UPDATE FROM FDP UNIT ON GMO APPLICATIONS

AD HOC MEETING WITH GMO INDUSTRY REPRESENTATIVES 19 MARCH 2025

Claudia Parisi
Ellen Van Haver
Silvia Federici
Front Desk and Workforce Planning Unit

efsa
EUROPEAN FOOD SAFETY AUTHORITY

OUTLINE

- Post-TR GMO dossiers
- Overview of most relevant changes in the update of EFSA GMO administrative guidance documents:
  - For new applications
  - For renewal applications
- Relevant information from EFSA's Catalogue of services
- Submission tips

POST-TR GMO DOSSIERS OVERVIEW

- 43 post-TR GMO dossiers have been received so far, since May 2022:

GM PLANTS:

- **10 new single events**
- **9 new stacked events**
- **20 renewals**: 3 in 2022 and 17 in 2024

GM MICROORGANISMS:

- **4 new applications** in parallel with FEED

GMO ADMINISTRATIVE GUIDANCE UPDATE: OVERVIEW OF CHANGES

Administrative guidance for the preparation of applications on GM plants

- **Appendix H:** Required information for bioinformatics analyses
- **Appendix I:** Required information for the 90-day feeding study
- Information on **Good Laboratory Practice** (GLP)
- Information on **Letters of Access** (LoAs)
- **Notification of studies** (NoS): Reference to Q.4 of Q&A on Practical arrangements
- Information on **confidentiality** of raw data and on **Intellectual Property Rights** (IPR)

Administrative guidance for the preparation of renewal applications on GM food and feed

- **Appendix F:** Required information for bioinformatics analyses
- **PMEM reports:** naming recommendations
- Information on **Good Laboratory Practice** (GLP)
- Information on **Letters of Access** (LoAs)
- **Notification of studies** (NoS): Reference to Q.4 of Q&A on Practical arrangements
- Information on **confidentiality** of raw data and on **Intellectual Property Rights** (IPR)

GMO ADMINISTRATIVE GUIDANCE UPDATE: APPENDICES

Appendix H (new applications)

ESFC Section: Molecular characterisation

Appendix F (RX applications)

ESFC Section: New info – Updated bioinformatics

Required information for bioinformatics analyses

Appendix H/F is a spreadsheet for submitting key bioinformatics information according to Regulation EC 1829/2003 and Commission Implementing Regulation EU 503/2013. The spreadsheet should be filled out by the applicant to facilitate harmonisation, transparency and clarity of the reported information. For GM plants with multiple transformation events, one spreadsheet should be filled out for each transformation event.

Appendix I (new applications)

ESFC Section: Toxicology assessment

Required information for the 90-day feeding study

Appendix I describes the information required for submitting a 90-day feeding study in rodents with whole GM food and feed under Regulation 503/2013 (EU). It includes tables with detailed description of the required information for the 90-day study, coming from various sources/obligations.

GMO ADMINISTRATIVE GUIDANCE UPDATE: GOOD LABORATORY PRACTICE

GMO studies (Article 4 of IR 503/2013):

- GLP for toxicological studies
- GLP or ISO for studies other than toxicological studies

GLP paragraph added to the GMO Admin GD to clarify the requirements on the acceptance of GLP studies (i.e. to be performed in GLP certified test facilities), in line with the information on EFSA website (GLP page)

Acceptance of GLP studies in application dossiers

EFSA accepts GLP studies that are performed in GLP certified test facilities located in an OECD member country or in a non-member country that adhere to the Mutual Acceptance of Data (MAD) system.

The OECD website provides a list of OECD members and MAD-adherent countries.

To find out whether a test facility is GLP-certified in an area of expertise, you should consult the respective *GLP monitoring authority*. The European Commission provides information on test facilities inspected by EU GLP monitoring authorities. If the test facility is located outside the EU, links to national websites on GLP are available on the OECD website.

We may accept studies that are conducted in a test facility located in a non-MAD adherent country under certain conditions, e.g. when the test facility has been inspected by an EU GLP monitoring authority and found to be GLP compliant for the respective area of expertise. Information on the GLP status of such a test facility can be obtained from the respective EU GLP monitoring authority.

Links to EU GLP monitoring authority contact points.

File naming recommendations

Annexes in new applications

All documents listed should be identified using a unique identification (e.g. Annex 2). The corresponding file name should contain the number and a short description of the content (e.g. Annex 2_protein expression.pdf). Reference in the main text to a specific document should be done using this unique identification for each cited document.

PMEM reports in RX

- Applicants are recommended to harmonise the naming of the files related to PMM/PMEM reports, so that the name of each file indicates:
  - the reporting year
  - the content of the file
  - the GM event(s) covered

Examples: *2019_PMEM report_GM event.pdf; 2022_Literature report_GM event.pdf*

- It is also recommended that the unique name of the file is used in the text of the core PMM/PMEM report to make reference to that supporting document.

