African Centre for Biosafety

Objection to Dow's application for field trials: MON89034xTC1507xMONNK603

24 June 2013

This submission has been endorsed by the Southern Cape Land Committee, P.O. Box 9015 George, contact Angela Conway, tel 044 8039900

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1. Introduction

The African Centre for Biosafety (ACB) is a non-profit organisation, working on biosafety issues, in the public interest. The ACB hereby places on record its objections to the application made by Dow AgroSciences to the Department of Agriculture Forestry and Fisheries (DAFF) for trial release of a multi-stack event. The event in question is MON89034 x TC1507 x MON NK603.

The application received by the ACB is marked "CBI Deleted". The location of field trial sites as well as measures to ensure isolation of trial crops has been deleted. References used in support of claims made by Dow have been deleted, most likely because they reference not peer-reviewed papers, but more corporate research designated as confidential. In addition, Dow sent more complete documentation with their application to the Executive Council (EC) for commodity clearance of this event in 2012, which is referred to in this application. The ACB has not been privy to this information. We note that no details of feeding studies whatsoever were provided by the applicant. No data is given on the safety of the chemicals to which the event is resistant, namely glufosinate and glyphosate. In fact, information on every single experiment carried out has not been made available. It is impossible under these circumstances for us to provide full and informed comment on a foodstuff that will enter the national food chain as a staple, should commercial release eventually be achieved. Regardless of the incomplete information provided to us, and on the basis of the documents received, our comments on the event are outlined below.

2. Summary of concerns

A thorough and rigorous independent scientific assessment of this application has been impossible due to the omission of large sections on grounds of it being 'confidential business information' (cbi). Other important information, such as the descriptions of the genetic modification of the single events and resultant phenotypic modifications, was omitted as Dow claims that this was already submitted to the Executive Council (EC): GMO Act for a previous commodity clearance (grain import) application. However, unlike the EC, the ACB was not privy to this information previously submitted.

Throughout the application, Dow asserts that MON 89034 × 1507 × NK603 is substantially, functionally and nutritionally equivalent to conventional maize. The theory of 'substantial equivalence' has been discredited by independent science, including in a joint South Africa – Norway biosafety project published in 2011.

The applicant also claims that because the 'stacked' MON 89034 × 1507 × NK603 was produced by the conventional breeding of single GM varieties, safety assessment of these individual parent varieties, and not MON 89034 × 1507 × NK603 itself, is satisfactory for risk assessment. The view held by the Genok Centre for Biosafety in Norway, the Codex Alimentarius guidelines for GM plants, and our GMO Act, is that the new stacked event should be subject to risk assessment.

There is a dearth of information regarding the description of the GM maize variety throughout the application. For example, though reference is made to southern blot analysis, this is not shown anywhere in the 'non-cbi' dossier, not allowing for independent verification. No mention is made of other characterisation techniques, such as polymerase chain reaction (PCR). Numerous studies have

noted that a combination of Southern blotting and polymerase chain reaction (PCR) should be used in GMO risk assessment.

Evidence of the lack of risk to human and animal health is equally scant. Vague reference is made to an animal feeding study, but no information is given to the study's duration, the number of animals used, or any information about control groups or the control group's diets. It is claimed that the Bt proteins present in this GM maize variety are 'functionally and structurally similar' to naturally occurring Bt proteins used in microbial pesticides, and that the Bt proteins themselves are not toxic to humans, animals or non-target insect pests and soil dwelling organisms. We cite multiple peer-reviewed articles that undermine these assertions, including a recent study in which pigs fed GM maize and soya suffered severe stomach inflammation compared to pigs fed the non-GM equivalents.

No discussion of the potential risks to human and animal health and the environment from glyphosate or glufosinate is made in the dossier, even though this GM maize variety has been engineered for the express purpose of being sprayed with these two chemicals. In fact, Dow even claims, that this variety will result in a reduction in overall pesticide use. We cite a number of studies that show that this technology has increased herbicide use and that glufosinate and glyphosate are associated with a plethora of health risks, including evidence from the USA and Europe that glyphosate has found its way into public water resources, and has been detected in people's urine. We note that glufosinate is being phased out in Europe due to health and environmental risks.

