ACB's Objection to Monsanto's Application for Commodity Clearance of MON 87708 × MON 89788 × A5547-127 Triple-Stacked Herbicide Tolerant Soybean

November 2017

On 7 April 2015 the African Centre for Biosafety officially changed its name to the African Centre for Biodiversity (ACB). This name change was agreed by consultation within the ACB to reflect the expanded scope of our work over the past few years. All ACB publications prior to this date will remain under our old name of African Centre for Biosafety and should continue to be referenced as such.

We remain committed to dismantling inequalities in the food and agriculture system in Africa and our belief in peoples' right to healthy and culturally appropriate food, produced through ecologically sound and sustainable methods, and their right to define their own food and agriculture systems.

www.acbio.org.za
PO Box 29170, Melville 2109, Johannesburg, South Africa. Tel: +27 (0)11 486 1156

1. INTRODUCTION

The African Centre for Biodiversity (previously 'Biosafety') (ACB) was established in 2003 and registered in 2004. ACB carries out research, analysis, capacity and movement building, and advocacy, and shares information to widen awareness and catalyse collective action and influence decision-making on issues of biosafety, agricultural biodiversity and farmer managed seed systems (FMSS) in Africa. The ACB's work both informs and amplifies the voices of social movements fighting for food justice and food sovereignty in Africa. The ACB has played an essential watch-dog role on new GMO permits in South Africa for a decade now, adding substantially to the discourse about the scientific assessment of GMOs, as well as issues of socio-economic impacts and democratic decision-making, through lodging substantive comments on at least 30 permit applications.

We are objecting to the commodity clearance of the triple-stacked GM soybean event MON 87708 x MON 89788 x A5547-127, due to concerns surrounding the lack of safety assessment data for this crop and the known toxicity of the three pesticides it is designed to tolerate. Its tolerance to three pesticides, glyphosate, glufosinate and dicamba will only increase the exposure of South African citizens to ever increasing amounts of chemicals in their food systems, while South African regulators are yet to fully establish legal limits for these chemical on our crops. Under these circumstances, we urge the Department of Agriculture, Forestry and Fisheries to decline approval until these safety uncertainties have been adequately addressed.

2. KEY CONCERNS

2.1 Molecular concerns

- Lack of information included in the characterisation of the inserted transgenes and disruption to host genome. These transgenes have been made synthetically and therefore have no history of safe use, so information should be provided. Evidence that the documented disruption to the host genome does not cause aberrant genomic activity should be tested.
- Introduced genetic elements, such as the cauliflower mosaic virus (CaMV) promoter sequences introduce known hazards that may introduce instability of the transgenes. Such risks have not been tested for.
- Agronomic/phenotypic alterations indicate that the genetic modification process has disrupted the plant genome activity and physiology. The applicant fails to provide experimental data from sensitive profiling techniques to confirm no alterations in transcriptome, proteome or metabolome has occurred.

2.2 Safety assessment

- The applicant claims substantial equivalence to conventional varieties without showing data that uses the latest global profiling techniques that allow for unbiased and sensitive screening of altered composition of plant constituents. Numerous studies have shown non-equivalence of GM crops. Claims of substantial equivalence are thus unfounded.
- 'History of safe use' cannot be claimed for this crop. The DMO protein conferring tolerance to dicamba shows limited homology to other proteins. Further, no history of consumption of varieties with three transgenes has occurred previously. The combined effects of these transgenes remain untested.
- Allergenicity studies are limited to predictive analyses that are not thorough enough to assess all potential allergenic properties of the transproteins.
- Mammalian toxicity remains completely untested for the whole plant. This is of upmost concern, considering this product is destined for the plates of South African citizens. The applicant should be asked to provide experimental data showing lack of toxicity in chronic mammalian feeding studies before claims of safety can be made.
- The effects of exposure to three herbicides with known adverse effects to all mammals of critical concern. These concerns remain untested by the applicant.

3. SUMMARY OF APPLICATIONS

Monsanto South Africa has applied for commodity clearance approval of triple-stacked genetically modified soybean MON 87708 x MON 89788 x A5547-127.

MON 87708 contains the mono-oxygenase (DMO) protein from *Stenotrophomonas maltophilia* intended to confer tolerance to dicamba herbicide.

MON 89788 contains the 5-enolpyruvylshikimate-3-phosphate synthase protein from *Agrobacterium sp.* strain CP4 (CP4 EPSPS) intended to confer tolerance to glyphosate herbicide.