GMO ADMINISTRATIVE GUIDANCE UPDATE

Admin GD updates on subjects presented in previous meetings

- ✓ **RFI response:** Free-text box to be used only to list the changes\new information introduced, while new information/justification to be added to the relevant section of the dossier.
- ✓ **Opening of additional sections of the dossier**: how to do it in practice.
- ✓ **Confidentiality of raw data**: How to deal with file formats than cannot be converted into .pdf files.
- ✓ **Intellectual property rights (IPRs)**: how to deal with articles/publications on which the applicant does not have IPRs
- ✓ **Letters of Access (LoAs):** clear distinction between the use of LoAs in applications for single events and for stacks
- ✓ **Notification of studies**: reference to Question 4 of Part B of the Questions and Answers on EFSA's Practical Arrangements: https://www.efsa.europa.eu/en/corporate-pubs/questions-and-answers-efsa-practical-arrangements

GMO ADMINISTRATIVE GUIDANCE INFORMATION

Additional studies in GMO renewals

ESFC Section
New information – Additional documents or studies performed by or on behalf of the applicant

- The main text should contain an overview of ALL unpublished studies produced, controlled or sponsored by the applicant or provided to the applicant by a third party and not previously submitted to the EU.
- Applicants should review and assess the relevance of these additional studies for molecular characterisation, human and animal safety and the environment.
- Any related study reports, raw data, certificate of analysis, etc. should be uploaded in the same ESFC section.

- If available, new data on the sequence of the event(s) for renewal, derived from seed lines containing this event(s) and giving rise to varieties imported to the EU close to the time of the renewal application, should be included.
  - Re-sequencing submitted as additional study should follow the Technical Note on the quality of DNA sequencing of 2024.
  - If the sequencing data is not available according to the Technical Note on the quality of DNA, the applicant should clearly state it in the main text of the additional study section.

SUPPORT INITIATIVES FOR APPLICANTS: FOCUS ON TELECONFERENCES AND TECHNICAL HEARINGS

Clarification teleconference

- Organised upon request of EFSA or the applicant
- It can be used during completeness check and risk assessment to:
  - clarify the rationale of questions raised by EFSA
  - ensure understanding of the questions by the applicant
- During completeness check, a clarification teleconference can also be used to clarify outstanding issues and a maximum of two requests may be submitted for the same application

Applicant's technical hearing

- Organised upon request of EFSA
- It can be organised during risk assessment
- The applicant is invited as a hearing expert to attend a specific agenda point of EFSA's Working groups or Panels meetings to:
  - clarify the additional information provided
  - clarify any outstanding issue on the application

Post-adoption teleconference

- Organised upon request of the applicant, EFSA reserves all rights to decide on it
- It can be used following the publication of EFSA scientific opinion to:
  - explain the scientific rationale of the final output
  - clarify the sources of evidence and the factors that influenced the outcome
- It is not meant to provide any scientific advice to applicants for future submissions

EFSA's Catalogue of support initiatives

Consult the catalogue for more details and contact information to request services

FINAL SUBMISSION TIPS

Sequencing package

- ESFC upload might be affected by the quality of the connection: we advise to re-check the uploaded package in ESFC before submitting the dossier
- Avoid long file/folder names and special characters (\ / : | < > * ? “ ,) which would prevent the upload of the sequencing package on EFSA platforms

SD0

Password-protected raw data

- Some applicants provide password-protected raw data together with the password in a separate file
- The principles of transparency, as reflected in preamble 28 and Article 38 of the General Food Law, request easy public access to disclosed data and information
- Accordingly, unnecessary steps for the public to access the data should be avoided

Submissions through Portalino

- Submission of complementary information following EFSA’s inconclusive scientific opinion (see Section 2.12 of Admin GD)
- PMM annual reports
- PMEM annual reports for cultivated GM crops

Slide 12

SD0 Are they aware of Azure? Is it needed to mention? In case just delete 'into Azure'
DE BERARDIS Sara, 2025-03-14T08:21:10.622

CP0 0 They should be aware. I will check with NIF. Long file names are OK for ESFC but then they give us issues for the upload in Azure.
PARISI Claudia, 2025-03-14T10:12:10.287

CP0 1 Indeed you were right. We reformulated in a more generic way. Thanks.
PARISI Claudia, 2025-03-14T11:02:33.328

THANK YOU FOR YOUR ATTENTION

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EUROPEAN FOOD SAFETY AUTHORITY

BACKGROUND SLIDES

SUBMISSION TIPS – RFI RESPONSES

RECOMMENDATIONS TO REPLY TO EFSA'S REQUEST FOR INFORMATION (RFI):

- When asked for missing information, please, integrate the missing information into the corresponding documents **of the dossier** or in the metadata of each document, as applicable. Do not only provide the information in the response to the RFI.

- Using the free-text box available in each section of the ESFC platform, indicate the changes made with a brief description of the new information provided.

