Member State comments received for discussion in future Committees

BE contribution:

Received on 19/12/2018

Belgian NRL-GMO opinion in Annex 1: Opinion of the Belgian NRL-GMO on the consequences of ECJ ruling of 25 of July on enforcement and more specifically on the analytical tools needed for this.

Received on 11/01/2019

As previously announced, here's some more feedback from Belgium. It's about monitoring issues in case of field trials with organisms obtained by new mutagenesis techniques:

- Method must be available for the detection of GMO targeting single nucleotide modification (ex qPCR or digital PCR or target PCR amplification followed by sequencing, no WGS - it is impossible to use this in field for plants).
- A priori knowledge of the frequency of the mutation in the nature is needed, especially in the tested non-GM cultivars. If this information is unknow, a pre-monotoring must be done in the tested non-GM cultivars to determine this natural frequency of mutation.
- Monitoring during the field trial to determine the frequency of mutation: Preliminary statistical study needs to be done to determine the number of samples to take during the field study in order to be able to test for significant deviation of the frequency of the mutation (due to GM) in comparison with the frequency of the natural mutation via statistical analysis.

BG contribution:

Received on 22/01/2019

Potential impact of the judgment of the Court of Justice of the European Union in Case C 528/16 within the framework of existing legislation

In Bulgaria, an interinstitutional working group comprising experts from: the Ministry of Agriculture, Food and Forestry, the Ministry of Environment and Waters, the Ministry of Health, the Agricultural Academy, the AgrobioInstitute, the National Center for Public Health and Analyzes and the Executive Agency for Variety Testing, Approbation and Seed Inspection discussed the impact of the judgment of the Court of Justice of the European Union (CJEU) in case C 528/16 regarding: control and traceability when placed on the market; field experiments and work in a controlled environment; the production of seeds and propagating material; patent protection and its impact on traceability; and research and development.

According to the judgments of the CJEU in case C 528/16, the new mutagenesis techniques (NMTs) lead to the creation of genetically modified organisms (GMOs) and their products are subject to: health and environmental risk assessments, market approval, labeling, traceability and monitoring.

The approach used in this CJEU decision, impacts also other methods included in the new selection techniques (NST) as presented in the publication of the Joint Research Center (2011) "New Planting Techniques: State and Prospects for Commercial Development"[1] and The EC Scientific Researches (2017) for "New Techniques in Agricultural Biotechnology"[2], since it considered all techniques/methods, which alter the genetic material of an organism in a way that does not occur naturally.

In addition, the CJEU decision enables Member States (MS) in their national legislation to categorize classical (chemical and physical) mutation as leading to the creation of GMOs or to continue to exclude it from the scope of GMO legislation.

The judgment of the Court of Justice in Case C 528/16 is largely based on Recital 17 of Directive 2001/18, therefore we need a strict definition when a technique is "traditionally used in a number of applications, and its safety has long been known ".

1. Control activities and traceability: conducting official laboratory tests.

The Control of NMTs products, in accordance with current GMO control, will be based on risk assessment and requires official identification and quantification methods or, in other words, there must be official methods to distinguish between NMT's plants and conventional ones. In addition, mutations derived from NMTs and from those with classical mutagenesis, which are often included in traditional selection programs and are often not fully documented, will also need to be reliable distinguished.

In this respect, we rely on the technical document, developed by the European Network of GMO Laboratories and the European Reference Laboratory for GM Food and Feed. Page **2** of **3**

From a technical point of view, any changes in the genome, which are done without introduction of a foreign genetic fragment, makes them virtually impossible to be reliable identified, such as the products obtained through NMTs, unless there is preliminary information on the modification. It is becoming even more difficult in the case of point mutations (replacement of single nucleotides) or deletion of part of the genome. And when it is not possible or very difficult to have an analytical protocol for detecting these small genome mutations, this could be considered as a technical barrier on the use of NMT's products under the rules of the World Trade Organization. Therefore, in that point a thorough legal analysis by the EC is needed with the active involvement of the MS.

Laboratory control of NMT's products can be performed if detailed information on the mutation is available. In the case of products with an edited genome, which are applied for placement of EU market, the mutation is known and the applicant provides a method and positive control. The only additional task, which possible needed is establishment of proper performance criteria of analytical methods for detection, identification and quantification for these products.

In a case of lack of certified reference materials, another issue will be metrological traceability conduction.

