ANALYSIS OF THE RECENT EUROPEAN COURT OF JUSTICE DECISION ON LEGAL STATUS OF GENE EDITING

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ABSTRACT

Science and the law have been in a fight over which one should lead the people. On July 25, 2018, the European Court of Justice interpreted 2001 European Union directive language and its scope about organisms obtained by means of technique/methods of mutagenesis. However, within 17 years scientists have invented new genome manipulation techniques.

Environmentalists and anti-OGM claim that the result of NPBTs is the same as genesis techniques in which DNA is inserted or deleted. On the other hand, in the US deletion mutagenesis, in which leaves no evidence behind, is treated different from insertion mutagenesis, which is considered in the same manner as traditional genetic engineering.

However, the benefits such as more quantity of GMO food in less time and fewer costs outweigh the environmental damages stemming from the overuse of herbicides. Furthermore, the use of herbicide is unavoidable even with the organisms obtaining from the mutagenesis, which the EU excludes from regulation.

This note will elaborate on the narrow concept of ECJ on the mutagenesis technique and considering them as GMOs with respect to EU regulation. The note concludes that most of the experts agree that gene editing techniques pose no important risk to the environment and human health; therefore, the ECJ opinion of 2018 is likely a step back for biotechnology science and the profits that it brings to society, especially to GMOs and NPBTs

ISSN 2581 3382

At the end, the note suggests as the optimal solution another ECJ opinion that overrules it or EU Parliament initiation enforcing a GMO Directive excluding organisms obtained from gene editing techniques from GMO Directive.

Keywords*:* OMG, Gene-Editing, European Court of Justice, NPBT, ECJ

OVERVIEW

Law and order exist to establish justice, and when they fail in this purpose, they become dangerously structured dams that block the flow of social progress.

Martin Luther King. Jr.

Science and the law (here included are its practitioners) always have been in a fight over which one should lead the people. Generally, in this symbiotic relationship, they helped each other to develop; however, there are many examples when the law and people who interpret it are reluctant to update with the changes that science and the technology bring in our lives. However, are not seventeen years enough time to be accustomed to new scientific approaches. On July 25, 2018, the European Court of Justice (hereinafter "ECJ") interpreted 2001 European Union directive language and its scope about organisms obtained by means of technique/methods of mutagenesis.

Within this period, scientists have invented new genome manipulation techniques (also known as genome editing or gene editing technologies) like oligonucleotide-directed mutagenesis, and zinc finger nuclease technology, cutting of DNA strands and tailoring genetic changes.[i] Moreover, the new generation gene editing techniques are applied in new plant breeding techniques (hereinafter "NPBTs") where the resultant genomes of the seeds and cells are mutated. Scientists expect that the alternative to classical plant breeding and transgenesis will improve crop varieties. Two of the most well-known NPBTs are CRISPR (clustered regularly interspaced short palindromic repeats),[ii] gene editing and TALENs (Transcription activator-like effector nucleases).[iii]

ISSN 2581 3382

The fear of the environmentalists and organizations against genetically modified organisms (hereinafter "GMO") is that the modern mutagenesis techniques differ from the traditional mutagenesis techniques or natural plant breeding; therefore, in EU some claim that the result of NPBTs is the same as genesis techniques in which DNA is inserted or deleted,[iv] known both as genetic engineering. On the other hand, in the US deletion mutagenesis, in which leaves no evidence behind, is treated different from insertion mutagenesis, which is considered in the same manner as traditional genetic engineering.

This note will elaborate on the narrow concept of ECJ on the mutagenesis technique and considering them as GMOs with respect to EU regulation. The optimal option would be that either the EU Parliament enforces a new regulation or the ECJ changes its approach; otherwise, the ECJ's opinion will impact the European economy and international relationships will be irreparable.

The note begins with a presentation of ECJ, then the historical background of how the legal battle of French NGO-s started against EU regulation, the questions the French government raised before the ECJ, and the suggestion of the Advocate General. The paper will present the ECJ final judgment, the risks and benefits of gene editing techniques. Lastly, the note will end with the suggestion for the optimal option with less harm for Europeans and international trade.