ESFC TABLE OF CONTENT: RFI INFO

- Each section of the dossier is unlocked for modifications by the applicant only in case Request of Information (RFI) is done by EFSA in that section
- Note that, with the simplified ToC, broader sections will be unlocked by the RFIs
- Please, always indicate the changes made in the dossier, also if not requested by EFSA (spontaneous changes)

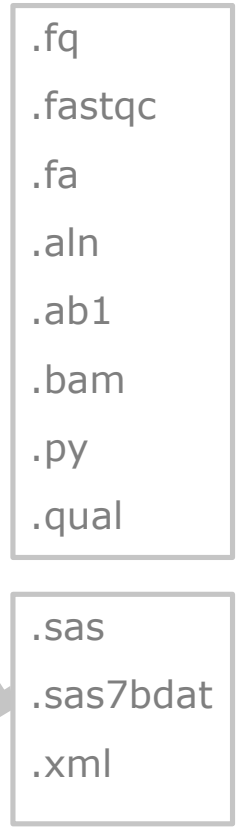
- In case of need for changes in sections that are NOT unlocked by an RFI:
  - If the application is with the applicant: re-submit your dossier at your earliest convenience, indicating the requests that have been addressed so far and the requests for opening additional section(s). We will then open the sections indicated.
  - If the application is with EFSA: send an email to FDP (FDP@efsa.europa.eu) clearly indicating the sections that need to be unlocked. As soon as we have completed the check, we will issue a new RFI and open all the needed sections.

Confidential raw data files

Raw data package:

- Sequencing
- Compositional analysis
- Agro-pheno analysis
- Tox 28-day study
- Tox 90-day study

Files typically included:



- Need a special software to be opened
- Not convertible into pdf
- Hundreds of files, in several subfolders
- Claimed as fully confidential by applicants

Confidential raw data files: current approach

CASE 1

- File entirely claimed confidential by applicant
- Files considered fully confidential in the preliminary evaluation

EFSA may accept the submission of a placeholder for the non-confidential version of the file

Files can be removed from the non-confidential version of the raw data package and can be replaced by a file that reports the LIST of all removed confidential files (one list per subfolder), mentioning that the files are considered confidential.

CASE 2

- File entirely claimed confidential by applicant
- Files NOT considered fully confidential in the preliminary evaluation

EFSA must perform a full confidential assessment

In the non-confidential version of the raw data package, applicants must provide, for each file, a corresponding document with the same name.

Please, note that this is **provisional** and **without prejudice to the outcome of the confidentiality assessment**.

SUBMISSION TIPS - REFERENCES

Articles/publications available in the public domain on which the applicant does not have intellectual property rights (IPRs)

- Flag as 'Yes (publicly available), IPR not owned' and include the bibliographic citation in the free-text box 'IPR reference'.

In case of a high number of references (and IPR not owned)

- The use of zipped folders is accepted
- Flag the full folder as 'Yes (publicly available), IPR not owned' and provide the list of bibliographic references in a separate pdf.

Subfolder "0.6_References" in the sequencing package (and IPR not owned)

- We advise the applicant to include the pdf reference files only in the confidential version of the folder and put a list of bibliographic references in the public version.

The list of bibliographic reference is published in Open EFSA upon validation, but not the corresponding IPR-protected pdf files.

LETTERS OF ACCESS (LOA)

EFSA legal services were recently consulted about the use of **Letters of access (LoA)** in post-TR dossiers, instead of confidential and non-confidential version of particular files. Main points:

- It is the responsibility of the applicant to provide all the data necessary for risk assessment (Art. 4(3) of Reg. 1829/2003)
- LoAs allow an applicant to use information for which a previous applicant had ownership (Art. 31 of Reg. 1829/2003).

HOWEVER:

- LoAs do not exempt the applicant from submitting that data in the application.
- EFSA shall make public, upon validation, all non-confidential dossiers and carries out a public consultation on the studies received (GFL Art. 38(1)c, 39b(1)a and 32c).

EFSA cannot accept a **single event** dossier that includes only LoA instead of a confidential and a non-confidential version of the corresponding studies/documents.

SPECIAL CASE:

- GM crops with **stacked events**: In accordance with IR (EU) No 503/2013, for the risk assessment of those events the applicant can refer to already submitted application(s).

NOTIFICATION OF STUDIES (NOS)

NoS obligations

- Studies must be notified prior to their starting date (art 32b of General Food Law)
- What falls within a definition of "study": Question 4, part B of Q&A to Practical Arrangements (update 28/08/2023)

Studies to be notified

- Stability, efficacy and safety studies
- Studies to demonstrate absence from the product of viable cells and recombinant DNA of a production microorganism

Studies exempted from NoS obligations

- Analysis to assess the **identity/composition of a product**, including the determination of its impurities and whole genome sequencing
- Analysis to determine **physico-chemical properties**
- **Method validation** studies

NOTIFICATION OF STUDIES (NOS)

Examples of **safety studies** to be notified in a GM plant application

- **Toxicity studies:** e.g., 90-day oral study, 28-day oral study, acute oral toxicity
- **Human or animal testing** for assessing the allergenic potential of Newly Expressed Proteins (NEPs)
- **Evaluating agronomic and phenotypic endpoints:** includes, among others, information on biotic and abiotic stressors, and addresses aspects relevant for the environmental fate and behaviour of the GM plant (thus going beyond the sole characterisation of the GM plant)

Examples of **studies exempted from NoS** in a GMO application

- **Molecular characterisation, protein characterisation, compositional analysis**: corresponds to analytical measurements to assess the identity/composition of the GM plant and to determine its physico-chemical properties