[1] https://ec.europa.eu/jrc/en/publication/eur-scientific-and-technical-research-reports/new-plant-breeding-techniques-state-art-and-prospects-commercial-development

[2] https://ec.europa.eu/research/sam/pdf/topics/explanatory_note_new_techniques_agricultural_biotechnology.pdf

For unauthorized NMT's products questions are significantly more. Sequencing analysis to detect unknown products developed by genome editing with subsequent bioinformatic analysis is required. It will be necessary to build a new infrastructure and significant capacity building to meet the requirements for detection of unauthorized NMT's products, which require considerable time, financial and human resources.

In this respect, a thorough discussion is needed between the MS coordinated by the EC on the rationality, appropriateness and proportionality of the proper control analyzes, required.

In addition, when complex products (such as most foods and feeds) have to be controlled, the task becomes even more difficult.

2. Conducting field trials and working in controlled conditions.

According to the decision of the CJEU, organisms obtained by gene editing are covered by GMO legislation. The main challenges with regard to the application of this legislation to the contained use and the release of organisms, developed by NMTs, into the environment are linked again to the lack of effective and efficient methods for their detection and identification. As noted above, a serious problem will be when the nature of the modification is not known in advance and the expected genetic changes are minor in comparison to the unmodified parental variety or strain. It will be extremely difficult to monitor for unregulated work or release into the environment. It is necessary to analyze a relatively large number of samples, when the nature of the GMO present is unknown. In general, detection and identification in this case would be difficult and sometimes impossible.

Potential monitoring costs would often be disproportionate to potential risks.

CZ contribution:

Received on 18/01/2019

Discussion following the ECJ decision on mutagenesis – response of the Czech Republic

January 2019

Detection - Statement of the Czech National Reference Laboratory for GMO

New breeding techniques, namely gene/genome editing, represent a useful tool for genetic improvement of agricultural organisms. Some examples have been shown and introduced on the market; products are under development either by companies or at the universities and research centres as experimental materials.

There are important aspects that should be taken into consideration and various scenarios assessed:

- Companies would place a product on the market along with information about the edited site and submit a method for detection and quantification. In principle an event specific method can be designed, validated and verified by reference laboratories. Financial resources will be needed to perform the validation and to purchase adequate chemicals and standards provided that PCR platform will be used (personal costs - 3 weeks of 2 persons, reference material, if available, PCR/qPCR reagents, overheads 20% covering power, water supply, support of technical/economy department) and costs for an accreditation of the method by an official accreditation body,

Increasing number of such organisms and derived products could be expected. No general screening protocols can be developed for such cases, multiplex and high throughput approach will be required. Laboratories will need probably more advanced equipment, incl. NGS machine and specialised operators.

- Numerous unauthorized products or products from countries where regulations are not applied could be present in imported goods or on the market. Assumed that NRL should identify such cases, not only equipment is needed but highly qualified bioinformation for data comparisons is necessary. It is questionable whether even wide knowledge of contemporary allelic variants in individual varieties and genetic resources could help to differentiate between natural and "induced" change. Cost - benefit analysis should be performed.

DK contribution:

Received on 24/01/2019

Provide timely **input to EURL GMFF/ENGL** in view of finalising the draft report.

- Comments have been coordinated with the Danish reference laboratory who send comments on January 15th 2019.

Provide information on **difficulties** Member States are confronted with (including impact on resources) **for** both **inspections and analytical testing** and to **share practices on inspections**

- In the report mentioned above, JRC will provide an overview of the detection issue as seen from a purely scientific/technical point of view. This is very helpful for MS. However, JRC will not provide an estimate of the cost involved in implementing the various suggested types of controls. MS need such a cost estimate before they decide on a future model of control. We would welcome if COM initiated an analysis of the cost involved in the various proposals presented by JRC.

Provide clear examples of **products challenging the implementation** of the legislation.

