under cover of the application of [an established] technique/method of mutagenesis … organisms may ultimately be obtained whose genetic material is different from those obtained by the application of that technique/method of mutagenesis, whereas it is precisely the experience gained as regards the latter organisms which enables establishing that the ["history of safe use" conditions are] satisfied."[17]

The ECJ applies this clarification, according to which findings obtained in other contexts are not relevant for the specific risk assessment at hand, to circumvention of the requirements of genetic engineering law in whatever form. However, the Court attaches particular importance to the finding that this applies not only to non-compliance with legislative requirements by reason of regulatory uncertainty but in particular also to the construction of supposed regulatory lacunae by individual stakeholders.

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[17] Paragraph 53 of the judgment.

In fact, the term Deckmantel ("guise") in the German version of the judgment always describes intentional conduct[18] and has therefore not been selected randomly. This interpretation is supported also by the English ("under cover of the application of a technique/method of mutagenesis conventionally used in a number of applications and with a long safety record") and French ("sous couvert de l'application d'une technique/méthode de mutagenèse traditionnellement utilisée pour diverses applications et dont la sécurité est avérée depuis longtemps") versions of the judgment.

Hence, the use of established techniques/methods as a "Trojan horse" in the regulatory sense is undoubtedly unlawful. The same applies, moreover, for the approach pushed keenly by some actors, namely, not to advance the development of suitable verification procedures, with disregard for obligations under the law, in order then to dispute the applicability or application of existing genetic engineering law on the basis that verification methods are absent.[19] In both situations the same applies, the companies concerned must comply with existing genetic engineering law and the competent authorities must enforce this.

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[18] The term "*Deckmantel*" (guise) denotes the "pretext under which someone does something in order to conceal his true motives and intentions". Compare https://www.duden.de/rechtschreibung/Deckmantel (accessed 16 February 2023).

[19] In this direction, see, for example, Faltus, "Mutagene(se) des Gentechnikrechts", (2018) *Zeitschrift für Umweltrecht* 524.

4. General necessity for risk assessment procedures

The inadmissibility of an approach seeking to disguise the applicability of existing genetic engineering law together with the impact of recital 17 of Directive 2001/18/EC to be read in light of the precautionary principle and detailing the meaning of Article 3 thereof means that, generally speaking, it is essential to carry out a risk assessment procedure under genetic engineering law. Conversely, to dispense with a procedure of that kind would automatically jeopardise the protected interests of human health and the environment.

"Consequently, the release into the environment or the placing on the market, without having carried out a risk assessment procedure, of organisms obtained by means of a technique/method of mutagenesis with characteristics distinct from those of a technique/method of mutagenesis which has been conventionally used in a number of applications and has a long safety record is likely, in certain cases, to entail negative effects, possibly irreversible and affecting several Member States, on human health and the environment, even where those characteristics do not relate to the processes of modification, by the mutagenic agent, of the genetic material of the organism concerned."[20]

[20] Paragraph 54 of the judgment.

Hence, in consistent case-law, the ECJ emphasises not only the relevance of the protected interests specified but also, above all, the importance of the procedural anchoring and circumscription of risk assessment with a view to protecting the legal interests concerned.

5. At the same time: necessary practical effectiveness of the exemption

The ECJ then turns subsequently to the remaining scope for application of the exemption provided for in Article 3(1) of Directive 2001/18/EC, read in conjunction with point 1 of Annex I B thereto. In this regard, above all, two considerations are important. First, it is only possible to identify the exemption’s detailed scope in light of the thoughts expanded earlier on the rule-exception relationship, on the protected interests and on the Directive's objective. Second, the ECJ points to the - methodically compelling - conclusion that the existence of an exemption implies, at the same time, that an actual scope must remain for the application thereof. Namely, an interpretation of any other kind would undermine the very raison d'être of the exemption.

“Nonetheless, to take the view that organisms obtained through the application of a technique/method of mutagenesis which has conventionally been used in a number of applications and with a long safety record is shown necessarily to fall within the scope of Directive 2001/18 where that technique/method has undergone any modification would be liable to render largely redundant

the exemption provided for in Article 3(1) of that directive, read in conjunction with point 1 of Annex I B thereto, since such an interpretation could make all forms of adaptation of techniques/methods of mutagenesis excessively difficult, even though that interpretation is not necessary to achieve the objective of protecting the environment and human health pursued by that directive, in accordance with the precautionary principle."[21]

This overall very balanced approach of the ECJ results, ultimately, in established techniques/methods of mutagenesis with a long safety record, and thus falling within the scope of the exemption from Directive 2001/18/EC, being permitted to remain excluded from the Directive's scope even in the event of one or more new characteristics being added provided certain conditions are satisfied.

