
A critical assessment of the paper ‘GM Soy: Sustainable? Responsible?’

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Table of contents

| | |
|---|----|
| Executive summary | 2 |
| 1 Introduction | 6 |
| 2 Response to claims relating to toxic effects of glyphosate and Round-up: evaluation of the safety of glyphosate. | 6 |
| 2.1 How do we know glyphosate is unlikely to harm humans and animals?..... | 6 |
| 2.2 Just how toxic is glyphosate? | 6 |
| 2.3 Does glyphosate cause birth defects? | 7 |
| 2.4 All things are poison..... | 9 |
| 3 Response to claims made about hazards of genetically modified foods and crops | 10 |
| 3.1 Genetic Engineering and GM foods | 10 |
| 3.2 How are GM foods regulated? | 12 |
| 3.3 The Devil is in the Details | 13 |
| 3.4 Lies, Damn Lies, and Statistics | 15 |
| 3.5 Whom do you believe? | 17 |
| 4. Response to claims made about the agronomic and environmental impacts of GM RR soy ... | 17 |
| 4.1 A claim that GM crops do not increase yields | 17 |
| 4.2 A claim that weed resistance to glyphosate is ‘the major agronomic problem associated with GM RR soy cultivation’ and that the GM HT technology is unsustainable’ | 18 |
| 4.3 The claim that GM HT soybean herbicide usage has increased to the detriment of the environment..... | 19 |
| 4.4 Claims about negative ecological and agronomic impacts of glyphosate use with GM HT soybeans | 25 |
| 5. Response to claims of negative socio-economic impacts of GM RR soy | 27 |
| 5.1 A claim of negative socio-economic impacts of soybean production in Argentina | 27 |
| 5.2 Claims of negative economic impacts in the US..... | 28 |
| 5.3 Claims that farmers pay too high a price for GM seeds and access to non GM seed is restricted..... | 28 |
| 5.4 A claim that Monsanto has a near monopolistic control over seed and agrochemical markets | 30 |
| References | 30 |

Executive summary

In 2010, Antoniou et al published a paper entitled *GM Soy: Sustainable? Responsible?* This made a number of claims of alleged negative impacts associated with the global use of genetically modified (GM) soybeans on human and animal health, on environmental safety and on socio-economic status.

This briefing note examined and assessed the main claims made in this paper.

1. *¹Claims of ‘a large and growing body of scientific research revealing serious health and environmental impacts. The adjuvants (added ingredients) in Roundup increase its toxicity. Harmful effects from glyphosate and Roundup are seen at lower levels than those used in agricultural spraying, corresponding to levels found in the environment’.*

No health impacts are documented in the published text; the majority of the scientific literature that shows a lack of (negative) health effects and a lack of safety problems is not mentioned or cited. There is no evidence that the adjuvant increases toxicity. The harmful effects that are seen at ‘lower levels than those used’ are a misleading statement in two-ways:

- The concentration sprayed is not the dose to which humans and animals will be exposed – what matters is what they ingest;
- The so-called harmful effects were observed only when routes of exposure that would not occur in actual usage are employed, as for example, injection of glyphosate directly into cells *in vitro* (because this route by-passes the absorption, distribution, metabolism and excretion system of whole organisms it is not a valid model for studying toxic effects).

2. *Claims that ‘The widespread spraying of glyphosate on GM Roundup Ready (RR0 soy, often carried out from the air, has been linked in reports and scientific research studies to severe health problems in villagers and farmers. A recently published study links glyphosate exposure to birth defects’*

Although the major route of application of glyphosate is not aerial application, it is sometimes sprayed from the air according to safety guidelines mandated by, for example, the Environmental Protection Agency (EPA) in the US, or equivalent agencies in other countries. Studies cited by Antoniou et al were not able, or did not attempt to establish a causal link between glyphosate and health problems (in the full text the authors claim only that the possible existence of a link should be investigated further); the study on birth defects does not even mention glyphosate *per se* but rather focuses on proximity to ‘pesticides’ without documentation of exposure or dose.

3. *A claim that ‘Contrary to claims by the GM industry and its supporters, the US Food and Drug Administration (FDA) has never approved any GM food as safe. Instead, it de-regulated GM foods in the early 1990s, ruling that they are ‘substantially equivalent’ to non-GM foods and do not need any special safety testing....In fact, ‘substantial equivalence’ has never been scientifically or legally defined’*

¹ Claims made in the report *GM Soy: Sustainable? Responsible?* are presented in italics to assist readers in following the analysis

The claim that the FDA has never approved a GM food as safe is a disingenuous play on words in that it misrepresents how the regulatory system works. Under US regulations, the FDA does not *approve* foods *per se* but rather accepts or rejects developers' evidence that their product is safe. Without exception, every GM product in the US market has been subjected to a safety review and the FDA has issued a letter to the developer that states that FDA has no further concerns about safety. It is noteworthy as well that most GM products have been *approved* for consumption in other countries that have a direct approval process.

The FDA has not declared that GM foods are '*substantially equivalent*' or that they do not require any specific testing. Antoniou et al distort, or fail to comprehend, that application of the substantial equivalence concept does not lead to a conclusion that two foods are substantially equivalent. Under this concept the composition of two foods are compared and it is assumed that components that are present in essentially equal quantities present similar benefits and risks. Further safety assessment is then focused on the *differences* in composition that are observed. The logic of this comparative safety assessment process is well documented in peer-reviewed scientific literature.

4. *Claims that 'a number of studies have found health hazards and toxic effects associated with GM RR soy. These include cellular changes in organs, more acute signs of ageing in the liver, enzyme function disturbances, and changes in the reproductive organs. While most of these studies were conducted on experimental animals, the findings suggest that GM RR soy may also impact human health. This possibility has not been properly investigated'*

Antoniou et al make these claims based on studies that:

- do not in fact claim harmful health effects were observed (ie, Antoniou et al misrepresent the findings of research);
- are flawed in design and execution and/or are inadequately described/documentated;
- do not follow internationally-established protocols for animal studies and toxicological evaluation, or
- apply *in vitro* approaches which are irrelevant for the study of harmful effects *in vivo*.

In each case, regulatory agencies in various countries have considered these reports and discounted their value in safety assessment. Original research reports and academic and regulatory agency reviews that conclude glyphosate (and its commercial preparations) are safe when used as directed are systematically ignored in the report.

5. *Claims that GM soy delivers low yields (ie, lower than conventional soy), interferes with nutrient uptake and increases plant susceptibility to pests and diseases*

In making these claims, Antoniou et al drew on unrepresentative and non peer reviewed papers, and ignored the significant literature that quantifies the benefits derived from using the technology; lower costs of production, additional weed management flexibility and convenience, the facilitation of no tillage production systems and the associated second crop (additional) soybean production in South America, and higher yields for some farmers (e.g. in

Bolivia and Romania). At the commercial farm level, there are no empirical studies that show statistically significant differences in yield between GM herbicide tolerant (HT) soybeans and conventional soybeans or in the rate of application of fertiliser or crop protection products (other than herbicides). This suggests that the claims made about negative impacts of nutrient uptake and pest/disease susceptibility are without foundation.

6. Claims that the major agronomic problem associated with GM RR soy cultivation is weed resistance to glyphosate and that the GM HT soy technology is unsustainable

These claims grossly exaggerate reality; there are currently only 21 weeds recognized as exhibiting resistance to glyphosate worldwide, of which several are not associated with glyphosate tolerant crops. It should, however, be acknowledged that where GM HT crops have been widely grown, some farmers have relied too much on repeated use of single herbicides like glyphosate to manage weeds and this has contributed to the development of resistant weed biotypes in some regions.

Whilst the overall level of weed resistance in areas planted to GM HT crops is still low, growers of GM HT crops are increasingly being advised to be more proactive and consistent with better agronomic practices based on the use of other herbicides (with different and complementary modes of action) in combination with glyphosate in their weed management systems, even where instances of weed resistance to glyphosate have not been found. Nevertheless, both reactive and proactive weed management programmes in GM HT crops continue to offer advantages relative to the conventional alternative and deliver better environmental profiles than the conventional alternative².

7. Claims that as a result of the widespread adoption of GM HT soybeans, herbicide usage has increased to the detriment of the environment

Antoniou et al (2010) cite non peer-reviewed, inaccurate and misleading papers to 'support' these claims. In particular, the main papers cited (by Benbrook in 2005 and 2009) rely on the author's assumptions about usage of herbicides on GM HT soybeans and its conventional alternative that do not reflect actual recorded practice (ie, overstate usage on GM HT soy and understate usage on conventional soy). The credible evidence in peer reviewed papers (e.g. Brookes G & Barfoot P (2011b) that have examined this issue shows that the adoption of GM HT soy has changed the profile of herbicides used to control weeds and facilitated many farmers adopting a no tillage production system. In some cases, this has resulted in increases in the amount of herbicide active ingredient applied to crops relative to the conventional alternative but the associated environmental profile of the herbicides used on GM HT soy has consistently been better than the conventional alternative.