A5547-127 contains the phosphinothricin N-acetyltransferase (PAT) protein from *Streptomyces viridochromogenes* to confer tolerance to glufosinate herbicide.

The triple-stacked event was generated by conventional breeding of the three above events.

4. MOLECULAR CONCERNS

4.1 Description of the recombinant DNA before and after modification

The transgenic material in the three parental single gene events as well as the final stacked event have been generated synthetically and therefore have no history of safe use in nature. A detailed description of the sequence of the transgenes should, therefore be provided. As stated in Annex I of Cartagena Biosafety Protocol, to which South Africa is a party:

> "It is important that a description of the nucleic acid introduced into the recipient organism be available. It provides information about all the genes including control elements that have actually been introduced…if there is introduced nucleic acid, then it will contain a number of elements with functions important to the production of a gene product; to the amount of gene product produced …These are important in considering how the introduced genetic information may be expressed in the modified organism."

Description of the parental single event lines as well as the stacked event fails to include sequence information, as it is CBI deleted. The applicant should be asked to provide sequence information to confirm integrity of the inserted transgenic material.

4.2 The CaMV 35S promoter

One of the parental event lines, A5547-127, uses the 35S promoter from the cauliflower mosaic virus (CaMV). Concerns surrounding the use of this promoter include the potential risks associated with the presence of viral gene VI within the promoter sequence, as well as the presence of a recombination hotspot. A 2012 paper entitled "Possible consequences of the overlap between CaMV 35S promoter regions in plant transformation vectors used and the viral gene VI in transgenic plants" raised concerns over the sequence overlap of the CaMV 35S promoter and gene VI, with gene VI potentially being expressed into the P6

protein (Latham & Wilson A 2012). A proper retrospective risk assessment on the gene VI fragment showed that the gene product is toxic to plants probably through, among other things, the inhibition of gene silencing, a necessary function universal to plants and animals; hence it is also likely to be toxic to animals, including humans. **The applicant has not mentioned this possibility, let alone checked for expression of this protein**. The promoter is also documented for carrying a recombination hotspot, which may increase potential for genetic rearrangements and horizontal gene transfer (HGT) (Ho et al., 1999). The promoter, contrary to claims by GM producers, is active in human cells and any horizontal transfer to human cells, therefore has the potential to disturb human gene expression (Ho, 2013). **The applicant has not provided information on the stability of the transgene and genome in the final stacked event after multiple generations.**

4.3 Characterisation of the indel

The applicant does not provide any details on the specific location of the transgenes in any of the individual or stacked events. There is no sequence information or description of the flanking genomic DNA provided.

The applicant, however, claims that sequence analyses demonstrate that "*MON 87708, MON 89788 and A5547-127 inserts and flanking regions are present and intact in the combined trait soybean product MON 87708 × MON 89788 × A5547-127*." The applicant goes on to state: "*The characteristics of the inserts and the 5' and 3' flanking sequences are conserved in this product*."

However, they fail to mention the confirmed loss of host genome DNA at flanking DNA regions in MON 87708 documented in the *EFSA Journal* (2013) on MON 87708 as a 899 base pair (bp) deletion and a 128 bp insertion adjacent to the 5' end of the insert, and a 35 bp insertion adjacent to the 3' of the insert, the consequences of which have not been evaluated. Though the *EFSA Journal* opinion states that these disruptions were not in regions of known soybean genes, interruptions of other regulatory elements in the genome could also potentially affect the activity of the genome. Such alterations in the host genome sequence could have unintended effects on the plant, potentially altering its physiology as well as compositional profile, which may alter nutritional or anti-nutritional status, and thus safety of the product following consumption.

Similarly, the *EFSA Journal* (2008) for MON 89788 states, "Sequencing of the parental soybean line showed that a 40 bp segment was deleted from the insertion site of the parental soybean and short novel DNA stretches (10 bp, 6 bp) were introduced during the insertion."

The applicant should provide *honest* details of disruptions to host genomic DNA in parental and stacked lines, and provide experimental analyses to show a lack of disruption to the host genome activity.

4.4 Description and characterisation of changes to the transcriptome, proteome and metabolome

The application fails to mention any profiling techniques that are now routinely employed to assess global changes in gene, protein and metabolite expression.