TWO WORDS ABOUT THE EUROPEAN COURT OF JUSTICE

The European Court of Justice, previously known as the Court of Justice of the European Communities before December 2009, was formed in 1952. Its primary duty is to interpret and observe the application of the EU Treaties. Twenty-eight judges, one from each EU member state, compose the Court, which is located in Luxembourg. Under the overall load of ECJ, the preliminary rulings occur at the highest number of cases per year; for example, in 2018, from 849 cases brought, 568 were a preliminary ruling request, which lasts on average for 3.1 months.[v]

A request for a preliminary ruling is a question asked by a national court when it is uncertain about the interpretation or validity of an EU act. The trial in the national Court stays the

ISSN 2581 3382

proceedings until an opinion from the ECJ.[vi] The Court of Justice does not decide the dispute itself. It is for the national court or tribunal to dispose of the case in accordance with the Court's decision, which is similarly binding on other national courts or tribunals before which a similar issue is raised.[vii]

GENE EDITING AND ITS IMPACT IN DIFFERENT COUNTRIES BEFORE JULY 25, 2018

At the time of the ECJ ruling on gene editing, only Spain and Portugal out of twenty-eight European Union members allow commercial GM crops, namely GM corn MON810.[viii] The leading countries that produce GM crops, mostly herbicide tolerance and insect resistance, are the United States, Brazil, Argentina, Canada, and India.[ix]

In the United States, the Department of Agriculture (hereinafter "USDA") does not regulate cisgenes or deletion mutants in new plant varieties, unless there are transgenes (from a different genera or species) and actually in the U.S. hundreds of mutagenized crops exist.[x] For instance, scientists acknowledge the greatest benefits of NPBTs derived from gene editing are "[t]their relative ease, precision, speed, and low cost . . . ."[xi] This is one of the reasons why, in the U.S., almost all soybean, cotton, and corn sold are genetically modified.[xii]

Although almost all scientists accepted that scientifically there are no side effects from consuming GMOs because insect resistant plants would reduce or eliminate the use of insecticides,[xiii] still people fear that GMOs are dangerous for health and the environment. In addition, they see GMOs as not natural products, raised mostly from the overuse of pesticides. On the other hand, people find GMOs as a key to fill the needs of developing countries, more mass of products with less cost and less labor or may be used to help to save fruits from diseases like citrus,[xiv] Papaya in Hawaii or Banana in Uruguay.[xv]

The first gap created between European Union countries (hereinafter "EU) stems from the definition of what is a GMO. Under Article 2(2) of GMO Directive, genetically modified organism means an organism, with the exception of human beings, in which the genetic

ISSN 2581 3382

material has been altered in a way that does not occur naturally by mating and/or natural recombination.

HOW DID IT START?

Article 3 of and Annex IB to the Directive [2001/18/EC] of March 12, 2001, prohibits the selling and marketing of GMOs within EU member states.[xvi] However, before this directive Spain in 1998[xvii] through governmental regulations chose not to join the rest of the EU countries to block farmers from growing GMO crops. EU regulations gave member states discretions on GMOs adoptions at that time.

Confédération Paysanne, and eight other Non-Government Organizations: Réseau Semences Paysannes, Les Amis de la Terre France, Collectif Vigilance OGM et Pesticides 16, Vigilance OG2M, CSFV 49, OGM : dangers, Vigilance OGM 33, Fédération Nature et Progrès sued the Prime Minister, and the Minister for Agriculture, the Food Processing Industry and Forestry because they refuse to annul Article K.531-1 of the French Environmental Code[xviii] that treats organisms obtained by mutagenesis technique as GMOs.[xix] Furthermore, the applicants have requested the Court to issue a moratorium on herbicide tolerant varieties obtained by mutagenesis.[xx] The new mutagenic techniques targeted the mutations in order to obtain a product that will be resistant to certain herbicides.[xxi] The use of herbicide on crops— according to the applicants —risk human and animal health and increase environmental pollution.

On October 17, 2016, the French Court, on the request of the defendants, suspended the pending case to refer to the ECJ for the preliminary ruling *sine qua non* the French trial court cannot move forward in a final judgment. Specifically, the Defendants ask the ECJ to clarify the GMO Directive on the mutagenesis exemption.

The questions that the French trial court arose to the ECJ were:

1. Do organisms obtained by mutagenesis constitute genetically modified organisms within the meaning of Article 2[xxii] of Directive [2001/18/EC] of March 12, 2001, known as "GMO Directive?"[xxiii] What about the mutagenesis techniques implementing genetic engineering processes are techniques listed in Annex IA, to which Article 2 refers?

ISSN 2581 3382

Consequently, does the exemption of Articles 2 and 3 of and Annexes IA and IB of GMO Directive related to precaution include the impact assessment and traceability measures of all organisms and seeds obtained by mutagenesis?

2. Do varieties obtained by mutagenesis constitute genetically modified varieties within the meaning of Article 4 of GMO Directive?[xxiv]

3. Do Articles 2 and 3 of and Annex IB to the GMO Directive give wide discretion to the Member States to define the regime to be applied to organisms obtained by mutagenesis?

4. The defendant's fourth question was whether the GMO Directive might impact the appearance of new plant varieties obtained by means of those techniques and the potential risks they represent for the environment and human and animal health.

The Opinion of the Advocate General

In January 2018, Advocate General Mr. Bobek (hereinafter "AG"), after gathering the opinion of Members who showed interest in the case and the Commission's opinion, suggested to the Court to answer only three out of fourth questions that the French government presented.