² Also, many of the herbicides used in conventional production systems had significant resistance issues themselves; this was, for example, one of the reasons why glyphosate tolerant soybeans were rapidly adopted, since glyphosate provided good control of these weeds

8. Claims about negative ecological and agronomic impacts of glyphosate use with GM HT soybeans

These claims draw heavily on non peer-reviewed papers that are inaccurate, make unsubstantiated claims.

9. Claims of negative socio-economic impacts

These are based on a combination of non peer-reviewed papers, press cuttings and misrepresentation of analysts work³. They also try to claim a link between the use of GM HT soybeans with all manner of social problems in South America, like unemployment and poverty in rural communities, concentration of agricultural production in the hands of a small number of large-scale operators and a perceived reduced level of food security. Antoniou et al ignore the consistent body of evidence in peer reviewed literature that quantifies the farm economic benefits that soybean farmers have derived from using the technology and of the additional production (of soybeans) that the technology has facilitated in South America (through its facilitation of no and reduced tillage production systems and wider cropping of 'second crop soybeans').

10. Claims that farmers pay too high a price for GM seeds and that access to non GM seed is restricted

These claims made, largely in respect of the US market, are highly dependant upon the assumptions used and perceptions of a cited author (Benbrook (2009b)) as to how seed markets work and farmers behave. The mainstream market evidence does not support the views expressed by Benbrook.

Overall, the paper *GM Soy: Sustainable? Responsible* contains very little credible science, is a catalogue of inaccuracies and makes misleading and inappropriate use of data. It includes a number of previously published allegations and concerns about the safety of GM crops, which have been examined and reviewed by regulatory authorities and independent specialists. In short, the paper provides nothing new or substantive to question the safety of GM crops.

The paper also claims '*that promised benefits to farmers of GM crops have not materialized and unexpected problems have arisen*'. There is, however, a significant and consistent body of peer reviewed literature that confirms the opposite, with GM crop technology proving very popular with the farmers that use it because of the agronomic, economic and environmental benefits it has consistently delivered.

³ In other words, taking out of context comments and conclusions of early analysis of impacts of GM crops in North America

1 Introduction

In 2010, a monograph entitled *GM Soy: Sustainable? Responsible?* was published by Antoniou M et al. This paper made a number of claims of alleged negative impact associated with the global use of genetically modified (GM) soybeans on human and animal health and safety, on the environment, agronomically and economically.

This briefing note presents an independent assessment, undertaken by Professor Bruce Chassy of the University of Illinois and Graham Brookes, agricultural economist at PG Economics.

The briefing note examines the main claims and literature cited by Antoniou et al (2010) and is structured into sections that largely correspond to the issues examined, and structure of the original report.

2 Response to claims relating to toxic effects of glyphosate and Round-up: evaluation of the safety of glyphosate.

2.1 How do we know glyphosate is unlikely to harm humans and animals?

The authors of *GM Soy: Sustainable? Responsible?* commence a discussion of the safety of glyphosate with the assertion that manufacturers claim glyphosate is a relatively safe herbicide since it inhibits an enzyme that is not present in humans or animals. While it is true that humans lack the enzyme inhibited by glyphosate, that fact does not in any way establish the safety of glyphosate; a demonstration of the safety of a chemical depends on rigorous toxicological evaluation. The lack of the target enzyme of glyphosate may, however, be a partial explanation for the fact that glyphosate is one of the safest pesticides in widespread use around the globe. The toxicological safety of glyphosate has been established through dozens of carefully designed and well executed scientific studies that have been published in the peer-reviewed scientific literature; studies that are largely ignored by the authors of the present study (see for example: Williams et al (2000), EU (2002), WHO/FAO (2004). The safety of glyphosate has also been rigorously evaluated by regulatory agencies around the world. Both the safety and efficacy of glyphosate have been established over almost 40 years of use in the field.

2.2 Just how toxic is glyphosate?

The authors refer to glyphosate as a toxic herbicide, perhaps in the hope that readers will assume that all *man-made chemicals* are highly toxic, however, they never tell the reader that glyphosate is equally toxic to the common cooking ingredients table salt and baking soda. The US Environmental Protection Agency (EPA) assigns glyphosate to the lowest class of toxic agents. It does not bio-accumulate in the body and it does not persist in the environment. More importantly, the compound is only partially absorbed through skin or by an oral route of administration in humans and animals; absorbed glyphosate is excreted largely unchanged in urine. A small amount is converted to AMPA, a metabolite that is similar in structure and

toxicity to glyphosate. The ADI for glyphosate (ADI = acceptable daily intake – a value that is 100-fold lower than the lowest level at which adverse effects are first observed in animal studies) has been set at 0.3g/Kg/day. That corresponds to about 21g – or about one heaping teaspoonful -- for a 70kg male human. That means that the average person could consume a teaspoonful each day and remain safely below the level at which adverse effects might be seen. The estimated highest daily intake for humans is about 5% of the ADI (<1% is typical) so exposure can be expected to remain far below levels of concern. A similar low level of exposure to AMPA has been estimated.

The authors note that the EU permits glyphosate residues in edible crops to be 20-fold higher than for any other herbicide; a similar high residue level has been set in Brazil. The authors attribute the setting of high residue levels to political pressure from Monsanto. There is, however, an extensive and well-documented record that regulatory agencies around the globe raised permissible residue levels because animal studies in numerous species of animals have established that high levels of exposure to glyphosate, and adjuvant-containing glyphosate preparations, throughout a lifetime resulted in no adverse-effects. No adverse effects have been seen in multi-generational studies. Studies have demonstrated repeatedly that glyphosate is not a mutagen, does not cause cancer, is not a teratogen, does not interfere with reproduction, is not an endocrine disrupter, and produces no neurological effects. Other studies have demonstrated that animals exposed to high levels of glyphosate display normal size and weight gain, metabolism, blood chemistry, organ weights and function, reproduction, skeletal development, physical activity and appearance (Williams et al (2000), EU (2002), WHO/FAO (2004); <http://extoxnet.orst.edu/pips/glyphosa.htm>)

2.3 Does glyphosate cause birth defects?

The monograph *GM Soy – Sustainable? Responsible?* highlights at some length a recently published study from an Argentine research group headed by Professor Andrés Carrasco⁴. The study reports that glyphosate caused birth defects when injected into chicken and frog embryos (Paganelli, et al (2010)). Professor Carrasco claims that the effects are not due to the adjuvant used in glyphosate preparations and that they depend directly on interference with “key molecular mechanisms” by glyphosate. Professor Carrasco asserts “The findings in the lab are compatible with malformations observed in humans exposed to glyphosate during pregnancy.” Since the publication of his work, Professor Carrasco has resigned his position and now travels throughout Argentina and South America speaking to audiences about the dangers of glyphosate. Professor Carrasco is a co-author of *GM Soy: Sustainable? Responsible?* As can be imagined, in a country that is the world’s 3rd largest producer of soybeans—over 95% of them herbicide-tolerant GM soybeans—Carrasco’s claims about the hazards of glyphosate received a great deal of attention from the scientific community, the government and the media. What the authors neglect to tell the reader is that critical reviews of the study have also been published (Mulet (2010), Palma (2010), Saltmiras et al (2010)) – an objective review would have

⁴ University of Buenos Aires Medical School

cited these letters which point out numerous deficiencies and flaws in the study published by the Carrasco group.

The critical problem with Carrasco's study is that the experimental design of the study is not appropriate for testing if glyphosate causes birth defects as claimed. In this study, glyphosate was injected directly into embryos. As a consequence, cells were exposed to extraordinarily high levels of glyphosate. These levels are far higher than would result from exposure to glyphosate residues in food or feed; the levels were so high that they could have lowered the intracellular pH to lethal levels. It is well known that direct injection of normally innocuous chemicals into cells and embryos can cause birth defects and other adverse effects. Caffeine⁵ and phenobarbital, for example, cause similar birth defects when injected into embryos (Kobayashi et al (1995)). Direct injection bypasses the protective embryo gel coat and short-circuits the normal route of exposure (eg. oral uptake or direct absorption through skin). In order to achieve the concentration of glyphosate used in the experiments from food or feed an oral dose of more than 6g glyphosate/Kg/day would have been required (Saltmiras et al (2010)). This corresponds to a 200 g rat consuming 60Kg/day of soybeans containing the EU maximum legally allowable residue level of 20mg/Kg!

What about the claim that the effects observed in laboratory experiments mirror birth defects observed in epidemiological studies in Argentina and Paraguay? The studies that are cited in Paganelli, et al (2010)) are flawed to the extent that no association between glyphosate exposure and birth defects can be drawn (Mulet (2010) Palma (2010), Saltmiras et al (2010)). It is instructive to consider the analysis of these claims provided in Saltmiras et al (2010):

" (b) Flawed premise: The authors provide no valid basis, other than an opinion, of an increase in the rate of birth defects in Argentina. The referenced epidemiology paper implied by the authors as justification for implicating glyphosate as a chemical of concern does not mention glyphosate or even distinguish between herbicide, insecticide, molluscicide, rodenticide, or fungicide potential exposures to pregnant women. This small epidemiological study, conducted in Paraguay, investigated associations between proximity or assumed exposure to pesticide use/storage and congenital malformations in neonates. The association between "living near treated fields" (distance and pesticide types unspecified) and congenital malformations was weak, with an odds ratio about six times lower than the reported association between pesticide storage in the home and congenital malformations. There is nothing unusual about the wide variety of birth defects reported in the Paraguay study and it provides no support for the authors' allegation that they "strikingly resemble the wide spectrum phenotypes resulting from a dysfunctional RA or Shh signaling pathway."

