EFSA misleads the European Commission and the public over GMOs

Werner Mueller, eco-risk.at, Vienna

May 2008

Summary

In a letter to DG Sanco of the European Commission, dated on 19 July 2007, EFSA made a seriously misleading statement. EFSA claimed that: „a large number of experimental studies with livestock have shown that recombinant DNA fragments or proteins derived from GM plants have not been detected in tissues, fluids or edible products of farm animals“ and “to date no recombinant DNA sequences have been found in any organ or tissue sample from animals fed GM plants”. However, scientific studies from Mazza et al. (2005) and Sharma et al. (2006) show that transgenic sequences have in fact been detected in animal tissues. Even though both studies are easily accessible from public scientific databases and even the European Commission was aware of them, neither study was cited by EFSA. Confronted with these two articles, EFSA reaffirmed its initial misleading statement which, given its inaccuracies, cannot be treated as scientific advice.

This incident raises serious implications over the reliability of EFSA’s scientific advice and calls into question the validity of the GMO approvals granted by the European Commission on the basis of EFSA’s advice.

EFSA provides incorrect scientific information

The European Commission (EC) asked EFSA whether transgenes and their products are incorporated into animal tissue. EFSA conducted a literature review which involved the 20 members of the GMO panel, along with three experts who were invited to contribute. In July 2007, EFSA submitted a letter to the EC (EFSA (2007a) – view Annex 1.) and a scientific statement (EFSA (2007b)). In both the letter and the statement, EFSA concluded that „a large number of experimental studies with livestock have shown that recombinant DNA fragments or proteins derived from GM plants have not been detected in tissues, fluids or edible products of farm animals“.
Based on a literature survey EFSA concluded “To date no recombinant DNA sequences have been found in any organ or tissue sample from animals fed GM plants” (EFSA (2007b) page1)

This statement was in direct contrast to scientific findings from two research groups published in 2005 and 2006. Mazza et al. (2005) detected fragments of the cry1A(b) genes in the blood, liver, spleen, kidney and muscle of pigs fed with GM maize (see Fig. 1 (= Figure 3 in Mazza et al. (2005) below – taken from the original publication).

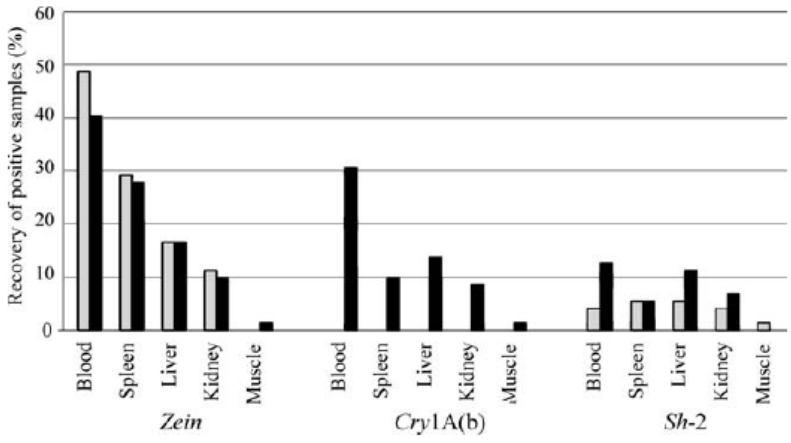

Figure 3. Recovery of positives samples (%) of the transgene and plant gene fragments in five tissues of animals from the control (■) and test (■) groups. The percentage of positives for each tissue is calculated as number of positives over 72 observations (3 PCR repetitions × 3 independent DNA isolations × 8 individuals).

Sharma et al. (2006) detected transgene fragments in the large intestine tissue of sheep and in the cecal tissues of pigs. From 36 pigs, one liver and one kidney sample (from different animals) were positive for a 278-bp fragment of the transgenic cp4 epsps gene.

Both studies can easily be retrieved from the scientific database PubMed - a service of the U.S. National Library of Medicine that includes over 17 million citations from MEDLINE and other life science journals for biomedical articles as far back as the 1950s. The links to the abstracts of both studies are below:

1. Sharma et al. (2006): http://www.ncbi.nlm.nih.gov/pubmed/16506822?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

2. Mazza et al. (2005): http://www.ncbi.nlm.nih.gov/pubmed/16245168?ordinalpos=16&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

It is highly unlikely that neither the EFSA GMO panel members nor other experts consulted by EFSA had not seen these studies during the 1-2 years after publication. In fact environmental groups like Friends of the Earth, GLOBAL 2000 and Greenpeace had already publicized the findings of the Mazza et al. study in December 2005.

