

## **Statement of the Scientific Panel on Genetically Modified Organisms on an evaluation of the 13-week rat feeding study on MON 863 maize, submitted by the German authorities to the European Commission**

**adopted on 20 October 2004**

### **STATEMENT**

At the request of the European Commission the Scientific Panel on Genetically Modified Organisms (GMO Panel) of the European Food Safety Authority (EFSA) has reviewed an evaluation report concerning GM maize MON 863 that was recently submitted by Germany. The GMO Panel has given careful consideration to the arguments set out in the report. Following its investigation of the report, and of the retrospective evaluation of renal tissues and data derived from the 13-week rat feeding study performed by independent peer reviewers, the GMO Panel concludes that there is no evidence presented in the report that changes the conclusions already reached by the GMO Panel earlier this year in its Opinions on the safety of the insect-protected genetically modified maize MON 863 (EFSA 2004a, b). These opinions state that the results of the rodent toxicity study with MON 863 maize did not indicate concerns about its safety for human and animal consumption.

An assessment of the report distributed by Germany is provided in annex.

### **BACKGROUND**

On 2 April 2004 the Scientific Panel on Genetically Modified Organisms adopted two opinions on genetically modified maize MON 863 (EFSA 2004a, b), following receipt of two questions from the Commission related to applications for the placing of the maize on the market by Monsanto under the Novel Food Regulation (EC) No 258/97 (EC, 1997) and the Directive 2001/18/EC on the deliberate release of genetically modified organisms (GMOs) into the environment (EC, 2001). The questions followed two separate scientific assessments which were initially made by the competent authorities of Germany and subsequently evaluated by all other Member States.

The GMO Panel concluded that 'the placing on the market of MON 863 maize is unlikely to have an adverse effect on human and animal health or the environment in the context of its proposed use'.

On 17 September 2004, the European Commission received from the German authorities an evaluation report on the 13-week rat feeding study on MON 863 maize to which reference was made during the meeting of the Regulatory Committee established under Directive 2001/18/EC on 20 September 2004. At that meeting it was decided to postpone the opinion of the Regulatory Committee on a draft Commission Decision

concerning the placing on the market of MON 863 maize as to allow time for clarification on the information that was circulated by Germany.

The Commission has sought scientific advice from EFSA as to whether this evaluation might have any impact on the former Opinions issued by the GMO Panel on this GM maize and in particular on the interpretation of the results of the 13-week sub-chronic toxicity study with rats.

## DOCUMENTATION PROVIDED TO EFSA

1. Evaluation of and Final Report on the summary report of the "13-Week Dietary Subchronic Comparison Study with MON 863 in Rats Preceded by a 1-Week Baseline Food Consumption Determination with PMI Certified Diet #5002 (Report MSL-18175/Covance Study No. 6103-293)"; Arpad Pusztai, 15 September 2004.
2. Retrospective Evaluation of Renal Tissues and data from Monsanto Co. Study CV – 2000 – 260 (MSL 18175): a 13 week Rat Feeding Study with MON 863 Corn, Pathology Peer Review, 003-RS-04; Hard, G.C. and Terron, A. (Covance Laboratories Study No 6103-293), 11 August 2004.
3. Supplemental Analysis of Selected Findings on the Rat 90-day Feeding Study with MON 863 Maize, Report MSL – 18175; Hammond, B.G. and Ward, D.P., Monsanto Co., USA, 24 May 2004.

## REFERENCES

- EC, 1997. Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients. Official Journal of the European Communities L43, 1-7.  
[http://europa.eu.int/smartapi/cgi/sga\\_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=31997R0258&model=guichett](http://europa.eu.int/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=31997R0258&model=guichett)
- EC, 2001. Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. Official Journal of the European Communities, L106, 1-39.  
[http://europa.eu.int/eur-lex/pri/en/oj/dat/2001/l\\_106/l\\_10620010417en00010038.pdf](http://europa.eu.int/eur-lex/pri/en/oj/dat/2001/l_106/l_10620010417en00010038.pdf)
- EFSA, 2004a. Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the Notification (Reference C/DE/02/9) for the placing on the market of insect-protected genetically modified maize MON 863 and MON 863 x MON 810, for import and processing, under Part C of Directive 2001/18/EC from Monsanto, The EFSA Journal (2004) 49, 1-25.  
[http://www.efsa.eu.int/science/gmo/gmo\\_opinions/381/opinion\\_gmo\\_06\\_en1.pdf](http://www.efsa.eu.int/science/gmo/gmo_opinions/381/opinion_gmo_06_en1.pdf)
- EFSA, 2004b. Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safety of foods and food ingredients derived from insect-protected genetically modified maize MON 863 and MON 863 x MON 810, for which a request for placing on the market was submitted under

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Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto, The EFSA Journal (2004) 50, 1-25.

