Policy Brief: Animal Feeding Studies for GMO Risk Assessment

Lessons from two large EU research projects

Genetically modified (GM) crops have aroused controversy in Europe and among contentious points is the conflicting evidence for possible effects on safety in animal testing studies. Between June 2012 and April 2018 the GRACE[1] and G-TwYST[2] projects, both funded by the European Commission, conducted research on the scientific value, design, procedures, analysis, and interpretation of animal feeding studies for the risk assessment of genetically modified food and feed. In the course of these projects several short- and long-term animal feeding studies were conducted with GM maize MON810, resistant to European corn borer and grown in Spain, and NK603 with tolerance to the herbicide glyphosate and grown in Canada. Given the controversial nature of this topic a particular emphasis was put on stakeholder engagement and transparency when planning and interpreting the animal feeding studies.

Regulatory context

The outcome of the GRACE project was intended to provide input to the review by the European Commission of the Implementing Regulation 503/2013 provision for a mandatory performance of 90-day animal feeding trials in rodents as part of the authorisation of GM food and feed (European Commission, 2013). According to this Regulation a 2-year carcinogenicity study with rats may also be requested by the European Food Safety Authority (EFSA) depending on the outcome of the 90-day animal feeding trials on a case-by-case basis. EFSA has been requested to assist the European Commission to provide supplementary guidance on key elements to consider for a 2-year carcinogenicity trial in rats with whole food/feed. G-TwYST was initiated in this context but also to address concerns about possible health impacts of GM maize, including those raised by a study on "Long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize" (Seralini et al., 2012/2014; EFSA, 2012).

Main conclusions

1. Neither the 90-day nor the long-term animal studies revealed any health risks of the GM maize tested. These findings support the conclusions based on previous steps of the risk assessment comprising the initial molecular characterisation of the genetic modification as well as the phenotypic, agronomic, and compositional analyses of the GM line in relation to its conventional counterpart and other non-GM lines.

2. In contrast to a study conducted earlier (Seralini et al., 2012/2014), the 2-year carcinogenicity animal feeding study performed by G-TwYST did not reveal any potential health risk associated with GM maize NK603.

3. In the absence of concerns identified during the GMO risk assessment procedures, we conclude that it is not possible to propose a science-based hypothesis for tailoring the design of the animal feeding studies. In contrast to the provision of the Implementing Regulation, GRACE and G-TwYST have demonstrated that the added scientific value of animal feeding studies without a targeted hypothesis is very limited and does not significantly reduce remaining uncertainties. Therefore, we do not see the need to continue with the mandatory requirement to conduct untargeted animal feeding studies for each novel GM plant. In the eventuality that there is a particular concern identified during the risk assessment procedures, a 90-day or extended animal feeding study might be justified. What constitutes a relevant concern would have to be decided on a case-by-case basis in the GMO risk assessment.

4. Such an approach would also be more compatible with the principles of Replacement, Reduction and Refinement (3R) of animal feeding trials, which is a legal requirement (European Commission, 2010). These principles carry the responsibility to ensure that any objective to perform an animal feeding trial with whole food/feed should be carefully evaluated, given the high number of animals needed for testing.

5. In the case that animal feeding trials are considered to be necessary, criteria to evaluate the scientific quality of 90-day and extended feeding trials with whole food/feed derived from GM plants have been proposed (Schmidt et al., 2016). These criteria should be taken into account when evaluating a rodent feeding trial in the course of a pre-market approval procedure for GMOs. Including an animal feeding study in a risk assessment that does not (fully) comply with the proposed quality criteria should be decided on a case-by-case basis. If rodent feeding studies on whole food/feed derived from GM plants are to be performed in the course of research projects not related to a pre-market approval procedure these should also comply with the proposed quality criteria.

6. The research also provided valuable insight on methodological innovations. *Omics* analyses of the GM plant material may help in the future to decide whether an animal feeding trial is scientifically justified and to develop a targeted hypothesis for the particular study.

For more information on the study plans, conclusions and recommendations from the 3 projects see:

- Conclusions and recommendations from the GRACE project
- Conclusions and recommendations from the G-TwYST project

References

EFSA (2012) Final review of the Séralini et al. (2012a) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA J. 10: 2986.

European Commision (2010). Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. Official Journal of the European Union, L 276/33-70, 20 October 2010.

European Commission (2013). COMMISSION IMPLEMENTING REGULATION (EU) No 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006.

Séralini GE et al.: first published in Food Chem. Toxicol. 50: 4221-4231, 2012; retracted in Food Chem. Toxicol. 63: 244, 2014; republished in Environ. Sci. Eur. 26: 14, 2014.

Schmidt K et al. (2016). Proposed criteria for the evaluation of the scientific quality of rat and mouse feeding trials with whole food/feed derived from genetically modified plants. Archives of Toxicology September 2016, Volume 90, Issue 9, pp 2287–2291.

Acknowledgement

GRACE and G-TwYST received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 311957 and no 632165 respectively.

1) GRACE is the acronym for GMO Risk Assessment and Communication of Evidence. This 3.5-year project conducted four 90-day subchronic toxicity and one 1-year chronic toxicity studies on rats fed with a diet containing GM maize MON810.

2) G-TwYST is the acronym for Genetically modified plants Two Year Safety Testing. This 4-year EU funded project conducted two 90-day studies and a combined chronic toxicity (1 year) and carcinogenicity (2 years) study on rats fed with a diet containing GM maize NK603: www.g-twyst.eu