Dow's application claims that the "Cry1A.105, Cry2Ab2 and Cry1F proteins exhibit toxicity towards certain lepidopteran insects but not against other insect orders," and is rapidly degraded in the soil and therefore shows no 'deleterious effects' on soil-dwelling organisms and aquatic species. A number of peer reviewed articles that contradict these claims are referenced. No mention at all is made of any environmental risk from glyphosate or glufosinate, nor the rapid emergence of insect populations resistant to Bt crops, and weed species resistant to glyphosate.

Dow does not adequately describe measures to prevent cross-pollination during fields trials, other than to say that adequate temporal and/or spatial isolation measures will be provided and that the trial sites will be fenced in. Contamination of commercial maize crops could impact negatively on farmer's livelihoods and the national maize market. We note a growing vocal consumer concern about the saturation of South African maize with GMOs, which has resulted in a number of food producers pledging to source GM-free maize for their products in recent months.

Dow's claims that small scale farmers have, and will continue, to benefit from the adoption of GM seeds is not borne out by independent research. For example, negative impacts have been recorded in the Eastern Cape's Massive Food Production Programme and in the Makhathini flats in Kwa-Zulu Natal. Stacked GM maize seed varieties, such as MON89034 x 1507 x NK603, are typically more expensive than their single trait counterparts. As the adoption of single and then stacked GM maize seed in South Africa has expanded, maize seed prices have continued to rise, prompting concern among commercial agricultural organisations. Small scale farmers do not have nearly as much representation, however, expert testimony to the Competition Tribunal in 2011 stated that maize seed price increases would make it impossible for small scale and subsistence farmers to continue farming.

Finally, there is a notable lack of capacity within South Africa to adequately monitor the potential human and environmental risks of GM crops and their associated herbicides. Although GM crops have been grown in the country for nearly 15 years, only one government post release monitoring study has been carried out. There is also virtually no testing of South African maize products for residues of glyphosate or other pesticides, or to monitor their presence in the environment or our water resources. It is unacceptable for government oversight to lag so far behind research, development and administration, while continuing to allow ever more controversial and complex events into our food chain and environment. Our authorities can and must set the pace to ensure safety.

This application has failed to adequately show that MON89034 x 1507 x NK603 is safe for human, animal and environmental health. Our submission points to a number of areas of scientific uncertainty that pose serious risks and require further research. The Precautionary Principle both obliges the EC and accords it the right to halt the introduction of this event into our environment until this research has been satisfactorily carried out. In addition, we do not believe that stacking genes to deal with insect and herbicide resistance is a reasonable response to these problems. It is clear that this strategy will lead to a cycle of further stacking, further resistance and increased use of agro-chemicals to deal with the problem. We show that alternative weed and insect management systems exist and are proving to be effective while in no way undermining agricultural yield.

3. Background

This is an application by Dow AgroSciences Southern Africa (Pty) Ltd. for a trial release (field experiments) of the multi-event stack, MON 89034 × 1507 × NK603, in the Republic of South Africa (South Africa). MON 89034 × 1507 × NK603 has been produced by crossing MON 89034, 1507, and NK603 maize lines using conventional breeding methods. The event is a three-trait maize that incorporates previously approved GE traits of herbicide tolerance (Roundup/Glyphosate and glufosinate herbicides) and insect resistance, produced by crossing these maize lines through conventional breeding.

The Executive Council approved commodity import status in 2012, but no imports have been made to date.

The respective resistances are conferred to the event by contributions of three recombinant maize lines as follows:

1. MON89034: Maize resistant to Lepidoptera (cry1A.105, modified cry2Ab2)
2. TC1507: Maize tolerant to glufosinate herbicide and resistant to Lepidoptera (cry1F, pat).
3. NK603 CP4 epsps, 5-enolpyruvylshikimate-3-phosphate synthase (Agrobacterium tumefaciens CP4) for glyphosate herbicide tolerance.

4. Case by case risk assessment and substantial equivalence

Throughout the application, Dow asserts that MON 89034 × 1507 × NK603 is substantially, functionally and nutritionally equivalent to conventional maize. They also claim the descriptions of the genetic modification of the single events and resultant phenotypic modifications have been provided to the EC formerly, with the commodity clearance application, and that these are fully applicable to the combined trait product.

