HELLENIC NATIONAL BIOETHICS COMMISSION

O P I N I O N

Genetically Modified Organisms in Agriculture and Consumption:

An Updated Approach

NATIONAL BIOETHICS COMMISSION

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I. Introduction

The Hellenic National Bioethics Commission met on several occasions to address the issue of updating its initial Opinion (Genetically Engineered Plants, 2000) regarding the ethical and social dimensions of the emergence of Genetically Modified Organisms (GMOs) in trade (food) and agriculture (seeds and feed).

This issue is part of the broader debate on agriculture, agricultural crops and food products in order to give prominence to the ethical, political and legal issues and search for sound policies at international and Union level. Already, over the first twenty years of the 21st century new data for globalized agriculture have emerged, such as: a) population growth, b) climate change, c) decrease in farming areas along with rural depopulation, d) declining biodiversity, e) increasing energy cost of food transportation and distribution, and f) food waste increase. The primary objectives set by the EU's agricultural policy are biosafety and sustainability. The EU policy focuses on respect for rights, delimitation of responsibilities of those involved in food production, distribution and consumption of food as well as on consolidation of moral values in legal arrangements to preserve soil, water and biodiversity. This framework also includes the use of technologies whose risk is scientifically assessed while related research is being promoted.[1]

More specifically, it was deemed necessary to update the Commission's Opinion given the international experience gained during the past twenty years from the use in food and feed, the evolution of the EU's legislation which started in 2001 and is continuously updated, but also the policy for implementing this legislation in our country throughout this period, with the involvement of different competent State Bodies and the contribution of scientific Bodies and Non-Governmental Organizations. Moreover, applying the new genome editing techniques (or gene editing) to plants of agricultural and commercial significance

[1] European Group of Ethics, No 24, Ethics of modern developments in agricultural technologies 2009-07-13 at: https://op.europa.eu/en/publication-detail/-/publication/9369a035-5a5e-45da-8e37-09717ed806d5/language-en/format-PDF/source-77404379.

raises new questions.

The Commission organized hearings with competent Bodies for plant growth and food control, with business operators, unions and scientific experts to discuss this issue. At the meeting of 24 September 2019 the following parties of Ministry of Rural Development and Food were invited to attend the hearing: a) Mr. Konstantinos Tzimas from the Food Quality and Safety Directorate, b) Mr. Spyridon Panagos, Head of the Department of Phytogenetic Resources and Biotechnology Products from the Directorate-General for Agriculture, c) Mr. Fotios Panagos from the Propageting Material of Cultivated Plant Species and Phytogenetic Resources Directorate, d) Mr. Argyrios Boulis from the Department of Feed Control of the Feed and Grazable Land Directorate and e) Mrs. Dionysia Stefanitsi from the Directorate-General of the General Chemical State Laboratory. At the meeting of 10 October 2019 the following parties were invited to attend the hearing: a) Mr. Dionysios Vlachos, Vice President of the Single Food Control Body (EFET) and b) Mrs. Elena Danali, campaign manager for sustainable agriculture GREENPEACE GREECE. Finally, at the meeting of 12 November 2019 the following parties were invited: a) From the Greek Seed Trade Association (EEPES) Mr. Efthimios Efthimiadis, President of the Board of Directors of EEPES, Mr. Alexandros Diamantidis, Director-General of EEPES and Evangelos Zagilis, Executive of EEPES, b) from the Organic Farmers' Union of Northern Greece Mr. Grigoris Datsiadis, agriculturist (he participated via skype), Mr. Giorgos Balias, Ph.D. in Law, Associate Professor at Harokopio University, Mrs Chrysa Kapartziani (lawyer, Ph.D. in Law at UOA) and Mr. Konstantinos Balias (lawyer).

II. Data

Genetic modification of plants aims to enhance existing characteristics by creating mutations or to acquire new desired characteristics by importing exogenous DNA/gene(s) even from different species. Either the so-called established techniques of genetic modification (i.e. microprojectile bombardment, electroporation, microinjection etc.) or the new genome editing techniques are used for the above purposes.