On the first question, the AG suggested that the exemption provided in Article (1) of Directive 2001/18 and its Annex 1 B covers all organisms obtained by any technique of which use recombinant nucleic acid molecules or genetically modified organisms. However, this regulation excludes mutagenesis obtained from one or more methods listed in Annex I B, such as mutagenesis, cell fusion, or traditional breeding methods via chemicals, radiation, or other physical stimuli to induce mutations.[xxv]

On the second question, the AG clarifies that Directive 2002/53 is the general law regarding organisms obtained by mutagenesis, while the GMO Directive is the *legis specialis* (specific law); therefore, the latter prevails in the interpretation overall EU secondary law or other general law such as Directive 2002/53. Thus, the AG suggested that the Directive 2002/53's catalogue of varieties of agricultural plants exclusively exempts varieties obtained by mutagenesis.[xxvi]

ISSN 2581 3382

As for the third question, the Advocate General proposed that Directive 2001/18 allows Member States to adopt measures governing organisms obtained by mutagenesis as far as they respect the EU law's obligation. [xxvii]

Lastly, on the fourth question, the Advocate General argued that the EU legislation, including also the GMO Directive, has been updated regularly to fit with the changes that happened in Europe. The fear of risk in human health or the environment without any scientific evidence is not enough; therefore, Article 2 and 3 of the GMO Directive and its Annexes I A and I B should be deemed valid.[xxviii]

ECJ Ruling and Arguments

The ECJ responds to three first questions and denied answering the fourth question, reasoning that the interpretation of Article 2 and 3 of Directive 2001/18 is not before the Court.

First, an organism obtained by mutagenesis constitutes a GMO under Article 2 of Directive 2001/18/EC, the ECJ ruled following the suggestion of the AG identically. Namely, the Court ruled that Article 2(2) of Directive 2001/18/EC of the European Parliament and of the Council must be interpreted as meaning that organisms obtained by means of techniques/methods of mutagenesis constitute genetically modified organisms. Moreover, the Court ruled that Article 3(1) of the GMO Directive and the point 1 of Annex 1B and recital 17[xxix] must be interpreted that only organisms obtained by means of techniques/methods of mutagenesis, which have conventionally been used in several applications and have a long safety record, are excluded from the scope of that Directive, like the wheat use for pasta that was mutagenized years ago by gamma radiation.

Indeed, it rarely happens that the ECJ diverges from the AG opinion. Even though the AG's opinion is not mandatory to the Court, the statistics show that the ECJ ruled according to his advice in 70% of the cases.[xxx] In this case, although the AG suggested that the organisms obtained by mutagenesis without mentioning the techniques of mutagenesis as the ECJ specifies, they can be exempted by the GMO Directive. While for the second part of the first answer, the AG suggested excluding all the organisms obtained by any technique of

ISSN 2581 3382

mutagenesis, which does not involve the use of recombinant nucleic acid molecules or genetically modified organisms produced with the method listed in Annex I B.

On the second question, the Court decided that Article 4(4) of Council Directive 2002/53/EC must be interpreted that genetically modified varieties 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 exempt from the obligations laid down in that provision. Again, it seems that the AG, in his suggestion, was more generous generalizing the concept of varieties obtained by mutagenesis. ECJ was more rigid and restricted the interpretation to varieties by means of techniques/methods of mutagenesis, which guarantee an already predictable outcome.

The ECJ ruled on the third question that Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex I B exempts from the EU GMO regulations, organisms obtained by traditional means of techniques/methods of mutagenesis, which have been used in a number of applications and have a long safety record. Furthermore, Member States are free to regulate such organisms, in compliance with EU law, in particular with the rules on the free movement of goods set out in Articles 34 to 36 TFEU or other obligations. In other words, the Member States have the discretion to define the regime to be applied to organisms obtained via mutagenesis under Articles 2 and 3, and Annex IB OF Directive 2001/18/EC. The AG's suggestion on this question was to allow EU members to regulate the gene editing organisms nationally in conformity with EU law.

POST-ECJ RULING AND TWO DIAMETRICALLY DIFFERENT VIEWS

Many expected that these new techniques might be considered as GMOs but would not be regulated by Directive. Indeed, the Court will treat the organisms from mutagenesis techniques equal to transgenic varieties that have foreign genes transposed in their organisms. While, the US will not do so for deletion mutants.