- Problems related to detection and control of imported products are important and difficult, but these awaits the JRC-report previously mentioned.
- As mentioned in the Annex III of Directive 2001/18/EC: “Future developments in genetic modification may necessitate adapting this Annex to technical progress or developing guidance notes on this Annex”. There is a need to adapt the demands for information in the dossier in connection to filing applications for deliberate release. E.g.:
    - Annex III B point C 2 and 3 do not apply for gene edited plants (“2. Nature and source of the vector used and 3. Size, source (name) of donor organism(s) and intended function of each constituent fragment of the region intended for insertion”).
    - Applicant is not able to provide information related to Annex III B point D point 12 (“12. Description of detection and identification techniques for the genetically modified plant”).
- We would welcome a clarification from the Commission on the interpretation of the GMO-definition and the mutagenesis-exemption vis a vis all the new techniques and applications that are currently available. A New Techniques Working Group has

previously addressed such questions, but following the ECJ-ruling they need to be addressed again. We need a common understanding and interpretation on a more technical level than what is provided by the ECJ-ruling.

IE contribution:

Received on 11/10/2018

Follow-up PAFF 11/09/2018

- Information relating to detection and quantification techniques - We will await the outcome of the work currently being undertaken by the EURL and the discussion taking place with the European Network of GMO Laboratories (ENGL) at its bi-annual meeting in October.
- Information on the intended control of imports of such products – It is proposed to carry out similar controls and checks on products produced from NBTs as those currently in place for GMOs. Until such time that official identification and quantification methods are established, the controls will be based on documentary checks

ES contribution:

Received on 11/10/2018

- **Detection and control:** methods for the detection of GMO produced with NBT are not available, so we can´t give specific instructions to our control bodies. We are aware about the possibilities and limitations of analytical methods to determine if the crop have emerged with NBT or with spontaneous or conventional mutation. It is also important to keep in mind the costs and resources needed to perform the controls.

FR contribution:

Received on 18/10/2018 (COM translation)

NOTE FROM THE FRENCH AUTHORITIES

Subject: Comments from the French authorities on the CJEU Judgment of 25 July 2018 in Case C-528/16

At the meeting of the Standing Committee on Plants, Animals, Food and Feed (SCPAFF), GMO section, held on 11 September 2018, the Commission called on the Member States to provide input on the various issues relating to the judgment of the Court of Justice of the European Union (CJEU) of 25 July 2018 on mutagenesis, with a view to preparing the

Regulatory Committee under Directive 2001/18/EC of 18 October 2018.

The French authorities wish to draw the Commission's attention to the following points.

- Detection and checks

We have sent the Commission a report from the national GMO reference laboratory at the Agency for Food, Environmental and Occupational Health and Safety (ANSES) on methods for detecting products generated by the new plant-breeding techniques.

Detection methods relating to applications for authorisation in the EU

The EU reference laboratory (EURL) reiterated at the SCPAFF meeting of 11 September 2018 that the detection method provided by the petitioner to support an application for authorisation must comply with the criteria for validation of detection methods, in particular, the criterion of specificity. This criterion means that the detection method allows a distinction to be made between the product for which the authorisation is being sought and any other product placed on the market.

The methods must also comply with the performance criteria concerning the limits of detection and quantification, specifically in order to facilitate checks on compliance with labelling provisions.

A EURL-validated detection method is one of the conditions required to obtain authorisation for the placing on the market of a GMO in the EU. According to comments from the EURL at the SCPAFF meeting of 11 September 2018, compliance with the criteria for validation of the methods could prove difficult, or even impossible, for certain organisms produced by new mutagenesis techniques.

The French authorities would like the EURL to specify the circumstances under which it would be possible to validate a detection method based on the current criteria.

Detection and monitoring of products not authorised in the EU

We would like to know which detection methods for products and which checks must be established by Member States to ensure that no products generated by new mutagenesis techniques are placed on the market in the EU without authorisation.

Various reports (produced by the scientific advice mechanism of the European Commission, the High Council for Biotechnology and ANSES) reveal that in most cases, it will probably be impossible to detect mutations if no information is available on their sequencing. The question also arises of attributing the mutation to a particular technique or to a natural variation.

Under these circumstances, compiling a register containing specific information on products generated by new mutagenesis techniques likely to be marketed appears to be the only option for Member States to ensure short-term monitoring of the markets in terms of surveillance and checks. On this point, Article 9(3) of Regulation 1830/2003 states that in order to help the Member States carry out checks, the Commission will ensure that a register is put in place containing information on authorised GMO sequencing and possibly information concerning GMOs which are not authorised in the EU.

In applying this Article, we request that the Commission put in place just such a register for

products generated by new mutagenesis techniques not authorised in the EU.

Monitoring of the information available in the international scientific and intellectual property databases could be set up at European level to help establish such a register.