> "The genome of MON 89034 × 1507 × NK603 therefore contains three different inserts, one derived from MON 89034, one derived from 1507, and one derived from NK603. Molecular characterisation, has confirmed that the structure and organization of MON 89034, 1507 and NK603 maize inserts in corresponding parental lines, are equivalent to those inherited by MON 89034 × 1507 × NK603 maize (Taylor *et al*., 2007; Schafer *et al*., 2008-Attachment C *CBI Deleted attachment*). Therefore, the molecular characterizations of the single events are fully applicable to the combined trait product. (p. 6)"

There is no way for us to verify this statement as the attachment referred to is *deleted as confidential business information.* There is also no peer reviewed material on this gene construct.

Substantial equivalence

Research recently published by the South African National Biodiversity Institute (SANBI) on MON810 has highlighted that long-held assumptions about substantial equivalence are false. SANBI carried out the first government research project on the environmental impacts of the single trait variety MON810 from 2008 to 2010, to fulfil their mandate as laid out in the National Environmental Management Biodiversity Act (NEMBA)(Act no. 10 of 2004).[1] While Monsanto safety data claims MON810 to be substantially equivalent to conventional maize[2], SANBI found in their study that, GM plants "grown in the same environment as the near isogenic-parent (non-GM counterpart), respond differently to the same environmental conditions, as shown by the differences in protein expression, for a number of proteins."[3] This is at odds with the assertion that MON810 and the near isogenic-parent are the same in every respect except for pest resistance conferred by Cry1Ab. The reasons for this are as yet unknown and the researchers recommended that, "Further research is needed to understand what types of proteins are expressed differently in different varieties of GM and non-GM plants under different environmental conditions"[4].

The implications for post-commercial monitoring are stated as, "Protein expression, and thus many protein-related unintended effects, is largely dependent on the environment and the genetic background of the crop plant. Due to the unpredictable nature of these unintended, unwanted effects, it is essential to monitor and identify such effects in field-based baseline studies in several growing conditions, and with several genetically modified varieties".[5]

MON810 has been growing in our environment and has been introduced into our food system for 12 years based on the false assumption that it is "substantially equivalent" to its conventional counterpart. The assumption of substantial equivalence has allowed GM producers to get away with dangerously scant safety testing. Unfortunately public research tends to lag very far behind corporate research and development, so this is only coming to light now. The application under consideration is asking for permission to release into our environment a combination of three traits,

while we have hardly begun to understand the environmental implications of the insertion of just one trait. We have not yet begun to understand the health implications at all.

Assessment of stacked varieties

Even if Dow did provide sufficient information for each individual event in MON 89034 × 1507 × NK603, a number of scientists, institutions and regulatory bodies (including South Africa) hold the view that assumptions on molecular characterisation and potential harm cannot be made without full assessment of the new stacked event in question.

According to the Genok centre for Biosafety (the competent national authority for biosafety of Norway), "the issue of combinatorial and/or synergistic effect of transgene proteins either with endogenous host proteins or with other inserted GM traits (e.g. "stacked" events) is an area of nascent scientific inquiry and must be carefully considered in the development and risk assessment of stacked event GMOs with respect to the implications on biodiversity and evolutionary consequences for crop genetic diversity. This will be an important area of investigation for risk research, as multi-trait (stacked) GMOs are poised to replace the current generations of GM crops used in global agriculture. More research in this area is needed" [6].

Under the Codex Alimentarius 'Guideline for the conduct of food and safety assessment of foods derived from recombinant-DNA plants' (2003), paragraph 14 states:

"Unintended effects in recombinant-DNA plants may also arise through the insertion of DNA sequences and/or they may arise through the subsequent conventional breeding of the recombinant-DNA plant. Safety assessment should include data and information to reduce the possibility that a food derived from a rDNA plant would have an unexpected, adverse effect on human health."[7]

The South African GMO Act stipulates that each single variety in a stacked event must be subjected to a safety assessment.[8] Our concern is the assumption of substantial equivalence, compounded by the fact that the synergistic effects of breeding the single events into the combined trait product are not taken into account. It is assumed that there will be no unintended or undesirable changes to endogenous or introduced traits and functions.

We cite research that has found unexpected and unwanted effects due to gene stacking under human and animal health as well as environmental impacts. We assert that safety of MON 89034x 1507 x NK603 should not be assumed safe because parent lines may have been assessed individually or in combination and found to be safe. MON 89034x 1507 x NK603 must be assessed as a new event and fully assessed as such.

