Soybean FG72 x A5547-127

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

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a. Assessment:
Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)

Study by Hoechst (Dr Arno Schulz) concerning the substrates of phosphinothricin acetyltransferase (PAT). PAT is present in herbicide-resistant (i.e. PPT-resistant) crops.

Amsterdam, 7 November 1999

Two studies that arrive at opposite conclusions, namely 1. Charles J. Thompson, 1987: Characterisation of the herbicide-resistance gene bar from Streptomyces hygroscopicus: 2. Dr Arno Schulz, 1993: L-Phosphinothricin N-Acetyl-transferase -Biochemical Characterisation - a report incorporated into Wehrmann 1996 (Schulz is co-author). The subject is the characterisation of the enzyme phosphinotricin acetyltransferase (PAT), and in particular the specificity of the substrates. The first study concerns the reaction of phosphinothricin (PTT) with acetyl co-enzyme A under the influence of PAT and compares this with a number of structural analogues of PPT. One of the analogues is L-glutamate. The products of the reaction were identified via a mass spectrogram and the equilibrium constants (affinity) determined. In addition to PPT, a number of structural analogues were tested to determine whether there was an acetylation reaction. L-glutamic acid was one of the substances investigated. Compared with PPT, the affinity of most of the substances was low; one substance did not react at all. In this test, where a numerically reportable reaction occurred to an identified product (the detection threshold is not an issue here) there does not appear to be any reason to doubt that glutamic acid is a substrate of PAT.

The second study concerns the reaction of a large number of amino acids, including L-glutamic acid, which was also involved in the first study, in a reaction mix together with a 100% excess of PPT in relation to the acetyl source acetyl co-enzyme A and PAT. Products of the reaction were identified using chromatography. Even with a very large excess of L-amino acid no products of reaction with the amino acids were found. Only acetyl phosphinothricin was found. The authors concluded that PAT very specifically has only PPT as a substrate. The following criticisms can be made of this conclusion, which conflicts with that produced in the first study. (Incidentally, the first study is cited in the bibliography to the second study): 1. No detection threshold was determined for acetylated L-glutamic acid. 2. The possibility of acetylated glutamic acid being a source of acetyl for the acetylation of PPT was ignored. This could have been tested in the study by adding acetylated glutamic acid to the reaction mix in a quantity above the detection threshold and examining whether this added quantity disappears during the reaction. Based on the results of the first study it could certainly be predicted to

disappear!! 3. The study was conducted using a reaction mix in which a large excess of a competing substrate, PPT, was present. Observations of the pure amino acids were not conducted. 4. There is no discussion whatsoever of the results of the first study, in particular as to why these were so different. 5. Essentially, the authors of the second study accuse the authors of the first study of fabrication, of fraud (the first study contains a wealth of numerical data; in the second there are no figures). In the second study this aspect is not fully explored. The background to the conclusion that PAT has only one substrate – PTT – is as follows: in herbicide-resistant (i.e. PPT-resistant) crops, PAT is present. In order to obtain approval for products to be placed on the market the toxicity of this gene-product must be examined. Could this gene-product react with the content of our GUT, e.g. with the – important – amino acid L-glutamic acid? It would cost a fortune in research to demonstrate that the dangers were minimal. For HOECHST, it would seem that total denial is a better strategy! We believe that the conclusion drawn in the second study is completely unfounded and that the so-called 'study' is unworthy of the name. It is an incompetent study and those persons who cite it need to be told about its incompetence. J. van der Meulen, L. Eijsten.
http://www.gentechvrij.nl/rvs9911.html

EU to restrict herbicide glufosinate

Category: Crop Protection Products Tags: EU , restrict , herbicide , glufosinate The European Commission has announced the restrictions for the use of the herbicide glufosinate, which will be effective from Nov 13, 2013.

The decision is based on the additional information provided by the notifier, the Commission considered that the further confirmatory information required had not been provided and that a high risk for mammals and non- target arthropods could not be excluded except by imposing further restrictions.

The active ingredient will only be authorised for band or spot application at rates not exceeding 750 g ai/ha (treated surface) per application, with a maximum of two applications per year.

