



Annual Report of preparatory work on the toxicological studies and animal feeding studies performed under the EFSA contract OC/EFSA/GMO/2014/01, Lot 2 during the period 1/3/2017 to 27/11/2018

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Annual Report of preparatory work on the toxicological studies and animal feeding studies performed under the EFSA contract OC/EFSA/GMO/2014/01, Lot 2 during the period 1/3/2017 to 27/11/2018

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Abstract

This report describes the tasks performed in the period 1/3/2017 to 27/11/2018 under the EFSA contract OC/EFSA/GMO/2014/01, Lot 2 on toxicological studies and animal feeding studies included in applications for market authorisation of genetically modified feed/plants under Regulation (EC) No 1829/2003. The tasks cover the check for study adherence to relevant EFSA guidance documents and to OECD Test Guideline no 407 (1995/2008), OECD Test Guideline no 408 (1998) and OECD Principles on Good Laboratory Practice. During the period covered by this report, preparatory work has been performed on six applications for GM plants submitted under Regulation (EC) No 1829/2003 for a total of three 28-day studies on newly expressed proteins and six 90-day studies in rodents on GM food/feed, using comprehensive checklist templates.

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Key words: OC/EFSA/GMO/2014/01 Lot 2, GMO-toxicity, compliance

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Summary

This annual report provides a summary of the work performed by the National Food Institute at DTU (here defined as Contractor) in the context of the Framework Contract No OC/EFSA/GMO/2014/01 - Lot 2, signed on 28/11/2013 (here defined as Framework Contract) for the period March 1, 2017 – November 27, 2018.

In the context of the Framework Contract, the Contractor provided preparatory work on toxicological studies and animal feeding studies in the context of applications on genetically modified (GM) plants, in accordance with the deliverables defined in Lot 2 tasks.

Based on comprehensive checklists developed by the Contractor in collaboration with the EFSA GMO Unit, the Contractor has reviewed the adherence to respective relevant guidelines of studies related to six applications for GM plants submitted under Regulation (EC) No 1829/2003, and provided a complete overview of each study covering abstract, summary, statistics, reports of compliance and deviations to the respective relevant guidelines. This preparatory work was performed on three 28-day studies on newly expressed proteins and six 90-day studies in rodents on GM food/feed. The aim of this work was to contribute to support the evaluation of GM plants submitted under Regulation (EC) No 1829/2003 by the Panel on Genetically Modified Organisms (GMO).

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

The Implementing Regulation (EU) No 503/2013 specifies risk assessment requirements for applications for market authorisation of genetically modified (GM) plants and derived products. It also provides indications on the methodological approach to follow for the comparative (compositional, agronomic and phenotypic) assessment and for toxicological studies¹.

With respect to the comparative assessment of GM plants and derived products, minimum requirements include the experimental design of field trials in order to ensure sufficient statistical power and reliable estimation of natural variability and the statistical analysis of the field trials carried out with the GM plant, the conventional counterpart and a set of non-GM reference varieties. The use of statistical mixed models and recommendations for the analysis of compositional, agronomic and phenotypic data from those field trials are further described in the Scientific Opinions on statistical consideration for risk assessment of GMOs and the Guidance for risk assessment of food and feed from genetically modified plants.

With regard to toxicological studies, general requirements are described in the Implementing Regulation (EU) No 503/2013, with reference to relevant regulations and guidelines for technical details, including Directive 2004/10/EC², OECD Principles of GLP³, Regulation (EC) No 440/2008⁴, the EFSA Scientific Committee Guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed.

A call for a framework contract for the preparatory support for the statistical evaluation of the comparative assessment of GM plant field trials (LOT 1) and for the evaluation of toxicological studies for GM plant food/feed safety (LOT 2) has accordingly been launched by EFSA.

The purpose for Lot 2 of the contract OC/EFSA/GMO/2014/01 is to provide preparatory support to the EFSA GMO Panel evaluation of the adherence of toxicological studies and animal feeding studies, performed for the safety assessment of GM plants, to the appropriate EFSA guidance documents and standardised guidelines, and to the Implementing Regulation (EU) No 503/2013. The task does not include the adherence to other guidelines to which the applicant may have referred to in the study reports.

The contract was awarded by EFSA to National Food Institute, Technical University of Denmark (DTU).

Contract title: Preparatory support for the statistical evaluation of the comparative assessment of GM plant field trials and for the evaluation of toxicological studies for GM plant food/feed safety, LOT2: Toxicological studies and animal feeding studies.

Contract number: OC/EFSA/GMO/2014/01

¹ 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.

² EC, 2004. Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances. Official Journal of the European Union, L50, 44-59.

³ OECD, 1998. Principles of Good Laboratory Practice (GLP) and Compliance Monitoring. <http://www.oecd.org/document>

⁴ COUNCIL REGULATION (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

2. Data and Methodologies

2.1. Data for Lot 2 – toxicological studies and animal feeding studies

In accordance with the purpose of Lot 2 of the Contract, data submitted to the Contractor included 28-day repeated oral toxicity studies in rodents on newly expressed proteins and 90-day feeding studies in rodents on whole food/feed.