There are additional compelling reasons to believe that neither glyphosate nor glyphosate resistant GM soybeans contribute to birth defects:

⁵ Caffeine is more than 10-fold more toxic than glyphosate (LD50 = 192mg/Kg in rats) but the average American consumes about 2 gm per day.

- A number of high quality animal feeding studies reported in the peer-reviewed literature have shown that no birth defects occur when animals are fed high levels glyphosate;
- Although production animals are routinely fed large quantities of GM-soybeans, no increase in birth defects has been reported;
- There is no epidemiological evidence that the incidence of birth defects has increased where GM soybeans have been introduced;
- An additional reason to believe that glyphosate does not cause birth defects is found in the Farm Exposure Study discussed by Saltmiras et al (2010) but not cited by Paganelli, et al (2010). In this study, serum levels of glyphosate were measured in farm family members who lived in close proximity to areas of intensive glyphosate spraying (Acquavella et al (2004)). The highest concentration of glyphosate observed in subjects was 0.04 µg/Kg body weight; 95% of subjects had levels that were below the lower limit of detection. These results demonstrate that in the real world, use of glyphosate results in very low levels of exposure and absorption. A number of high quality animal studies that demonstrate that glyphosate does not cause birth defects, reproductive problems, or cancer at levels of exposure millions of times higher than the levels measured in human subjects who had been exposed to glyphosate. These results may also provide a sound basis for disregarding other reports cited by Paganelli, et al (2010) that claim adverse effects of glyphosate (e.g. cancer).

Professor Carrasco has responded to the criticism of his groups' publication (Carrasco (2011)). The response does not fully respond to the criticism of his work, but instead raises additional issues and examples while rejecting all data and papers produced by the industry (see also sub-section 3.5 'Whom can we trust?').

The reader is encouraged to study Professor Carrasco's letter and judge for themselves if he has made his case. It is noteworthy as well that Professor Carrasco is a co-author of *GM Soy: Sustainable? Responsible?*⁶

2.4 All things are poison.

Paracelsus (Philippus von Hohenheim, 1493-1541), considered to be the father of the modern science of toxicology, taught us "*all things are poison, it is only the dose that makes that a thing is not a poison.*" As previously noted, glyphosate is about as toxic as table salt or baking soda. The authors of *GM Soy: Sustainable? Responsible?* ignore a body of scientific literature that establishes

⁶ The European Commission's Health and Consumers Directorate-General (DG SANCO) "invited Germany, the original Rapporteur Member State which evaluated glyphosate prior to its EU-wide approval in 2001, to provide its views on the above studies, the validity of their methodology, and, importantly, their relevance to the normal evaluation and application of glyphosate as a pesticide". In the Session on 22-23 November 2010, of the Standing Committee on the food chain and animal health, Section Phytopharmaceuticals – Plant Protection Products Legislation, it was reported that "the German authorities came to the conclusion that the above studies had been performed under highly artificial conditions, extremely different from what can be expected in agricultural circumstances, and that it is hardly possible to predict adverse effect on mammals on this basis". "Germany therefore concludes that the findings of the studies do not put into question the current EU risk assessment for the substance and the products used in the EU that contain this substance with regard to human health."

the relatively low toxicity of glyphosate, while they cite a handful of dissenting papers. These papers share one or more common shortcomings. In many cases the dose used in the experiments (e.g, with animals, cells, embryos) was unrealistically high; high levels of many chemicals *per se* can damage cells. The authors frequently compare these doses to the commercial concentrate that is sprayed on crops rather than to the dose that corresponds to the level of oral intake that can be estimated from the residue level in food or feed multiplied by the average daily intake. The route of exposure can also dramatically affect the outcome of a toxicological evaluation. As noted previously many chemicals that are innocuous when swallowed are toxic when injected into cells. Most outlying studies that claim adverse effects of glyphosate follow this design (Paganelli, et al (2010), Benachour and Séralini (2009). In order to avoid such methodological traps, internationally accepted standardized protocols are used in toxicological evaluations appearance (Williams et al (2000), EU (2002), WHO/FAO (2004)). The studies cited by *GM Soy – Sustainable? Responsible?* generally do not follow standardized protocols or regulatory guidelines.

3 Response to claims made about hazards of genetically modified foods and crops

3.1 Genetic Engineering and GM foods

Humans have been genetically modifying crop plants (as well as animals and microbes) for thousands of years (Parrott (2010), Chassy (2010a), Chassy (2010b)). Almost none of our crops are natural in the sense that they do not occur as such in nature but are descendents of wild plants that have been domesticated. The process of domestication introduced genetic changes that improved yield, cultivation, harvesting, size, taste, colour, palatability and a host of other traits that made them more desirable to plant and eat. Domesticated plants have typically lost the ability to grow in the wild and must be planted, nurtured, and harvested by farmers. While ancient farmers depended on random changes that occurred in plants as a source of genetic diversity for the production of new varieties, by the 19th century crop breeding began a migration into laboratories where breeders learned to accelerate the rate of DNA mutation in plants which shortened the time required for production of new crop varieties for agriculture. The first transgenic⁷ microbe was produced in 1973 and the first transgenic GM plant was reported in 1982.

Gene transfer methods allowed scientists to produce organisms containing new traits such as resistance to specific insects, viruses, or herbicides. *GM Soy: Sustainable? Responsible?* asserts that genetic engineering produces combinations of genes that would not naturally occur in nature as if this fact by itself should be a concern. That statement is not precisely accurate. While it is true that such combinations are highly unlikely to occur naturally – that is why biotechnologists accelerate them in the laboratory – it is in fact possible that such an event could happen since the pieces of DNA that are used in transgenic plants occur naturally, and it is now

⁷ “Transgenic” in this case means that pieces of DNA containing a whole gene or several genes were been linked together in a laboratory and inserted into a living organism by a process called transformation. The technology is also called recombinant DNA technology (rDNA), or the new biotechnology.

known that genes naturally transfer between organisms by a process called horizontal evolution.

The important question is if transferring genes *in vitro* between organisms poses increased risks of harm to humans, animals, or the environment. An expert panel convened by the National Academy of Science (USA) studied that question and concluded that transgenic breeding posed no new or different risks compared to conventional breeding (NAS (1987)). NAS has revisited the question over the last 25 years with three additional expert panels all of which have come to the same conclusion. The Royal Society (London), the German and French Medical Societies, the International Council for Science, the OECD and numerous other scientific societies, medical societies and national academies of science around the world have all come to the same conclusion: transgenic breeding is simply breeding, if the new trait that is introduced presents no unacceptable risks, then the crop plant should be as safe as any other.

The authors of *GM Soy: Sustainable? Responsible?* disagree with a global scientific consensus that GM plants pose no special risks. They describe GM plants as unnatural and claim that they could be harboring unintended and potentially harmful genetic changes since the inserted genes might produce unanticipated effects in alien hosts and the act of inserting them could have disrupted the chromosomes of the plant in unforeseen ways. There are three lines of evidence that support the conclusion reached by the NAS 25 years ago that GM crops pose no special risks.

All breeding involves changing DNA, and all changes in DNA pose the chance that unintended changes might occur (Cellini (2004), Parrott (2005), Parrott (2010)). It is certainly true that breeding can produce unintended and unforeseen effects. A major part of the plant breeders' efforts are devoted to selecting plants for further study that display the fewest unintended effects and which most closely resemble the parental variety in all aspects except the intended changes that are sought. *In vitro* transgene insertion is a more precise and better defined means to introduce a new trait than are the more random and chaotic methods used by breeders before the introduction of rDNA technology. Fewer more precise and better-understood changes imply that fewer unintended effects will be created.

Until recently, plant breeders did not have the tools that would allow them to trace the numerous DNA-changes that occur during the process of conventional plant breeding. Thirty years of research in molecular genetics of plant breeding has now demonstrated that transgene insertion produces fewer and less disruptive genetic changes than other modalities of plant breeding that are used to develop new crop varieties (Parrott (2005), Parrott (2010)). Genomic, proteomic and metabolomic analyses support the conclusion that plant varieties produced using transgene insertion more closely resemble the parental strain in gene expression, protein content (the proteome), and composition (the metabolome) than do different varieties of the same crop (Ricroch et al (2011)).

Abundant evidence now supports the conclusion that genetic engineering is *less likely* to unintended adverse effects than are other methods of breeding. From a scientific perspective, it is ironic that the more precise and presumably less risk technology of genetic engineering has become the focus of controversy.