The latest studies in relation to GM crops reveal that the genetic modification process has the potential to disrupt endogenous gene expression in the plant, which can introduce human and environmental hazards as well as agronomic disturbances. Mesnage et al., (2016) used such techniques to analyse proteome and metabolome profiles of GM maize variety (previously shown in regulatory risk assessment with the basic tests to be substantially equivalent), detecting altered levels of proteins and metabolites indicative of oxidative stress, alterations in levels of enzymes involved in glycolysis metabolism, as well as Krebs cycle involved in energy production. Metabolome alterations also included a 28-fold rise in polyamines, which play multiple roles in cell growth, survival and proliferation; they can be either toxic or protective, depending on the context. This highlights the limitations of the tests carried out by the applicant, which may miss alterations that can now be detected with modern profiling techniques.

A study on golden rice also revealed that outcrossing of the GM rice engineered to have increased beta-carotene content of a local Indian rice variety revealed stunted growth related to disruption of growth hormone and photosynthesis levels ascribed to the genetic modification process by the researchers (Bollinedi et al., 2017).

Analysis of the seed weight of parental line MON 87708 indeed shows a reduction in seed weight in comparison to its conventional counterpart, which EFSA (2013??) concluded "might be either incidental or indicative of unintended effects due to the genetic modification". This finding should have initiated detailed analysis of genomic activity in order to understand how and what differences are occurring as result of the genetic modification process. The applicant also states that the final stacked event showed significant alterations in grain moisture, more days to 50% flowering, and higher susceptibility to bacterial blight disease and Cercospora leaf spot disease.

The applicant should be asked to provide profiling data for MON 87708 × MON 89788 × A5547-127 as part of a hazard identification procedure. This is particularly important considering the disruptions in the host genome flagged up by EFSA, alterations in agronomic and phenotypic traits, and previous evidence of genetic modification disruptions to plant physiology and composition.

5. SAFETY ASSESSMENT

Establishing the food and feed safety of MON 87708 × MON 89788 × A5547-127 is essential, considering it is destined for human and animal consumption.

However, it is critical to note that the applicant fails to present ANY experimental evidence from feeding studies that MON 87708 × MON 89788 × A5547-127 does not cause toxicity to mammals.

Nonetheless, numerous claims of safety have been made by the applicant. For example, the applicant concludes that: 1) MON 87708 × MON 89788 × A5547-127 is compositionally equivalent to conventional varieties of maize; 2) MON 87708 × MON 89788 × A5547-127 has a history of safe use; 3) the proteins of MON 87708 × MON 89788 × A5547-127 have no structural similarities to known toxins or other biologically active proteins that could cause adverse effects 4) the transproteins of MON 87708 × MON 89788 × A5547-127 are rapidly digested in mammalian gastrointestinal systems, and 5) the MON 87708 × MON 89788 × A5547-127 variety does not induce mammalian toxicity.

5.1 Issues regarding substantial equivalence

Substantial equivalence is a concept that states that if a new food is found to be 'substantially equivalent' to an already existing food product, it can be treated the same way as the existing product with respect to safety. It allows for the comparison of a GM line to any existing variety within the same species, and even to an abstract entity made up of ingredients from a collection of varieties. A GM variety can, therefore, have the worst traits of many different varieties and still be deemed substantially equivalent. This concept has been widely criticised by biosafety analysts for its crudity and flexibility in interpretation, as well as the procedures. These only compare gross measurements of, for example, total carbohydrates, proteins and sugars, which cannot begin to tackle issues of safety. The applicant, therefore, makes unsubstantiated claims of substantial equivalence that remain untested for any safety assessment.

These basic comparative tests of only 50 analytes included in the application do not allow for detailed and unbiased detection of compositional differences, and have since been shown to be outdated. This is highlighted by recent studies that have used more sensitive 'omics' global profiling technologies that analyse alterations at the genomic, RNA, protein and metabolite level, with the ability to analyse hundreds or even thousands of molecules at once. Such techniques have revealed differences in GM crops compared to their conventional counterparts that were not detected with the basic tests performed for standard risk assessment, including a 28-fold rise in potentially toxic polyamines in a GM maize variety (Mesnage et al., 2016).

Even with these basic tests, **6 components out of 50** (arginine, oleic acid, behenic acid, ADF, NDF and vitamin K1 in seed) showed a statistically significant difference ($p<0.05$) between MON 87708 × MON 89788 × A5547-127 and the conventional control.

Instead of relying on substantial equivalence analysis, the applicant should incorporate "omics" global profiling techniques now being used routinely in research laboratories.

