

Soybean MON 89788

Organisation: Farmer

Country: Portugal

Type: Individual

a. Assessment:

4. Conclusions and recommendations

Very important that farming have real access to new technologies and modern plant varieties. That will allow us to protect the soil and the environment were we live.

Organisation: The European GMO-free Citizens (De Gentechvrije Burgers)

Country: The Netherlands

Type: Others...

a. Assessment:

b. Food Safety Assessment:

Toxicology

Do GMOs Accumulate Formaldehyde and Disrupt Molecular Systems Equilibria? Systems Biology May Provide Answers V. A. Shiva Ayyadurai*, Prabhakar Deonikar Systems Biology Group, International Center for Integrative Systems, Cambridge, MA, USA Email: *vashiva@integrativesystems.org Received 17 June 2015; accepted 7 July 2015; published 10 July 2015 Copyright © 2015 by authors and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY). <http://creativecommons.org/licenses/by/4.0/> Abstract.

Safety assessment of genetically modified organisms (GMOs) is a contentious topic. Proponents of GMOs assert that GMOs are safe since the FDA's policy of substantial equivalence considers GMOs "equivalent" to their non-GMO counterparts, and argue that genetic modification (GM) is simply an extension of a "natural" process of plant breeding, a form of "genetic modification", though done over longer time scales. Anti-GMO activists counter that GMOs are unsafe since substantial equivalence is unscientific and outdated since it originates in the 1970s to assess safety of medical devices, which are not comparable to the complexity of biological systems, and contend that targeted GM is not plant breeding. The heart of the debate appears to be on the methodology used to determine criteria for substantial

equivalence. Systems biology, which aims to understand complexity of the whole organism, as a system, rather than just studying its parts in a reductionist manner, may provide a framework to determine appropriate criteria, as it recognizes that GM, small or large, may affect emergent properties of the whole system. Herein, a promising computational systems biology method couples known perturbations on five biomolecules caused by the CP4 EPSPS GM of *Glycine max* L. (soybean), with an integrative model of C1 metabolism and oxidative stress (two molecular systems critical to plant function). The results predict significant accumulation of formaldehyde and concomitant depletion of glutathione in the GMO, suggesting how a “small” and single GM creates “large” and systemic perturbations to molecular systems equilibria. Regulatory agencies, currently reviewing rules for GMO safety, may wish to adopt a systems biology approach using a combination of *in silico*, computational methods used herein, and subsequent targeted experimental *in vitro* and *in vivo* designs, to develop a systems understanding of “equivalence” using biomarkers, such as formaldehyde and glutathione, which predict metabolic disruptions, towards modernizing the safety assessment of GMOs.

Ayyadurai, V.A.S. and Deonikar, P. (2015) Do GMOs Accumulate Formaldehyde and Disrupt Molecular Systems Equilibria? Systems Biology May Provide Answers. *Agricultural Sciences*, 6, 630-662. <http://dx.doi.org/10.4236/as.2015.67062>

Nutritional assessment

5. Barbosa HS, Arruda SCC, Azevedo RA, Arruda MAZ. New insights on proteomics of transgenic soybean seeds: evaluation of differential expressions of enzymes and proteins. *Anal Bioanal Chem*. 2012;402(1):299-314. doi:10.1007/s00216-011-5409-1

6. Arruda SCC, Barbosa HS, Azevedo RA, Arruda MAZ. Comparative studies focusing on transgenic through cp4EPSPS gene and non-transgenic soybean plants: an analysis of protein species and enzymes. *J Proteomics*. 2013;93:107-116. doi:10.1016/j.jprot.2013.05.039

Others

“Basis — Inadequate evidence for oncogenicity in animals. Glyphosate was originally classified as C, possible human carcinogen, on the basis of increased incidence of renal tumors in mice.”

https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0057_summary.pdf

3.2 Lankas, 1981 Testicular interstitial cell tumors In this 2-year study in Sprague-Dawley rats conducted by Bio/dynamics, EPA reports a significant trend of testicular interstitial cell tumors in males, with pairwise comparison significant even after multiple comparisons adjustment (0.039). It appears that EPA misreported the high-dose incidence rate in Table 4.1 (6/44 = 14%, not 12%).