EU member states must amend or withdraw existing product authorizations in accordance with Regulation (EC) No 1107/2009 by Nov 13, 2013. They may set a grace period of up to one year for use of existing stocks. New approvals should include the application of drift-reducing nozzles and spray shields, together with relevant labelling.

Glufosinate obtained EU approval for use in apple orchards in 2007. Source: EUR-Lex
http://news.agropages.com/News/NewsDetail---9598.htm

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b. Food Safety Assessment:
Toxicology

Court Rules Against Monsanto, Allows California To Put Cancer Warning On Roundup. January 27, 2017 3:27 PM http://sacramento.cbslocal.com/2017/01/27/court-rules-against-monsanto-allows-california-to-put-cancer-warning-on-roundup/

Allergenicity

Statements by mothers in the USA, where GMOs are not labelled as such.

"When my son was born he fussed a lot, the whole day, wouldn't nap. I breast fed until he was three months old. And because his gut was not right, he fussed and I could never console him. I tried all the gassy meds, not sure they are considered meds. Once on formula the fussing continued, we switched to different formulas, but not until we switched to parent's choice organic, Walmart, his fussing stopped, he began taking naps. As a toddler, I fed him Cheerios, a main staple in our house. The tantrums began; two hours at a time couple times a day. This was with head banging or slamming his head into the wall repeatedly. He wouldn't let me hold him, not even touch him. Can you imagine not cuddling your baby? I cried every day. I had watched the movie Food Inc. It touched on a subject I wasn't familiar with. After watching Genetic Roulette, I cleaned out the cupboards. After doing this, within two weeks my sons tantrums stopped completely, he started smiling, crawling into my lap for cuddles. I had no idea that was the issue. Even now when he gets something conventionally/GMO poison, he'll have another tantrum like in the past. So if there's a question as to where it's from-what kind of seed, I don't take it. So for me and my family, we bow out from being a guinea pig."- Stephanie Vanderyacht

"My husband was in the hospital 5 times last year. Doctors wanted to remove part of his intestine because it was so infected instead doctors pumped him full of antibiotics for a week when he got out of hospital I changed his diet and all our family food choices to NON- GMO foods WOW what a difference he's doing great and food never tasted so good! I will march sign petitions anything to reclaim our healthy labelled food choices. God Speed JUST SAY NO TO GMO'S ….MAAM!" Rhonda Bryne, MAA

My 7 year old son was diagnosed with asthma and needed glasses inside of two weeks. I started learning about asthma and natural ways to control it. Then I found out about GMO. I removed my family from GMO foods/drinks. My 7 year old went from needing a nebulizer 3x's a day to not at all. His asthma disappeared. He also no longer had the stigmatism that required glasses. The eye Dr. said he must have had 'some sort of inflammation' that is now gone for whatever reason. The reason was removing GMO from our diets. He was recommended for retention last year. This year, he is at the top of his class. Karen L.~Moms Across America. The above testimonials are a sampling of the hundreds of testimonials which Moms have sent to us. More see:
http://www.momsacrossamerica.com/zenhoneycutt/mom_s_testimonials

Others

Rising demand for organic and non-GMO grains outpaces U.S. production By Ken Roseboro Published: February 22, 2017 Issue: March Category: Organic/Sustainable Farming

Organic imports rise sharply as U.S. corn and soybean growers contemplate premiums, risk-reward scenarios Increasing consumer demand for organic and non-GMO foods led to a sharp rise in organic grain imports in 2016—prompting food manufacturers to explore new incentives for U.S. growers transitioning to organic production, according to a new report from CoBank. While U.S. production of non-GMO crops has risen, domestic production of organic corn and soybeans remains well short of demand. CUT http://non-gmoreport.com/articles/rising-demand-organic-non-gmo-grains-outpaces-u-s-production/

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4. Conclusions and recommendations

The European GMO-free Citizens do not want any GMOs on their plates, not as colorants, aromas, flavourings or similar, medicines, biological products or vaccines, GM flowers with altered colours, or crops. And no laundry detergents with GM enzymes.