5.2 'History of safe use'

There is no history of safe use of MON 87708 × MON 89788 × A5547-127 as the transgenes have been synthetically made. This is exemplified by the applicant's admission that the transgene product conferring tolerance to dicamba, called DMO, shows only up to a 41% identity to other proteins present in other species.

Further, there is no history of safe use of consumption of the triple-stacked variety. Nevertheless, the applicant states:

> "Conventional breeding has a history of safe use for combining genetic information for the improvement of crop plant varieties (CLI, 2011). There is no evidence that these inserts behave differently when combined by traditional breeding and therefore the traits in MON 87708 × MON 89788 × A5547-127 are expected to perform in the stack in the same way they do in the respective single."

However, combinatorial effects may occur due to interactions between the novel transproteins and metabolites produced in the stacked variety. For example, having multiple Bt toxins may have cumulative or synergistic effects on non-target organisms.

This is the basis for the EU regulation that requires risk assessment of stacked traits, which defines a stacked event derived from conventional breeding of existing single event GM varieties as a "new entity" (Regulation (EC) No 1829/2003). It takes into account the possibility of stacked varieties showing disturbances in transgene and host genome stability, expression of novel proteins, and potential synergistic/combinatorial interactions between the individual modifications. Such interactions in stacked events have been documented in stacked maize that carries both Bt toxins and glyphosate tolerance, showing alterations of transgene expression in the stacked versus single event lines (Vilberte et al., 2016).

5.3 Allergenicity assessment

The testing of allergenicity was based solely on bioinformatics predictions and not experimental data. The applicant states that they used an eight-amino acid sliding window search to specifically identify similarity of the potentially novel peptides to known allergens.

The 2001 FAO/WHO consultation on the assessment of possible allergenicity due to GM foods, however, had suggested moving from eight to six identical amino acid segment searches. Codex Alimentarius Commission (2004) notes, "*The smaller the peptide sequence used in the stepwise comparison, the greater the likelihood of identifying false positives, inversely the larger the peptide sequence used, the great the likelihood of false negatives, thereby reducing the utility of comparison*". Using six amino acids for comparison would therefore be more precautionary, and in line with the thrust of the GMO Act and the Cartagena Protocol on Biosafety, to which South Africa is a Party.

Further, soybean is one of the eight food groups known to elicit allergic responses in humans. Despite this, the applicant has presented no experimental data on the whole plant to show if the genetic modification process has increased allergenic properties or constituents of the plant.

The applicant should be asked to provide experimental data in laboratory animals showing a lack of allergenicity to the whole plant MON 87708 × MON 89788 × A5547-127.

5.4 Mammalian toxicity

The applicant fails to provide any experimental data to show a lack of toxicity of the whole plant MON 87708 × MON 89788 × A5547-127 in either acute of long-term feeding studies.

Al the above claims of safety can, therefore, be regarded as assumption-based and not evidence-based. Parental lines have not been tested either, with only the transprotein derived from bacteria being used in 14-day feeding trials. This is not sufficient to rule out adverse toxicological effects of parental lines, let alone the triple-stacked event.

We urge that the applicant be required to submit chronic mammalian feeding study data for MON 87708 × MON 89788 × A5547-127. Such experiments should use soybean that has been applied with glyphosate, glufosinate and dicamba, to reflect real-life exposure that would occur following consumption of this crop.

5.5 Pesticide toxicity

The critical health issue of pesticide toxicity has not been raised by the applicant. Further, this crop will be the first triple-herbicide tolerant variety to enter the South African market. This raises novel concerns surrounding the potential combinatorial toxicity resulting from exposure to glyphosate, glufosinate and dicamba and their metabolites.

The cultivation of GM crops tolerant to herbicides has led to a sharp increase in pesticide use, with 15-fold rises documented in the US (Benbrook, 2012) and an 858% rise documented in Argentina (Ávila-Vázquez, 2015). The rising use is being reflected in the pesticide burden in people. A new 2017 study now shows that glyphosate levels in US citizens has risen dramatically from 1993 to 2016 (Mills et al., 2017) from a mean of 0.024 to 0.314 µg/ml in 70 participants. This can, therefore, only be expected for the additional herbicides glufosinate and dicamba. Indeed, glufosinate has already been detected in urine of Canadian citizens (Aris & Leblanc., 2011).