Since the marketing of the first genetically modified tomato in 1995, the circulation of food (mainly soy), feed and exceptionally seeds for cultivation is sparing within the EU, contrary to the rest of the world where these products cover a significant percentage of the cereal grain cultivation. Prior to being placed on the European market, the products' safety is assessed as set out in the European legislation, namely centrally by the competent European authority European Food Safety Authority (EFSA) and the European Commission. A risk assessment process by accredited laboratories is set out for the genetically modified organisms in particular to the extent possible given that the assessment of the long term effects of the genetic modification of organisms entails a higher level of uncertainty.

In European societies there are serious concerns both within the scientific community, regarding risk uncertainty, and within the civil society amongst involved parties, businesses, cultivators and ecologists. Hence, the general public lacks comprehensive information due to difficulty in objective information based on ethical principles, and due to preconceptions. This information however, is necessary for the citizens to build trust in scientific research. Therefore, the current concerns focus on the new genome editing technologies. The new genome editing technologies are based on the use of specific enzymes, namely nucleases, and include the Zinc Finger Nucleases (ZFNs), the Transcription Activator-Like Effector Nucleases (TALEN) and the Clustered Regularly Interspaced Short Palindromic Repeats/associated protein-9 nuclease (CRISPR/Cas9).[2] Thanks to its simplicity, effectiveness and flexibility, CRISPR/Cas9 is the most widely used tool in genome editing. These new genome editing technologies cause targeted changes in an organism's genome, namely point mutations (changes in a single DNA base) or more complex changes (in several DNA bases), and as a matter of fact, they make it feasible to simultaneously modify more than one gene.

Contrary to the established and conventional techniques of genetic modification by transgenesis, the new genome editing techniques cause mutagenesis in the genome without importing new genes, namely without creating transgenic organisms. Although these technologies provide greater flexibility in

[2] More information in Mollaki V. And Vidalis T. 2016, Gene editing. Report for the National Bioethics Commission.

genetic modification they pose -especially CRISPR/Cas9- a risk of creating off-target mutations. For instance, CRISPR/Cas9 has already been applied to plants and as a matter of fact it was feasible to simultaneously modify (mutagenize) multiple loci. However, according to studies, there are legitimate concerns about the unknown consequences of potential off-target mutations,[3,4,5] as well as about potential off target cuts and the toxicity of these systems in comparison with conventional techniques of mutagenesis.

Given that the plants or seeds which are genetically modified using technologies such as CRISPR/Cas9, are intended for consumption by humans or animals, the issue of their safety is deemed significant. An equally important issue is the relatively high level of uncertainty in the assessment of long-term effects of their release into the environment, both physical effects (on human and animal health, as well as on plant and animal biodiversity) and social effects (tendencies for creation of monopoly and restriction of cultivators' and citizens' rights). As a matter of fact, the low cost and the relatively easy application of the new technologies make it easier to generalize their use.

III. Issues of bioethics and law

The Commission considers that, from an ethical and social perspective, the use of GMOs in agricultural crops, feed and food for consumption ought to promote, by all appropriate means, the right to adequate and safe food, including the innovative technologies in combination with the principles of precaution, justice and respect for diversity. The aforementioned rights and principles are weighted in order to counterbalance the legitimate interests and freedoms of individual and collective bodies of action, sustainability of the environment and future generations.