https://www.centerforfoodsafety.org/files/sap-glyphosate-cancer-comments--cfs-20161_35863.pdf

https://file.scirp.org/pdf/AS_2015071017323113.pdf

TIME: I Won a Historic Lawsuit, But May Not Live to Get the Money

“Evidence revealed in the trial included internal Monsanto records that included discussions of “ghostwriting” scientific papers that asserted the safety of its products and plans to discredit an international agency that declared the main ingredient in Roundup, a chemical called glyphosate, to be a probable human carcinogen” Quote By CAREY GILLAM 7:48 AM EST http://time.com/5460793/dewayne-lee-johnson-monsanto-lawsuit/?utm_source=twitter.com&utm_medium=social&utm_campaign=social-share-article

Bound to fail: The flawed scientific foundations of agricultural genetic engineering (part 2)
<https://www.gmwatch.org/en/news/latest-news/18593>

This quote is from a second commentary on the same theme by the London-based molecular geneticist Dr Michael Antoniou, this time from the standpoint of molecular biology. Part 1 of this series of two articles is here: <https://www.gmwatch.org/en/news/latest-news/18582>

"However, in-depth molecular profiling analysis of transgenic plants shows that transgenic procedures invariably result in a spectrum of unpredicted alterations, not only in the function of the inserted foreign transgene but also of the plant's host genes. This in turn results in unintended changes in the plant's biochemistry."

4. Conclusions and recommendations

“The soy line in question has the cp4 epsps gene, which means that the plants have become tolerant to herbicides whose active substance is glyphosate.”

“MON 89788 is substantially equivalent to other soybean, except for its tolerance to glyphosate”. Part III Cartagena Protocol

Our comment: So, they're not the same!

“Under the assumption that the DNA sequence of the event in soybean MON 89788 considered for renewal is identical to the sequence of the originally assessed event, the GMO Panel concludes that there is no evidence in renewal application EFSA-GMO-RX-011 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on soybean MON 89788”. 2.3. Scientific opinion of the GMO Panel

“Under the assumption” is not science.

Has RIKILT taken food safety tests? We agree with the comment from Austria, France, Hungary, Norway and Germany that, because the herbicide Roundup (active substance:

glyphosate) is used in this GM soybean and the bean has been made resistant to the herbicide, the safety of this food for humans and animals needs to be researched. We therefore request an internal review. We dispute the claim that the GMO Panel is not competent to conduct such a review, partly in the light of the following:

"85 It is plain, as was stated in paragraphs 49 and 62 above, that the request for internal review is admissible, in this case, only to the extent that it claims that the authorisation decisions contravened provisions of environmental law within the meaning of Regulation No 1367/2006. Article 4(1)(a) and Article 16(1)(a) of Regulation No 1829/2003 provide that the food and feed concerned must not be placed on the market if they cause adverse effects on human health, animal health or the environment. The 305423, MON 87769 and MON 87705 soybeans constituted, when being cultivated, elements modified by human intervention that were in interaction with the natural environment. Accordingly, genetic modifications of those elements of the environment were liable to have consequences for their nutritional value or to represent a risk for food safety and constituted therefore matters within the scope of environmental law within the meaning of Regulation No 1367/2006."

Source: InfoCuria – Case-law of the Court of Justice. JUDGMENT OF THE GENERAL COURT (Seventh Chamber) 14 March 2018 (*) Environment - Genetically modified products – Regulation (EC) No 1367/2006 – Regulation (EC) No 1829/2003 – Genetically modified soybeans MON 87769, MON 87705 and 305423 — Rejection of an application for internal review of market authorisation decisions – Concept of ‘environmental law’ – Article 10 of Regulation No 1367/2006”. Case T-33/16, Applicant: TestBioTech eV (Munich, Germany) (represented by: R. Stein, Solicitor, K. Smith QC, and J. Stevenson, Barrister); Defendant: European Commission (represented by: J. Tomkin, L. Pignataro-Nolin and C. Valero, acting as Agents). Please regard the entire judgment as an integral part of the present document. <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:62016TJ0033&from=NL>