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6. Labelling proposal

Labelling in the Netherlands is a farce. If labelling is carried out, it should be effective and subject to strict supervision, especially in the case of GMOs obtained through parallel importing, which might contain prohibited GMOs, such as certain genetically modified sugars. Dairy products from genetically modified animals and all other uses that are not labelled at present, such as vitamins, enzymes, colorants, flavourings, etc., should also be labelled. The European GMO-free Citizens of Lelystad have found out that:

All American (genetically modified) products at Jumbo are incorrectly labelled. Jumbo places the following warning as standard on all its products from the American range: ‘American products may contain genetically modified raw materials’, even on the ‘GMO Free’ products. Consumers are therefore unable to determine whether or not a product contains genetically modified organisms (GMOs). This undermines the basic principles of compulsory labelling of genetically modified food: • consumers have the right to know what they are eating • the freedom of consumers to choose whether or not to consume GMOs. Furthermore, such products may contain ingredients that are prohibited in the EU. This applies to all the American products from the Jumbo range (at least 36 products). Jumbo therefore infringes Dutch legislation concerning compulsory GMO labelling, in particular the Dutch Novel Foods Decree and EU Regulation No 1830/2003. GMOs must be labelled as such in the EU. The wording to be used is specified exactly and must not be deviated from. 5 July 2015 Request to the NVWA (Dutch Food and Consumer Product Safety Authority) to enforce the law at Jumbo. Because this behaviour by Jumbo undermines the principles of freedom of choice and the right of consumers to know what they are eating, we have asked the NVWA to intervene. (more info>>)

1 September 2015 Ruling by NVWA: Jumbo must change the labelling on all American products. The NVWA immediately started an investigation at the request of the European GMO-free Citizens. Quotation from the NVWA's letter of 1 September 2015: ‘Appropriate measures have been taken by the NVWA and the sales organisation to stop the deviation. The

incorrect information was removed from the website, or amended, on 14 August 2015. The said data were also amended on the labels'. (full text of the NVWA's letter >>). All's well that ends well? Unfortunately, Jumbo is still making a mess of things.

This is because in the meantime (2 September 2015), we have noticed the following with regard to the new labels: • products labelled as containing genetically modified wheat. GM wheat is prohibited in the EU; • products labelled as containing GMOs but stated as GMO-Free on the packaging; • products without any labelling (no Dutch declaration list); • we have no confidence in Jumbo actually checking whether the ingredients in these American products really are permitted. After two interventions by the NVWA, Jumbo has still not put its house in order!! The NVWA had in fact already taken action regarding Jumbo on 9 March 2015, at the request of the European GMO-free Citizens. To date, around 30 completely unlabelled American GM products have been involved. Quotation from NVWA ruling of 9 March 2015: a NVWA inspector took samples for examination. That examination revealed that the labels did not meet the legal requirements. The NVWA took appropriate action (more info>>).
4 May 2016: The initial products were then finally correctly labelled by Jumbo after repeated requests by the European GMO-free Citizens, a European consumers' platform, to the NVWA. But what will happen if it starts using a different importer? And there are still articles that are incorrectly labelled on the shelves, with no Dutch text on the label stating that the product contains genetically modified (= manipulated) organisms. We are keeping an eye on things! 8 November 2016. Now Poptart labels have been found at Jumbo that are very difficult to read, not just on one kind of packaging, but on several.
http://www.gentechvrij.nl/DossierJumbo_2.html

Via Facebook:

Miep Bos Jumbo Supermarkets 28 February: Dear Jumbo, we have now found yet another US product with incorrect labelling in one of your shops. Does it or does it not contain GMOs? 'Bevat mogelijk GMO' [May contain GMOs] is not permitted under the EU directive.

Jumbo Supermarkten: Hello Miep, that is a good point. And it is not the intention. We will ask our colleagues what the situation is. Can you perhaps also send us a photo of the barcode? 28 February at 22:04

Jumbo Supermarkten: Hello Miep, We have contacted the supplier and the product has been withdrawn from the range. Thank you for drawing this to our attention. 20 March at 10:14
https://www.facebook.com/photo.php?fbid=324595777937632&set=o.156928557716372&type=3&theater¬if_t=photo_comment¬if_id=1488315874763235 24 March 2017 Soft drinks Coca Cola Vanilla and A&W and Cheetos (cocktail biscuits, carton) at Jumbo do not bear any indication that they are produced using genetic engineering. Cheetos don't even have a Dutch label. These products are manufactured in the USA and obtained through parallel importing. Jumbo should investigate this.

