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How much evidence does it take for EFSA to admit they are unsure about safety? – The case of genetically modified herbicide resistant rice LL62.

April 2009

SUMMARY

Rice is a staple food for 2.5 billion people. For many of those people, including European citizens, it can make up a large proportion of the diet. Since rice is such an important component of many people's daily food, an application for the approval of genetically modified (GM) rice deserves the utmost scrutiny.

The evidence against glufosinate – the herbicide that LL62 rice is tolerant to – is so strong that it is among the 22 agrochemicals that will soon have to be phased out in the EU. It is a questionable double standard that based on the newly adopted Regulation on pesticides[1] the EU decided to phase out glufosinate, and at the same time even considers approving a glufosinate tolerant plant for import. This implies two serious contradictions:

- The EU protects its own farmers and soil from a dangerous pesticide, but encourages chemical companies to increase its use outside of Europe.
- The EU does not protect its own consumers as there is a high likelihood that glufosinate will be eventually imported as residues on rice.

The European Food Safety Authority (EFSA) has failed to properly address the problem of contamination of rice cultivated in Europe. Contamination could result from *"accidental spillage of imported viable GM rice during transport through rice growing areas"* - according to EFSA. Since European consumers continuously reject GM food, such contamination could jeopardise the viability of European rice cultivation on which many farmers and traders depend.

Regrettably, in its opinion on LL62 rice[2] EFSA has failed to properly address several issues. Many uncertainties characterise the evaluation of LL62 rice, including:

- irregularities at the molecular level,
- compositional differences between LL62 rice and conventional rice that could be important for food safety, and
- serious issues of human and animal toxicity related to glufosinate ammonium, the herbicide sprayed on LL62 rice.

Greenpeace therefore urges the European Commission and the EU member states to reject Bayer's application on the basis of the precautionary principle.

[1] Regulation of the European Parliament and of the Council on the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC

[2] http://www.efsa.europa.eu/EFSA/Scientific_Opinion/gmo_ej588_LLRICE62_opinion_en,0.pdf

1) Human and environmental health effects of glufosinate

Bayer has genetically engineered LL62 rice to tolerate higher doses of its own herbicide, glufosinate.

A 2005 EFSA review of glufosinate has brought its future into question together with that of its application to GM glufosinate tolerant crops.[3] Serious issues of human and animal toxicity have been identified. The most worrying risk in relation to the import of rice is the impact of residues of glufosinate on human health. EFSA, in its review of glufosinate ammonium, noted that:

- the toxic residue level in potatoes on which glufosinate had been used posed *'an acute risk for toddlers'*;
- *'a high risk to mammals'* has been identified;
- farmers using glufosinate on genetically engineered maize were being exposed to unsafe toxic concentrations, even when protective equipment was being used; and
- a *'high risk'* had been identified for insects and wild plants even outside the sprayed fields, which might lead to a serious loss of biodiversity.

A European Commission working group suggested classifying glufosinate as a *'possible risk of harm to the unborn child'* and that it *'may impair fertility'*.[4] The EFSA study from 2005 states very clearly: *"the critical effect of glufosinate-ammonium is severe effects on reproduction toxicity*".[5]

In early 2009, the EU adopted legislation that regulates the production and licensing of agrochemicals.[6] It sets clear criteria for the approval of these products, forbidding the authorisation and re-authorisation of agrochemicals classified as toxic for reproduction, carcinogenic or mutagenic. Based on these cut-off criteria, 22 currently-authorised agrochemicals, including glufosinate, cannot have their marketing licence extended.

2) GM rice is likely to contaminate EU rice crops

EFSA, in its opinion on LL62 rice[7] acknowledges that contamination of EU rice crops could occur:

> *"The GMO Panel concludes that there is a possibility that GM rice could enter cultivation through accidental spillage of imported viable GM rice during transport through rice growing areas. The frequency of cross-pollination between the imported viable GM rice and cultivated or weedy rice will be directly related to levels of such spillage and subsequent establishment of GM populations in rice fields."*

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[3] EFSA Scientific Report (2005) 27: 1-81. Conclusion on the peer review of glufosinate. http://www.efsa.eu.int/science/praper/conclusions/895/praper_ej27_conclusion_glufosinate_en1.pdf.