3.2 How are GM foods regulated?

GM foods differ from conventionally bred food and feed plants in one other important way: their safety is assessed before they are introduced into the market. Crops bred using older methods that produce numerous random changes in the genome are not subjected to pre-market safety review. Perhaps this is because there is a long history of safe use of plant breeding to provide improved varieties of these edible foods and feeds. In marked contrast, transgenic crops are subjected to a rigorous safety assessment prior to approval and marketing that seeks to evaluate 1) if the inserted DNA presents could be harmful, 2) if the newly introduced trait could produce adverse effects, or 3) if any unintended or unforeseen adverse changes have occurred. The process takes many millions of dollars and 5-10 years to complete for each new crop as regulators around the world demand detailed data on every aspect of the molecular structure, composition, and effects of consumption of each new variety.

The claim that the FDA has never approved a GM food as safe is a disingenuous play on words in that it misrepresents how the US regulatory system works. The authors are apparently trying to create the false impression that there is no pre-market testing or regulatory oversight of GM food and feed safety in the US. Under US regulations, the FDA does not *approve* foods *per se* but rather accepts or rejects developers' evidence that their product is safe. Thus, under US law and unlike law in the EU and some other countries, the developer and marketer are liable for damage caused by a product, not the regulatory agency. Without exception, every GM product in the US market has been subjected to a safety review and FDA has issued a letter to the developer that states that FDA has no further questions or concerns about safety; receipt of the letter indicates that the developer has satisfactorily completed a pre-market consultation with FDA. The authors fail to mention that many of GM products that have received a letter from FDA have been *approved* for consumption in other countries that have a mandatory approval process. GM-soy has been reviewed and approved for use as food or feed by regulators around the globe; it is the world's leading GM crop. Regulatory agencies have reviewed the studies and claims presented in *GM Soy: Sustainable? Responsible?* and found them to be without merit.

The FDA has not declared that GM foods are "*substantially equivalent*" or that they do not require any specific testing. The authors distort, or fail to comprehend, that application of the substantial equivalence paradigm does not lead to a conclusion that two foods are substantially equivalent. Under this paradigm the composition of two foods are compared and it is assumed that components that are present in essentially equal quantities present similar benefits and risks. Further safety assessment is then focused on the *differences* in composition that are observed. The logic of this comparative safety assessment process is well documented in the peer-reviewed scientific literature (Chassy et al (2004), Chassy et al (2008)).

GM soy has been cultivated commercially since 1996. It is planted on a greater land area than any other GM crop. The GM soybeans have been used to feed domestic animals and as a protein and food ingredient source for human food; over 200 million metric tons of GM soybeans were harvested in 2010. Although many unfounded claims of harmful effects have been made, no documented and verified report of harm to humans or animals has appeared.

3.3 The Devil is in the Details

The authors of *GM Soy: Sustainable? Responsible?* find fault with the EU regulatory approval process applied to GM crops because whole food feeding studies in animals are not required by regulation. They then present a series of claims of adverse effects on health caused by herbicide-tolerant GM soy that are based on animal feeding studies. The report singles out a multi-generation study (Brake and Evanson (2004)) for criticism and asserts that poor quality studies are used to support the approval process.

Animal studies that are submitted to regulators are required to follow internationally accepted guidelines for design and conduct; the US Food and Drug Administration (FDA), the Organisation for Economic Co-operation and Development (OECD), the US Environmental Protection Agency (EPA) and other international bodies have published guidelines for appropriate conduct of studies (see in Cromwell (2003), Hartnell (2007)). Experiments are performed under GLP (Good Laboratory Practices) and are typically conducted by bonded and certified laboratories. Misconduct or misrepresentation of studies is a felony punishable by fines and/or imprisonment.

Animal studies that have followed international guidelines have consistently produced data that has satisfied regulators around the globe that the GM crop being assessed produced no adverse effects in animals. And it can be fairly argued that the regulatory review process is far more rigorous than is the peer-review process employed by scientific journals. This is because standardized protocols and guidelines must be carefully followed using GLP, more extensive data sets are required, there is no length limitation to the size of the data set and often no limitation on length of time for the review, and the process is conducted by internal agency scientists as well as a panel of expert independent academic experts. It is far easier to publish a faulty paper – a point to which is returned to below – than it is to gain approval of a faulty GM product. In fact, none has thus far been approved.

Brake and Evanson (2004) conducted an extended 4-generation rigorously designed study of GM soy that focused on any potential impacts on mammalian testis which are a powerful surrogate for overall good health; the study included data on growth rates and animal health. Data indicated there were no observable differences between test and experimental groups, rates of reproduction were no different, and not a single mortality was observed in the course of the study. The authors criticize the study because it did not “look for toxic effects in other organs” and no evidence was presented that the experimental and control soybeans were in fact different. A comparison of the chemical composition of the two diets used in the study was reported. We would also observe that no attempt was made to evaluate soy-derived isoflavone

phytoestrogen content of diet. This is important since soy isoflavones might be expected to have a direct effect on the reproductive system.

The Brake and Evanson study focused on multi-generational reproductive effects. It did not follow internationally accepted guidelines for animal studies – it was a research study -- and the data were not used to support the approval of GM-soy. Why then do the authors of *GM Soy: Sustainable? Responsible?* devote attention to this study? There are two reasons: 1) they most likely could not find fault with the numerous high quality studies that have been submitted to regulatory agencies, and 2) the Brake and Evanson study directly contradicts claims of reproductive failure observed in GM soy feeding studies reported by Ermakova that were not published in the peer-reviewed literature (Marshall (2007)).

The report states in regard to the Brake and Evanson study:

“Several aspects of the study are poorly described. The authors do not state the amount of non-GM soy that was put into the non-GM diet. They do not specify the amount of either diet consumed by the mice. The feeding protocol, weights of each animal, and growth pattern related to feed intake are not recorded. All these factors are relevant to a rigorous nutritional and toxicological study and yet are not accounted for.”

Let's for the moment accept these criteria and also add the requirement that closely related varieties of soy should be used as test and control, the diet composition, the GM content of the test (GM) and control (conventional) soybeans, and the isoflavone content of the soybeans should be reported. If we then look at the collection of papers that are cited to support the claim the GM-soy causes adverse health effects we find that *none of the papers cited by the authors meets the criteria they set in their criticism of Brake and Evanson!* And none fully meet the additional criteria added by the present author. It should not shock the reader to be told at this point that with but one exception (amount of ration consumed per diem), this is part of the data set specified by international guidelines and this data is supplied to regulatory agencies by developers of GM products.

It is instructive to observe just how little attention the studies cited in the report give to the data expectations of the report's authors. For example, a series of papers by a group headed by Malatesta are cited (Malatesta et al (2002) and others). Each of the papers provides only the following scant description of soybeans, diet, composition, and animal feeding and growth determination:

“Twelve female Swiss mice were fed ad libitum on a standard laboratory chow (Mulino & Frantoio del Trasimeno, Castiglione del Lago, PG, Italy) containing 14% GM soybean (Padgett et al (1995); in parallel, 12 (control) mice were fed on the same diet with wild soybean. Both animal groups started their respective diets at weaning. The animals were weighed and then killed by cervical dislocation at 1, 2, 5 or 8 months of age.”

The studies cited in the report do not meet the very criteria that the authors themselves (and international accepted guidelines) set for conduct of the animal feeding studies. There are a great many other deficiencies in the studies that claim adverse effects of feeding GM soy cited by the authors; some of these are reviewed at <http://academicsreview.org>

3.4 Lies, Damn Lies, and Statistics

It is instructive to read exactly what the cited studies actually conclude about health effects of feeding GM soy. For example, a study cited by the report as documenting the harmful effects of GM soy concludes (Tudisco et al (2006)):

“Anyway, since no diseases were detected in treated animals and serum activities of all the enzymes showed similar levels between the groups, it should be over-speculative to assess that the GM diet is responsible for that but it is a fact that the synthesis of LDH changed in more than one organ and such results should be taken into account for future research.”

A careful review of the studies cited in the report reveals the following:

- None conform to internationally accepted protocols;
- Most do not compare closely related soybeans, and;
- None of the peer-reviewed papers actually demonstrates a harmful or adverse health effect – at best what can be concluded is that a few statistically significant differences were observed between test and control groups. A few of the studies apply *in vitro* models that are not relevant for the study of harmful effects *in vivo*. Not all of the studies cited were published in peer-reviewed journals, one of these (Velimirov et al (2008)) has been reviewed and rejected by EFSA (European Food Safety Authority) and retracted by the study’s sponsors⁸. A careful reading of the citations shows that cited studies may not even show what the authors claim. For example, the report claims that GM soybeans have 27% more trypsin inhibitor than conventional soybeans (Padgett et al (1996)); while the Padgett et al paper concludes no differences in trypsin inhibitor content were observed.

Setting aside deficiencies in studies and citations, there is a much more compelling reason to disregard the claims of adverse effects on the health of animals and the dangers of consuming GM soybeans claimed in *GM Soy: Sustainable? Responsible?* It turns out that whole food animal feeding studies are not very useful for determining the safety of a food or feed (Chassy et al (2004)). That is why EFSA does not require or recommend whole food animal studies (EFSA (2008)). These kinds of studies must be performed very carefully, they are tedious and expensive, the results are often difficult to interpret, and at the end of the day the studies have very little power to discern if harmful effects will occur or not (Chassy et al (2004); see also

⁸ The report neglects to inform the reader that the journal has withdrawn their support from one study that was cited. Quist and Chapella, 2001 was not the target of a coordinated campaign against it but rather the editors of Nature received so many letters from scientists pointing out the flawed methods and data analysis that they withdrew their support. The authors fail to note that another detailed study could not verify the Quist and Chapella report (Ortiz-Garcia et al (2005)).

