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Health and Food Safety Directorate General

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Section *Regulatory Committee 2001/18/EC*
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SUMMARY REPORT

A.01 Application of the GMO legislation to medicinal products for human use in the context of the COVID-19 pandemic. Presentation by Commission and discussion.

The Commission introduced the agenda item, referring to the Coronavirus outbreak which has created an unprecedented public health emergency. In this situation of health crisis, the EU is confronted with questions about the application of the GMO legislation to medicinal products for human use, in particular as regards the conduct of clinical trials with GM vaccines and the administration of GM medicinal products in emergency or urgent situations.

The Commission provided clarification on the email sent to the Member States on 30 April, about the regulatory flexibility under the GMO legislation to accelerate clinical trials with GM vaccines and treatments against COVID-19 and the use of GM medicinal products for COVID-19 prior to marketing authorisation, under national early access schemes or in exceptional circumstances.

The Commission also provided a summary of the discussion with MS experts in the teleconference of 13 May 2020 about the application of the GMO framework to the conduct of clinical trials and possible use of vaccines against COVID-19 before a marketing authorisation is granted.

One Member State called for an EU harmonised approach and questioned who would be responsible in case of environmental damage. Another Member State confirmed the difficulties in applying the GMO legislation to medicinal products.

Four Member States supported the maintenance of an environmental risk assessment, to be performed with a proportionate and case-by-case approach.

The Commission took note of the comments of Member States and confirmed that the work with the national experts on the pharma-GMO interplay will continue.

A.02 Seed sampling and testing: follow-up of Regulatory Committee of 18 October 2018. Exchange of views and endorsement on seed testing convergence (Commission Recommendation 2004/787/EC).

The Regulatory Committee of October 2018 requested the Commission to coordinate the work between Member States with a view to achieve a higher convergence of national practices on the seed testing and sampling. The Commission accepted to convene an ad-hoc technical working group (WG) to this end, while reminding that the zero-tolerance, applicable to GM-presence in conventional seeds, remains in place.

The Commission presented the result of four intensive WG meetings, which builds on an existing Recommendation 2004/787/EC. The Committee endorsed the document and agreed to make it public as an attachment to the minutes. The Commission and the Member States agreed to discuss the issue in the light of possible future practical experience. Further to the request of Member States, the Commission agreed to elaborate a document enumerating the practical aspects of notifying non-compliant seed lots.

A.03 French draft legal acts reviewing, *inter alia*, the status of mutagenesis techniques used *in vitro*. Presentation by the Commission and discussion.

The Commission provided a short overview of the notification received on 7 May from the French authorities concerning three draft legal acts under preparation to answer to the injunctions issued by a decision of the Conseil d'Etat on mutagenesis. France had sent the notification also to the Member States.

The Commission clarified that the notified French draft legal acts were still under assessment by Commission services and that the discussion would not prejudge the Commission's follow up to the notification.

The Commission then informed the Member States on:

- the mandate recently sent to EFSA to provide a scientific analysis as to whether the distinction between *in vitro* and *in vivo* random mutagenesis techniques is scientifically justified; the output is expected by the end of September 2021;
- the letter sent to Member States requesting information, by 30 June 2020, on *in vitro* mutagenesis techniques in plant breeding;
- the meeting of the Standing Committee on Plants, Animals, Food and Feed, Section Seeds and Propagating Material for Agriculture and Horticulture of 12 June, where the issue would have also been discussed.

FR provided clarifications on the French draft legal acts and the decision of the Conseil d'Etat. FR also referred to a note sent to the Commission and the Member States requesting support for the implementation of the draft legal acts.

Seven Member States raised concerns on the challenge to gather information. The Commission clarified that the need for information was related to the scope of the Conseil d'Etat decision/French draft legal acts, namely on the techniques of *in vitro* random mutagenesis on plant cells cultured *in vitro*. The scope should include agriculture but also other purposes such as ornamental and forestry. In view of the short deadline, Member States agreed to provide available information by 30 June with the possibility to integrate further data at a later stage.

A.04 A Farm to Fork Strategy for a fair, healthy and environmentally friendly food system. Presentation by the Commission.

The Commission made a presentation on the recently adopted Farm to Fork (F2F) strategy.

Two Member States welcomed the F2F strategy.

Four Member States commented that the text of the F2F strategy on the Commission study on new genomic techniques (NGTs) did not reflect accurately the request of the Council, as it mainly focused on the potential of these techniques to improve sustainability along the food supply chain.

Further to these comments, the Commission confirmed that, as requested by the Council, the study under preparation focused on the status of novel genomic techniques under Union law in light of the Court of Justice's judgment in Case C-528/16. The Commission emphasised that the services were working on the study as intended, with an objective and neutral approach and that the sustainability potential of NGTs was one of the many aspects addressed in the questionnaire to Member States and stakeholders. The Commission concluded that the final content of the study and follow up were not yet known, as the services were still assessing the high amount of information received.

Member States were satisfied with this clarification.