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

Type: Others...

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a. Assessment:
4. Conclusions and recommendations

I fully endorse the statements by Miep Bos, spokesperson for De Gentechvrije Burgers, who has previously also sent you observations on the herbicide-tolerant, genetically modified soybean FG72 x A5547-127. All observations signed by Miep Bos, spokesperson for De Gentechvrije Burgers, on behalf of Wieteke van Dort. Lelystad. www.gentechvrij.nl

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

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a. Assessment:
b. Food Safety Assessment:
Toxicology

http://www.boerenlandvogels.nl/sites/default/files/2017-04/srep39328%20%281%29.pdf
Non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide

The impairment of liver function by low environmentally relevant doses of glyphosate-based herbicides (GBH) is still a debatable and unresolved matter. Previously we have shown that rats administered for 2 years with 0.1 ppb (50 ng/L glyphosate equivalent dilution; 4 ng/kg body weight/day daily intake) of a Roundup GBH formulation showed signs of enhanced liver injury as indicated by anatomorphological, blood/urine biochemical changes and transcriptome profiling. Here we present a multiomic study combining metabolome and proteome liver analyses to obtain further insight into the Roundup-induced pathology. Proteins significantly disturbed (214 out of 1906 detected, $q < 0.05$) were involved in organonitrogen metabolism and fatty acid β-oxidation. Proteome disturbances reflected peroxisomal proliferation, steatosis and necrosis. The metabolome analysis (55 metabolites altered out of 673 detected, $p < 0.05$) confirmed lipotoxic conditions and oxidative stress by showing an activation of glutathione and ascorbate free radical scavenger systems. Additionally, we found metabolite alterations associated with hallmarks of hepatotoxicity such as γ-glutamyl dipeptides, acylcarnitines, and proline derivatives. Overall, metabolome and proteome disturbances showed a substantial overlap with biomarkers of non-alcoholic fatty liver disease and its progression to steatohepatosis and thus confirm liver functional dysfunction resulting from chronic ultra-low dose GBH exposure. Source: Mesnage R et al. (2017) Scientific Reports 7, Article number: 39328 srep39328 (1).pdf

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5. Others

Supplementing our previous concerns.

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

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a. Assessment:
b. Food Safety Assessment:
Toxicology

http://www.boerenlandvogels.nl/sites/default/files/2017-04/srep39328%20%281%29.pdf
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5. Others

Supplementing our previous concerns. Compiled by M. Bos. on behalf of Ms W. van Dort.

Organisation: Testbiotech
Country: Germany
Type: Non Profit Organisation

a. Assessment:
Molecular characterisation

Regarding parental events: Soybean FG72 was produced using the ballistic method. As the application for soybean FG72 shows, several copies of the additional DNA inserted in the plants´ genomes revealed defragmentation and other unintended characteristics in the size and orientation of the copies. Risks were not assessed in depth by EFSA.

In soybean A5547-127, the gene construct was shown to be unintentionally divided into two parts; and parts of the DNA show reverse orientation and deletions. There were some open reading frames identified that can give rise to unintended gene products in the plants. Risks were not assessed in-depth by EFSA.

Regarding FG72 x A5547-127: Differences in the expression of the HPPD protein were found between the single and the stacked event in measurements derived from field trials in the US (EFSA, 2017a): "The reported expression levels of HPPD W336 in most tissues in the stack were lower than in the single (maximum ratio of twofold), although with overlapping ranges."

Further, data generated in Brazil give a clear indication that the stacking of the event influenced the level of protein expression: "Overall levels of HPPD W336 for both FG72 x A5547-127 and FG72 were low; levels of HPPD W336 in FG72 9 A5547-127 were below the method's limit of quantification, whereas in the single they were quantifiable."

As a result, further investigations are necessary to assess the combinatorial genomic effects.

