GREENPEACE

Regulatory systems for GE crops a failure: the case of MON863.

March 2007

New peer-reviewed evaluation[i] of Monsanto's data shows MON863 should not have been approved in EU or elsewhere

MON863 is a genetically engineered (GE) insect resistant maize (corn) that expresses a Bt-toxin (Cry3Bb1). This toxin, which stems from a micro-organism (*Bacillus thuringiensis*), is meant to protect the maize against the corn rootworm pest. This GE maize is different from other GE maize plants (Mon 810, Bt11, Bt 176) already placed on the market, as they produce another toxin (Cry1Ab), which is toxic to the European corn borer. Further, GE maize MON863 contains an antibiotic resistance marker gene (ntpII conferring resistance to kanamycin).

Greenpeace and others have previously stated several times (see Chronology of MON863) that the data submitted in support of market approval for this GE maize gives rise to serious concerns regarding the food safety of MON863. However, significant findings found in a 90 day rat feeding study are generally dismissed by the regulatory authorities, e.g. by the European Food Safety Authority (EFSA)[ii], as *"not considered as biologically relevant"*, or *"incidental findings".*

This new evaluation is the first independent evaluation of data submitted by a biotech company for regulatory approval of a GMO for food/feed published in a peer-reviewed scientific journal. The new evaluation shows that, far from being not of biologically relevance, the statistical differences found should be grounds for a recall of the GE crop. This GE maize should not have been approved, for cultivation or food/feed, in the EU or anywhere else in the world.

New evaluation highlights MON863 poses risk to human and animal health

Scientists from CRIIGEN (Committee for Independent Research and Genetic Engineering, based at the University of Caen, France), have analysed the data obtained from a feeding trial submitted by Monsanto in support of its application to the EU to market MON863.

The independent scientists found that after the consumption of MON863:

- **There were *"signs of toxicity"* in the liver and kidney of the test animals**. Analysis of blood, urine, liver and kidneys showed signs of disruption to kidney/liver function. The researchers conclude that *"the two main organs of detoxification, liver and kidney, have been disturbed".*
- **Weight gain was different.** Rats showed slight but dose related significant variations in growth for both sexes, resulting in 3.3. % decrease in weight for males and 3.7 % increase for females.

1. Chemical data indicate disruption of liver/kidney function

Although some chemical differences did show up in the original Monsanto data, the European Food safety Authority (EFSA) stated "*Whilst some statistically significant differences were observed, these differences were not considered as biologically relevant since they fall within normal variation ranges.*"[iii] However, a closer examination of the data in this new study shows differences in blood and urine chemistry between rats fed MON863 and rats fed non GE maize (including blood sugar and fats, urine phosphorus and sodium) that were either discounted or not recognised. The authors of this new evaluation state: *"It appears that the statistical methods used by Monsanto were not detailed enough to see disruptions in biochemical parameters"*

The new evaluation suggests that these results are of biological relevance as they suggest disruption to liver/kidneys, which indicate that MON863 is causing toxicity in rats.

2. **Differences in weight gain between rats fed GE and non GE maize**

The authors analysed the weight gain growth curves - something that Monsanto failed to do, even with their published data[iv]. The authors proved there were significant differences in the weight gains, with differences between male and females. Together with the indications of liver/kidney function, the authors suggest that this could be due to *"endocrine disruption and/or hormonal metabolism differences"*. Although Monsanto did find some differences in weight gain, they simply discarded them by comparing to historical or population data, rather than the control (fed non GE maize), which is the normal and valid comparison. The cause of the differences in weight gain was never investigated by Monsanto. However, Seralini and colleagues (the authors of this new study) suggest that a further investigation into sexual hormones could explain some of the observations.

Cause of toxicity not known

It is not known whether the signs of toxicity are caused by the Bt protein, or from some changes in the plant's own DNA caused by the genetic engineering event.

MON863 cannot be considered safe for food/feed

The authors of this new evaluation have shown that there are serious concerns over the food and feed safety of MON863. These concerns have simply been dismissed where they should have been ground for the rejection of the GM crop. At the very least, the differences should have been investigated further.

The authors of this evaluation state ***"it cannot be concluded that GM corn MON863 is a safe product".*** This conclusion of the independent scientists is in stark contrast to those from regulatory authorities who have approved MON863 who deemed it is as safe as its non GE counterpart. In countries where MON863 is approved (Australia, Canada, China, the EU Japan, Korea, Mexico, Philippines, Taiwan, United States), the regulatory authorities have failed to recognise the warning signs in a GE crop. They have recommended a GE crop that has potential to cause adverse effects on health for approval.