"Therefore, it must be held that the fact that a technique/method of mutagenesis includes one or more characteristics distinct from those of a technique/method of mutagenesis conventionally used in a number of applications and which has a long safety

[21] Paragraph 55 of the judgment.

record justifies the exclusion of the exemption provided for in Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B thereto, only in so far as it is established that those characteristics are likely to result in modifications of the genetic material of the organism concerned that differ, by their nature or by the rate at which they occur, from those obtained by the application of that second technique/method of mutagenesis."[22]

In other words, modifications of the genetic material must, having regard to the parameters specified as decisive, that is, the nature or rate of the modifications concerned, be "unremarkable". Where divergences arise, there is, thus, on the contrary, no justification to presume an exemption.

6. Application of findings to *in vitro* applications

Having prepared the regulatory field in this way, the ECJ then proceeds to the application of the relevant parameters to the context of *in vitro* applications of specific interest in the present case. In accordance with its general approach of applying an interpretation consistent with general legal methods, the Court thus reaches the conviction that the *in vitro* application of an existing *in vivo* technique does not result necessarily, simply because of the modified conditions of its application, in the categorisation of the organism concerned as a genetically modified organism (GMO).

[22] Paragraph 56 of the judgment.

"However, in the case in the main proceedings, the referring court is specifically called upon to determine whether the application *in vitro* of a technique/method of mutagenesis initially used *in vivo* may fall within that exemption. It is therefore necessary to ascertain whether the EU legislature considered that the fact that a technique/method involves *in vitro* cultures is decisive for determining whether or not such an application falls within the scope of Directive 2001/18.

In that regard, the EU legislature did not consider that the genetic modifications inherent in the *in vitro* cultures, to which the referring court makes reference, justified the fact that the organisms affected by such modifications necessarily constituted "GMO's" subject to the risk assessment procedures referred to in Part B and Part C respectively of Directive 2001/18."[23]

The Court then determines the legislative intention on the basis of three different considerations. On the one hand, the Court observes that *in vitro* culture is not included in the illustrative list of techniques which, pursuant to Article 2(2)(a) of Directive 2001/18, read in conjunction with Part 1 of Annex I A thereto, must be regarded as producing a genetic modification that results in a GMO.

On the other hand, the ECJ refers to Article 2(2)(b) of Directive 2001/18, according to which the techniques listed in Annex I A, Part 2, are not considered to result

[23] Paragraph 57 et seq. of the judgment.

in genetic modification. However, Part 2 of that annex is worded as follows: "Techniques referred to in Article 2(2)(b) which are not considered to result in genetic modification, on condition that they do not involve the use of recombinant nucleic acid molecules or genetically modified organisms made by techniques/methods other than those excluded by Annex I B: (1) *in vitro* fertilisation, …." Thus, according to the Court, the fact that the application of that technique presupposes an *in vitro* culture was not, as such, regarded by the EU legislature as precluding from the outset the application of the exemption.[24] In addition, the Court refers to the exemption for cell fusion involving the exchange of genetic material by way of traditional selection methods, which is applied *in vitro* to isolated cells – and which, nonetheless, pursuant to Article 3(1) of Directive 2001/18, read in conjunction with point 2 of Annex I B thereto, remains excluded from the Directive's scope.[25]

Finally, the ECJ draws attention also to Article 2(2)(b) of Directive 2001/18, read in conjunction with point 3 of Part 2 of Annex I A thereto, pursuant to which, according to the Court, the EU legislature chose not to make the

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[24] Paragraph 60 of the judgment.
[25] Paragraph 61 of the judgment. Of procedural interest is the Court's indication that submissions to this effect by the French Government and the Commission were not contradicted.

regime applicable to polyploidy induction dependent on whether or not it is applied *in vitro*, although the *in vitro* application of that technique had long been known at the time the directive was adopted.[26] Hence, to not apply the exemption to an organism obtained *in vitro* using a technique already established *in vivo* would be to disregard the fact that the EU legislature did not consider that those effects were inherent in the definition of the scope of that directive.[27]

These observations convincingly reflect the findings on the provision's starting point. However, the statement found in certain press reports on the judgment that, in the ECJ's assessment, all *in vitro* random mutagenesis is now excluded from the Directive's scope, is certainly incorrect.[28] Rather, according to the unambiguous statements of the Court, *in vitro* random mutagenesis that is not "linked" to an established *in vivo* technique and/or for reasons mentioned results in a risk that is

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[26] Paragraph 62 of the judgment. Here, too, of procedural interest is the statement that submissions to this effect by the Commission were not contradicted.