European Commission has more scientific expertise than EFSA

The European Commission was aware of the studies of Mazza et al. (2005) and Sharma et al. (2006). In a response to the EFSA statement on the fate of recombinant DNA fragments or protein in meat, milk and eggs from animals fed with GM feed, published on 20 July 2007, the European Commission along with the UK Food Standards Agency (FSA) inquired about further relevant literature references (Sharma et al. (2006), Dugan et al. (2003), Mazza et al. (2005) and Guertler et al. (2007)) and specifically whether or not they had an impact on EFSA's conclusion that "a large number of experimental studies with livestock have shown that recombinant DNA fragments or proteins derived from GM plants have not been detected in tissues, fluids or edible products of farm animals like broilers, cattle, pigs or quails". (EFSA (2007c))

From this it is clear that the EC and the UK FSA wanted to know why EFSA had not taken into account the relevant scientific literature in its statement.

EFSA seriously misleads the European Commission and the public

Confronted with these scientific studies, EFSA stated that there is no need to change its opinion or review and republish its statement:

"In conclusion, these additional references do not change the following conclusions as drawn in the EFSA statement:

(1) Biologically active genes and proteins are common constituents of foods and feed in varying amounts. After ingestion, a rapid degradation into short DNA or peptide fragments is observed in the gastrointestinal tract of animals and humans.

(2) To date, a large number of experimental studies with livestock have shown that recombinant DNA fragments or proteins derived from GM plants have not been detected in tissues, fluids or edible products of farm animals like broilers, cattle, pigs or quails."

EFSA saw also no need to change their claim that "To date no recombinant DNA sequences have been found in any organ or tissue sample from animals fed GM plants"

For EFSA to reaffirm its statement that transgenic DNA had not been found in animal tissue when the two studies by Mazza et al. (2005) and Sharma et al. (2006) clearly showed they had, is seriously misleading and ignores the scientific facts. It is unclear why EFSA refuses to state that transgenic fragments have been detected in tissues of farm animals. It is also unclear why the European Commission continues to ask EFSA for scientific advice when the advice it has provided in this case was not scientific but selective and biased.

The relevance of the findings of Mazza et al. (2005) and Sharma et al. (2006)

Proteins and interestingly nucleic acid can act as pathogen-associated molecular patterns. Why nucleic acid is identified by human (mammalian) pattern-recognition receptors (PRRs) is still not fully clear, but some argue that nucleic acids represent a uniform conserved molecular pattern, allowing recognition independently of continuous evolutional changes to the outer membrane or capsid components of pathogens. (Pawar et al. (2006))

Also the Toll-like receptors are evolutionary conserved among species (Akira et al. (2006)). Some nucleic acid sequences seem to be "evolutionary conserved" and represent a universal code which is identified as a sequence from a pathogen by the innate immune system. This universal knowledge is passed from generation to generation. The most striking difference between nucleic acid-specific Toll-Like-Receptors and the other Toll-Like-Receptors is their localization within an intracellular compartment, which may contribute to their ability to differentiate between self and nonself DNA/RNA sequences (Pawar et al. (2006)).
There are several receptors in the human immune system which can bind foreign nucleic acids (DNA and RNA). Two different ways in which the immune system detects DNA/RNA from viruses, microorganisms and self DNA have been identified so far – as the following figure shows:

1. Recognition in the endosome by Toll-like-receptors TLR
2. Recognition in the cytoplasma by retinoic acid-inducible gene1 (RIG-1) and MDA5