Greenpeace demands an immediate and complete recall of MON863 from the global market. We also call upon governments to undertake an urgent reassessment of all other authorised GE products and a strict review of current testing methods.

---

[i] Séralini, G-E, Cellier, D. & Spiroux de Vendomois, J. 2007. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Archives of Environmental Contamination and Toxicology DOI: 10.1007/s00244-006-0149-5. Hepatorenal = of or pertaining to the liver and kidneys.

[ii] EFSA 2004. 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 Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto (Question No EFSA-Q-2003-121).Opinion adopted on 2 April 2004. The EFSA Journal 50: 1-25

[iii] 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. http://www.efsa.eu.int

[iv] Hammond, B., Lemen, J., Dudek, R., Ward, D., Jiang, C., Nemeth, M. & Burns, J. 2006. Results of a 90-day safety assurance study with rats fed grain from corn rootworm-protected corn. Food and Chemical Toxicology 44: 147-160.

The MON863 case - a chronicle of systematic deception

August 13, 2002: The Monsanto company submits to the German authorities an application to import genetically engineered MON863 maize into the EU. This submission contains a 90-day rat feeding study.

MON863 is a genetically modified corn that expresses a Bt-toxin. This toxin is a modified version of the delta endotoxin Cry3Bb1 which originates from the microorganism *Bacillus thuringiensis*. The genetic manipulation is aimed at protecting maize plants against a pest called corn rootworm (*Diabrotica* spp.).

MON863 differs from other Bt-corns already placed on the market (MON810, Bt11, Bt176), which produce a modified Cry1Ab toxin conferring resistance to a pest called European corn borer (*Ostrinia nubilalis*), in that it produces an artificial Cry3Bb1 toxin. In addition to the modified Cry3Bb1 toxin gene MON863 contains an antibiotic resistance marker gene.

Outside the EU MON863 is approved for cultivation in the USA and Canada, and for food and feed in Australia, China, Japan, Korea, Mexico, the Philippines and Taiwan.

Based on the results of the 90-day rat feeding study presented in the application the Monsanto company concludes: “Toxicological parameters evaluated were survival, clinical signs, body weight changes, food consumption, clinical pathology, organ weights, and macroscopic pathology. There were no test article related changes in any of the aforementioned toxicological parameters”.

In the conclusions of the rat feeding study provided by Monsanto one can find a disturbing fact, namely that the feeding study was performed by a third company (Covance Laboratories), but the statistical analysis of the data was made by Monsanto itself.

September 2002: Experts at the French Genetic Engineering Commission (CGB, Commission du GÃ©nie BiomolÃ©culaire) raise critical questions regarding the toxicological test data derived from the rat feeding study with MON863.

April 8, 2003: The German competent authorities publish their assessment of the MON863 application. In their report they state that the amino acid sequence of the Cry3B1 toxin produced by the MON863 maize has similarities to some other toxins. Most notably, the German authority found some “homologies to sequences from *Clostridium bifermentans*, *Caenorhabditis elegans*, *Vibrio cholerae* and *Bacillus popilliae.*” These homologies are of high relevance in respect to human and animal health. Despite the similarities to other toxins found the German authorities did not investigate the results from the 90-day rat feeding study in detail and therefore failed to find out if there might be some indices for mammalian

toxicity. Instead, the German authorities interpreted the similarities found “as being biologically irrelevant due to lack of indications of mammalian toxic activity.”

The 90 day rat feeding study which shows significant changes in the blood of the animals was mentioned in the German assessment report as follows: “From this extensive study, it can be deduced that even after long term oral exposure to MON863 maize kernels, no harmful effects are to be expected.” The German report does not mention any significant findings, but by and large repeats Monanto's conclusion that “… no substance-specific biologically relevant effects were seen in comparison to controls …".

June 2003: A narrow majority of the French CGB's expertsapproves the results of the MON863 tests.

November 10, 2003: The French group CRIIGEN (Committee for Independent Research and Genetic Engineering) appeals to the French Commission CADA (Commission of Access to administrative Documents) in order to obtain the reports of CGB referring to significant health effects in the rat feeding study.

The French authorities had declared the CGB reports as being confidential, but CRIIGEN wins the case and presents the reports to journalists (see below).