As recently reported by ACB (2017), **there are no established safe levels** for these pesticides in foods. Conversely, evidence of toxicity of these pesticides and their metabolites is well documented in the scientific literature. Of critical importance to the South African context is that legal limits on pesticide residues for many food crops are yet to be established or fully regulated. **There appears to be no 'maximum residue level' (MRL) set for either glufosinate or dicamba on soybeans**, and in 2017 an MRL for glyphosate on soybean was established for the first time.

While safe levels are yet to be fully established, evidence of adverse effects of exposure to the three relevant pesticides is well documented. Glyphosate has been recently classified as a probable human carcinogen by the oncology arm of the WHO, the International Agency for Research on Cancer (IARC), forcing a delayed decision on its re-approval in the EU, yet to be resolved. Over 150 studies have shown adverse effects of glyphosate to humans and the environment (see Ávila-Vázquez, 2015 for a fully-referenced extensive review).

Glufosinate has also been shown in many studies to have adverse toxic effects on humans, such that its use was restricted in 2013 by the European Union. Toxic effects of glufosinate have been linked to its glutamate neurotransmitter-mimicking effects. This has been shown to disrupt brain signalling, resulting in learning and memory deficits, structural changes in the brain and impaired brain development in laboratory animals (Herzine et al., 2016;

Laugeray et al., 2014; Lantz et al., 2014; Meme et al., 2009; Calas et al., 2008;). In humans, paternal exposure has been linked to developmental defects in children (Garcia et al., 1998).

Dicamba is a synthetic hormone that has been linked to toxic effects, including reproductive and developmental toxicity in both regulatory and independent peer-reviewed studies. Multi- generation reproductive studies reported increased abortions, decreased food consumption and weight gain, with offspring displaying skeletal abnormalities (US Environmental Protection Agency, 2005). Low doses have also been shown to induce endocrine disruption (Zhu et al., 2015). Regulatory data submitted to EFSA has also shown mutagenic and toxic effects of dicamba. Toxic effects, including chromosomal aberrations caused by the metabolite DCSA, have also been noted by EFSA (2013). This metabolite is present on GM dicamba tolerant crops but the issue of pesticide toxicity or that of their metabolites has not been raised in the application.

These studies highlight the lack of scientific consensus surrounding the safety of these pesticides. We urge the applicant be asked to submit toxicity studies of the combined effects of the three pesticides and their metabolites to confirm lack of toxicity to the South African population, who will be exposed to these chemicals.

6. CONCLUSIONS

The above summaries of pesticide toxicity show that their safety is far from established, resulting in continued controversy over their approvals amongst national and regional regulatory bodies. The introduction of triple-stacked herbicide tolerant soybean into the South African market is risking the very safety of South Africa's soybean supply, adding further to other herbicide tolerant varieties already on the market. This will only result in increased toxic pesticide burden in the bodies of exposed people and animals.

We urge the government of South Africa to decline the approval of this crop until all the safety uncertainties that ACB has raised can be addressed by the applicant, and regulatory levels of safe legal limits of residues in foods are established by government.

REFERENCES

ACB (African Centre for Biodiversity) (2017) *No safe limits for toxic pesticides in our foods: Comments on draft regulations for MRLs*. https://acbio.org.za/wp-content/uploads/2017/07/No-Safe-Limits-for-Toxic-Pesticides-in-Our-Food.pdf.

Aris A & Leblanc S (2011) Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. *Reprod Toxicol* 3: 528–33.

Ávila-Vázquez M (2015) Devastating impacts of glyphosate use with GMO seeds in Argentina. *Banishing Glyphosate*. Special ISIS report. http://www.i-sis.org.uk/Banishing_Glyphosate.php.

Benbrook C (2012) Impacts of genetically engineered crops on pesticide use in the US – the first sixteen years. *Environmental Sciences Europe* 24: 24. doi: 10.1186/2190-4715-24-24.

Bollinedi H, S GK, Prabhu KV, Singh NK, Mishra S, Khurana JP, Singh AK (2017). Molecular and Functional Characterization of GR2-R1 Event Based Backcross Derived Lines of Golden Rice in the Genetic Background of a Mega Rice Variety Swarna. *PLoS One* 9:12(1):e0169600.

Calas AG Richard O, Même S, Beloeil JC, Doan BT, Gefflaut T, Même W, Crusio WE, Pichon J, Montécot C (2008) Chronic exposure to glufosinate-ammonium induces spatial memory impairments, hippocampal MRI modifications and glutamine synthetase activation in mice. *Neurotoxicology* 29: 740–7.