Parrott and Chassy:

<http://www.agribiotech.info/details/Is%20This%20Study%20Believable%20V6%20final%2002%20print.pdf>).

A particular difficulty with animal studies is in interpretation of the statistical analysis of the data. This has been a subject of some debate, for example, Séralini and his associates have published a series of papers which reinterpret the statistical analysis of animal studies performed on GM corn presented to the European Food Safety Authority (EFSA) in support of an application for regulatory approval by Monsanto, and EFSA has published a critical rejection of the analysis (Séralini et al (2007), Doull et al (2007)). Séralini, and the authors of a number of papers cited in the report, as well as the authors of the report itself, have confused statistical significance with harm.

When large numbers of measurements are taken on large number of animals and the statistical differences are evaluated, a small number of comparisons between groups of animals will always appear to reveal statistical differences. This results from normal random biological variation. These differences do not mean that a treatment has harmed the animals; it is incorrect to conclude that a difference in weight of kidneys or livers observed between groups that were fed GM versus non-GM soy means that those organs were adversely affected. Proof of an adverse effect requires a demonstration of actual harm. This in turn requires histopathologists, physiologists, pathologists, anatomists and toxicologists to examine the animals (including organs, tissues, and serum) and establish that real harm has occurred. To be real, such harmful effects must be reproducible and must follow a normal dose-dependent response.

A key indicator of toxicity is that a toxic feed will usually change several related parameters at the same time, for example, a liver toxicant will not only cause an enlarged liver, it will decrease serum albumin levels. If inter-related linked differences of this sort are not seen, it is evidence of random variation.

Experts use their professional judgment in interpreting small statistical differences and often dismiss as meaningless random biological variability that an opponent of GM crops sees as evidence of adverse effects.

Opponents of GM crops are far from alone in their misunderstanding of the meaning of statistical significance, many scientists make the same mistake and the scientific literature is full of erroneous conclusions based on untested statistical differences that at the very best only point to the need for additional experiments (Goodman (2008)). It has been argued that many research studies are false; Ioannidis pointed out that “Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true” (Ioannidis (2005)). The inherently low power, small numbers, natural variability, and the lack of reproducibility, place whole food feeding studies into the category of studies that are unlikely to produce meaningful results.

Critics of GM often claim that the studies they cite are demonstrations of real harm. They demand that multi-generational studies should be performed as a follow-up. Some ask for studies in humans that are virtually impossible to perform and even less likely to produce meaningful results than whole food animal studies (Chassy et al (2004)). Non-experts are no doubt concerned if not swayed by these arguments. The scientific reality is that whole food animal studies are of little value in assessing safety. The reader is left to decide if they believe that using animals in pointless studies is even moral or ethical.

3.5 Whom do you believe?

The authors of *GM Soy: Sustainable? Responsible?* portray a world in which large companies control regulatory agencies, policymakers, and scientists, and dominate the marketplace. The industry stifles the opposition to their products from telling the truth about their products and suppresses the science that proves harmful effects. They would have us believe that scientists, companies and regulators are willing to turn a blind eye to the purported harm caused by GM products out of greed or fear. They offer us a potpourri of bad papers and poor arguments, many of them unpublished or anecdotal in nature, and misinterpretations and exaggerations abound. The report is highly selective in citation of the literature in an attempt to stack the deck against GM soy. This is not the way science is supposed to work. None of the reports' authors is a toxicologist, nutritional scientist, or food scientist and none has published research in the area of food safety assessment. All openly oppose GM soy and other GM crops. It is conceivable that they are simply unaware of the extensive food safety literature that they have overlooked, but given the clear bias against GM soy, this seems unlikely.

An alternative view holds that hundreds of research studies have been published over the last 30 years that support various aspects of the safety of GM crops and specifically GM soy. There is a global scientific consensus among independent and objective scientists that GM technology is as safe as any other. Extensive studies have been presented to regulators in support of applications for approval of GM products and regulators have considered *the weight of all of the evidence* and have approved GM products in countries across the globe. The experience with GM crops—including GM soy—has been very positive. No adverse effects to human and animal health have been observed. Ultimately each of us must decide for ourselves whom and what we will believe.

4. Response to claims made about the agronomic and environmental impacts of GM RR soy

4.1 A claim that GM crops do not increase yields

This claim ignores the (positive) impacts on yields associated with the adoption of GM insect resistant technology, that have been consistently identified in peer reviewed literature (e.g. Bennett R et al (2004), Brookes (2008), Ghouse M (2006), Hutchison et al (2010), Marra M et al (2002), Pray C et al (2002)), and focuses exclusively on yield effects associated with the use of GM herbicide tolerant (GM HT) technology used in soybeans. The use of this GM HT

technology has primarily delivered important cost savings for most farmers who have used the technology (cost reductions being the main 'target of the technology'), with some also reporting yield and production benefits (e.g. see Brookes G & Barfoot P (2009). The image portrayed by Antoniou et al is based largely on a combination of non peer reviewed, un-representative and, in some cases, dis-credited reports (e.g. Gurian-Sherman D (2009). Reality is different, with the overwhelming experience of farmers who have used HT technology in soybeans being one of similar yields between the first generation⁹ of GM HT soybeans and conventional alternatives (ie, no operational yield gains), but with the GM HT option delivering important cost savings, additional weed management flexibility and convenience and the facilitation of no and reduced tillage production systems (e.g. Qaim M & Traxler G (2005), Carpenter J & Gianessi L (1999). Some GM HT soybean farmers have also experienced higher yields from improved weed control. For example, an average yield gain of over 30% in the early years of adoption in Romania (Brookes (2005)). In addition, the use of GM HT technology, by facilitating the adoption of no tillage production systems in South America has shortened the production cycle for soybeans enabling many farmers to plant a second crop of soybeans in the same season (after wheat). This additional (second crop) production accounted, for example, in 2009 for 20% of the total Argentine soybean crop.

4.2 A claim that weed resistance to glyphosate is 'the major agronomic problem associated with GM RR soy cultivation' and that the GM HT technology is unsustainable'

This is an exaggeration of reality; there are currently 21 weeds recognized as exhibiting resistance to glyphosate worldwide, of which several are not associated with glyphosate tolerant crops (www.weedscience.org). For example, there are currently eleven weeds recognized in the US as exhibiting resistance to glyphosate, of which two are not associated with glyphosate tolerant crops. It should, however, be acknowledged that where GM HT crops have been widely grown, some, limited incidence of weed resistance to glyphosate has occurred. In addition, it should be noted that the adoption of GM HT technology has played a major role in facilitating the adoption of no and reduced tillage production techniques in North and South America. This has probably contributed to the emergence of weeds resistant to herbicides like glyphosate and to weed shifts towards those weed species that are not well controlled by glyphosate. A few of the glyphosate resistant species, such as maretail (*Conyza Canadensis*) and palmer pigweed (*Amaranthus Palmeri*) are now reasonably widespread in the US, especially maretail, where there are several million acres infested, and palmer pigweed, in southern states, where over a million acres are estimated to exhibit such resistance. In Argentina, development of resistance to glyphosate in weeds such as Johnson Grass (*Sorghum halepense*) is also reported.

⁹ The first (generation) GM herbicide tolerant trait was commercially introduced in 1996 and has been widely grown since then. A second generation of GM herbicide tolerant soybeans has been commercially available to farmers in the US and Canada since 2009. This latter, second generation provides operational yield gains of over 5%

This resistance development should, however, be placed in context. All weeds have the ability to develop resistance to all herbicides and there are hundreds of resistant weed species confirmed in the International Survey of Herbicide Resistant Weeds (www.weedscience.org), as cited above and reports of herbicide resistant weeds pre-date the use of biotech herbicide tolerant crops by decades. Where farmers are faced with the existence of weeds resistant to glyphosate, there is a need to adopt reactive weed management strategies incorporating the use of a mix of herbicides (i.e. the same way as control of other herbicide resistant weeds).

In recent years, there has also been a growing consensus among weed scientists of a need for changes in the weed management programmes in GM HT crops, because of the evolution of these weeds towards populations that are resistant to glyphosate. While the overall level of weed resistance in areas planted to GM HT crops is still low, growers of GM HT crops are increasingly being advised to be more proactive and include other herbicides (with different and complementary modes of action) in combination with glyphosate in their weed management systems, even where instances of weed resistance to glyphosate have not been found.

This proactive approach to weed management is therefore the principle strategy for avoiding the emergence of herbicide resistant weeds in GM HT crops. A proactive weed management programme also generally requires less herbicide, has a better environmental profile and is more economical than a reactive weed management programme.

At the macro level, the adoption of both reactive and proactive weed management programmes in GM HT crops has already begun to influence the mix, total amount and overall environmental profile of herbicides applied to GM HT soybeans, cotton, corn and canola. This is shown in analysis by, for example, Brookes and Barfoot (2011b), where the usage and mix of herbicides on GM HT crops in the US has increased marginally in recent years. Relative to the conventional alternative, however, the overall environmental profile of herbicides used with GM HT crops and the economic impact of the GM HT crops continues to offer advantages¹⁰.