[4] Classification R63 and R60, respectively, as suggested by the EU Commission Working Group on C&L. Searchable working database at: http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=cla

[5] EFSA Scientific Report (2005) 27: 1-81. Conclusion on the peer review of glufosinate. http://www.efsa.eu.int/science/praper/conclusions/895/praper_ej27_conclusion_glufosinate_en1.pdf, page 17

[6] Regulation of the European Parliament and of the Council on the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC

[7] Opinion of the Scientific Panel on Genetically Modified Organisms on an application (reference EFSA-GMOUK-2004-04) for the placing on the market of glufosinate tolerant genetically modified rice LLRICE62 for food and feed uses, import and processing, under Regulation (EC) No 1829/2003 from Bayer CropScience GmbH1., The EFSA Journal (2007) 588, 1-25 http://www.efsa.europa.eu/EFSA/Scientific_Opinion/gmo_ej588_LLRICE62_opinion_en,0.pdf

Although feral population of rice may not be an issue in the EU, the passing on of LL genes from the GM rice to weedy rice would be a highly serious issue in many areas. Once the LL genes are in weedy rice, they would not be able to be eradicated because of the feral populations of weedy rice, which persist and would provide a reservoir of LL genes that would contaminate conventional rice.

Some of the imported grain may already be hybrid between cultivated and weedy rice, so if a spillage occurs, these LL genes are ready to enter the weedy rice population. EFSA acknowledges this:

> *"The applicant states … A proportion of the imported GM rice will be viable grains in the so called 'paddy rice' fraction. Hybrid grains between LLRICE62 and weedy rice plants might also occur within this fraction."*

But instead of recommending rejection, EFSA simply says that prevention of contamination is part of the risk management, which is outside of their remit. However, no surveillance can ensure there is no germination of spilled seed. EFSA has failed in its responsibility to protect EU rice growers.

> *"The GMO Panel advises that appropriate management systems should be in place to restrict seeds of LLRICE62 entering cultivation as the latter requires specific approval under Directive 2001/18/EC or Regulation (EC) No 1829/2003. These should include management measures to prevent LLRICE62 spillage into EU rice growing areas and subsequent establishment of GM plants and outcrossing. The efficacy of these measures should be reported as part of the general surveillance activities."*

It should be understood that most of the rice produced in Europe is consumed in Europe. Contamination of European rice supplies would be even more financially devastating than contamination was to the US rice industry (see below) where the population remained largely unaware that it was being fed contaminated rice. Consumers will not buy rice if it is contaminated and contamination is likely to persist for at least several years.

Since 2006, there have been almost continual contamination surprises of rice around the world.[8] Even more incredible is that no GM rice has been commercialised anywhere in the world - these contamination cases result from field trials.

Bayer's history of contamination alone suggests that contamination fears and risks are higher than with other companies. Starlink (2001), Topas (Australia 2005) and LL601, 62, 604 (2006) represent only the worst cases of contamination involving Bayer. They also represent the worst cases of GM contamination globally. In many cases, it isn't known how the contamination occurred, with Bayer citing an "Act of God"[9] causing contamination by Bayer's GM rice variety LL601. Will the hand of God strike again?

It is estimated that the total cost to the US rice industry could be as high as 1.2 billion dollars.[10] The scale of the contamination that occurred in the US and the staggering

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[8] GM Contamination Register: http://www.gmcontaminationregister.org

[9] Answer and Defenses of Bayer CropScience et al. to Plaintiffs Consolidated Class Action Complaint, 21 June 2007 http://www.bayerricelitigation.com/PDFs/Bayer%20Rice%20--%20Part%201%20of%20Defendants'%20Answer%20to%20Master%20Consolidated%20Amended%20Class%20Action%20Complaint%20--%20062107.pdf

[10] Greenpeace 2007. Risky Business. Economic and regulatory impacts from the unintended release of genetically engineered rice varieties into the rice merchandising system of the US. http://www.greenpeace.org/international/press/reports/risky-business

costs associated with that contamination makes ignoring of contamination quite clearly reckless.

The complete failure of regulatory systems to prevent contamination – including in the EU which is widely held to have the most stringent rules globally – suggests that allowing LL62 rice to be introduced on the basis of a monitoring plan that is unlikely to be successful is unacceptable. The risk of contamination alone justifies rejection of Bayer's application.

3) Serious irregularities regarding the genetic insert

There are many irregularities at the molecular level with LL62. Most critically there are a total of 19 open reading frames (ORFs). These ORFs are created by the genetic engineering process and could produce unintended proteins or interfere with normal plant proteins. 19 is an exceptionally high number of ORFs. However, EFSA discounts these ORFs on the basis that they do not show significant similarities to rice proteins, toxins or allergens. But this does not preclude the fact that products from these ORFs may, in fact, interfere with the normal function of the rice plant.

Any adverse effects, even potentially highly important ones, caused by these ORFs may not have been detectable in Bayer's field trials. Indeed, these ORFs may only be activated in times of stress. In other words, adverse effects may only become apparent under conditions of stress, e.g. drought.