M.01 Novel genomic techniques

The Commission gave a short procedural update on the progress regarding the on-going study on the status novel genomic techniques, as requested by the Council.

This document was endorsed during the meeting of the Regulatory Committee under Directive 2001/18/EC held on 4 June 2020.

Seed testing convergence

In addition to the provisions of Commission Recommendation 2004/787/EC[1], seed testing for adventitious GMO presence should be based on and take into account the following points:

1. Risk based sampling plans

Amongst other, risk based sampling plans for testing the adventitious GMO presence in seeds take into account the following factors for targeting sampling:

- Plant species:
    - Species for which GM events are known: for species for which many GM events are known (e.g. soy, maize, oil seed rape, cotton), the risk for adventitious GMO presence can be higher, justifying increased sampling or targeting. Sampling of species for which no knowledge of a GMO exists may be useful where the methods for detection of GMOs or for screening approaches are available.
    - Biology of the species: the mode of reproduction, and especially, the potential for dispersion and persistence in the environment by pollen and seeds can justify a higher sampling frequency or more targeted testing.
    - The areas cultivated at national level for the species for which GM events are known;
    - Sampling should take into account that seed lots of a given species/crop could be contaminated by seeds of GM varieties of another species/crop that is commercially grown in the region where the seed multiplication has taken place.
- Origin:
    - For countries in which GMOs are grown commercially, the cultivated area by species or crop, the proportion of GMOs versus non-GMOs for a given species, and the local traceability systems are important elements. Higher ratios GMO / non-GMO can increase the likelihood of adventitious GMO presence and thus warrant higher sampling frequencies. Information on the efficacy of local traceability or geographic

[1] Commission Recommendation 2004/787/EC on technical guidance for sampling and detection of genetically modified organisms and material produced from genetically modified organisms as or in products in the context of Regulation (EC) No 1830/2003 (O.J. L 348, 24.11.2004, p. 18)

spread of GMO cultivation can influence the sampling frequency / plans.

  - For some origins, safeguard measures apply.

- Volume of imported seed: higher quantities of imported seed warrant a higher number of samples.
- Size of the seed lot: for a given species, targeted sampling of larger lots can be advantageous, as this generates information for larger cultivated surfaces.
- Any other parameter influencing the risk of presence of GMOs in seeds, such as information related to accidental or illegal release, GMO field trials (current or past), operator's practices, past results of official controls etc. Newly available information can be a reason to adjust a predefined sampling frequency.
- For sampling high value seeds or small lots of seed, smaller sample size should be compensated by other checks (e.g. operator's production process, segregation, traceability, and testing of parent plant material etc.).

The information on these parameters is assessed to establish risk based sampling plans with a suitable sampling frequency and targeting adapted to the risk of GMO presence in seeds for the different possible situations. Changing situations trigger a regular review of this assessment.

Amongst other, the following sources of information may be useful:

- On GM species and events: the EU Register of authorised GMOs[2], international databases, such as those of the OECD[3], of the Biosafety Clearing House[4] of the Cartagena Protocol, of FAO[5], or those developed by other organisations (e.g. ISAAA[6], EUginius[7]).
- Quantitative data: European statistical database Eurostat, customs data, national statistical data relating to agriculture and the agricultural economy, data published by professional organizations and operators of the seed sector etc.

2 https://webgate.ec.europa.eu/dyna/gm_register/index_en.cfm
3 https://biotrackproductdatabase.oecd.org/
4 http://bch.cbd.int/database/lmo-registry/
5 http://www.fao.org/food/food-safety-quality/gm-foods-platform/en/
6 http://www.isaaa.org/gmapprovaldatabase/
7 http://euginius.eu/euginius/pages/home.jsf

2. Time/Moment of sampling

Sampling and testing of seed should be performed as early as possible and before planting. Where possible sampling and testing of seed should be integrated in the seed certification process. Ideally, the results on the sampled seed lots should be available prior to distribution and planting of the seeds. The use of a database compiling the test results can be helpful in immediately informing the concerned institutions / parties to take measures and avoiding duplication of efforts.

3. Sampling methods and sample size

Sampling methods should be in accordance with the latest version of the ISTA (International Seed Testing Association) 'International Rules for Seed Testing'[8]. The working sample (sample used for the preparation of the test portion) should consist of 3000 seeds. For seed potatoes, the working sample should consist of 200 tubers; from each tuber a small part of similar weight (e.g. 1 g) should be taken.

4. Analytical aspects

4.1. Sample preparation

Sample preparation is performed in accordance with the '*Guidelines for sample preparation procedures in GMO analysis*' prepared by the ENGL ad hoc working group on "sample preparation procedures"[9].

An optional washing step may be included in the sample preparation procedure[10]. In case of coated seeds, the pellets can be depelleted as described in the ISTA Rules (Chapter 11). In case of treated seeds, the washing step can be done under running water. In both cases, the washed seeds should be dried overnight in a warm dry place on moisture absorbing material, e.g. filter paper.