4.3 The claim that GM HT soybean herbicide usage has increased to the detriment of the environment

As with the claims on yield impacts, Antoniou et al (2010) cite non peer-reviewed, inaccurate and misleading papers (notably Benbrook (2009a)) to 'support' their claims. More specifically:

- a) The claims made in the cited report (Benbrook) about changes in pesticide use on soybean (and other) crops in the US during the first 13 years of biotech crops (1996-2008) are based on inaccurate assumptions and extrapolations of data from the United States Department of Agriculture (USDA) National Agricultural Statistical Service (NASS), which annually produces reports on 'Agro-chemical usage on crops'. These NASS

¹⁰ Also, many of the herbicides used in conventional production systems had significant resistance issues themselves; this was, for example, one of the reasons why glyphosate tolerant soybeans were rapidly adopted, since glyphosate provided good control of these weeds

surveys do not annually collect pesticide usage data on all field crops and the last time pesticide usage data on soybeans was collected related to 2006. Furthermore USDA NASS data does not differentiate pesticide usage between biotech and non biotech crops. It is therefore impossible to present any data on herbicide use for GM HT soybeans versus conventional soybeans directly from USDA NASS survey data.

Therefore the frequent reference in the Benbrook work to NASS-based data (notably for the last few years for total usage on each crop and all usage differentiated into biotech versus conventional) is misleading and disingenuous to USDA NASS – many readers might gain the impression that the report is using the government data source when, in fact, crucial parts of the data used, on which conclusions and arguments are drawn, do not draw from this source but are founded on the author's (inaccurate) use assumptions (see below for additional comments).

- b) The only comprehensive source of pesticide usage data on field crops in the US is GfK Kynetec, an independent, private sector source of data on agricultural input usage in the US¹¹. This dataset goes back to 1998 and covers every year (including 2008, the final year of Benbrook's analysis). It also provides data disaggregated into usage on biotech versus conventional crops. A comparison of the actual average usage volumes for herbicide active ingredient use per acre on biotech HT crops from this dataset compared to the assumed usage rates by Benbrook shows that he overstates herbicide active ingredient on biotech crops. Over the period 1998-2008, Benbrook overstates the amount of herbicide active ingredient used on the biotech HT corn, cotton and soybean crops by 63.4 million lbs (28.75 million kg) compared to actual usage recorded in the GfK Kynetec dataset (equal to 6% of the total herbicide active ingredient used on these crops in this eleven year period).
- c) Assessment of the amount of pesticide usage that would be used on the three crops of corn, cotton and soybeans in the US, if the entire crops were conventional requires the use of assumptions about what herbicides and insecticides might reasonably be expected to be used in the absence of biotechnology. Applying usage rates for existing conventional crops is one approach (e.g. using the average values identified from the disaggregated data in the GfK Kynetec dataset). However, this provides significant under estimates of what usage would be in the absence of biotechnology, as the conventional cropping dataset used to identify pesticide use relates to a relatively small share of total area of each of the US crops of corn, cotton and soybeans. The reasons why this conventional cropping dataset is unrepresentative of the levels of pesticide use that might reasonably be expected to be used in the absence of biotechnology include:
 - i) Whilst the levels of pest and weed problems/damage vary by year, region and within region, farmers' who continue to farm conventionally are often those with

¹¹ Not an industry-sponsored dataset, as inaccurately described by Benbrook

relatively low levels of pest or weed problems, and hence see little, if any economic benefit from using the biotech traits targeted at these agronomic problems. Their pesticide usage levels therefore tend to be below the levels that would reasonably be expected to be used to control these weeds and pests on an 'average infested' farm. A good example to illustrate this relates to the US cotton crop where, for example, in 2008, nearly half of the conventional cotton crop was located in Texas. Here levels of bollworm pests (the main target of biotech insect resistant cotton) tend to be consistently low and cotton farming systems are traditionally of an extensive, low input nature (e.g. the average cotton yield in Texas was about 82% of the US average in 2008);

- ii) Some of the farms continuing to use conventional (non biotech) seed traditionally use extensive, low intensive production methods (including organic) in which limited (below average) use of pesticides is a feature (see, for example, the Texas cotton example above). The usage patterns of this sub-set of growers is therefore likely to understate usage for the majority of farmers if all crops were conventional;
- iii) Many of the farmers using biotech traits have experienced improvements in pest and weed control from using this technology relative to the conventional control methods previously used. If these farmers were to now switch back to using conventional techniques, based on pesticides, it is likely that most would wish to maintain the levels of pest/weed control delivered with use of the biotech traits and therefore some would use higher levels of pesticide than they did in the pre biotech crop days.

In analyses of pesticide use changes arising from the adoption of biotech crops undertaken by Brookes & Barfoot in their annual global assessments of the impacts of biotech crops¹², the above pitfalls of using this data to assess the conventional alternative are discussed. Brookes & Barfoot therefore do not use the average recorded levels of pesticide use on the relatively small US conventional cropping area to estimate the likely usage if the whole US crop was no longer using biotechnology, but apply a more reasonably representative approach largely based on a consensus of opinion from extension advisors across the US as to what farmers might reasonably be expected to use in terms of crop protection practices and usage levels of pesticide¹³. In addition, the usage levels identified from this methodology are cross checked (and subject to adjustment) against historic average usage levels of key herbicide and insecticide active ingredients from the GfK Kynetec dataset to minimise the scope for overstating likely usage levels on the conventional alternative.

¹² AgbioForum 8 (2&3) 187-196 of 2005, 9 (3) 1-13 of 2006, 11 (1), 21-38 of 2008 and 12 (2), 184-208 of 2009 and GM Crops 2.1, January-March 2011

¹³ In other words Brookes & Barfoot draw on the findings of work by Carpenter & Gianessi (1999 & 2002), Sankala & Blumenthal (2003 & 2006), Johnson & Strom (2008). These authors consulted with in excess of 50 extension advisors in almost all of the states growing corn, cotton and soybeans and therefore provided a reasonably representative perspective on likely usage patterns

In contrast, Benbrook's approach is based on personal assumptions of herbicide use for biotech versus conventional crops and extrapolation of average trends in total crop active ingredient use (from an incomplete dataset). Benbrook also does not present any information about typical weed control regimes that might be expected in conventional systems. Not surprisingly, this resulted in significant under estimation of usage on conventional alternatives when compared to the values derived from a consensus of extension advisers.

In some cases, estimates by Benbrook are significantly lower than the actual recorded levels of use on the existing small US conventional cropping areas of corn, cotton and soybeans. For example, Benbrook uses an assumed average herbicide active use level on conventional soybeans in 2008¹⁴ of 0.49 lbs/acre, compared to the recorded average level of herbicide usage on conventional soybeans in 2008 of 1.76 lbs/acre (source: GfK Kynetec dataset).

Coupled with the overestimates of usage on the biotech HT crops referred to above, this points to major overestimation of the herbicide use changes associated with the adoption of biotech HT traits in the US (relative to what might reasonably be used in the absence of biotechnology trait use). This is the main reason why Benbrook's claims differ markedly from more representative, reliable and credible analysis that has been published in peer reviewed scientific journals (e.g. Brookes & Barfoot (2011b)), which estimated that biotech crop adoption in the US reduced pesticide spraying in the US, e.g. by 357 million lbs (162 million kg; -7.1% 1996-2007) relative to what might reasonably be expected if the crops were all planted to conventional varieties.

Benbrook (2005) also used the same flawed methodology of inaccurate assumptions and extrapolations to make claims about changes in herbicide use in Argentina. The dataset cited and drawn on by Benbrook (2005), like the USDA NASS dataset in the US, does not differentiate usage between GM HT and conventional soybeans. In fact, this dataset does not even provide a breakdown of herbicide use by crop; it simply reports total usage of individual pesticide active ingredients in the country.

Consequently, all conclusions drawn by Benbrook about usage of glyphosate on soybean crops in Argentina are entirely based on his inaccurate assumptions about use. In contrast, analysis presented in peer reviewed work by Brookes and Barfoot (eg, 2011b)) applies the same approach as referred to above, namely reporting actual usage on GM HT crops (based on private market research datasets) and estimating what might reasonably be used on a conventional alternative to deliver the same level of weed control, based on consultation with farm advisors.

Drawing conclusions from trends in pesticide usage on the three crops should also be placed within the context of the following issues:

- a) Comparisons with what might reasonably be used in the absence of biotechnology. During the period since biotech traits have been widely used in US agriculture, the

¹⁴ Which accounted for 8% of the US soybean crop in 2008

alternative weed and pest control chemistry available to farmers have undergone some change and therefore a more meaningful assessment should be made with what farmers might use as an alternative. This is the approach taken by authors such as Sankala and Blumenthal (2003 and 2006) and Johnson and Strom (2008) in the US (and used as a basis of the analysis by Brookes & Barfoot), drawing on discussions with a representative cross section of extension advisors (see above);

- b) Drawing on the most recent assessment covering the period 1996-2009, the above suggests that if US soybean farmers wished to obtain the same levels of weed control for conventional crops as delivered through use of biotech herbicide tolerant crops, it would require approximately the same amount of active ingredient use per ha/acre on soybeans;
- c) Since the mid 1990s, the use of no and reduced tillage production systems has become commonplace in US agriculture. Whilst such systems were applied by some farmers prior to the widespread availability of biotech herbicide tolerant crops, the availability of this technology has consistently been cited by farmers as an important facilitator of no/reduced tillage production systems. In no/reduced tillage systems weed control is primarily delivered through use of herbicides compared to a combination of herbicide use and ploughing in a conventional tillage system. Key to staying in no/reduced tillage production systems is cost effective weed control.

