Regulation (EU) No 503/2013
90-day studies on GM food/feed: technical aspects

GMO ad hoc meeting with industry representatives, 13 June 2019

efsa
European Food Safety Authority

Outline

- Technical aspects – test material
- Procedural aspects – OECD TG 408 (2018)

Outline

- Technical aspects – test material
- Procedural aspects – OECD TG 408 (2018)

- What
- Source
- Characterisation
- Incorporation rate, maize

Test material

Test material: WHAT

- **TEST MATERIAL**
  - the whole GM food/feed, i.e. a complex matrix from the GMP, composed of many individual substances
  - treated with the intended herbicide(s) in case of HT GM

- **TEST DIET = formulated test material**

  a balanced diet incorporating the test material as an ingredient

- **CONTROL MATERIAL/DIET**

  same considerations as above

Regulation (EU) No 503/2013
EFSA Scientific Committee, 2011
EFSA, 2014

Test material: WHAT

- **Herbicide-tolerant crops**
  (EFSA to Europabio, 10/4/2019)

  - The material treated with the intended herbicide(s) and the conventionally-treated material should be evaluated to capture all possible unintended effects linked to the genetic modification.

    EFSA Panel on Genetically Modified Organisms (GMO). 2011a Scientific opinion on Guidance for risk assessment of food and feed from genetically modified plants.
    EFSA GMO Panel, 2011b. Guidance document on Selection of Comparators for the Risk Assessment of GM Plants.

  - However, in the context of 90-day studies, EFSA considers that to minimize the number of used animals it is sufficient to test feed from GM material treated with the IH(s) since this is considered the most representative consumption material

  → *The genetically modified food and feed analysed should be relevant to the product to be consumed"*

    Reg.(EU) 503/2013, Annex II, II, 1.4.4.1

Test material

Test material: SOURCE

- **Requisite (EFSA, 2014):**

  The test material used in the 90-day feeding study should be a representative sample of the field trials material supporting the comparative assessment.

  Feasibility: storage, stability and yield aspects

- **Situation**

  The test material derives from *ad hoc* studies; no justification provided.

- **Question to Europabio**

  Can Europabio expand on feasibility aspects?

Test material: SOURCE

- *Ad hoc* studies

  - Production plan of the GM and of the control lines
  - Information on herbicide treatments (IH and conventional)
  - Information on the selected control material and the tested GM line (breeding tree)

Test material

Test material: CHARACTERISATION

- Based on GLP requisites

OECD SERIES ON PRINCIPLES OF GOOD LABORATORY PRACTICE AND COMPLIANCE MONITORING
Number 1
OECD Principles on Good Laboratory Practice (as revised in 1997)

OECD SERIES ON PRINCIPLES OF GOOD LABORATORY PRACTICE AND COMPLIANCE MONITORING
Number 19
Advisory Document of the Working Group on Good Laboratory Practice on the Management, Characterisation and Use of Test Items (2018)

Test material: CHARACTERISATION

TEST MATERIAL

- **Identity**
  - Unique identifier
  - DNA/New protein(s)
- **Batch number**
- **Purity**
  - No other GM events
- **Composition**
  - Constituents (supporting diet preparation)
  - Pesticides
  - Other contaminants
- **Stability** in the case of multiple batches used
  - DNA/New protein(s)
- **Integrity**

Test material: CHARACTERISATION

TEST DIET

- **Identity**
  - DNA/New protein
- **Batch number**
- **Purity**
  - No other GM events
- **Composition**
  - Ingredient
  - Constituents
  - Pesticides
  - Other contaminants
- **Homogeneity, concentration, stability** of the test material in the diet

CONTAMINATION

- Presence of **intended herbicides (and metabolites)** and of **other GMPs** in the diet should be investigated and discussed.

EFSA (European Food Safety Authority), 2015.
Scientific Report: Review of results published by Mesnage et al. (2015) in PLoS ONE and the laboratory findings communicated by Dr Samsel to Farm Wars. EFSA Journal 2015;13(10):4258, 12 pp.
doi:10.2903/j.efsa.2015.4258

Homogeneity and concentration

It may not always be technically possible to generate information on homogeneity and concentration for a test item administrated or formulated, and the lack of such data and its impact on the validity of a study should be justified (OECD, 2018)

The FFWG of the GMO Panel acknowledges that the analytical determination of homogeneity and concentration of complex test materials such as GM plants materials into formulated diets could be technically challenging if no practical methods are available.