References:

EFSA (2017a) Scientific opinion on application EFSA-GMO-NL-2013-120 for authorisation of genetically modified soybean FG72 x A5547-127 for food and feed uses, import and processing submitted in accordance with Regulation (EC) No 1829/2003 by Bayer CropScience LP and M.S. Technologies LLC. EFSA Journal 2017;15(4):4744, 23 pp. doi:10.2903/j.efsa.2017.4744

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

Agronomic characteristics The data on agronomic characteristics also indicate genomic effects or – and this would also need to be assessed – genome x environmental interaction:

“However, for the endpoints stand count (early and final) and plant vigour the per-site summary statistics revealed that the observed differences can be mainly attributed to data derived from the sites where soybean FG72 x A5547-127 introgressed into MST39 was tested (maturity group 3 sites), where a reduction of ca. 50% was observed. Such reduction was not observed for the single events FG72 and A5547-127 previously assessed by the GMO Panel (EFSA GMO Panel, 2011c, 2015). The GMO Panel requested further information, but from the submitted data, it was not possible to fully characterise the observed differences.”

The results from the field trials should be assessed in more detail, looking at specific interactions between the additional DNA and the genetic background of the different plant varieties, as well as interaction between the environment and the genome.

Composition Around half of the data assessed showed significant differences compared to the non-GM variety:

“The combination of test of difference and test of equivalence could be applied to the remaining 61 endpoints, with the following results:

Statistically significant differences between soybean FG72 9 A5547-127 (untreated) and the non-GM comparator were identified for 28 endpoints. 25 All the endpoints fell under equivalence category I. Statistically significant differences between soybean FG72 9 A5547-127 (treated) and the non-GM comparator were identified for 39 endpoints. 26 All the endpoints fell under equivalency category I.”

Although these differences were classified under category I, the high number of significant changes, in combination with the genomic effects and differences in the agronomic characteristics, should be investigated further.

But EFSA failed to require further studies e.g. Omics studies (proteomics, transcriptomics, metabolomics) to assist the compositional analysis and the assessment of the phenotypical changes. Investigations of changes in content of miRNA which can be taken up from the gut and render biological effects across border of life domains (Zhang et al., 2012). Exposing the plants to a wide range of defined biotic or abiotic stressors to assess the true range of possible changes in the plants´ composition. More varieties inheriting the trait should have been included to investigate how the gene constructs interact with the genetic background of the plants.

Further, as experts from Member States explain (EFSA, 2017b), due to the expression of the HPPD W336 protein, FG72 x A5547-127 and FG72 are resistant not only to isoxaflutole, which belongs to the isoxazoles, but possibly also to other herbicide families, e.g. triketones and pyroxazoles. In this respect, the transgenic trait has not been described comprehensively and the comparative assessment should possibly consider GM material that has also been treated with other herbicides.

As experts from Member States further explain (EFSA, 2017b), the plants were either treated, or not treated, with the three complementary herbicides in combination. It cannot be ruled out that the effects of isoxaflutole, glyphosate and glufosinate work against each other and cancel each other out - therefore, comparative assessment studies should also include GMO treated with each of the herbicides separately.

Based on the available data, no final conclusions can be drawn on the safety of the plants.

References:

EFSA (2017b) Application EFSA-GMO-NL-2013-120 by Bayer CropScience, Comments and opinions submitted by Member States during the three-month consultation period, Register of Questions, http://registerofquestions.efsa.europa.eu/roqFrontend/ListOfQuestionsNoLogin?0&panel=ALL

Zhang, L., Hou, D., Chen, X., Li, D., Zhu, L., Zhang, Y., Li, J., Bian, Z., Liang, X., Cai, X., Yin, Y., Wang, C., Zhang, T., Zhu, D., Zhang, D., Xu, J., Chen, Qu., Ba, Y., Liu, J., Wang, Q., Chen, J., Wang, J., Wang, M., Zhang, Q., Zhang, J., Zen, K., Zhang, C.Y. (2011) Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA. Cell Research, 22(1): 107-126.

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b. Food Safety Assessment:
Toxicology

No feeding studies were presented with the whole food and feed: A subchronic 90-day feeding study of sufficient quality was provided for soybean FG72 but it suffered from major methodological deficiencies and was rejected by EFSA. No subchronic 90-day feeding study was provided for soybean A5547-127. No feeding study with stacked soybean FG72 x A5547-127 was presented.