[http://www.efsa.eu.int/science/gmo/gmo\\_opinions/383/opinion\\_gmo\\_07\\_en1.pdf](http://www.efsa.eu.int/science/gmo/gmo_opinions/383/opinion_gmo_07_en1.pdf)

EFSA, 2004c. Guidance document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed. The EFSA Journal, 99, 1-94.

[http:// www.efsa.eu.int/science/gmo/gmo\\_guidance/660\\_en.html](http://www.efsa.eu.int/science/gmo/gmo_guidance/660_en.html)

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## ANNEX

1. The safety testing strategy for GM food/feed or derived components is described in detail in the recently published Guidance document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed (EFSA, 2004c). The risk assessment strategy for GMOs is based on the comparison of the GMO and derived products with their non-GM counterparts. The underlying assumption of this comparative assessment approach for GMOs is that traditionally-cultivated crops have gained a history of safe use for the normal consumer or animals as food or feed products. This comparison is the *starting point* of the safety assessment which then focuses on the environmental or food/feed safety and nutritional impact of any intended or unintended differences identified.
2. The animal feeding trials with MON 863 maize kernels have been carried out in accordance with the GLP guidelines as developed by OECD. Formulation of diets containing test, control and reference material was carried out according to standardised protocols, on the basis of a certified commercially available rodent test diet, which was adjusted in order to balance nutritional requirements. Besides the GM maize and the parent control line, six commercial maize lines were tested as reference.
3. In animal toxicity studies of GM food/feed or derived products, test animals are usually fed with commercial diets supplemented with the GM test material, while control animals receive diets supplemented with control material, which should be non-GM, preferably isogenic material. Clinical, biochemical and (histo)pathological analysis should focus on the potential of the test component to induce adverse changes in biological parameters. Evaluation of observed changes includes amongst others (i) type, severity, incidence and spontaneous occurrence, (ii) whether changes are treatment related, and (iii) appreciation of normally expected biological ranges in parameter values. In case *statistically* relevant changes have been identified in biological parameters, their natural variations must be taken into account in order to assess the *biological* relevance. To this end the use of animals of the same strain and age, fed with diets containing other commercial maize varieties, is most relevant.
4. The suggestion made in the evaluation report to supplement the 11% test diet with maize from the parent line instead of material from the commercial maize line would lead to a 'dilution' of potential differences between the test and control line, and is therefore not recommended. The suggestion to add a 'spiked' control group, containing material from the parental line supplemented with the transgenic product isolated from the GM maize is worthwhile in case there are indications of the occurrence of unintended effects with the GM food/feed derived product. This is however not the case with MON 863 maize. The Panel would not recommend the use of spiked control groups on a routine basis.
5. Common food consumption and growth features of the animals fed with the various test diets were observed which reflect normal biological variations with a few outliers in each test group. The Panel did not find any indication of poor animal management, as suggested in the evaluation report.

6. The Panel has paid particular attention, as detailed in its Opinion, to the relevance of the statistically significant differences observed in some clinical parameters and individual kidney weights of test and control animals. Whilst some statistically significant differences were observed, these differences were not considered as biologically relevant since they fall within normal variation ranges. Since no differences in white blood cell or lymphocyte counts were observed, nor changes in spleen weights and appearance, or enlarged lymph nodes, the Panel does not consider it meaningful to further investigate the immune responsiveness of the animals as suggested in the evaluation report.
7. The Panel has noted some differences in the pathology data derived from a microscopy examination of kidneys from test and control animals. In male animals of the test group a higher incidence in focal chronic inflammation and tubular regeneration was observed compared to the incidences in control animals and in female test animals a lower incidence in tubule mineralization. These changes were considered by the Panel as spontaneous lesions or incidental findings and not treatment related.
8. In addition, at the request of the applicant, the kidney tissues were re-evaluated by two independent consulting veterinary pathologists, who conducted a blind study using masked slides. All anatomic regions of all kidneys were scanned at appropriate magnifications to ensure that no renal lesions were excluded. The lesions observed by the original study pathologist were considered by the review pathologists to represent components of the chronic progressive nephropathy syndrome, a spontaneous kidney disease occurring in most rat strains. All microscopic changes were of minimal or mild severity and not considered as treatment related.