ISSN 2581 3382

For the environmentalists and anti-GMOs organizations, the ECJ's judgment has been a triumph. Here is how the Corporate Europe Observatory's agribusiness campaigner Nina Holland reacted after the ECJ decision:

> "This is a big victory for the environment, farmers, and consumers. It clarified that EU decision-makers have to ensure that products from these new techniques are possessed for potential food safety and environmental risks and that they are properly labeled as GMOs . . . Big agribusiness corporations will continue their lobbying in Brussels to escape EU safety rules for the new GMOs, ..."[xxxi]

Also, this opinion reinforces what another country did to regulate the free-foreign DNA mutagenesis products; respectively, New Zealand did so in 2016 via High Court opinion to regulate plant gene editing[xxxii] and Argentina in 2015 with a resolution to exclude free foreign DNA plants from the product-based GMO regulation. However, such jurisdictions should be aware that the category of plants that they will regulate is as safe as mutagenesis organisms that these jurisdictions do not regulate.[xxxiii] Moreover, if one use chemical or radiation mutagenesis, we cannot tell what genesis the intervention might impact.

On the other side, for the scientists, plant genetics, the agro-food industry, and farmers, especially crop breeders, the ECJ ruling has been a setback ruling. This regulation means in the language of numbers five years for the risk assessment by the European Food Safety Authority plus a year for improvement for the risk management process by Commission. In short, it needs a crop industrialist for around six years to import mutagenesis products.

The issue is whether the (i) EU should maintain the position announced by the ECJ that GMO Directive of 2001 covers mutagenesis, as well, or (ii) the EU needs to have a new approach after eighteen years adopting new regulations parallel with science evolution on mutagenesis and overturning the ECJ opinion. The latter seems to be the most acceptable approach on which even the EU members are pressuring the EU Parliament to enact for a new directive.[xxxiv]

ISSN 2581 3382

The Split of the EU countries on Gene Editing Techniques

The ECJ ruling split the customers, scientists, farmers, and politicians in pro-GMOs and the anti-GMOs groups. The supporters of GMOs seek the immediate need to overrule the judgment of the EU Parliament to intervene with new Directive. On the other side, anti-GMO groups applauded the ECJ opinion and pushed the politicians to stay devoted to what the Court decided.

Fears from Organisms Obtained from Gene Editing Technologies

Those who take the view that the new techniques should be exempt from GMO legislation generally argue that the final product is very similar to products generated using conventional breeding techniques or that similar changes could also occur naturally.

Consumers fear gene editing organisms, namely crops or other plants because they doubt that the genes in a living organism may change unpredictably. However, with this logic those consumers should be afraid even from sunlight which can cause a mutagen due to the UV wavelength.

The suspicion and the fear exist among a few scientists, too. For example, Dr. Michael Antoniou, a molecular geneticist at King's College London, supports ECJ ruling on gene editing because the tools are not precise, the outcomes are unpredictable, and the scientists have little control over the outcome.[xxxv] Simply put, gene editing technologies regulated by authorities will ensure that these products will be subjected to safety checks and carry a GMO label. However, this opinion is not supported by data, and the author gives his opinion as a medical researcher and as an Agrobiotech researcher.[xxxvi] Furthermore, if the scientists suspect the CRISPR/Cas9 system's precision what is their opinion on chemical mutagens or radiation, whose mutagenesis procedures are far less specific.

The outcome from the herbicide-resistant crops produced by traditional methods manifest the same issue for the environment and health as the new generation of herbicide-resistant crops; however, European farms are worried more about the methods than the result and are pleased that the conventional crops are exempted from the regulation.[xxxvii] Do they know that even

ISSN 2581 3382

conventional crops are also genetically modified because, after one thousand years of civilization, no plants look like its wild ancestors, an exception maybe Jerusalem artichoke. Maybe the genome technology has so quickly developed that we find people's mindset unprepared?

Furthermore, campaigners are more concerned about the precision of the editor who, for a small mistake, may affect a crop's health issues and environmental risks.[xxxviii] CRISPR/Cas9 gene editing technique is impossible to track in a modified organism, so it will be difficult to catch the unscrupulous breeders.[xxxix] The concern is more profound with human CRISPR-based medicine mistakes where the outcome is irreversible.

The international trade relationship with Anti-GMO countries is another issue that the pro-GMOs group raises. The EU adheres to the UN Cartagena Protocol on Biosafety and shall respect all the other countries and members Protocol to refuse certain GMOs, but only if the EU knows what exports there are by controlling and labeling certain GMOs varieties.[xl] One hundred sixty-six countries have signed this Protocol thus far; however its supplement, the Nagoya-Kuala Lumpur Supplementary Protocol Liability and Redress, which is related to living modified organisms, entered in force on March 5, 2018, and is signed by fewer member countries than ratified the Cartagena Protocol,[xli] which show a reluctance of the members to take further steps regarding GMOs regulation. Lastly, some herbicide-resistant crops developed using chemical mutagenesis have caused an environmental problem because of herbicide-resistant weedy plants.