Codex Alimentarius Commission (2004) *Guideline for the conduct of food safety assessment of foods derived from recombinant-NA plants* (CAC/GL 45-2003). Rome: Food and Agriculture Organization of the United Nations and World Health Organization.

EFSA (2008) Opinion of the Scientific Panel on Genetically Modified Organisms on application (reference EFSA-GMO-NL-2006-36) for the placing on the market of the glyphosate-tolerant genetically modified soybean MON89788, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. *EFSA Journal* 758: 1–23.

EFSA (2013) Scientific Opinion on application EFSA-GMO-NL-2011-93 for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. *EFSA Journal* 11(10): 3355.

García AM, Benavides FG, Fletcher T & Orts E (1998) Paternal exposure to pesticides and congenital malformations. *Scand J Work Environ Health*. 24(6): 473–80.

Herzine A Laugeray A, Feat J, Menuet A, Quesniaux V, Richard O, Pichon J, Montécot-Dubourg C, Perche O, Mortaud S. (2016) Perinatal exposure to glufosinate ammonium herbicide impairs neurogenesis and neuroblast migration through cytoskeleton destabilization. *Front Cell Neurosci* 10: 191.

Ho MW (2013) Natural versus Artificial Genetic Modification. *Entropy* 15: 4748–4781.

Ho MW, Ryan A & Cummins J (1999) Cauliflower Mosaic Viral Promoter – A recipe for Disaster? *Microbial Health and Disease* 11: 194–197.

Lantz SR, Mack CM, Wallace K, Key EF, Shafer TJ, Casida JE (2014) Glufosinate binds N-methyl-D-aspartate receptors and increases neuronal network activity in vitro. *Neurotoxicology* 45: 38–47.

Latham J & Wilson A (2013) Potentially dangerous virus gene hidden in commercial GM crops. *Sci. Soc*. 57: 4–5.

Laugeray A Herzine A, Perche O, Hébert B, Aguillon-Naury M, Richard O, Menuet A, Mazaud-Guittot S, Lesné L, Briault S, Jegou B, Pichon J, Montécot-Dubourg C, Mortaud S. (2014) Pre- and postnatal exposure to low dose glufosinate ammonium induces autism-like phenotypes in mice. *Front Behav Neurosci,* 8, 390.

Meme S, Calas AG, Montécot C, Richard O, Gautier H, Gefflaut T, Doan BT, Même W, Pichon J, Beloeil JC. (2009) MRI characterization of structural mouse brain changes in response to chronic exposure to the glufosinate ammonium herbicide. *Toxicol Sci* 111: 321–30.

Mesnage R, Agapito-Tenfen SZ, Vilperte V, Renney G, Ward M, Séralini GE, Nodari RO & Antoniou MN (2016) An integrated multi-omics analysis of the NK603 Roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process. *Sci Rep* 19 (6): 37855. doi: 10.1038/srep37855.

Mills PJ, Kania-Korwel I, Fagan J, McEvoy, Laughlin GA & Barret-Connor E (2017) Excretion of the herbicide glyphosate in older adults between 1993 and 2016. *JAMA* 318: 1610–1611. doi:10.1001/jama.2017.11726.

Suarez I, G Bodega & Fernandez B (2002) Glutamine synthetase in brain: Effect of ammonia. *Neurochem Int* 41: 123–42.

Science in Society. 2015. *Banishing Glyphosate*. A Special I-SIS Special Report. http://www.i-sis.org.uk/ Banishing_Glyphosate.php.

US Environmental Protection Agency (2005) EFED Reregistration Chapter For Dicamba/Dicamba Salts. Office of Prevention, Pesticides and Toxic Substances, Office of Pesticide Programs, US Government Printing Office EFED Re-registration Chapter For Dicamba/Dicamba Salts. Washington, DC.

Vilperte V, Agapito-Tenfen SZ, Wikmark OG & Nodari RO (2016) Levels of DNA methylation and transcript accumulation in leaves of transgenic maize varieties. *Environ Sci Eur*. 28: 29

Zhu L, Li W, Zha J & Wang Z (2015) Dicamba affects sex steroid hormone level and mRNA expression of related genes in adult rare minnow (*Gobiocypris rarus*) at environmentally relevant concentrations. *Environ Toxicol* 30(6): 693–703. doi: 10.1002/tox.21947.