In addition, certain third countries such as Argentina and Brazil have introduced a procedure which aims to subject products generated by new mutagenesis techniques to a prior examination on the basis of a file before taking a decision on their legal status. This ensures that the authorities of these countries have data even on products that are not subject to regulation.

The French authorities would ask the Commission to hold discussions with third countries, particularly in the context of trade agreements, in order to specify the conditions whereby the data required for detection of these products could be passed on to the European authorities.

Finally, in the event that it would appear impossible to detect certain non-authorised products that are likely to be marketed, it would be a good idea to examine their impact in terms of potential risks to health and the environment and, where appropriate, the management of these risks.

The French authorities remain at the disposal of the European Commission for further reflection on this topic.

Received on 11/01/2019 (translation to EN pending)

Objet : contribution des autorités françaises à la suite de l'arrêt CJUE du 25/07/2018 dans l'affaire C528/16, en complément de la note du 17/10/2018

Par courrier électronique du 18 décembre 2018 et suite aux réunions du Comité réglementaire de la directive 2001/18/CE du 18 octobre 2018 et du CPVADAAA OGM du 3 décembre 2018, la Commission européenne a invité les États membres à compléter les informations déjà fournies sur différentes questions liées à la mise en œuvre de l'arrêt de la Cour de Justice de l'UE (CJUE) du 25 juillet 2018 sur la mutagénèse.

En complément de leur note du 17 octobre 2018, les autorités françaises souhaitent faire part des informations suivantes à la Commission.

1- Information sur les ressources nécessaires à la mise en œuvre des méthodes de détection pour les produits issus des nouvelles techniques de mutagénèse

Des précisions sont apportées ci-dessous concernant les moyens nécessaires à la mise en œuvre de méthodes de détection en routine, sur la base du rapport de l'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et de travail (ANSES) sur les méthodes de détection des produits issus des nouvelles techniques de sélection des plantes, déjà transmis à la Commission.

S'agissant des cas où les séquences à rechercher sont connues, les techniques actuelles (PCR) et le matériel déjà disponible au sein des laboratoires nationaux de référence (LNR) pourront toujours être utilisés. La performance des méthodes reste toutefois à préciser, en particulier pour les mutations de petite taille, ce qui nécessite des travaux de mise au point par les laboratoires. Comme pour les OGM issus de transgénèse, le coût des analyses sera lié au nombre de cibles à rechercher. Il faut toutefois également bien prendre en compte que la détection d'une mutation ne permet pas

d'inférer de manière fiable la nature technologique ou naturelle de celle-ci.

S'agissant des cas où aucune information n'est disponible sur la séquence à rechercher, l'ANSES n'identifie aucune technique permettant la détection de mutations. Les méthodes reposant sur le séquençage de génomes complets pourraient permettre de détecter des séquences exogènes inconnues mais pas les mutations et à condition de connaitre de manière exhaustive les génomes et leur variabilité naturelle au sein des espèces concernées, alors que l'on n'approche aujourd'hui ceux-ci que de manière très partielle et incomplète car on ne réalise souvent que le séquençage d'un « génome de référence » d'un seul individu pour une espèce donnée. Elles ne pourraient donc être utilisées que dans les cas où des séquences exogènes importantes seraient présentes dans le génome à l'issue du processus de la mutagénèse. La mise en œuvre en routine de techniques de séquençage de génomes complets ne pourrait être envisagée qu'à long terme. Ces techniques nécessitent des investissements importants (coût d'un séquenceur : 250 000 à 650 000 €). De plus, cette approche nécessite une technicité et des compétences en bio-informatique qui ne sont pas présentes dans tous les LNR français. Cette approche fait actuellement l'objet de recherches exploratoires à l'ANSES pour la détection de séquences exogènes (doctorat en cours 2016-2019). Elle nécessite encore d'importants travaux de recherche et de mise au point avant qu'une utilisation ne puisse être envisagée dans le cadre de contrôles officiels.

LT contribution:

Received on 18/01/2019

Please find bellow information about the situation in the the Republic of Lithuania regarding the new mutagenesis techniques:

1. Provide to the JRC and reference laboratories **any questions and information concerning analytical issues.**
Harmonised EU strategy for detection, identification and validation of new mutagenesis techniques would be welcome.

2. Provide timely **input to EURL GMFF/ENGL** in view of finalising the draft report.

The implementation of methods for the detection of genome-edited crops depends strongly on the prior knowledge of the sequence alteration. If the analytical procedure for detection and identification of a genome-edited product would be assessed by the EURL.