The application of proper diet preparation procedures and regular evaluations of the mixing methods can be useful to confirm the homogeneity and concentration of the test material "whole food/feed" in the diet.

The applicant should **duly document** the diet preparation procedures in place in the facilities, in which the test material is added into diets, and justify that these guarantee diet homogeneity and the proper concentration of the respective test or control items.

Webnotes FFWG May 2019

Stability

The test facility should be provided with information on the stability of the test item under storage and test conditions, or the test facility should determine such information. The stability of the test item can only be assured if the material is handled and stored appropriately and is used before expiration. (OECD 2018)

The FFWG of the GMO Panel considers that information on the expiration dates of the constituents of the formulated diets, as declared by the diet manufacturer, can be regarded as sufficient to prove their stability, provided that this information is duly documented.

Identification of the event and/or of the newly expressed proteins in the test material and formulated diets after the conclusion of the in-life phase of the toxicological studies should be conducted to further corroborate their stability.

Webnotes FFWG May 2019

GLP

If the test item is supplied prepared as a mixture, as a formulation or in a vehicle, and the data on homogeneity, concentration and stability is not generated in a GLP test facility, the impact on the validity of the study and the integrity of the test item should be assessed. (OECD 2018)

The FFWG of the GMO Panel considers that, if the diets are prepared and analysed in non-GLP facilities, the application of standardised procedures and quality measures can be considered adequate and not to impacting on the outcome of the studies, provided that these are **duly documented**.

Webnotes FFWG May 2019

Integrity of the test material

Harvesting

- Date
- Storage conditions till the next phase
- Transportation conditions

Processing

- Date
- Storage conditions till the next phase
- Transportation conditions

Incorporation in the diet

- Date
- Storage conditions till the next phase
- Transportation conditions

Administration

- Storage conditions

duly documented !

Maize

incorporation

rate

Maize incorporation rate

- Steinberg et al, 2019 reported in a recent study that a diet incorporating 50% maize did not lead to a nutritional imbalance in rats after a 90-day feeding period.

Steinberg et al. 2019. Lack of adverse effects in subchronic and chronic toxicity/ carcinogenicity studies on the glyphosate-resistant genetically modified maize NK603 in Wistar Han RCC rats. Archives of Toxicology https://doi.org/10.1007/s00204-019-02400-1

- Further confirmation is needed before this 50% maize incorporation rate is generally applicable.
- **The 50% inclusion rate should be considered when planning new 90-day feeding studies with maize.**

Webnotes FFWG May 2019

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EFSA to Europabio 22/11/18 & 10/4/2019

Ad hoc meeting with all industry representatives (**24-25 October 2018**):

- need to comply with the most up-to-date internationally agreed guidelines
- the date of initiation of a study is the driver for defining the applicable guidelines.

- **90-day studies with a date of initiation before 25 October 2018 will be assessed against OECD TG408 1998**
- **90-day studies with a date of initiation after 25 October 2018 will be assessed against the OECD TG408 2018**
- Studies performed before 25 October 2018, with single events as part of a stack application currently under assessment will not be subject to new standards and guidelines if 're-submitted' in an upcoming stack application.

EFSA to Europabio 22/11/18 & 10/4/2019

- Such an approach is fully in line with EFSA's procedural principle regarding the implementation of its guidelines and guidelines internationally agreed. New guidelines are not implemented in a retroactive manner, and never applied to existing studies/information.

- As clarified at our ad hoc meeting with industry representatives in 2017, new guidelines are only applied to dossiers reaching EFSA after their publication, or in the case where, for ongoing applications, new data/studies should be generated.


Thank you!
Questions?

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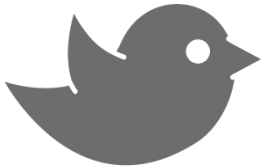

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