The Risk of Implementing the ECJ Opinion on Gene Editing Techniques

The first impact of the ECJ on the GMO Directive is on EU innovation and global agricultural trade. Having different approaches on NPBTs and the mutagenesis crops will cause, in the worst scenario, blocking of the imports from other countries. For instance, Africa, as one of the biggest importers of crops to the EU, uses CRISPR to develop disease-resistant varieties of crops, and after the ECJ opinion, the import of these crops to the EU needs review. An impartial third party, like the World Trade Organization as a global trade authority, may address this issue.[xlii]

ISSN 2581 3382

Furthermore, EU scientists will have undue hardship even when they want to experiment in a trait because of the long procedure required from the EU considering the NPBTs as GMOs and regulating them.

Also, the decrease of GMO trait fields and restriction of innovation will deter investment and drive EU scientists to move abroad, and the EU members will face the "brain drain" effect. This is the reason why scientists in 2013 from many companies addressed this issue of risk evaluation and future benefits of gene techniques by sending a letter to the EU institutions.[xliii] Furthermore, this EU approach against NPBTs has discouraged scientists from "[u]sing novel techniques, rejecting research funding applications, and shifting research investment out of the EU."[xliv]

Foreign developers will be reluctant to use the gene editing technology, as well, because to introduce GMOs in the EU, even though it has not incorporated any foreign DNA, would take years and a lot of money to be approved for consumption.[xlv]

Benefits of Gene Editing Technologies

Those who consider that the new techniques should fall within the scope of GMO legislation contend that the processes used mean that plants bred using the new techniques are, in fact, genetically modified. However, the EU should not regulate the new gene editing technologies under GMO Directive because it is not updated with the changes that the scientists came up with during all of this seventeen-year period from the first day when the Directive came in force to the ECJ opinion on July 25, 2018.

First, the mutagenesis technology is a different modification technology from the genesis that the GMOs had in consideration when they provided its strict regulation. Now, organisms derived from deletion mutagenesis techniques result in a mutation without having foreign gene material in their genome. Scientists can produce a new DNA combination without cutting or pasting, or they can replace DNA precisely in the genome of the organism to achieve the desired result. With that said, a scientist offers another product through gene editing techniques while the GMO directive and ECJ have in mind another type of modified genetic organism.

ISSN 2581 3382

Second, gene editing technologies speed up the improvement and commercialization of new varieties, which means more products, less time for less money. For this reason, agribusiness actors support this technology.[xlvi]

Third, politicians who have concern for the macro-perspective of their countries also support this approach because it will be able to respond to the need of "population growth, climate change, and the constant evolution of pathogens."[xlvii]

Fourth, another benefit of the gene editing techniques is that a deletion or base editing mutation is easily detected because it is the product of a specific process rather than a mutation derived by conventional breeding.[xlviii] CRISPR techniques will allow the (1) farmers to save using less water, less fertilizer and fewer pesticides for their crops, and (2) customers to have safer, tastier, and healthier food.[xlix]

Scientists' point of reference regarding gene editing differs from the ECJ's Court because of the former concerns more about the final products where the later from the techniques used to the final products.[l] This is a big difference between regulation in the US and the EU. The former tends to regulate the product and the latter the process.

The immediate need to change the GMOS directive

The EU Gene Editing Directive and ECJ interpretation, unless it is changed in the near future, will show harmful effects in many perspectives such as the economy, international relationships, and brain drain. One of the explanations why countries have different approaches toward organisms obtained by new gene editing technologies is how they defined the GMOs.

First, the vague language of the ECJ providing that the newer techniques “might” prove to be similar to the risk associated with the transgenesis is not scientifically based and, coming from the highest Court of the EU, obviously brings uncertainty to the citizens. Furthermore, in its vague and unelaborated language, the ECJ did not define what the threshold for the "number of applications is," and what determines "a long safety record." Both elements constitute mutagenesis that is exempted by GMO Directive regulation. This is one of the divergences that the AG had with the ECJ. The former advised the Court that these two elements of “popularity”

ISSN 2581 3382

and "safety record "should not be references whether the EU should regulate organisms obtained by mutagenesis techniques.[li]

Second, the impact of ECJ on the GMO Directive in EU innovation will be irreparable. That discourages the scientists from inventing new approaches because they will face the legislature or court interpretation that is not coherent and has no scientific basis. Therefore, a wrong interpretation of a technique or method would setback the scientists. An illustration of discouraging innovation is the impact the ECJ will cause to virtually riskless agriculture breeding techniques and products. They will be overregulated, and small agro-businesses or researchers will not want to waste time inventing a technique, when its product needs the "overwhelming" EU authorization to label, manufacture, or import them.[lii] Furthermore, gene engineers will try to find new employers overseas because even experimental trials will not be allowed.