More specifically, regarding the safety and potential risks for the environment and public health arising from the use of GMOs, there is no doubt that

[3] Hajiahmadi Z, Movahedi A, Wei H, et al. Strategies to Increase On-Target and Reduce Off-Target Effects of the CRISPR/Cas9 System in Plants. Int J Mol Sci. 2019;20(15):3719.
[4] Zhang Q, Xing HL, Wang ZP, et al. Potential high-frequency off-target mutagenesis induced by CRISPR/Cas9 in Arabidopsis and its prevention. Plant Mol Biol. 2018;96(4-5):445-456.
[5] Xu W, Song W, Yang Y, et al. Multiplex nucleotide editing by high-fidelity Cas9 variants with improved efficiency in rice. BMC Plant Biol. 2019;19(1):511.

even conventional crops of agricultural products or free trade of conventional food and feed can be seriously questioned too. In the case of crops, intensive production requires using conditioning chemicals or pesticides which are proven to be associated with risks for the environment and health. Respective risks have also been identified in conventional food and feed, which are usually processed for the acquisition of characteristics and their preservation.

However, in the case of GMOs the difference lies in the uncertainty of the risks arising from their use. Contrary to conventional products – in which case risks are normally considered to be known, therefore preventable – in this case, lack of scientifically proven knowledge about gene functions and their interaction with external factors maintains ambiguities regarding the probability, exact nature and risk severity which raises more serious doubts. It is reasonable to suppose that these doubts will be limited as genetic information will continue to be disclosed, but today we are not yet able to confirm sufficient data for a full risk recording and assessment.

In the light of the above, the critical ethical issue arising is whether this uncertainty itself could constitute a ground for the total exclusion of GMOs from the use in agriculture and consumption until we obtain sufficient risk data. The precautionary principle can be interpreted in a narrow or broad manner. In the narrow sense it means that if there aren't any scientific data available and there is a risk of irreversible environmental damage, then such a technology should not be further implemented. In the broad sense, which is adopted by the European Commission, it means that it should be carefully implemented, assessing the consequences of each GMO release into the environment taking things step-by-step. Activation of this principle presupposes that potential dangerous consequences of a phenomenon, product or procedure have been identified and that scientific assessment does not allow the risk to be determined with sufficient certainty.[6] The Commission is of the opinion that adopting the "precautionary principle" in the broad sense makes it imperative to take appropriate measures for a controlled

[6] European Commission Communication (COM (2000) 1 of 2 February 2000) on the precautionary principle, available at https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2000:0001:FIN:EN:PDF.

product trade. It is important to stress how crucial continuous research on GMO safety is, in order to accurately identify risks and possibly prevent them with measures, which will gradually become more proportionate, accurate and effective. Such research requires, in particular, guarantee of independence and thus it should be financed by public funds.

The Commission also notes that financial aspects are also included in the relevant ethical and social concerns about who is benefited and who is harmed by the introduction of GM plants, food and feed. Introducing new products in crops and especially in trade that are protected as patents obviously affects financial competition. An important problem is the fact that GMO crops tend to predominate conventional crops in other countries (especially in North and South America). Indeed, if the predominance of GMO crops is due to contamination of conventional crops, which causes farmers to turn to GM crops and actually depend on monopoly conditions in GM seeds production, then the restriction of their economic freedom is illegitimate. This should be borne in mind in the preparation of a national policy regarding cultivation of approved GM plants in particular, under the options given by the EU legislation.

As regards the implementation of this legislation, the Commission notes the need for continuous update due to the technological developments, as applied by the EU institutions throughout the period of 30 years since its initial adoption. This update seems to follow a double trend as regards the responsibility for decision-making: a) decisions regarding GMO trade are made centrally at the EU level and b) final decisions regarding crops are taken at the Member State level. However, it is pointed out that in both cases the assessment of the environmental risk posed by GMOs for human, animal and plant health is conducted under the supervision of the State according to the guiding principles of the European Food Safety Authority.[7]

Regarding trade, it is crucial to provide appropriate information to consumers in order for them to be able to select the nutritional products to be consumed by them and their dependants. The Commission finds that, despite the provisions of the legislation, checks carried out both at the Union and the national level - particularly

[7] The procedure is defined by Directive (EU) 2018/350 for the assessment of the environmental risk posed by GMOs in combination with MD 1371/99270 (Β΄1865) 27.05.2019.

regarding the import of products from third countries- are not able to ensure absolute certainty regarding the presence of GM ingredients. This applies even in cases where the percentage of GM ingredients may exceed the acceptable "horizontal" safety threshold (0.9%) foreseen in the legislation. Hence, the information for consumers remains insufficient.