3. Provide information on **difficulties** Member States are confronted with (including impact on resources) **for** both **inspections and analytical testing** and to **share practices on inspections.**

National Reference GMO laboratory of Lithuania (National Food and Veterinary Risk Assessment Institute) needs more workshops and training for detection and identification of a genome-edited product.
In the meantime, Lithuania does not carry out control and surveillance of organisms obtained by new mutagenesis techniques because the comprehensive data on the species to which these methods were applied and the nature of alterations made to the genome are lacking. Another

issue – it is essential to have harmonised EU procedure for detection and identification of the organisms obtained by new mutagenesis techniques.

NL contribution:

Received on 04/10/2018

Dutch implementation issues of the Court's decision– as requested by the EU Commission October 5, 2018

How do we cope with import control?

The Netherlands Food and Consumer Product Safety Authority (in Dutch: NVWA) carries out import controls that can consist of both a document check and a physical check on the batch to be imported. The basis for this check is a risk-based approach in which the country of origin, type of product and crop are taken into account. If necessary, when legislation or recent events require so, accents can be placed on specific products and/or specific countries. For example on Chinese rice products.

The Human Environment and Transport Authority in the Netherlands (in Dutch: ILT) controls import parties with a risk-based approach. This approach is based on a database that combines data on global gmo activities, the environmental risk and the transport flows.

Information about detection possibilities and/or databases

The JRC (European Reference Lab) has drawn up a document about the detection possibilities. This has been sent to the European Network for GMO laboratories (Dutch members are: NVWA and RIKILT; RIKILT is also a National Reference Lab) and this document will be published in the plenary meeting in October. We are working on a joint response and have already had a discussion about this. RIKILT and NVWA are of the opinion that the possibilities for the NBT crops distinguished from conventional crops are currently very limited. In the future, when NBTs will also be able to bring about greater changes in plants (which is already happening now in microorganisms) this opinion can change, but at the moment in most cases we will not be able to make the distinction. Moreover, in our monitoring programs we work especially with complex products and that makes it even more difficult in practice. Conversely, it is possible to analyze risk-based: when specific new properties are known, and especially when the associated DNA sequence (more or less) is known, we can develop specific methods for this and detect these properties. This may concern properties that may pose a risk to people, animals or the environment. In single plant material (or animal material) there are more possibilities, but the development of this type of methodology is still in its infancy and needs to be dealt with even further.

Received on 24/12/2018

During the meetings of SCOPAFF on September 11th, 2018 and the Regulatory Committee under Directive 2001/18 on October 18th, 2018, Member States Competent Authorities were requested to provide any information relevant to the implementation of the Court ruling.

The following information was requested in particular[3]:

[3] The listed requests are, for the most part, paraphrased from the Summary Report of the Regulatory Committee 2001/18/EC meeting on 18 October 2018 and complemented by personal notes of the meeting of SCOPAFF on 9 September 2018.

1. Regarding official controls: to share information on the difficulties they are confronted with (including impact on resources) for both inspections and analytical testing, and to share good practices on inspections
2. Provide or describe specific examples of products or specific situations where the implementation of the legislation would be challenged
3. To discuss with national laboratories to provide timely input to EURL GMFF/ENGL in view of finalising the draft report, and provide to the JRC and reference laboratories any questions and information concerning analytical issues.

Part of the requested information was provided in our e-mail of October, 5th following the information requests during SCOPAFF in September. In order to maintain oversight and provide answers in a structured manner, our answers to all of the requests described above are listed below. Answers that were copied from the earlier NL input are indicated with a *.

1. Official controls and analytical testing

* The Netherlands Food and Consumer Product Safety Authority (in Dutch: NVWA) carries out import controls that can consist of both a document check and a physical check on the batch to be imported. The basis for this check is a risk-based approach in which the country of origin, type of product and crop are taken into account. If necessary, when legislation or recent events require so, accents can be placed on specific products and/or specific countries. For example on Chinese rice products.

As requested during the meeting of the Regulatory Committee 2001/18/EC in October, some more information is hereby provided on the use of document checks in import controls.

Based on article 5, Regulation 1830/2003, information on the use of GMOs in a product "is transmitted in writing to the operator receiving the product". This type of information regarding imported goods can usually be obtained from the accompanying (transport) documentation. However, this is only helpful if the exporting country requires a GMO status to be mentioned in these documents.