[8] Chapter 2 «Sampling» is freely available at https://www.seedtest.org/en/Rules/free-rules-chapters-_content---1--3410.html

[9] available at http://gmo-crl.jrc.ec.europa.eu/ENGL/docs/WG-SPP-Final-Report.pdf

[10] See for example Point 6.3 in the report of the ENGL Working Group „Seed Testing" (htpp://gmo-crl.jrc.ec.europa.eu/ENGL/docs/WG-SeedTesting-Report.pdf)

4.2. Subsampling

Sub-sampling approaches should be favoured for seed testing, according to the report of the ENGL Working Group "Seed Testing"[11] and considering the relevant ISTA Rules (Chapter 19) and associated statistical tools (e.g. Seedcalc[12]), and (draft) international standards (ISO CD 22753[13]).

4.3. GMO screening aspects

GMO screening methods are selected based on, amongst other, the screening strategy, the type of sample, the control plan objectives etc. The use of screening methods validated against the EURL-ENGL minimum performance criteria[14] is recommended. Validated screening methods are available in the GMOMETHODS database[15].

Screening strategies can be designed with the help of web tools like the JRC GMO Matrix[16] and EUginius[17], combining a number of different screening methods. For advice, CEN/TS 16707:2014[18] can be used. For species where screening methods do not cover all GMOs, event-specific methods need to be applied additionally to cover all the possibilities.

4.4. Expression of results

The format of expression of result described in EN ISO 24276, EN ISO 21569 and EN ISO 21570 should be applied.

Results of the qualitative PCR analysis should be expressed along the following lines:

- for PCR positive results as "for sample X, target sequence Y was detected"; the identity of the GMO may be included, if available.
- for PCR negative results as "for sample X, target sequence Y was not detected;

The LOD of the method is x % (provide unit of measurement) determined by using material ABC (*identify the reference material*)".

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11 available at http://gmo-crl.jrc.ec.europa.eu/ENGL/docs/WG-SeedTesting-Report.pdf

12 Last version available at https://www.seedtest.org/en/statistical-tools-for-seed-testing-_content---1--3449--1102.html

13 ISO/CD 22753 Molecular biomarker analysis - Method for the statistical evaluation of genetically modified organisms analysis results obtained in testing sub-sampled groups of seeds and grains— General requirements and definitions. Available at https://www.iso.org/standard/73822.html

14 Definition of Minimum Performance Requirements for Analytical Methods of GMO Testing (2015) ENGL; available at: https://gmo-crl.jrc.ec.europa.eu/doc/MPR%20Report%20Application%2020_10_2015.pdf

15 available at http://gmo-crl.jrc.ec.europa.eu/gmomethods/

16 http://gmo-crl.jrc.ec.europa.eu/jrcgmomatrix/

17 http://www.euginius.eu/euginius/pages/home.jsf

18 Available at https://standards.cen.eu/dyn/www/f?p=204:110:0::::FSP_PROJECT:40277&cs=1A5C2C34E988871457536EADE6326EA81

If a qualitative analysis result provides information on the GMO content (e.g. that the content is below x %), the unit of measurement (mass/mass; copies/copies; number of GM seeds/number of total seeds) for the percentage should be provided.

For quantitative PCR results the content of GMO (*specify GMO*), the unit of measurement, the measurement uncertainty and the practical LOQ should be given.

Whenever the subsampling approach has been adopted for seed quantification, the unit of measurement is the percentage by number of seeds.

4.5. Test report

The test report should be in accordance with EN ISO/IEC 17025 and should provide the following information (or be traceable to):

Date of sampling
Date of sample arrival in laboratory
Sealing of the sample: absent / official or non-official / description (integrity)
Identity of sampling organisation
Seed treatment: yes/no
Analysis start and end dates
Plant species
Variety**
Official lot number
Country of production**
Number (or weight) of seeds in working sample (and used in the analysis)
Number of sub-samples**
Number (or weight) of seeds per sub-sample (used for grinding)**
Result of the analysis***
PCR method(s) used (reference)
Limit of detection of PCR method(s)

* if other than official.

** when applicable

*** the expression of result of the analysis is described in point 4.4.

5. Proficiency testing

Participation in the proficiency tests organised by the EURL GMFF provides a good opportunity for demonstrating the laboratory competence regarding procedures from DNA extraction until measurement and expression of results. Participation in GMO proficiency tests specifically organised for seed testing (e.g. organised by ISTA) is encouraged.

6. Counter analysis

Counter analysis can have a deviating result from the first analysis result due to the Poisson distribution of adventitious (very low level) presence of GMO seeds. Consequently, a negative counter analysis result does not exclude the presence of GMO seeds in the lot when a first analysis detected GMO.

7. Information to COM and other MSs

When sampling and testing of a lot of seed originating in another MS country or traded with another MS country reveals a non-compliant result, the MS will immediately inform the COM of the findings by e-mail. Following bilateral and internal validation, COM will subsequently share the info with all Member States.