[27] Paragraph 63 of the judgment.

[28] See, for example, the unattributed news item, EuGH gewährt Ausnahme für In-vitro-Zufallsmutagenese, https://www.lto.de/recht/nachrichten/n/eugh-200118eg-in-vitro-zufallsmutagenese-genetisch-vernderte-organismen-landwirtschaft-umwelt-auswirkungen/ (accessed 17 February 2023); Lehmann, Pflanzenzüchter begrüßen EuGH- Urteil zur grünenGentechnik, https://www.agrarheute.com/management/recht/pflanzenzuechter-begruessen-eugh-urteil-gruenen-gentechnik-603220 (accessed 17 February 2023).

relevant for the purposes of genetic engineering law falls unreservedly within the scope of Directive 2001/18/EC.

The overall effect of the Court's statements is to require, quite correctly, a greater focus on the core questions and fundamental policy choices of European genetic engineering law. This means that, generally speaking, what is decisive is less the nuances of detailed concepts but rather the avoidance of all risks to the protected interests of human health and the environment and compliance with the precautionary principle, established in primary law, and with other higher-ranking law. By reason of the clear emphasis placed on these guiding principles not only for the legal dispute at hand but also for future interpretations, the core principles of European environmental law and of genetic engineering law embedded therein are fundamentally strengthened.

In this context, it is likely going forward that, from the perspective of certain actors, it will be (even) more difficult to assert, in the interests of an alleged need for legislative revision, the existence of supposed regulatory lacunae in European genetic engineering law or, in the other direction, to justify the attempted construction of certain technologies as “unregulated”, in order to circumvent existing legal requirements.

Approaches of that kind could be observed, in particular, following the judgment of the Court in Case C-528/16, visibly seeking to undermine the clear findings of the ECJ by way of certain “micro-discourses”. The Court’s

call, seen in the present case, for an approach that minimises risk, in accordance with the objectives of primary law, is a robust counter to such attempts.

IV. Answers to the questions referred

Whereas the Advocate General in his Opinion called for a reformulation of the questions referred,[29] the Court abstains from this, thereby confirming, without the need to examine in detail the persuasiveness and viability of the Advocate General's arguments, that the questions did not require a new "reading" of that kind.

1. Question 1

The essence of the ECJ's preliminary considerations, according to which a modification of the setting from *in vivo* to *in vitro* is not, as such, of any preeminent relevance for the detailed specification of the exemption under genetic engineering law then also dictates the concrete wording of the answer to the first question.

"In the light of the foregoing, the answer to the first question is that Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B to that directive and in the light of recital 17 thereof, must

[29] See on this Spranger, Ad hoc expert opinion on the Opinion of the Advocate General in Case C-688/21, commissioned by the German Federal Agency for Nature Conservation, January 2023.

be interpreted as meaning that organisms obtained through the application of a technique/method of mutagenesis which is based on the same processes of modification, by the mutagenic agent, of the genetic material of the organism concerned as a technique/method of mutagenesis which has conventionally been used in a number of applications and has a long safety record, but which differs from that second technique/method of mutagenesis by virtue of other characteristics, shall, in principle, be excluded from the exemption laid down in that provision, provided that it is established that those characteristics are likely to lead to modifications of the genetic material of that organism which differ, by their nature or by the rate at which they occur, from those obtained by the application of that second technique/method of mutagenesis. However, the effects inherent in *in vitro* cultures do not, as such, justify the exclusion from that exemption of organisms obtained by the *in vitro* application of a technique/method of mutagenesis which has conventionally been used in a number of *in vivo* applications and has a long safety record with regard to those applications."[30]

For the reasons set out in detail above, this approach is convincing.

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[30] Paragraph 64 of the judgment.

2. Question 2

As in its answer to the first question the ECJ concluded that the effects inherent in *in vitro* cultures do not justify from a regulatory perspective an "exemption from the exemption" if the corresponding technique/method has conventionally been used in a number of *in vivo* applications and has a long safety record with regard to those applications,[31] no account must be taken, at any rate in the circumstances of the present case, of the effects inherent in techniques/methods involving *in vitro* cultures.[32] For this reason, the ECJ dispenses entirely with a substantive assessment of the second question.[33]

Although the ECJ's reasoning on the second question is comprehensible from a technical perspective and arguably necessary as a matter of "judicial self-restraint",[34] it would naturally have been extremely interesting had the Court set down limits on the sources of inspiration that are relevant in justifying a sufficient "history of safe use". Without pushing the Court's findings too far, the following conclusions may be reached, nonetheless, that are crucial going forward in the identification of viable sources of inspiration.