An example of a specific combination of document checks and physical checks are the requirements for the import of Chinese rice products laid down in Commission implementing decision 2011/884.

* The Human Environment and Transport Authority in the Netherlands (in Dutch: ILT) controls import parties with a risk-based approach. This approach is based on a database that combines data on global gmo activities, the environmental risk and the transport flows.

The Dutch expert on detection and identification (from RIKILT, the Dutch national reference lab) communicates with the JRC on a regular basis to discuss any analytical issues.

2. Specific examples of products or specific situations where the implementation of the legislation would be challenged

At the moment, we are not aware of any such products or situations.

3. Provide input to EURL GMFF / ENGL and JRC

The Dutch expert on detection and identification (from RIKILT Wageningen University & Research, the Dutch national reference lab) has provided input for the EURL GMFF/ENGL report.

* RIKILT and NVWA are of the opinion that the possibilities for the NBT crops distinguished from conventional crops are currently very limited. In the future, when NBTs will also be able to bring about greater changes in plants (which is already happening now in microorganisms) this opinion can change, but at the moment in most cases we will not be able to make the distinction. Moreover, in our monitoring programs we work especially with complex products and that makes it even more difficult in practice. Conversely, it is possible to analyze risk-based: when specific new properties are known, and especially when the associated DNA sequence (more or less) is known, we can develop specific methods for this and detect these properties. This may concern properties that may pose a risk to people, animals or the environment. In single plant material (or animal material) there are more possibilities, but the development of this type of methodology is still in its infancy and needs to be dealt with even further.

AT contribution:

Received on 21/01/2019

AT input to the follow up PAFF 03/12/2018 – new mutagenesis techniques

• Provide to the JRC and reference laboratories any questions and information concerning analytical issues

- *AT sees an urgent need to follow a proactive approach for solving the challenges regarding detection of products produced by NBT. We expect that the EURL GMFF/ENGL report provides substantial input as well as clear recommendations for the next steps in this issue*

• Provide timely input to EURL GMFF/ENGL in view of finalising the draft report.

- *Input from AT is provided directly via* [redacted] *who is member of the drafting team of the EURL GMFF/ENGL report*

• Provide information on difficulties Member States are confronted with (including impact on resources) for both inspections and analytical testing and to share practices on inspections

- *AT is of the opinion that there is an urgent need for developing of analytical methods and strategies to identify and inspect products developed with new mutagenesis techniques. Until this methods and strategies are available, the only way to conduct controls will solely depend on the documents provided and total traceability.*

• Provide clear examples of products challenging the implementation of the legislation.

- *All products, where the genetically modification consists of point mutations will challenge the implementation of legislation. Although it is possible to detect such a point mutation, it will*

be difficult to distinguish if this mutation is the result of a natural mutation, non directed mutagenesis or new mutagenesis techniques until there will be new detection methods are developed.

PL contribution:

Received on 22/01/2019

with regard to issues concerning new mutagenesis techniques (e-mail below), please find Polish comments on that matter.

Regarding analysis of food, our national reference laboratory pointed out the following difficulties:

- basically we agree with the comments raised by the UK;
- evolving a common strategy in the matter of organisms (plants) that have been produced by new mutagenesis techniques will be a huge challenge for reference laboratories, since implementing new methods of detection of such organisms is possible under condition that changed sequence is known;
- contrary to GMOs obtained by transformation procedures, plants obtained by new mutagenesis techniques are characterized by an alteration of an existing DNA sequence occurring at a precise genomic site, thus, the new analysis method must lead to detection this unique target sequence;
- In recent years, an innovative technique of "reading"? sequences called "NGS" has been shown. This method seems to be used for analysis, but it is available for detection well known sequences with a simple composition, therefore for composite and processed food products this method may not be feasible;
- we see the need of establishing data base for detection methods for plants created by the new mutagenesis techniques (as it is done for testing GMOs which are authorized in the EU, or GMOs from third countries);
- additionally, for interpretation of analytical results, the sequencing and assembling a plant variety genome database is necessary;
- taking into account the diversity of plant genome, there is a concern that analytical problems may show up, e.g. spontaneous mutations, the need to get information concerning different species of plant (which leads to the need of enormous database of plants and its genomes);
- for plants created by new mutagenesis techniques (similarly to non authorized GMOs), analysis based on sequencing need to be used. Such methods are very expensive (expenditures related to new equipment, costs of implementing and maintaining this method, reagents, additional human resources), currently our NRL does not has this capability;
- after deciding by the EURL GMFF about detection methods, GM laboratories will have to implement it and use it for official controls purpose. This situation, will have an impact on the number and promptness of analysis, as well as the number of food samples.