Third, the exemption of the gene editing technique to plants incentivizes secret and unregulated field trials with CRISPR plants. For example, the Flemish Institute for Biotechnology experimented with CRISPR maize in 2017–2018 without being registered as a GM trial under the EU GMO Directive.[liii] These field tests raise concerns about biosafety measures although without knowing precisely what was being attempted, one cannot be sure.

Fourth, the ECJ decision, if the EU holds tight to this approach, will disrupt global agricultural trade and EU trade relationships with other countries. In particular, that Directive provides that GMOs must be authorized following an assessment of the risks, which they may present for human health and the environment, and also makes them subject to traceability, labelling, and monitoring obligations because the techniques and methods of mutagenesis alter the genetic material of an organism in a way that does not occur naturally.[liv] This is one of the reasons why it would be so difficult to detect.

The lack of information or misleading information made people believe that the GMOs are "bad things" or a menace.[lv] The recent data shows that the people's approach to NPBTs has ameliorated some of that concern and that will be higher if they will have more information on the label or [i]nformation of product safety is shared.[lvi] A suggestion would be to inform the consumers or farmers via labeling the uncertainties that the product may impose.

ISSN 2581 3382

Other Countries' Approaches to Gene Editing Techniques

One approach that the EU Parliament can have as a model when they enforce the new Directive is the United States Department of Agriculture (USDA) regulation, which decided not to regulate gene edited plants if the resulting mutations are the same as that mutation would come naturally or from a traditional breeding technology,[lvii] except Foreign DNA insertions would still be regulated. It is suggested to use science and facts regarding precaution approaches rather than using emotion or fear.

The precautionary approach a main principle-based approach that regulates new technologies, is not suggested as the best solution to the GMO regulation because it uses science and other factors to lead the final judgment,[lviii] For example, the Precautionary Principle (PP) is included in the Rio Declaration of 1992, and in the Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity, which entered into force in 2003. The U.S. and Argentina did not ratify the latter, which is ratified by China, EU, Italy, Japan, New Zealand, and the Republic of Korea.

In addition, another precautionary approach can be considered by the ECJ on GMO Directive of 2001. However, experts consider the PP more than an attempt to replace the factors of the risk-based approach;[lix] In addition application of the precautionary approach leads to the conclusion rather than to "[a]n argument for greater security."[lx]

The difference between the precautionary principle followed by ECJ and the "evidence-based approach" is that for the former environments, ecologists or medical doctors impose regulatory measures even if the harm is not scientifically proven yet, while the latter imposes regulatory measures when the environment and health harm is proven.[lxi]

Another solution is that countries adopt the precautionary approach in order that society absorbs gene editing methods gradually in agriculture. Social acceptance of agricultural biotechnology will grow if the government tries to define, regulate, and accept the precautionary approach, which regulated the harm of the consequences of the gene editing technique before the risk happens.[lxii] Hence, the case-specific risk assessment and the application of the precautionary principle is necessary. According to Tetsuya Ishii, "Food

ISSN 2581 3382

safety assessments are necessary before placing gene edited crop products on the market, as hazardous substances, such as modified proteins with allergenicity, could be unintentionally produced due to the off-target mutations in the food products."[lxiii] However for all these decades producing plant genetic engineering, the reported case of unintentional allergenicity are highly rare.

CONCLUSION

In conclusion, most of the experts agree that gene editing techniques pose no important risk to the environment and human health; moreover, in 2016, more than a hundred Nobelists signed a letter to reject the anti-GMO campaign because that is misleading the society about GM foods and crops.[lxiv] Thus, the ECJ opinion of 2018 is likely a step back for biotechnology science and the profits that it brings to society, especially to GMOs and NPBTs.

Modern gene editing technology can cause lower intended disruption to the host genes than an earlier technique for genetic modification. Simply said, the new gene editing technology does not exclude "off-target" effects, but the likelihood of that happening would be less frequent than the conventional genetic modification techniques.[lxv]

Although it is debatable if the ECJ opinion is either a prohibition on innovation or a pseudoscience; indeed, the judges approach following the precautionary principle will slow the EU gene editing innovation because of the rigid precautionary measures in contrast with the "evidence-based approach."

In a balancing test measuring the risks, advantages, and disadvantages of gene editing techniques, the benefits such as more quantity of GMO food in less time and fewer costs outweigh the environmental damages stemming from the overuse of herbicides. Furthermore, the use of herbicide is unavoidable even with the organisms obtaining from the mutagenesis, which the EU excludes from regulation.

Thus, the optimal solution to the actual situation caused by the ECJ opinion in 2018 is another ECJ opinion that overrules it or EU Parliament initiation enforcing a GMO Directive excluding

ISSN 2581 3382

organisms obtained from gene editing techniques from GMO Directive. From a long-term perspective, international trade may oblige the EU authorities to accept the evidence-based approach like the U.S., and not all GMOs will be regulated because of the biotechnology; the legislators should rely more on scientists.