2.2. Methodologies

In accordance with the scope of this contract, the Contractor was requested to check that toxicological studies and animal feeding studies provided in GMO applications submitted under Regulation (EC) No 1829/2003 fulfilled requirements of EFSA GMO Panel Guidance (EFSA, 2011a), and the EFSA Scientific Committee Guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed (EFSA, 2011b) and in Regulation (EU) No 503/2013. The check included verification that technical requirements by other relevant regulations and guidelines (including Directive 2004/10/EC⁵, OECD Principles of GLP⁶, Regulation (EC) 440/2008⁷) are fulfilled.

Specifically the Contractor provided for each study submitted by EFSA:

1. detailed description of the adherence of the toxicological studies to the appropriate guidelines;
2. identification of potential lack of adherence to the appropriate guideline documents in the toxicological studies that can result in questions to complement their assessment;
3. a summary report and a power point presentation highlighting the main issues in terms of design of the study and adherence to relevant guidelines and legislation; this covered abstract, summary, statistics, reports of compliance and deviations to the respective relevant guidelines.

A kick-off meeting with EFSA representatives (Procurement team and the scientific officers acting as contact persons for the contract) took place in Parma at the 19 February 2015. Templates for the compliance checklist of 28-day toxicity studies on newly expressed proteins and of 90-day toxicity studies in rodents on whole food/feed towards the relevant EFSA guidance documents and OECD Technical guidance documents were developed. These templates supported the check for adherence of 90-day studies on GM food/feed in rodents to the recommendations given by EFSA guidance documents (EFSA, GMO Panel 2011; EFSA Scientific Committee, 2011, EFSA, 2014); to OECD TG 408 (1998); to GLP (OECD, 1998, EC, 2004), incorporated into Implementing Regulation (EU) No 503/2013.

⁵ EC, 2004. Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances. Official Journal of the European Union, L50, 44-59.

⁶ OECD, 1998. Principles of Good Laboratory Practice (GLP) and Compliance Monitoring. <http://www.oecd.org/document>

⁷ COUNCIL REGULATION (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

3. Assessment/results

Using the agreed checklists, in the period covered by this report (1/3/2017-27/11/2018) the Contractor finalised the assessment of the adherence to relevant guidelines of four 28-day studies and 12 90-day studies included in six GMO applications submitted to EFSA under Regulation No 1829/2003 (Table 1).

Table 1: EFSA contract OC/EFSA/GMO/2014/01, Lot 2. Studies evaluated by the Contractor during the period 01/03/17 to 27/11/2018/02/17

Application no	EFSA-Q-no	Study type	Submission date ^a
AP109	EFSA-Q-2012-00617	28-day	August 30, 2017
AP121	EFSA-Q-2014-00719	90-day	March 2017
AP133	EFSA-Q-2016-00583	90-day	January/February 2017
AP135	EFSA-Q-2016-00688	90-day	January/February 2017
		90-day	July 11, 2018
		90-day	
AP136	EFSA-Q-2016-00707	90-day	March 1, 2017
AP137	EFSA-Q-2016-00775	90-day	March 1, 2017
AP138	EFSA-Q-2016-00857	90-day	March 1, 2017
AP140	EFSA-Q-2017-00263	28-day	September 26, 2018
		90-day	February 7, 2018
AP142	EFSA-Q-2017-00398	28-day	May 4, 2018
		90-day	
AP143	EFSA-Q-2017-00424	90-day	May 4, 2018
AP145	EFSA-Q-2017-00487	90-day	May 4, 2018
RX-002	EFSA-Q-2016-0047	28-day	October 30, 2018

a. Date of submission of the studies by EFSA to the Contractor.

4. Conclusions

Based on comprehensive checklists developed by the Contractor in collaboration with the EFSA GMO Unit, in the period covered by this report (1/3/2017-27/11/2018) the Contractor has reviewed the adherence to the respective relevant guidelines of studies related to 14 applications for GM plants submitted under Regulation (EC) No 1829/2003, and provided a complete overview of each study covering abstract, summary, statistics, reports of compliance and deviations to the respective relevant guidelines. This preparatory work was performed on four 28-day studies on newly expressed proteins and 12 90-day studies in rodents on GM food/feed.

References

- 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
- DIRECTIVE 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances.
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- OECD Principles of Good Laboratory Practice (as revised in 1997) Environment Directorate Organisation for Economic Co-operation and Development Paris 1998
- OECD guidelines for the testing of chemicals 407 (1995) - Repeated Dose 28-Day Oral Toxicity Study in Rodents
- OECD guidelines for the testing of chemicals 407 (2008) - Repeated Dose 28-Day Oral Toxicity Study in Rodents
- OECD guideline for the testing of chemicals 408 (1998) - Repeated Dose 90-day Oral Toxicity Study in Rodents