Controlling imported products for new breeding techniques

The Customs supervises products according to an annual plan. Products produced with mutagenesis will be included in the annual GMO supervision plan. At the moment methods for the detection of GMOs produced with new breeding techniques are not available. We are waiting for the commission to publish suitable methods.

Other comments

Reliable methodology for the detection of products modified with novel mutagenesis methods is absolutely required to ensure legal certainty. This is especially crucial for organisms with point and deletion mutations, which may be challenging to tell apart from any natural counterparts. Also, a constantly updated listing of products on the market outside EU is essential to focus the supervision on relevant products. Estimates are needed about the amount of additional supervision resources needed annually to ensure sufficient supervision capacity within EU. A certificate describing which breeding method was used in the development of a particular animal, plant or microbial strain could help supervision, but it would also constitute a substantial administrative burden in the various production chains.

Received on 18/01/2019

Statements of the supervisory Authorities for Gene Technology Act on the implementation of ECJ ruling on new mutagenesis techniques

The Finnish supervisory authorities for the Gene Technology Act (377/1995) provided the following statements when the Board for Gene Technology requested about the use of novel mutagenesis techniques (NMTs) in Finland and the implementation and effects of the ECJ ruling on NMTs.

(Unofficial courtesy translation.)

Finnish Food Authority:

Finnish Food Authority sees that since the detection of organisms produced by NMTs is practically impossible by analytical means, official controls or self-monitoring by operators cannot be performed in practice. Mere document-based controls pose compliant and non-compliant actors in a very unequal position, which can have serious consequences for the competitiveness of the players. Moreover, limiting the use of NMTs within the EU places European plant breeders in a disadvantageous position in relation to operators in other countries. In the EU, the approval procedure for GMOs is slow, which is unfavorable for plant breeders or other users of new technologies. According to Finnish Food Authority, it is most important to assess the safety of new products on the basis of the product's characteristics, not based on the technology used.

The organisms produced by NMTs can in practice be detected analytically only by genomic sequencing. Finnish Food Authority has the potential for both Sanger and whole genome sequencing. The target genes modified by NMTs may sometimes be the same as those previously used for conventional gene transfer. In these cases, a targeted search for a mutation by sequencing could be theoretically possible. However, even if the mutated site is detected, finding out how the mutation has occurred - naturally or with various chemical or irradiation-induced or targeted mutagenesis methods - is virtually impossible.

An additional problem is that the food and feed analyzed contain several ingredients. Each of them should be sequenced in its entirety and compared to the genomic databases, which are not complete even for crop plants. Since each variety differs from the genome of other varieties of the same species, there should also be a genomic database for each variety. Given that the amount of target genes, species and varieties increases as a result of NMT use, detection of GMOs produced by new mutagenesis methods and not approved in the EU is therefore virtually impossible.

From the control point of view, the amount of GM material in GMOs approved in the EU is also crucial. If food/feed contains an GM ingredient produced by NMTs and approved in the EU, but the food/feed is not labeled as GM material, the amount of GM material should be analyzed so that the control authority can make a decision on labeling on the basis of the analysis results. If conventional quantitative real-time PCR (QPCR) cannot be used for analysis, it is virtually impossible to analyze the amount of GM material. Whole genome sequencing is considerably more expensive than today's common Q-PCR used to analyze GMOs, and the resources for such an analysis are limited.

Finnish Food Authority considers that while ECJ ruling as unambiguous, it does not take into account that the control authorities should have a possibility to carry out their supervision task. Supervision is carried out both in written documents and by taking samples and analyzing them. If there is no adequate documentation and/or analytical controls cannot be performed in the absence of any methodology or because of their costs, this effectively prevents effective enforcement.

Finnish Environment Institute SYKE:

SYKE does not see reason to focus its supervisory activities at this point to any NMT applications. If the use of NMTs becomes more common, SYKE's supervisory obligations will increase and additional resources are needed. SYKE does not have technical capability to detect and identify NMT organisms. SYKE does not carry out independent development work for the detection methods for supervision purposes, but relies on collaboration with other authorities, such as Customs and Finnish Food Authority. SYKE states that once the operator has provided legitimate information on the application of NMTs, controls are carried out on the same principles as for the conventional GMOs.