Dutch comment: “The Dutch CA has assessed the renewal dossier with respect to the environmental, food and feed safety of MON 89788 soybean and has no comments or requests for additional information in relation to the safety of this GM event”. Norway comment: VKM welcomes information on herbicide residue levels and their relevant metabolites in applications for herbicide tolerant GM plants. Data on glyphosate residue levels, including relevant metabolites, in plant material from field studies would support the assessment of food, feed, and environmental safety.

Answer: “This issue falls outside the remit of the GMO Panel.” References EFSA (European Food Safety Authority), 2008. Opinion of the Scientific Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO

Application EFSA-GMO-RX-011 (soybean MON89788) Comments and opinions submitted by Member States during the three-months consultation period (Annex G)

Our comment: We are ashamed to be Dutch, why has the Dutch CA lost its moral compass? Austria, France, Hungary and Norway all ask for data on the safety of this GM soya because of health issues of humans and animals. It will be high time this important issue will be an important one to address the safety of these GM soybean - and other GM products! If this is not possible then change the law!

The GM-free Citizens are supported by St. Natuurwetmoeders (Bussum) and St. Ekopark (Lelystad).

5. Others

Bayer:

Monheim, November 21, 2018 – Bayer will soon include safety study summaries of glyphosate on its dedicated transparency platform. This next step will mark the first anniversary of the company's Transparency Initiative, having been launched on 7 December 2017. <https://media.bayer.com/baynews/baynews.nsf/id/Bayer-to-offer-access-to-its-owned-glyphosate-studies> Our comment: Let's wait for those studies before you okay this GMO soya!

6. Labelling proposal

Not applicable until the safety for humans and animals has been thoroughly researched.

Organisation: The European GMO-free Citizens (De Gentechvrije Burgers)
Country: The Netherlands
Type: Others...

a. Assessment: Others

Press release

11.12.2018 Parliament calls for more transparency on the authorisation of pesticides and additives in the food chain Food law

Today, Members of the European Parliament have just voted in favour of greater transparency around the authorisation of pesticides, GMOs and additives in the food chain. Following the call of over 1.4 million people in the largest ever European Citizens' Initiative (ECI "Stop Glyphosate") for more transparency in the authorisation of pesticides, in April 2018 the

European Commission proposed a new regulation: "Transparency and sustainability of EU risk assessment in the food chain". The regulation will have an impact on the General EU Food Law and other legislation, for example on the authorisation of genetic engineering, pesticides and food additives. Fragment <https://www.greens-efa.eu/en/article/press/parliament-calls-for-more-transparency-on-the-authorisation-of-pesticides-and-additives-in-the-food-chain/#lang-es>

5. Others

This is a supplement to our previous complaints.

Organisation: Testbiotech
Country: Germany
Type: Non Profit Organisation

a. Assessment: **Molecular characterisation**

EFSA should have requested data that takes into account the increased number of times that glyphosate is sprayed because of problems with herbicide resistant weeds (see, for example, Benbrook, 2016). A higher number of applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genome activities in the plants. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018).

This aspect, which is the most relevant in regard to the re-assessment of this event, was completely ignored by EFSA. EFSA should have requested that Monsanto submit data from field trials sprayed with the highest dosage of the complementary herbicides that can be tolerated by the plants, also including repeated spraying. The material derived from those plants should have also been assessed using Omics techniques to investigate changes in the gene activity of the transgene and in the natural genome of the plants.