April 2, 2004: The European Food Safety Authority (EFSA) publishes its opinion on Monsanto's MON863 application.

In their conclusion the EFSA's experts state, “The results of the 90-day sub-chronic rodent studies do not indicate adverse effects from consumption of MON863 and MON810 and the Panel concludes that there are no concerns over their safety.”

In its opinion EFSA mentions the significant findings in the rat feeding study as follows: “Some differences were observed in haematological parameters, including total white blood cell, lymphocyte and basophil counts.” But EFSA plays down these findings with a very general statement, saying that “These differences are not considered to be biologically meaningful since they fall within the standard deviation of the reference control population.”

Moreover, EFSA plays down significant findings in kidney weights observed in the rat feeding study: “The overall conclusion is that no differences in relation to feeding in MON863 maize were observed on kidney weights, kidney weights relative to body weights and kidney weights relative to brain weight.”

Finally, EFSA discusses some microscopic pathological changes in kidneys. “However, a statistically significant lower incidence of mineralized kidney tubulus was noted for rats fed

33% MON863 maize compared to those fed the control maize during histopathology after termination. These findings are not considered to pose concerns over the safety of MON863 maize."

April 23, 2004: After CRIIGEN succeeded in accessing the report of CGB, the French newspaper *Le Monde* exposes the MON863 scandal. The newspaper covers the significant changes in the blood of rats, which were fed with MON863, and reveals that the CGB's experts had expressed safety concerns.

May 2004: Greenpeace requests the data from the rat feeding study with MON863 from the German authorities.

August 4, 2004: In a response to the German authorities Monsanto denies access to data, and only provides a short "Supplemental analysis of selected findings on the rat 90-day feeding study with MON863 maize".

August 2004: CRIIGEN asks the French Ministry of Agriculture for access to the original toxicological data from animal feeding trials done with MON863 maize, NK603 maize, Bt11 maize and GT73 oilseed rape.

January 20, 2005: The French Ministry of Agriculture confirms that the original data from the toxicological tests should be confidential.

March 21, 2005: The German authorities announce that the data from the rat feeding study shall be given to Greenpeace. Monsanto appeals against the decision of the German authorities and submits the case to the Cologne administrative court.

June 1, 2005: Bruce Hammond (a scientist at the Monsanto company) sends in a further evaluation of the rat feeding data to the "Food and Chemical Toxicology" scientific journal . The data are published in 2006. In his conclusion the author states, "The summary prepared by the GMO Panel of the European Food Safety Authority best captures the prevailing scientific conclusions regarding the findings from this study. EFSA concluded that the results of the 90-day rodent study do not indicate adverse effects from consumption of maize line MON863".

June 9, 2005: The Cologne administrative court decides that Monsanto has to give their rat feeding study data to Greenpeace.

June 20, 2005: The Muenster Higher administrative court (Germany) reaffirms that the data from the rat feeding study shall be given to Greenpeace. Greenpeace publishes the complete rat feeding study (more than 1000 pages) on the internet.

June 24, 2005: The Council of EU environment ministers votes on market authorisation for MON863 for animal feed. The majority of the ministers abstain or vote against the authorisation. As a qualified majority for either rejecting or approving the application fails to be reached, the final decision reverts to the European Commission.

September 15, 2005: An independent expert on biostatistics from the University of Hamburg makes a written statement to Greenpeace on the statistical design of Monsanto's rat feeding study. The expert states, “Significant differences were indeed found in the study, and afterwards were classified as irrelevant. (This is as if a marksman had shot at a wall and the rings of a target were drawn around where the shot had made a hole, and it was then maintained he had hit the target dead centre.)”

October 2005: A confidential study prepared on behalf of the Austrian government concludes that “A complete re-evaluation of the study would be indicated, but as the design and the methods are inadequate, a repetition of the study seems desirable.”

October 24, 2005: The Council of EU agriculture ministers vote on market authorisation for MON863 maize for food. As a qualified majority for either rejecting or approving the application fails to be reached, the final decision reverts to the European Commission .

Just before the meeting of the EU agriculture ministers experts from the French CRIIGEN group publish a report on the first findings from the evaluation of Monsanto's rat feeding study data. In this evaluation all data from Monsanto's rat feeding study were retyped and subjected to comprehensive statistical analysis. The report states that the “findings clearly indicate major failures of statistical analysis as performed by Monsanto.” CRIIGEN calls for a complete reassessment of all data from the rat feeding study.