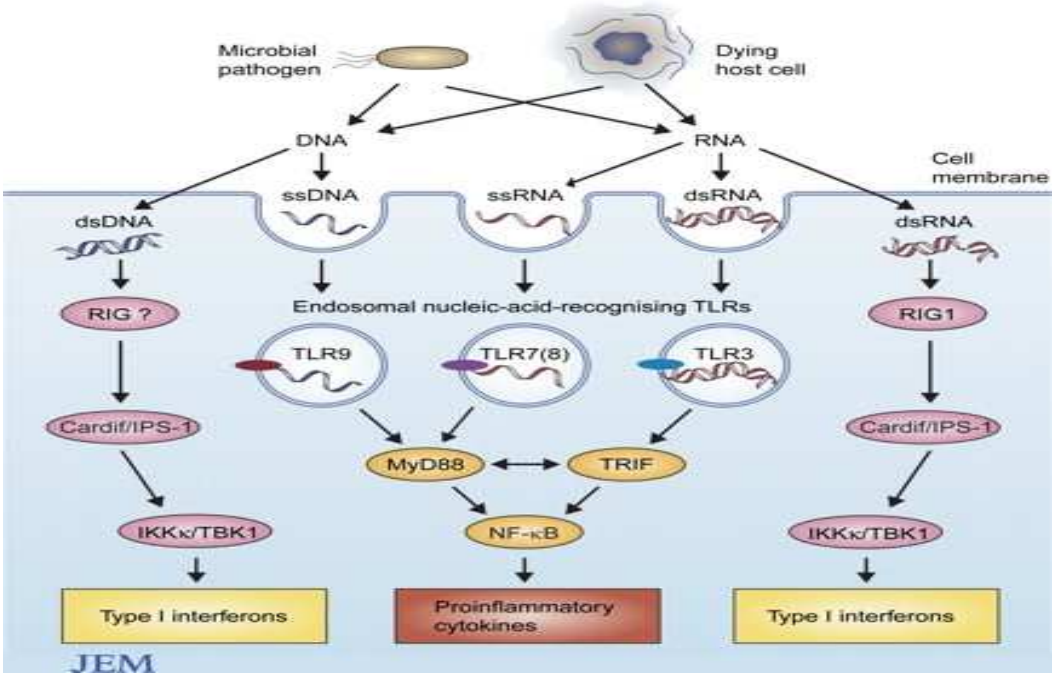

Figure 2: DNA/RNA recognition pathways in innate immune cells (WAGNER and BAUER (2006))

Reviews on DNA/RNA recognition receptors in the immune system are provided by Akira et al. (2006) and Pawar (2006). Furthermore, Rachmilewitz et al. (2004) show that nucleic acid from food interacts with the human immune system. Mazza et al. (2005) and Sharma et al. (2006) have shown that fragments of synthetic transgenes have been traced in the blood and therefore it is highly likely that they interact with the human immune system, just as natural sequences do. How synthetic nucleic acids from genetically modified plants interact with the human immune system has so far not been analyzed by EFSA. (Mueller (2007) provides a more detailed analysis of the interaction between not self DNA and the immune system and its implications for the risk assessment of GMOs.)

Conclusions

The EFSA GMO panel has, in this case, failed to provide the EC and the public with scientifically correct information. All EC decisions on GMO-approvals are based upon the opinions of EFSA. That all GMO-applications are exclusively reviewed by EFSA before making a recommendation to the EC, raises serious implications, if EFSA fails to provide the EC with correct scientific information. For this reason it is inappropriate to continue with the practice of resubmitting incomplete scientific opinions to EFSA. Based on EFSA's advice, GM food has been approved for the consumption of more than 400 million citizens in the European Union. These revelations call into question the validity of the GMO approvals granted by the EC on the basis of this advice. As such, a complete overhaul of the GMO approvals process is urgently needed and the EFSA GMO panel must be replaced by independent scientists who will provide unbiased and accurate scientific information.

References:

Akira S, Uematsu S, Takeuchi O (2006): Pathogen recognition and innate immunity. Cell 124(4): 783-801.

EFSA (2007a): Letter to Robert Madelin regarding the EFSA statement on the fate of recombinant DNA or proteins in the meat, milk or eggs of animals fed with GM feed. http://efsa.europa.eu/EFSA/Non_Scientific_Document/EFSA_letter_DNA_proteins_gastroint,0.pdf

EFSA (2007b): Statement on the fate of recombinant DNA or proteins in the meat, milk or eggs of animals fed with GM feed published 19 July 2007 http://efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178623095798.htm

EFSA (2007c): Minutes of the 37th Plenary Meeting of the scientific panel on genetically modified organisms held on 22-23 November 2007 in Brussels, Belgium (Adopted on 18 December 2007) EFSA/GMO/380

Mazza R, Soave M, Morlacchini M, Piva G, Marocco A. (2005): Assessing the transfer of genetically modified DNA from feed to animal tissues. Transgenic Res. 2005 Oct;14(5):775-84.

Mueller W (2007): Effect of foreign (=not self) DNA/RNA on the Human Immune System in regard to Genetically Modified Plants; published online http://www.eco-risk.at/ http://www.eco-risk.at/de/stage1/download.php?offname=FOOD-DNA-risk&extension=pdf&id=69

Pawar RD, Patole PS, Wornle M, Anders HJ (2006): Microbial nucleic acids pay a Toll in kidney disease. Renal Physiology 291(3): F509-F516.

Rachmilewitz D, Katakura K, Karmeli F, Hayashi T, Reinus C, Rudensky B, Akira S, Takeda K, Lee J, Takabayashi K, Raz E (2004): Toll-like receptor 9 signaling mediates the anti-inflammatory effects of probiotics in murine experimental colitis. Gastroenterology 126(2): 520-528.

Sharma R, Damgaard D, Alexander TW, Dugan ME, Aalhus JL, Stanford K, McAllister TA. (2006): Detection of transgenic and endogenous plant DNA in digesta and tissues of sheep and pigs fed Roundup Ready canola meal. J Agric Food Chem. 2006 Mar 8;54(5):1699-709.

Wagner H, Bauer S (2006): All is not Toll: new pathways in DNA recognition. Journal of Experimental Medicine 203(2): 265-268 including supplements from http://www.jem.org/content/vol203/issue2/images/large/481fig1.jpeg