Therefore, health risks stemming from feeding whole food and feed cannot be assessed. This kind of data should have been requested, especially in awareness of the high number of significant changes in compositional analysis, the effects observed on plant characteristics and the observed genomic effects.

Further, testing of whole food and feed is especially relevant for assessing potential health effects resulting from the combination of the residues from spraying with glyphosate, isoxaflutole and glufosinate.

The application of the complementary herbicides is part of regular agricultural practice in the cultivation of herbicide-resistant plants. Therefore, it can be expected that the residues from spraying will always be present in the harvest and could be seen as inevitable “constituents”. In general, EFSA considers residues from spraying with the complementary herbicide to be outside the remit of the GMO panel. However, from a scientific and regulatory point of view, it cannot be justified that herbicide-resistant genetically engineered plants are assessed for health risks whilst at the same time residues from spraying with complementary herbicides are left aside. Health risk assessment cannot be reduced to what is required under Regulation 396/2005 (Pesticide Regulation) since this assessment does not take the specific pattern of exposure and relevant cumulative effects into account.

Due to the specific agricultural practices that go along with the cultivation of herbicide-resistant plants, there are specific patterns of applications, exposure and occurrence of specific

metabolites and an emergence of combinatorial effects that require special attention. For example, large-scale commercial cultivation of these plants results in a strong selective pressure on weeds to develop resistance to the herbicides (Sammons & Gaines, 2014). This problem is also relevant for health risk assessment, since it has led to increasing amounts of glyphosate being sprayed (Benbrook, 2016) and subsequently more residues in the harvest (Cuhra, 2015). Specific agricultural practices applied in the cultivation of these herbicide-resistant plants mean that, for example, specific patterns of applications, exposure, occurrence of specific metabolites and emergence of combinatorial effects all require special attention. Herbicide-resistant plants are meant to survive the application of the complementary herbicide while most other plants will die after short time. Thus, residues of glufosinate, glyphosate and isoxaflutole, their metabolites and additives to the formulated product might accumulate and interact in the plants.

As a publication by Kleter et al. (2011) shows, using herbicides to spray genetically engineered herbicide-resistant plants does indeed lead to patterns of residues and exposure that are not taken into account in regular pesticide registration. Further, according to a reasoned legal opinion drawn up by Kraemer (2012), from a regulatory point of view, residues from spraying with complementary herbicides have to be taken into account in the risk assessment of genetically engineered plants.

In regard to the pending application, there are specific reasons for concern: Isoxaflutole is classified as “probably carcinogenic” (see: Reuter, 2016), or classified as a suspected human carcinogen (EFSA, 2016). Further, there are ongoing discussions about whether glyphosate is “probably carcinogenic” (IARC, 2015). In addition, glufosinate is about to be phased out in the EU due to negative health impacts (EU Pesticides Database, 2017).

In 2016, EFSA presented its peer review of the pesticide risk assessment of the active substance isoxaflutole (EFSA, 2016), which clearly shows major data deficiencies in regard to the requirements of Pesticide Regulation 396/2005. As a result, EFSA was unable to set MRLs for isoxaflutole and its metabolites for applications to genetically engineered soybeans.

Furthermore, in 2015, EFSA presented the results of the risk assessment of glyphosate. EFSA stated in its opinion (EFSA, 2015a) that there were not enough data available on the application of glyphosate to genetically engineered plants resistant to the herbicide. For this reason, EFSA was unable to deliver a conclusive risk assessment on the actual risks of residues from spraying with glyphosate and the various glyphosate formulations.

Consequently, the EFSA assessment cannot show that genetically engineered soybeans sprayed with isoxaflutole, glyphosate and glufosinate are safe.