Benbrook, C.M., 2016. Trends in glyphosate herbicide use in the United States and globally. *Environ. Sci. Eur.* 28, 3. <https://doi.org/10.1186/s12302-016-0070-0>

Fang, J., Nan, P., Gu, Z., Ge, X., Feng, Y.-Q., Lu, B.-R., 2018. Overexpressing Exogenous 5-Enolpyruvylshikimate-3-Phosphate Synthase (EPSPS) Genes Increases Fecundity and Auxin Content of Transgenic Arabidopsis Plants. *Front. Plant Sci.* 9. <https://doi.org/10.3389/fpls.2018.00233>

Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)

There have been huge changes in the last ten years in the way that glyphosate-resistant plants are cultivated. Therefore, new field trials should have been requested from the applicant. Due to the changes in weed populations, it has to be expected that these plants can and will be exposed to higher and repeated dosages of glyphosate. Higher applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence plant composition and agronomic characteristics. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018).

This aspect, which is the most relevant in regard to this specific event, was completely ignored in the risk re-assessment. The issues of practical conditions prevalent in large scale cultivation and increasing weed occurrence were left aside.

EFSA should have requested that Monsanto submit data from field trials sprayed with the highest dosage of the complementary herbicides that can be tolerated by the plants, also including repeated spraying. The material derived from those plants should have been assessed using Omics techniques to investigate changes in plant composition and agronomic characteristics.

Fang, J., Nan, P., Gu, Z., Ge, X., Feng, Y.-Q., Lu, B.-R., 2018. Overexpressing Exogenous 5-Enolpyruvylshikimate-3-Phosphate Synthase (EPSPS) Genes Increases Fecundity and Auxin Content of Transgenic Arabidopsis Plants. *Front. Plant Sci.* 9. <https://doi.org/10.3389/fpls.2018.00233>

Further, data representing more extreme environmental conditions, such as those caused by climate change, would have been necessary.

New field trials are also necessary since new standards for conducting the trials and assessment of the data are now requested in the EU (see Regulation 503/2013).

b. Food Safety Assessment: Toxicology

Both the EU pesticide regulation and the GMO regulation require a high level of protection for health and the environment. Thus, in regard to herbicide-resistant plants, specific assessment of residues from spraying with complementary herbicides must be considered to be a prerequisite for granting authorisation. In assessing the safety of the products derived from the soybeans, the assessments made by the Pesticide Panel in 2015 (EFSA 2015) and 2018 (EFSA 2018b) have to be taken into account. They state that: «In the framework of the renewal, representative uses were proposed for conventional crops only and residue trials on glyphosate tolerant GM crops were not provided.» (EFSA 2015)

“For genetically modified crops, data were sufficient to derive MRL for sweet corn (EPSPS modification) and cotton seed (EPSPS modification), noting that MRLs should be tentative

pending on the submission of confirmatory methods for enforcement of AMPA and N-acetyl-glyphosate. For sugar beet roots, maize and soybeans (EPSPS modification), soybeans (GAT modification) and rapeseeds (GOX modification), the available data were insufficient to derive MRLs and risk assessment values.” (EFSA 2018b)

The conclusion that has to be taken from these EFSA reports (2015 and 2018 b) is that the existing data are not sufficient to conclude on the overall safety of the soybeans for import.

Further, while the GMO panel considers the assessment of the toxicity of the residues from spraying to be outside its remit, it is the duty of the GMO panel to consider and assess the specific metabolism in the plants and the specific metabolites that might occur in the plants after application of the complementary herbicides. These residues might show a specific pattern or accumulation that only occurs in this specific event. The pesticide panel can only assess the toxicity of these metabolites, if the GMO panel request specific data on metabolism and metabolites, also considering the various formulas, mixtures and combination of the complementary herbicides. So even if it is the case that the pesticide panel only has to assess the toxicity of these metabolites, it is the duty of the GMO panel to request these specific data that are needed to conclude on the safety of the plants.

In addition, as mentioned, higher applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genome activities in the plants. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018). These changes can have a serious impact on health since soybeans are known to produce many bioactive compounds such as allergens and oestrogens.

There are further relevant issues: for example, the potential impact on the intestinal microbiome also has to be considered. Such effects might be caused by the residues from spraying since glyphosate has been shown to have negative effects on the composition of the intestinal flora of cattle (Reuter et al., 2007) and poultry (Shehata et al., 2013). New research also shows an increase in resistance to antibiotics due to selective pressure caused by exposure to glyphosate (Kurenbach et al. 2018). In general, antibiotic effects and other adverse health effects might occur from exposure to a diet containing these plants (see also EFSA, 2018c); these were not assessed under pesticide regulation.