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[31] Paragraph 64 of the judgment.
[32] Paragraph 65 of the judgment.
[33] Paragraph 66 of the judgment.
[34] See in general, for example, Dederer, Die Architektonik des europäischen Grundrechtsraums, (2006) *Zeitschrift für ausländisches öffentliches Recht und Völkerrecht* 575 (620-621).

- The Court considers recital 17 of Directive 2001/18/EC decisive – now as a matter of consistent case-law – in giving specific expression to the exemption provided for in genetic engineering law.[35]

- Recital 17 sets out, above all,[36] two relevant individual criteria: to have been used conventionally in a number of applications and to have a long safety record.[37]

- Additions to the substance of these two criteria must continue to reflect the objectives of the Directive, its protected interests and the precautionary principle.[38]

However, this necessarily implies, for example, that publications from which no insights on the conceivable effects for human health and the environment can be derived are, as such, in principle, not of any significance in justifying a "history of safe use". Similarly, isolated observations of genetic engineering processes carried out in laboratory conditions do not provide a comprehensive picture of conceivable effects in open-field situations.

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35 Paragraph 43 of the judgment.
36 On closer examination, these criteria can certainly be broken down even further. Compare Spranger, Die "history of safe use" im europäischen Gentechnikrecht, (2021) *Natur und Recht* 746-751.
37 Paragraphs 47 and 43 of the judgment.
38 Paragraphs 47 and 44 of the judgment.

V. Summary of the main findings

Making numerous references to its judgment in Case C-528/16, the Court maintains in the present judgment all the key findings reached in that earlier judgment and establishes the existence of consistent case-law on the "interpretation of Article 3(1) of Directive 2001/18".

The foundations established on this basis are of paramount importance for the future development of European genetic engineering law. As a result of the interplay between the ordinary law requirements of Directive 2001/18/EC and, in particular, the precautionary principle under primary law, as emphasised now in consistent case-law, clear limits are set on the possibility to amend even the "ordinary rules" of genetic engineering law in the event of a revision to Directive 2001/18/EC.

Stressing the wording and objective of Directive 2001/18/EC, the Court emphasises convincingly the need for a strict interpretation and application of the exemption for mutagenesis. Further, application of the rule-exception relationship implies that a technique/method of mutagenesis that meets the conditions for having a "history of safe use", and thus is regarded as having a safety record of sufficient duration, may, when combined with other characteristics, result in previously unknown risks.

The ECJ expressly recognises the possibility of such risks that may result from the application in new contexts of established technologies categorised as safe. Combining established "processes of modification of the genetic material of the organism concerned" with "other characteristics" may, in the ECJ's assessment, "lead to genetic modifications of the organism concerned which …, by their nature or by the rate at which they occur," differ from those obtained by the application of the original technique/method.

Consequently, at the same time, the ECJ holds that even established techniques, in other words, those benefiting from the scope of the exemption from Directive 2001/18/EC may not be regarded "automatically" in every context as sufficiently safe. This analysis by the ECJ is of relevance beyond the limited facts of the case also for the discussions surrounding SDN-1 and SDN-2. Namely, the finding that even established techniques "in new contexts" may lead, among other things, to risks that are of relevance for genetic engineering law stands naturally in stark contrast to the assumption by some stakeholders that new forms of genetic engineering involving only "small modifications" are unproblematic.

The Court expressly counters the risk "that, under cover [in German: *Deckmantel*] of the application of [an established] technique/method of mutagenesis …" GMO fall outside the scope of Directive 2001/18/EC. This deliberate wording in the German version – confirmed by a comparison with the English and French versions of the judgment – is clearly intended to prevent, beyond the individual case, tendencies of circumvention (for example, through the construction of supposed regulatory lacunae).

In the light of the interests protected under legislation, risk assessment procedures are, as a rule, indispensable.

Hence, although the exemption from genetic engineering law must be interpreted strictly, conversely, it may not be wholly deprived of its scope. Established techniques/methods of mutagenesis with a long safety record, and thus falling within the scope of the exemption from Directive 2001/18/EC, may therefore remain excluded from the Directive's scope even in the event of one or more new characteristics being added provided that this does not result in risks that are relevant for the purposes of genetic engineering law. In relation to the *in vitro* random mutagenesis at issue in the present case, the Court presumes that the exemption may be extended in this way.

Viewed globally, the effect of the Court's findings is to require, quite correctly, a greater focus on the core questions and fundamental policy choices of European genetic engineering law. This means that, generally speaking, what is decisive is less the nuances of detailed concepts but rather the avoidance of all risks to the protected interests of human health and the environment and compliance with the precautionary principle, established in primary law, and with other higher-ranking law.