Regarding crops, the Commission notes that the statutory ability of a Member State to prevent the cultivation of GMOs approved at Union level could be based on non-scientific reasons (political, social, financial etc.), which eventually render it ultimate. However, the respective decision should be based on sufficient justification because except for indiscriminately excluding the application of genetic editing technologies, it constitutes an exception to the unhindered exercise of the economic freedom within the European market.

From a legal perspective, according to the Commission, the issue whether the application of the new technologies such as CRISPR/Cas9 falls under the GMOs case and consequently the centralized authorization system according to the relevant European and national legislation has been fully resolved. The Conseil d'État of France referred to the Court of Justice of the European Union for a preliminary ruling concerning the organisms which are produced by mutagenesis using the new technologies.[8,9] On 25 July 2018 the Court of Justice held that the organisms which are produced by targeted mutagenesis techniques are considered to be GMOs since they modify the genome and they do not occur naturally and, therefore, they fall under the relevant European legislation about GMOs. On the contrary, according to the Court of Justice, the organisms which are produced by natural mutagenesis or by mutagenesis using the conventional techniques for which there is a long history of safety constitute an exception. It is worth noting the remark of the Court of Justice that the new genome editing techniques make it feasible to produce genetically modified varieties at a pace and in quantities that are impossible in the case of the conventional techniques of random mutagenesis. In the light of the above, the Court of Justice included the organisms produced by the new technologies in the GMOs,

[8] Judgement of the Court of Justice (Grand Chamber) of 25 July 2018 available at http://curia.europa.eu/juris/documents.jsf?num=C-528/16.

[9] Court of Justice of the European Union. Press Release No 111/18 available at https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf.

pursuant to Article 191.2 (formerly Article 174 TEC) providing inter alia that the Union's policy for the environment aims at a high safety level and is based on the principles of precautionary and preventive action.

In Greece the issue has long been resolved because there is an express legislative provision according to which the mutagenesis techniques (or the plant cells fusion techniques as well) fall under the scope of the European Directive relevant to Article 3 of the Ministerial Decision No38639/2017/2005 (Β΄1334) of 21.09.2005 which was the adaptation to Directive 2001/18/EC for the intentional release of genetically modified organisms into the environment and their placing on the market as products or product components.

At this point, Charalabos Savvakis, member of the Commission, expressed a dessending opinion, pointing out his disagreement with the previous decision of the Court of Justice of the European Commission regarding the new methods of genome editing, and also the European legislation about GMOs, and considering that, in any case, the safety issue must be decided by the product itself and not by the methodology of its production. Moreover, he pointed out that Bioethics Commissions should express their independent opinion. As a result, it is out of question that Bioethics Commissions are bound by the court decision at any level. On the contrary, they must criticize them, wherever this is ethically justified.

Although it has been clarified that concerning their risk assessment process new technologies fall under the conditions applicable to GMOs, issues are posed regarding their acceptance and effective use as well as product placing on the European Union market. As a matter of fact, this issue is of the greatest importance for the national legislators who, according to the latest amendment of the European legislation, are responsible for allowing or prohibiting their use and distribution depending on the wider framework of their agricultural policy.[10] Controversy has

[10] It is about Directive 2015/412/EU which enabled each State to allow or prohibit the release and placing on the market of genetically modified organisms for purposes other than scientific. In Greece Ministerial Decision No2775/128090 (Β΄4287) of 08.12.2017 was adopted on that matter prohibiting them due to: a) the particular characteristics of the Greek crops (landraces and varieties of plant species), b) apiculture, c) local agricultural structures and practices to ensure the ecosystem sustainability and d) cultivation to produce high added value goods in alpine and insular conditions, with small plots of land that make it impossible to practically apply coexistence measures to avoid unintended contamination of conventional and organic plants with genetically modified plants.

already been aroused[11] about the existing European legislative framework, namely whether it is appropriate to include the new technologies based on the following arguments: a) it will not always be possible to distinct mutations created by their application from those caused by natural mutagenesis, b) it will stop European research and its application, while it will fail to effectively prevent the distribution within EU of products produced in third countries using the new technologies and, c) it could be replaced by a safety assessment system and not be based on the technology by which the product was produced.