The use of biotech herbicide tolerant crops with one or two broad spectrum herbicides (glyphosate or glufosinate) has delivered this for farmers (most importantly it has enabled farmers to stay in no/reduced tillage systems). A consequence of using no/reduced tillage systems is that the amount of herbicide active ingredient use per acre/ha tends to rise because chemical weed control is replacing a mechanical (plough) control mechanism. As such, 50% to 60% of the herbicide active ingredient use applied to crops in no/reduced tillage production systems is typically used as a burn-down, pre-emergence and is associated with maintaining the no/reduced tillage system;

- d) Whilst no/reduced tillage production systems can use higher amounts of herbicide active ingredient use than conventional tillage systems, no/reduced tillage systems deliver carbon emission savings that do not arise from conventional, plough-based systems. The scope for biotech HT crops contributing to lower levels of carbon emissions via facilitation of no/reduced tillage systems comes from two principle sources¹⁵:
 - Reduced fuel use from not ploughing. The fuel savings associated with not ploughing results in carbon dioxide emission savings of 88.81 kg/ha if no till is used

¹⁵ See Brookes & Barfoot (2011b)

and 35.66 kg/ha if reduced till is used. In 2009, the carbon dioxide savings from reduced fuel use from ploughing on GM HT soybean crops were 1,088 million kg¹⁶;

- By reducing the need to rely on soil cultivation and seed-bed preparation as means to getting good levels of weed control, more carbon remains in the soil, leading to lower carbon emissions. The no tillage (NT) system is assumed to store 300 kg of carbon/ha/year, the reduced tillage (RT) system stores 100 kg carbon/ha/year and the conventional (CT) system releases 100 kg carbon/ha/year¹⁷. In the context of global GM soybean production, the average level of carbon sequestered per ha increased by 42.3 kg carbon/ha/year (from 101.7 to 144 kg carbon/ha/year). This resulted, in 2009, to savings in carbon dioxide emissions of 13,236 million kg.

Overall, global GM HT soybeans contributed, in 2009, to the equivalent of removing 14,324 billion kg of carbon dioxide from the atmosphere or equal to removing nearly 6.37 million cars from the road for one year.

- e) No/reduced tillage also results in enhanced soil quality and reduced levels of soil erosion (in direct contrast to the claims made in Antoniou M et al (2010).
- f) The amount of pesticide active ingredient used per acre/ha is a fairly crude and poor measure of environmental impact. It does, for example, not pick up the benefits referred to earlier relating to lower levels of pesticide concentrations in water courses. An alternative measure used by several analysts is the Environmental Impact Quotient (EIQ) developed at Cornell University in the 1990s. The EIQ distils the various environmental and health impacts of individual pesticides in different GM and conventional production systems into a single 'field value per hectare' and draws on key toxicity and environmental exposure data related to individual products. It therefore provides a better measure to contrast and compare the impact of various pesticides on the environment and human health than weight of active ingredient alone.

Applying this methodology to global GM HT herbicide use changes, the analysis by Brookes and Barfoot (2011b), estimated that whilst the use of GM HT soybeans has reduced herbicide spraying by 2.2% (in terms of the weight of active ingredient applied) between 1996 and 2009, the associated environmental impact associated with herbicide use on the area planted to GM HT soybeans, as measured by the EIQ indicator, fell by a larger 16%. It is interesting to note that Antoniou M et al (2010) cite the paper Bindraban et al (2009) as concluding that the herbicides used with GM HT soybeans had a more

¹⁶ Taken as indicative of the savings in the corn: soybean rotation

¹⁷ The actual rate of soil carbon sequestered by tillage system is, however dependent upon soil type, soil organic content, quantity and type of crop residue, so these estimates are indicative averages

damaging environmental profile than conventional soybeans in Argentina. This was not the conclusion drawn by Bindraban et al¹⁸.

4.4 Claims about negative ecological and agronomic impacts of glyphosate use with GM HT soybeans

These claims draw heavily on non peer-reviewed papers that are inaccurate, make unsubstantiated claims and attribute impacts to GM HT soybeans that are due to a combination of factors and circumstances. Examples include the following:

- *A claim that the expansion of soybean production has resulted in a decline in soil fertility and an increase in soil erosion.* Given that the majority of soybean production in South America (notably Argentina and Brazil) is based on the use of GM HT soybeans and no/reduced tillage, the mainstream literature on impacts of no tillage does not support this conclusion. In contrast, the 'widely accepted' consensus is that no tillage system contributes to reducing soil erosion and enhancing soil fertility;
- *A claim that nutrient uptake and yields are adversely affected.* This is simply not reflected in the numerous farm level studies of impact of GM HT soybeans, where yields of GM HT soybeans have tended to be similar to conventional soybeans (ie, no statistically significant differences) for the majority of farmers, with some GM HT soybean growers also seeing increases in yields relative to the conventional alternative (see, for example Fernandez W et al (2010));
- *A claim that glyphosate use results in increased severity of various plant diseases, impairs plant defence to pathogens and diseases and immobilises soil and plant nutrients rendering them unavailable for plant use (based on Johal G & HuberD (2008)).* Issues relating to the effects of herbicides like glyphosate on pathogen pressures on GM HT soybeans were reviewed in Bindraban et al (2009). Their literature review identified the following key points; a) theoretically the application of a broad-spectrum herbicide like glyphosate used with GM HT crops should not affect the susceptibility of a crop, b) in certain tissues and environmental conditions it is possible that a crop could become more susceptible to diseases (Cerdeira et al (2007)), c) in laboratory conditions, glyphosate could inhibit the growth and development of certain pathogens whilst enhancing the pathogenicity and virulence of others, though the authors of this research (Termorshuizen and Lotz (2002)) questioned whether any of these effects would be of significance in the field given the low persistence of glyphosate in the environment and d) the application of glyphosate in a greenhouse trial was found to be preventative or curative on soybean rust (a common fungal disease: Feng et al (2005)).

¹⁸ Which found the environmental impact, as measured by the EIQ indicator, was marginally worse than conventional soybeans in one region of Argentina. Bindraban et al also acknowledged that other research examining the same issue with the same indicator for the whole of Argentina found the environmental impact of GM HT soybeans to be marginally better than impact of herbicides that might reasonably be expected to be used on conventional soybeans

At the farm level, it is noted that there are no empirical studies that show statistically significant differences in yield between GM HT soybeans and conventional or in the rate of application of crop protection products (other than herbicides);

- *Claims that no till leads to soil compaction and increased soil acidity.* These may be impacts associated with the adoption of no tillage systems in South America (the lack of tillage makes it more difficult to add lime to soils) but are not considered important for farmers if crop response and yield are as good or better than the tillage-based alternative. As most farmers who have adopted no tillage have not found poorer crop response or inferior yields using no tillage, these issues are not considered important;
- *Claims that no tillage production systems are linked to increased fertiliser application rates in Argentina.* In no tillage systems, a thick layer of mulch (crop residues) is an important part of the production system and helps deliver benefits of higher levels of soil moisture and temperature. The presence of the mulch can, however, potentially result in less efficient and slower uptake of fertiliser by crops, and therefore could result in farmers increasing fertiliser rates to compensate. Bindraban et al (2009) suggested that the amount of fertiliser used on no tillage systems is marginally higher than in conventional tillage systems (but identical for GM HT soybeans and conventional soybeans under either tillage system). However, this view is not supported by extension and government advisory services that record farm crop profitability (gross margin data). This source shows that fertiliser rates of application (and costs) are the same for no tillage as conventional soybean production systems (and records no difference between fertiliser application rates and costs for GM HT soy and conventional soybeans under each tillage system). Overall, it would appear that fertiliser rates tend to be the same, or possibly marginally higher under no tillage production systems, but do not differ between GM HT soybeans and conventional soybeans under the same production (tillage) system;
- *Claims that the widespread use of GM HT soybeans has resulted in a loss of species and biodiversity.* To support this claim, Antoniou et al cite work from the UK, where GM HT soybeans are not grown, and draw on a single, non peer reviewed paper from Argentina. The issue is a complex one and was examined in detail by Bindraban et al (2009). This work indicated that there are circumstances where the herbicides used in GM HT soybeans may contribute to reducing biodiversity. For example, through improved weed control it reduces weed biodiversity. Weeds are a source of food for wildlife and a source of plant pathogens. However, Bindraban et al (2009) concluded that it is not known what effect improved weed control has on the part played by weed biodiversity in soybean production or the agro-ecosystem in general. Equally, these analysts stated that GM HT soybeans may benefit biodiversity in and around fields through the adoption of no tillage, which increases soil biodiversity, and in turn benefits above ground biodiversity. Overall, their conclusion was GM HT soybeans '*probably has a different impact on biodiversity in and around fields than conventional soybeans*'.