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[ii] CRISPR stands for clustered regularly interspaced short palindromic repeats is a technique, which edits DNA sequences in the genomes, also named as cut-paste-replace technique. *See generally* Anthony King, *What the ECJ ruling means for gene editing*, CHEMISTRY WORLD, (July 25, 2019), available at https://www.chemistryworld.com/news/what-the-ecj-ruling-means-for-gene-editing/3009305.article.

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[iv] Unlike transgenesis, mutagenesis is a set of techniques that make it possible to alter the genome of a living species without the insertion of foreign DNA. Mutagenesis techniques have made it possible to develop seed varieties that are resistant to selective herbicides. *See generally* Court of Justice of the European Union, PRESS RELEASE No 111/18, Luxembourg, July 25, 2018.

[v] *See further* THE COURT OF EUROPEAN JUSTICE, https://curia.europa.eu/jcms/jcms/P_80908/en/ (last visited November 6, 2019).

[vi] Court of Justice of the European Union, PRESS RELEASE No 111/18, Luxembourg, July 25, 2018
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[vii] *Id*.

[viii] *See supra* note 3. *See also supra* note 2.

[ix] Esra Seyran & Wendy Craig, *New Breeding Techniques and Their Possible Regulation*, 21 AGBIOFORUM (2018).

[x] *See supra* note 2 at 4.

[xi] *See supra* note 8 at 6.

[xii] *Recent Trend in GE Adaption*, UNITED STATES DEPARTMENT OF AGRICULTURE, ECONOMIC SERVICE RESEARCH, available at http://www.ers.usda.gov/data-products/adoption-of-genetically-engineered-crops-in-the-us/recent-trends-in-ge-adoption.aspx (last visited September 18, 2019).

[xiii] Nina Federoff, former President AAAS says, "This is probably the safest technology that human beings have ever invented," however, I think that nothing is absolute in science and that would be a faulty logic.

[xiv] *See Citrus Diseases*, UNITED STATES DEPARTMENT OF AGRICULTURE, ANIMAL AND PLANT (MAY 18, 2016) available at https://www.aphis.usda.gov/aphis/resources/pests-diseases/save-our-citrus/soc-citrus-diseases (last visited November 10, 2019).

[xv] *See also* Arango Isaza et al., *Combating a Global Threat to a Clonal Crop: Banana Black Sigatoka Pathogen Pseudocercosporafijiensis (Synonym Mycosphaerellafijiensis) Genomes Reveal Clues for Disease Control*, (2016) available at http://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1005876.

[xvi] Pursuant to Article 3(1) of the directive: "This Directive shall not apply to organisms obtained through the techniques of genetic modification listed in Annex I B."

[xvii] Paula Fernandez-Wulff, *Why and How Spain Became the EU's Top Grower of GMOs*, OUR WORLD, UNITED NATIONS UNIVERSITY, Dec. 19, 2013, available at https://ourworld.unu.edu/en/why-and-how-spain-became-the-eus-top-grower-of-gmos (last visited December 5, 2019).