In any case, the Commission deems appropriate to give prominence to the bioethical issues arising by agricultural and nutritional policy-making, including the use of GM technologies in crops, food and feed in order to raise awareness between citizens about two subjects. On the one hand, this is necessary because of the need to generally address the ethical purposes of agriculture and the dilemmas arising concerning the nutrition of the world population and the maintenance of the Earth's production capacity, biodiversity and natural ecosystems and intergenerational justice. On the other hand his is necessary because of the need to involve the public in a dialogue with the scientific community, to promote transparency and information in order for citizens to be aware and participate in decision-making.

[11] Statement by the Group of Chief Scientific Advisors. A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive. Available at https://ec.europa.eu/info/publications/status-products-derived-gene-editing-and-implications-gmo-directive_en.

IV. Recommendations

In the light of the above, the Commission recommends that:

1. Scientific research must be continued to further verify the safety of the products produced by the new genome editing technologies and the risks they pose for human health, in light of the lack of sufficient data on their long-term safety. As long as the level of uncertainty about their behavior and consequences on the environment remains high, the precautionary principle should be implemented in order to protect the ecosystem's integrity.
2. Studies and risk assessment of the new genome editing technologies must be conducted by reliable and specific accredited Bodies in conditions adjusted to the Greek environment and natural ecosystem, particularly as regards the risk of depopulation referring to the Greek biodiversity conditions. It is also recommended that the possibility of taking measures be explored to avoid contamination of conventional or organic crops by GMO crops in case of cross-border contamination.
3. Research must be strengthened regarding agriculture in general and agricultural crops in all dimensions, focusing on exploring the consequences of climate change on crops, especially in Mediterranean countries, but also on the particular characteristics of both the geomorphology of the Greek soil in combination with the evolution of agriculture and the Greek gastronomic culture with scientifically recognized high nutritional value.
4. A more effective national system of electronic control of the products approved at the EU level circulating in the Greek market must be established to provide more accurate information to consumers. This system will support the environmental risk assessment of GMOs, as well as the monitoring of immediate and delayed toxic and allergic reactions to human and animal health, which the European legislation has delegated to the Member States.
5. Consumers must be informed and this must include the results of both positive and negative risk assessments of GMOs at the European level. Even if the approved products do not raise risk concerns about human health, their selection or not by the consumer may be based on other reasons which ought to

be respected (i.e. philosophical, religious or political opposition to the specific technology and its use for confronting hunger or climate change at international level). In that context, the necessary information of the consumer is not limited only to protecting his/her health, but it also strengthens his/her freedom to choose his/her food and to form an integrated view.

6. To systematically raise public awareness particularly to all levels of education about the assessment of this kind of technologies and the ethical issues, the rights and the principles arising from agriculture and nutrition, focusing on distributive justice and the need to cover the gap between those who lack life's essentials and those who contribute to the increase of food waste and abuse of natural resources due to dietary habits. The development of GMO technologies in agriculture and nutrition can be ethically assessed only as a part of a social effort guided by science which is trusted by the citizens. Eventually, the public perception of risk depends on how and by whom it is defined, especially during the initial stage of technology development, on counterbalance with advantages and on its distance from the people who are conducting the assessment. Hence, it is recommended to promote a comprehensive approach of all the advantages and disadvantages and realize the global interdependence.

The Commission reserves the right to return to this issue provided that new data emerge, regarding the issue of safety of the products produced using the new genome editing techniques.

Athens, 22 June 2020.