5. Response to claims of negative socio-economic impacts of GM RR soy

5.1 A claim of negative socio-economic impacts of soybean production in Argentina

This claim essentially draws from non peer-reviewed papers and press cuttings. The authors also try to claim a link between all manner of social problems such as unemployment and poverty in rural communities, concentration of agricultural production in the hands of a small number of large-scale operators and a perceived reduced level of food security on soybean production systems.

Social issues such as poverty, unemployment in rural communities and the structure of agricultural production are affected by many factors, of which economics is an important driver. Reductions in the levels of rural employment in agriculture have been a feature of agricultural development long before the advent of GM HT soybeans, and the adoption of this technology reflects a desire by Argentine farmers to use the best available technology to boost their incomes and improve competitiveness on both domestic and world markets. The additional income generated by GM HT soybeans between 1996 and 2009 in Argentina has been \$9.75 billion (Brookes and Barfoot (2011a)). These farm income gains have added to rural farm household incomes which, when spent on goods and services, have had a positive 'knock on' effect on local, regional and national economies.

The technology has also contributed to additional soybean production via its facilitating role in the adoption of no tillage production systems (which has shortened the production cycle). This advantage enables many farmers in Argentina to plant a crop of soybeans immediately after a wheat crop in the same growing season. The second crop, additional to traditional soybean production, has added 79.3 million tonnes to soybean production in Argentina between 1996 and 2009. This additional production, together with the contribution of the technology to improving competitiveness (through cost reductions) has earned Argentina important export income that would otherwise not have occurred. In turn, taxes imposed on soybean exports have been an important source of revenue for the Argentine government and hence contributed to the provision of public services.

In relation to the structure of agricultural production, changes in this are influenced by several, mainly economic factors, and it is interesting to note that Bindraban et al (2009), when examining this issue, concluded that *'GM soy probably facilitated an increase in the scale of farming but the availability of GM soy was not a decisive factor in the process'*. Bindraban et al (2009) also concluded that *'the production methods associated with RR soy are equally suitable for mono-cropping as those associated with conventional soybeans. Prior to the introduction of RR soy in Brazil, large scale operations mono-cropping soy also expanded rapidly. Evidence of the role of GM soy in facilitating mono-cropping is inconclusive'*.

5.2 Claims of negative economic impacts in the US

To 'support' this claim, Antoniou et al (2010) refer to two public sector reports (USDA (2002) and Gomez-Barbero & Rodriguez-Cerezo (2006) that examined early years of adoption when the technology was not in the best available seed germplasm and when farmers were in a learning phase in respect of using the technology. The real world evidence relating to usage by US soybean farmers is totally different to that portrayed by Antoniou et al (2010).

After 15 years of adoption, more than 93% of US soybeans use GM HT technology. This alone suggests that US farmers derive important economic benefits from using the technology; *if they didn't why would they use it?* More importantly, there is a consistent body of evidence in peer reviewed literature that quantifies the farm economic benefits that US soybean farmers have derived from using the technology. For example, for the period 1996-2009, this amounted to additional direct farm income of \$11.17 billion (Brookes & Barfoot (2011)).

5.3 Claims that farmers pay too high a price for GM seeds and access to non GM seed is restricted

These claims again largely draw from non peer reviewed work and press cuttings. These claims, in respect of the US market, are highly dependant upon the assumptions used and perceptions of the author (Benbrook (2009b)) as to how seed markets work and farmers behave. The mainstream market evidence does not support the views expressed by Benbrook. More specifically:

- *Size of premia paid for seed with specific traits or characteristics:* The absolute amounts farmers pay for seed and the size of premia for additional traits, or organic versus conventional versus biotech seed costs are of limited relevance. *It is the size of premia or extra cost relative to the benefit farmers derive from the seed that matters.* During the period 1996-2009, the average net income gain (after deducting the extra cost of biotech seed) from using biotech seed in the US was \$39.5/ha (Brookes and Barfoot (2011a)) for GM HT. These net average gains provide a primary reason why in 2010, 93% of the total US plantings to soybeans used seed containing biotech traits;
- *Seed choice/use and profitability:* If farmers' fail to see benefits, usually in the form of higher returns and income from using (more expensive) biotech traited-seed, they won't use the seed. Farmers are likely to switch to conventional (or organic) seed, change to growing a different crop or take up a different activity/enterprise. For Benbrook to suggest that US farmers are dependant on biotech companies, are increasingly transferring income to biotech companies and have little choice, is disingenuous to the intelligence, management capabilities and business skills of US farmers;
- *Possible net transfer of income from farmers to biotech companies:* the evidence does not support any assertion that soybean farmers are now paying too much for seed. In terms of the share of the total 'benefit cake' between farmers and the supply chain (of technology companies, plant breeders, seed companies, seed producing farmers and

sellers of seed to farmers), US farmers have received the majority (64%), with 36% retained by the supply chain in the 1996-2009 period¹⁹ (Brookes & Barfoot (2011a)). This is broadly in line with historic divisions of benefits from the application of other input technologies in agriculture;

- *Reasons why farmers use biotech seed:* There are a number of reasons why US farmers have rapidly adopted biotech seed. The important and consistent increase in profitability has been a primary driver of adoption (see above). These improvements in profitability have arisen from a combination of yield increases (mostly associated with use of GM insect resistant corn and cotton traits) and cost reductions (found both in herbicide tolerant and insect resistant crops).

These benefits are well documented in peer reviewed scientific literature²⁰. As well as these direct farm income benefits there are more intangible benefits such as greater management flexibility, convenience, more time to undertake off-farm activities, improved production risk management and better quality crops. These are more difficult to value in monetary terms but analysis by US researchers at North Carolina University²¹ estimated these to be between \$4.86/acre (\$12/ha) and \$10.12/acre (\$25/ha) for HT crops;

- *Recent market developments:* In 2008/09, the price of all agricultural inputs (including seed and crop protection products) rose, largely because of increases in the cost of production. During this period, the part of the cost of seed specifically related to a biotech trait (seed technology premium) increased for some traits (notably HT traits) but remained largely unaltered for others. In addition, the price of glyphosate rose more significantly than prices of other herbicides resulting in a net reduction in the cost saving associated with adoption of biotech HT technology relative to conventional alternatives²². Nevertheless, the continued use of biotech traits by US farmers in the last three years reflects the significant benefits that most of them continue to derive from using the technology relative to the additional costs paid for the technology;
- *The seed market:* The dominance of seeds containing biotech traits in Argentina, Brazil, Paraguay and the US soybean sectors reflects market demand at the farm level. Changes in the price, availability and effectiveness of seed and crop protection products are features of these markets. New seed and crop protection products develop market share on the basis of their effectiveness and financial attractiveness to farmers relative to alternatives. They are inevitably replaced in time because of declining effectiveness and/or the availability of better performing products. This 'product life cycle' occurred

¹⁹ The corresponding figures for GM HT soybeans are 91.5% to farmers and 8.5% to the supply chain in Argentina and 74% to farmers and 26% to the supply chain in Brazil (Brookes and Barfoot (2011a))

²⁰ See for example, the references in Brookes G & Barfoot P (2011a). Despite this evidence Benbrook claims that US farmers have derived little or no yield or income gains from using biotech traits

²¹ Marra M & Piggott N (2006)

²² Prices of glyphosate in 2009 have, however recently fallen back to 2007 levels for most brands

before biotech traits were available in seed, applies equally in today's marketplace, and will continue;

- *Competition in the seed market:* If there is perceived to be limited competition in the biotech seed market this is not a biotech regulatory approval issue. Matters relating to the nature of product availability, pricing and forms of competition in a market like seed are typically addressed through market and competition regulations. It should, however, also be noted that the regulatory requirements for biotech traits tend to be significantly higher than the requirements for other seed. This adds considerably to the cost of bringing biotech traits to the marketplace making it more difficult for small and medium sized seed businesses to enter the market. Therefore this represents a regulatory driven barrier to entry into the seed market. In addition, it is important to recognise the rationale for, and role of patents. These play a key role in rewarding investment and risk in the development of new technology, not just in the plant breeding sector. Patents provide a period of market control over who can sell and licence a new product in order to reward the risk of investment. After patents have expired other plant breeders can take advantage and apply the same technological advances. In the absence of this type of market protection, investments in new trait and product development are likely to be lower, resulting in lower levels of productivity and crop improvement.

5.4 A claim that Monsanto has a near monopolistic control over seed and agrochemical markets

As indicated above, the structure of competition in markets is a commercial policy issue not a biotechnology regulatory approval issue. The evidence presented above in relation to the seed market and the share of the 'benefit cake' also suggests that this claim lacks credibility. In addition, it is difficult to see how Monsanto has a monopolistic control over global glyphosate markets, given the herbicide active ingredient has been 'off patent' for many years and is made by a wide range of companies. In South America the majority of glyphosate used probably derives from China.

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