These ORFs should have cause EFSA to issue a negative opinion, but instead EFSA has dismissed these as unimportant just by saying:

> "*Based on the analyses provided the putative ORF amino acid sequences identified from LLRICE62 do not present any significant sequence identity with known toxins and allergens or with rice genes of known function.*"

As explicitly stated in Commission Decision 2002/623, areas of scientific uncertainties should be clearly identified in the evaluation ('*the overall uncertainty for each identified risk has to be described*'). Panel opinions generally have not done so. EFSA opinions often do not state where the scientific uncertainties arise even though it is legally binding to do so. EFSA once again, is only giving scant regard to uncertainties in any of their opinions for GM products. An assessment of the scientific uncertainties in an EFSA opinion is crucial to enable risk managers (e.g. the European Commission and the Member States) to make judgements in the public interest.

4) The GM insert interrupts a plant gene

During the genetic engineering process, the genetic cassette has integrated in a coding sequence of an endogenous gene (i.e. belong to the rice plant). The interruption of a genetic construct into the coding region of an endogenous gene has a high potential for unexpected and unpredicted effects.

ORF 5 is caused by the GM insert interrupting a plant gene. EFSA says:

> *"Although ORF-5 did show sequence similarities with rice mRNA and with two hypothetical rice proteins, no specific function could be ascribed to these*

putative proteins. Furthermore, bioinformatic analysis revealed no homology with a ribosome binding site or with core promoter sequences. This indicates that ORF-5 is not transcribed and this was confirmed by Northern analysis."

In other words, "this interruption to the plant gene may cause a protein with unknown function to be produced but we don't think it will be expressed, based on our current knowledge". However, Monsanto also assured regulatory authorities that the ORFs produced by the unintended fragments were not transcribed in their Round-up Ready soya, yet later they were found to be transcribed.

Our knowledge of how genomes work, and in particular how genes function and are controlled is incomplete. Indeed, new discoveries are made each year.[11] It may be that there are controls on whether this ORF is expressed or not. And if it becomes expressed unexpectedly, e.g. during a time of stress, what would the effects be? It is completely unknown. This may well be a cause of unexpected and unpredictable effects that could occur later on (e.g. Bt maize is more prone to aphid attack because of unexpected and unpredictable changes in sap chemistry).[12]

The interruption of a coding region of a plant gene caused by the genetic engineering process should be grounds enough to invoke the precautionary principle and reject the import of this GM rice into the EU as a foodstuff.

5) Compositional analysis raises food safety questions

EFSA acknowledges that there are differences between LL62 and a comparator line:

"*the compositional data obtained from individual locations showed statistically significant differences in the level of several compounds.*"

Incredibly, these differences are then dismissed because they are not consistent throughout the years. But with all the molecular irregularities, couldn't these compositional differences be indications of effects seen in certain years under certain stresses?

EFSA further dismisses the compositional differences because they fall "*within the ranges determined for the commercial varieties and in agreement with the natural variability*". But the GM rice should be compared to its sister non-GM rice, not the much broader range of rice composition generally.

EFSA is failing its job of protecting consumers and the environment by dismissing these significant differences, especially as they occur in conjunction with the molecular irregularities. The GM rice cannot be called "substantially equivalent" to non GM rice. These compositional differences could be important for food safety. At the very least, EFSA should be calling for further investigations to find out the physiological reasons for these compositional differences.

[11] see for example The ENCODE Project Consortium. Nature 447: 779-816.

[12] Faria, C.A., Wäckers, F.L., Pritchard, J., Barrett, D.A. & Turlings, T.C.J. 2007. High susceptibility of Bt maize to aphids enhances the performance of parasitoids of lepidopteran pests. PLoS ONE 2: e600.

6) Nutritional Assessment is worthless

In the nutritional assessment, significant differences were found:

> "*Significant differences were found only in the hot weight at study termination and in the weight gain in the middle phase of the study between the two control groups and the group of pigs fed LLRICE62 treated with glufosinate*."

and

> "*There were also significant differences in total weight gain, feed conversion efficiency and the hot weight at study termination between the group of pigs fed LLRICE62 treated with conventional herbicides and group of pigs fed LLRICE62 treated with glufosinate.*"

EFSA dismisses these studies on the basis that "*the compositional analysis of the GM and non-GM rice show similarity in constituents*". However, these "similarities" in composition are only because EFSA has dismissed the significant differences.

Therefore, the nutritional assessment tells us nothing about food or feed safety of the GM rice.

CONCLUSIONS

The precautionary principle must be invoked when scientific information is insufficient, inconclusive, or uncertain and where there are indications that there could be potentially dangerous effects on the environment, or on human and animal health. The precautionary principle must be applied in case of potential risks, even if these risks cannot be fully demonstrated or quantified or their effects determined.

The EU must not establish double standards on toxic herbicides. The EU considered glufosinate to be too toxic for use in Europe and thus must not allow the import of a glufosinate tolerant food product as well as not endorse its use outside Europe.

Given the fact that even after EFSA's assessment there remain many uncertainties and knowledge gaps with regard to the food and environmental safety of Bayer's LL62 rice and that glufosinate is a highly toxic herbicide, Greenpeace urges the European Commission and EU member states to reject Bayer's application.