National Supervisory Authority for Welfare and Health (Valvira):

At present, the focus of gene editing is in the therapeutic use of edited cells, which does not cause population-level health risks. So far, the clinical and preclinical trials of GM organisms in general have been performed as contained use.

Valvira would prioritize monitoring the use of gene editing in poorly characterized organisms with a short history of use, as well as in organisms with toxic, pathogenic or detrimental properties. Special attention should be based on large-scale use of organisms with a short history of use e.g. as production platforms.

Regular GMO monitoring methods can be used when the user has notified the use of gene editing for deliberate release, as the notifier must present the detection and identification methods for the organism in the B-notification. Illegal use can be supervised by direct requests of information for the relevant operators as well as by following new products to be launched on the market and by making more detailed studies on whether their properties might arise from NMTs. Such properties could include e.g. disease resistance, rapid growth, shortened generation time, or phenotypic changes (taste, color, shelf life).

According to Valvira, extending the scope the GMO regulation to gene editing requires new supervising practices and thus extra resources. Their extent depends on how widely NMTs will be used in and outside EU. Gene editing may not be regulated in all countries of import, which has to be taken into account in controls. Also, more users will start using gene editing as the methods become easier and cheaper. Some of them may neglect the notification requirements, especially as it may not be possible to unquestionably prove the use of gene editing. Crop research will probably move outside the EU to countries which are not regulating gene editing extensively. On the other hand, introduction of new technologies in itself could make plant breeding for the Finnish climate economically viable, potentially starting GM plant cultivation in Finland. Gene editing can also be an economically viable way to modify a number of sites in the genome, so the range of properties to be modified is likely to expand. NMTs also allow modifying such prokaryotes or eukaryotes (including eukaryotic microbes) for which effective molecular biology tools have been lacking. Supervision must be prepared for a much wider range of both species, applications and users.

For the time being, Valvira has not used laboratory analyses to control the use of GMOs or their spread into the environment, and Valvira does not have its own analytics service. If needed, the analytical services will be obtained from external actors on a case-by-case basis. When the modifications made with NMTs do not differ from those induced by traditional mutagenesis or from natural mutations, there is no laboratory analysis method to undeniably demonstrate the use of gene editing technology.

For the detection of the organisms which have been notified, the methods described in the application can be used. On suspected unauthorized use, the operator would be requested information on the origin of the organism, its characteristics and the genetic material affecting the

At the moment, no effects are seen when it comes to trading of tree based products in relation to analysis and control, but this could change.
Future problems are predicted with international exchange of plant material, when the outside world does not intend to regulate mutagenesis where no external DNA is present in the end product. If there is no reason to label research material as regulated material in the country of origin, we have no possibility to control if mutagenesis with methods that are regulated in the EU has taken place at some point. This creates a legal and credibility problem given that the quality of products is currently guaranteed by analysis.
When research and plant breeding are moved outside of the EU, there is a risk that the crops that were originally developed in EU countries will be imported back into the EU. This could partly be the case for seeds for cultivation within the EU but also for consumer ready products. Since there are no detectable differences between crops that have been developed with modern and traditional plant breeding techniques, it is questioned how the control of such import would be possible. There is a risk that food and ingredients produced with the new techniques of mutagenesis, will still be on the EU market, in spite of the efforts of the EU to limit the use of these techniques.
If a genome edited crop would after all be produced, the current EU legislation for traceability and labelling of GM crops would obstruct commercialisation since it will be very difficult to produce a method to identify and distinguish mutations when only one or a few nucleotides have been changed. In practice, the ruling therefore means a ban on genome edited crops.

UK contribution:

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•Details of the advice given to control bodies/local enforcement authorities

The detection of products arising from gene editing will be extremely challenging and the availability of databases and reference materials will be fundamental in achieving any solution. An expert from our National Reference Laboratory has been involved in producing the EURL explanatory note on the detection of GM food/feed originating from genome editing. We have been in contact with the UK National Reference Laboratory for GMOs and with our GMO Inspectorate about the implications of the CJEU judgment but we have not issued detailed advice to them.

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FERA note in Annex 2: Technical notes on the ‘detectability problem’ of GE