January 13, 2006: Despite the concerns raised by EU member states, members of the EU parliament and 10,000 cyberactivists alerted by Greenpeace, the EU Commission authorises the placing on the market of foods and food ingredients derived from MON863 maize.

February 2006: Greenpeace (and other NGOs) meet with the GMO Panel of EFSA and present case studies on failures and shortcomings in risk assessment of EFSA..During the meeting the experts of EFSA reject the demand to reassess the MON863 data.

April 12, 2006: The European Commission announces that EFSA's standards should be improved. Statistical protocols and the assessment of long term effects are explicitly mentioned.

March 31, 2006: Based on the previous assessment of MON863 EFSA publishes further positive opinions on three genetically modified maize plants which were produced by the

combination of MON863 with other genetically modified maize lines - MON863 x MON810, MON863 x NK603, MON863 x MON810 x NK603). According to an analysis by Greenpeace the GE hybrid maize in animal feeding studies produced significant effects related to possible health impacts.

A summary of the application can be downloaded at
http://www.transgen.de/pdf/zulassung/Mais/MON863_Mon863xMON810_summary.pdf

http://www.greenpeace.de/fileadmin/gpd/user_upload/themen/gentechnik/Monsanto_Rattenfuetterungsstudie.pdf

http://www.agbios.com/dbase.php?action=ShowProd&data=MON863 /
http://www.cofepris.gob.mx/pyp/biotec/OMG.pdf

See footnote 2, page 27.

See footnote 2, page 23.

Assessment Report of the Robert Koch Institute in Accordance with Directive 2001/18/EC
http://www.transgen.de/pdf/zulassung/Mais/MON863_MON863xMON810_assessment.pdf

See page 10, footnote 6 above

See page 10, footnote 6 above

See page 13, footnote 6 above

See page 13, footnote 6 above

http://www.efsa.europa.eu/etc/medialib/efsa/science/gmo/gmo_opinions/381.Par.0001.File.dat/opinion_gmo_06_en1.pdf

See page 3, footnote 11 above

See page 14, footnote 11 above

See page 15, footnote 11 above

See page 15, footnote 11 above

L'expertise confidentielle sur un inquiÃ©tant maÃ¯s transgÃ©nique. Le Monde, April 23, 2004.

Hammond, B.G., Dudek, R. Lemen, J.K. & Nemeth, M.A. (2006), Results of a 90-day safety assurance study with rats fed grain from corn borer-protected corn. Food and Chemical Toxicology 44(7): 1092 - 1099.

http://www.greenpeace.de/themen/gentechnik/anbau_genpflanzen/artikel/monsantos_gen_mais_mon_863_studie_ueber_fuetterungsversuche_an_ratten/

http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/793&format=HTML&aged=0&language=EN&guiLanguage=en

Full information about the written statement is only given from Greenpeace upon request

Evaluation of the report on a Subchronic Toxicity Study with Mon863 Maize. Report for the Federal Ministry for Health and Women, 70420/0166-IB/B/12/2005. (Full information from Greenpeace only upon request.

http://europa.eu/rapid/pressReleasesAction.do?reference=PRES/05/258&language=en

http://www.greenpeace.de/fileadmin/gpd/user_upload/themen/gentechnik/MON_863_French_report_statistics.pdf

http://europa.eu.int/eur-lex/lex/LexUriServ/site/en/oj/2006/l_034/l_03420060207en00260028.pdf

http://www.efsa.europa.eu/de/stakeholder_stakeholder/technical_meetings.html

http://europa.eu/rapid/pressReleasesAction.do?reference=IP/06/498&format=HTML&aged=1&language=EN&guiLanguage=en

http://www.efsa.europa.eu/etc/medialib/efsa/science/gmo/gm_ff_applications/more_info/505.Par.0009.File.dat/gmo_ov_op3_en1.pdf /
http://www.efsa.europa.eu/etc/medialib/efsa/science/gmo/gm_ff_applications/more_info/703.Par.0009.File.dat/gmo_ov_op6_en1.pdf /
http://www.efsa.europa.eu/etc/medialib/efsa/science/gmo/gm_ff_applications/more_info/720.Par.0010.File.dat/gmo_ov_op7_en1.pdf

http://www.greenpeace.de/fileadmin/gpd/user_upload/themen/gentechnik/greenpeace_mon863_mon810_hybrid_03.pdf

6