As a result, the toxicological assessment carried out by EFSA is not acceptable.

EFSA (2018b). Reasoned Opinion on the review of the existing maximum residue levels for glyphosate according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2018;16(5):5263, 230 pp. <https://doi.org/10.2903/j.efsa.2018.5263>

EFSA GMO Panel (2018c) Comments from the experts of Member States on the scientific opinion on the assessment of genetically engineered soybean MON 89788 (application EFSA-GMO-RX-011). Accessed via the register of EFSA, <http://registerofquestions.efsa.europa.eu/roqFrontend/login?0>

EFSA, (2015). Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. EFSA J. 13, 4302. <https://doi.org/10.2903/j.efsa.2015.4302>

Kurenbach B., Hill A.M., Godsoe W., van Hamelsveld S., and Heinemann J.A. (2018) Agrichemicals and antibiotics in combination increase antibiotic resistance evolution, PeerJ, DOI10.7717/peerj.5801, <https://peerj.com/articles/5801/>

Reuter T., Alexander T.W., Martinez T.F., McAllister T.A. (2007) The effect of glyphosate on digestion and horizontal gene transfer during in vitro ruminal fermentation of genetically modified canola. *J Sci Food Agric* 87:2837–2843

Shehata A.A., Schrödl W., Aldin A.A., Hafez H.M., Krüger M. (2012) The effect of glyphosate on potential pathogens and beneficial members of poultry microbiota in vitro. *Curr Microbiol* 6(4):350–358

Allergenicity

No data were presented to show that plant composition is unchanged in regard to allergenic potential.

As mentioned, higher applications of glyphosate will not only lead to a higher burden of residues in the harvest, but may also influence the expression of the transgenes or other genome activities in the plants. The changes in plant gene activity might also be caused by interference in the metabolism of the plant hormone auxin (Fang et al., 2018). These changes can have serious impacts on health since soybeans are known to produce many allergens.

Consequently, the assessment in regard to allergenicity cannot be regarded as conclusive.

Fang, J., Nan, P., Gu, Z., Ge, X., Feng, Y.-Q., Lu, B.-R., 2018. Overexpressing Exogenous 5-Enolpyruvylshikimate-3-Phosphate Synthase (EPSPS) Genes Increases Fecundity and Auxin Content of Transgenic Arabidopsis Plants. *Front. Plant Sci.* 9. <https://doi.org/10.3389/fpls.2018.00233>

Others

According to Regulation (EU) No 503/2013, the applicant has to ensure that post-market monitoring (PMM) is developed to collect reliable information on the detection of indications showing whether any (adverse) effects on health may be related to GM food or feed consumption (see also EFSA, 2018c). Thus, the monitoring report should at very least contain detailed information on: i) actual volumes of the GE soybean imported into the EU, ii) the ports and silos where shipments of the GE soybean were unloaded, iii) the processing plants where the GE soybean was transferred to, iv) the amount of the GE soybean used on farms for feed, and v) transport routes of the GE soybean.

Environmental monitoring should be run in regions where viable kernels of the GE soybean are transported, stored, packaged, processed or used for food/feed. In case of losses and spread of the GE soybean, all receiving environments need to be monitored.

Furthermore, environmental exposure through organic waste material, by-products, sewage or faeces containing the GE soybean during or after the production process, and during or after human or animal consumption should be part of the monitoring procedure (see also EFSA, 2018c).

EFSA GMO Panel (2018c) Comments from the experts of Member States on the scientific opinion on the assessment of genetically engineered soybean MON 89788 (application EFSA-GMO-RX-011). Accessed via the register of EFSA, <http://registerofquestions.efsa.europa.eu/roqFrontend/login?0>

4. Conclusions and recommendations

The EFSA risk assessment cannot be accepted.