In addition, there are many other substances such as oestrogens, allergens and antinutritional compounds present in the plants that in interaction with trait-related characteristics might act as stressors: There is a considerable amount of literature indicating that glyphosate formulations can act as so-called endocrine disruptors (see, for example, Thongprakaisang et al., 2013; Çağlar & Kolankaya, 2008; de Liz Oliveira Cavalli et al., 2013; Omran & Salama, 2013). Endocrine effects were found when young rats were exposed to soy milk in combination with glyphosate (Nardi et al., 2016). Since soybeans also produce a number of plant oestrogens with hormonal activity (de Lemos, 2001), there might be some synergistic or additive interaction with the residues from spraying with glyphosate formulations.

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). Further, Bremmer and Leist (1997) examined the possible conversion of NAG to glufosinate in rats. Up to 10% deacetylation occurred at a low dose of 3 mg/kg bw as shown by the occurrence of glufosinate in the faeces. The authors concluded, however, that most of the conversion was caused by bacteria in the colon and rectum although toxicity findings indicate partial bioavailability (Bremmer & Leist, 1997, see also EFSA 2017 (b)).

As a result, there is a huge gap in the safety assessment of the genetically engineered soybeans that cannot be filled by adjustments to the MRLs applicable under the Pesticide Regulation. Consequently, the impact of residues from spraying in the plants must be assessed before the soybeans can be declared safe. The failure to do so poses real safety risks to humans, animals and the environment generally.

In any case, 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 addition, cumulative effects have to be investigated if a plant contains or produces other compounds of potential toxicity.

It should be acknowledged, that no new methodology is needed to assess the health risks emerging from the combinatorial application of the herbicides and their potential interaction with the other plant constituents. There is, for example, no need to apply methods such as the Monte Carlo Risk Assessment (MCRA) because the majority of potential stressors can be expected to occur in a fixed combination and follow a specific pattern of exposure. Rather, the methods currently available (in vivo and / or in vitro) are sufficient to assess the health effects: For example, Regulation (EC) No 1907/2006 (REACH) provides guidance on how substances that are in fact mixtures (isomeric mixtures, MCS (multi-constituent substance) and UVCB (substances of unknown or variable composition, complex reaction products or biological materials) should be assessed for their PBT/vPvB (persistent, bioaccumulative and toxic) properties. In general, due to the nature of "substances of unknown or variable composition, complex reaction products or biological materials" it is not possible to make reliable predictions about the additive, or synergistic, or antagonistic mode of effects. Therefore, such substances have to be tested as a mixture, not as single compounds. For example, chronic feeding studies are a well-established method to generate the relevant data.

References:

Benbrook, C.M. (2016) Trends in glyphosate herbicide use in the United States and globally. Environmental Sciences Europe, 28(1): 3.

Bremmer, J.N. and Leist, K.-H. (1997) Disodium-N-acetyl-L-glufosinate; AE F099730 - Hazard evaluation of Lglufosinate produced intestinally from N-acetyl-L-glufosinate. Hoechst Schering AgrEvo GmbH, Safety Evaluation Frankfurt. TOX97/014. A58659. Unpublished. (see FAO publication on https://web.archive.org/web/20060101000000*/http://www.fao.org/ag/agp/agpp/pesticid/jmpr/Download/98/glufosi3.pdf)

Çağlar, S., & Kolankaya, D. (2008) The effect of sub-acute and sub-chronic exposure of rats to the glyphosate-based herbicide Roundup. Environmental toxicology and pharmacology, 25(1): 57-62.

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Allergenicity

There are several relevant issues regarding allergenicity and the immune system that were left aside in EFSA risk assessment: The residues from spraying might lead to adjuvant effects in the plant´s allergens. No non-IGE-mediated immune reactions were assessed although these effects must be considered relevant (Mills et al., 2013). The assessment did not take the risk for more vulnerable groups of the population, such as infants (EFSA, 2010), into account. No blood samples from patients with a known allergenicity to soybeans were investigated. An analysis published by EFSA experts and other scientists recently found that, in general, open questions remain regarding the allergenicity assessment of genetically engineered plants, especially in the case of engineered soybeans (Selb et al., 2017).

Overall, the assessment is insufficient to exclude impacts on the immune system.

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5. Others

The risk assessment by EFSA is not acceptable in its present form. It does not identify knowledge gaps and uncertainties and fails to assess toxicity, or impact on immune system and the reproductive system. The monitoring plan has to be rejected because it will not make essential data available.