ISSN 2581 3382

[xviii]Article L. 531-1 of the French Environmental Code defines a genetically modified organism as an "organism whose genetic material has been modified other than by natural mating or recombination."
[xix] Opinion of Advocate General, Case C-528/16 (January 18, 2018) at 2.
[xx]*Id.* at 15.
[xxi]*Id.* at 5.
[xxii] Article of this Directive provides: (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 recombination. Within the terms of this definition: (a) genetic modification occurs at least through the use of the techniques listed in Annex I A, part 1; (b) the techniques listed in Annex I A, part 2, are not considered to result in genetic modification; (3) "deliberate release": any intentional introduction into the environment of a GMO or a combination of GMOs for which no specific containment measures are used to limit their contact with and to provide a high level of safety for the general population and the environment."
[xxiii] GMO Directive regulates the GMOs' release into the environment and into the EU market. Also, the Directive regulates the traceability, labeling, and monitoring of all GMOs in EU members. However, this Directive treats mutagenesis differently as organisms obtained from specific techniques of GMOs.
[xxiv] Article 4(4) of Directive 2002/53 provides, "In the case of a genetically modified variety within the meaning of Article 2(1) and (2) of Directive 90/220/EEC, the variety shall be accepted only if all appropriate measures have been taken to avoid adverse effects on human health and the environment."
[xxv]*EU Court Extends GMO Directive to New Plant Breeding Techniques*, FOREIGN AGRICULTURE SERVICE,(July 27, 2018), available at https://apps.fas.usda.gov/newgainapi/api/report/downloadreportbyfilename?filename=EU%20Court%20Extends%20GMO%20Directive%20to%20New%20Plant%20Breeding%20Techniques_Brussels%20USEU_Belgium%20EU-28_7-27-2018.pdf.
[xxvi]*Id.*
[xxvii] *See supra* note 19 at 16.
[xxviii] *Id.* at 20.
[xxix] "This Directive should not apply to organisms obtained through certain techniques of genetic modification which have conventionally been used in a number of applications and have a long safety record."
[xxx] *See* Carlos Arrebola, Ana Julia Mauricio, & Héctor Jiménez Portilla, *An Econometric Analysis of the Influence of the Advocate General on the Court of Justice of the European Union*, 5 Cambridge J. Int'l & Comp. L. 82, (2016).
[xxxi] *See supra* note 1. A question would be what if CRISPR/Cas9 is used to produce a deletion mutant and it is not claimed as a GMO? It would be impossible to prove since no tracks are left behind.
[xxxii] Tetsuya Ishii, *Crop Gene-Editing: Should We Bypass or Apply Existing GMO Policy?* 23 SCIENCE & SOCIETY, no. 11, (2018) at 947.
[xxxiii] *Id.* at 949.
[xxxiv] *The EU Future of New Breeding of New Plant Breeding Techniques*, Special Report, EUROACTIVE.Com (May 2019), available at http://eurac.tv/9QiU.
[xxxv] Michael Antoniou, The EU Must not de-Regulate Gene-Edited Crops and Foods, EURACTIV.COM (updated July 8, 2019), https://www.euractiv.com/section/agriculture-food/opinion/the-eu-must-not-de-regulate-gene-edited-crops-and-foods/.
[xxxvi] *Id.*
[xxxvii] Ottoline Leyser, GM *Crop Ruling Shows Why the EU's Laws Are Wholly Inadequate*, THE COVNERSATION.COM, (July 27, 2018, 11:48 am EDT), http://theconversation.com/gm-crop-ruling-shows-why-the-eus-laws-are-wholly-inadequate-100675.
[xxxviii] *See supra* note 2.
[xxxix] Except they will need to be plant molecular biologists and not farmers.
[xl]*See supra* note 1 at 4.
[xli] *See further* Convention on Biological Diversity.
[xlii]AgBioForum, 21(1), 2018 at 8.
[xliii] Ricarda A. Steinbrecher& Helena Paul, *New Genetic Engineering Techniques: Precaution, Risk, and the Need to Develop Prior Societal Technology Assessment*, 59:5 Science and Policy for Sustainable Development,38, 39-44 (2017) https://doi.org/10.1080/00139157.2017.1350011.
[xliv] Rim Lassoued, Stuart J. Smyth, Peter W. B. Phillips, & Hayley Hesseln, *Regulatory Uncertainty Around New Breeding Techniques*, 9 FRONTIERS IN PLANT SCIENCE, 1291 page 3 (2018) available at www.frontiersin.org (last visited November 11, 2019).
[xlv] Matt Ridley, *Absurd ECJ Ruling will hurt farmers and Push up Prices,"* (July 27, 2018), https://www.thetimes.co.uk/article/absurd-ecj-ruling-will-hurt-farmers-and-push-up-prices-kvhw5cwzp.
[xlvi] *See supra* note 3 at 499.

ISSN 2581 3382

[xlvii] *Id.*
[xlviii] Christopher M. Holman, *A Fractured International Response to CRISPR-Enabled Gene Editing of Agricultural Products*, Mary Ann Liebert, Inc, 38 Biotechnology Law Report 3 No. 1 (2019) at 7.
[xlix] *Id.*
[l] *Id.* at 21.
[li]SDA Foreign Agriculture Service, *EU Court Extends GMO Directive to New Plant Breeding Techniques*, no. E18052 (July 27, 2018).
[lii]*Id.*
[liii]*See supra* note 1 at 5.
[liv] Court of Justice of the European Union, PRESS RELEASE No 111/18, Luxembourg, July 25, 2018, Judgment in Case C-528/16 Confédération Paysanne and Others v. Premier Ministre and Ministre de l'Agriculture, de l'Agroalimentaire et de la Forêt.
[lv] *See supra* note 44 at 3.
[lvi]*Id.*
[lvii] *See supra* note 3 at 501.
[lviii] *See supra* note 44.
[lix] Gary E. Marchant, The precautionary principle: an 'unprincipled' approach to biotechnology regulation. Journal of Risk Research 4 (2), 143–157.
[lx]*See supra* note 44.
[lxi] Eva Gelinsky & Angelika Hilbeck, *European Court of Justice Ruling Regarding New Genetic Engineering Methods Scientifically Justified: Commentary on the Biased Reporting About the Recent Ruling*, Environment Science Europe (December 20, 2018) available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6302053/.
[lxii] *See supra* note 32 at 950.
[lxiii]*Id.* at 949.
[lxiv] *See supra* note 43.
[lxv] *See supra* note 48 at 6.

ISSN 2581 3382