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5. Description of the genetic and resultant phenotypic modifications of the GMO

Stability of the integrated DNA inserts for each individual event in the stacked event under question (MON 89034, 1507 and NK603) is demonstrated by reference to southern blot analysis. However, no pictorial illustration of the Southern blot is present in the application. Without this, it is impossible for an independent reviewer to verify this.

Further, it is not clear from the dossier whether the applicant has made use of other procedures for profiling the rDNA before and after modification. Numerous studies have noted that a combination of Southern blotting and polymerase chain reaction (PCR) should be used.

For example, in their commentary on detecting the many small and/or complex products of multiple insertion sites, Kohli et al[9] said: "Mehlo et al. (2000) studied seven transgenic maize lines with multicopy transgene loci and found that every line showed some form of transgene rearrangement in at least one copy. Importantly, some of these rearrangements could be detected by sequencing and/or PCR, but were too subtle to be picked up by Southern blot analysis, the predominant technique used to characterize transgene loci. The authors speculated that undetected 'minor' rearrangements might be extremely common…However, sequencing and PCR analyses by themselves would provide an incomplete picture of transgene organization because, depending on the location of the sequencing and PCR primers, some major rearrangements might not be detected. Therefore, *PCR, sequencing and hybridization provide complementary information regarding locus structure.*" [emphasis added][10] [11]

"Characterization of the inserted DNA merely using PCR is not sufficient, as it does not unambiguously reveal the number of insertion sites and the copy number of inserted genes. Either Southern blots or a combination of PCR and Southern blotting yields better results. Inserts at one site may be concatemers of the same sequence. In particular, the ends of the inserts adjacent to plant genomic DNA have to be carefully analysed to determine whether any truncated open reading frames start within the insert or the plant genomic DNA that might yield transcripts that span plant genomic DNA and might also produce fusion proteins."[12]

Genetic stability of TC1507

On p. 5 Dow claims that “Segregation analysis was performed on two stages in the breeding process and the data provide evidence of the stable inheritance of the genetic elements introduced into maize line 1507”. No further data to back up this claim has been made available to the ACB, so we are unable to verify this statement. In addition, we could find no peer reviewed literature on the stacked event under consideration. Research has shown that the parent line of TC1507 is not genetically stable, and raised problems regarding current detection methods.

Morriset *et al* published a report in 2009 that found “a single nucleotide polymorphism (SNP) in the promoter region of TC1507 maize that clearly contradicts the applicant claim of genetic stability of the parent lines. The detected SNP negatively affected the detection of this event by the method approved by the European Network of GMO Laboratories (ENGL), showing that genetic instability is not only a concern for expressional changes but also for detection purposes. Also, genetic variations have been detected in commercial variants of MON810 (Aguilera et al. 2009; Aguilera et al. 2008). The latter study showed that ARISTIS BT did not contain the MON810 insert as expected and that CGS4045, even though it expressed the BT toxin, gave no amplicons in PCRs performed with MON810 event specific primers. MON810 event specific PCR is constructed to span the insertion junctions of the event and plant DNA, therefore this study shows that the event specific detection does not work in the genetic background of CGS4045 due to either SNPs/truncation at the PCR target and/or junction site or that the train is inserted elsewhere in the CGS4045 maize genome.

According to the applicant, MON 89034 x 1507 x NK603 has been field tested in USA in 2006, 2007 and 2008. The applicant should therefore provide information on the stability of the insert over multiple generations as well as compositional data and expression analyses over all three growing seasons"[13].

6. Animal and Human Health

Details pertaining to the human health, animal health and environmental safety of MON 89034 × 1507 × NK603 have been submitted with the application for commodity clearance of MON 89034 × 1507 × NK603 which was approved on 12 April 2012. (p. 19) The ACB has not been privy to this data and is only able to comment on the summary supplied, without the benefit of many references given as these have been *CBI deleted.*

Animal feeding experiments

"Animal feeding experiments was using whole-grain MON 89034 × 1507 × NK603 fed to broiler chickens, did not indicate any nutritional effects or safety concerns for MON 89034 × 1507 × NK603." (p. 21)

An important statistical analysis of chicken feeding studies conducted to 2004 found that most were incapable of detecting moderate to low level health effects in the short time of testing on chickens, and thus may miss important adverse effects that would be possible over the lifetime of humans.[14] The study assessed the power of tests to determine the adequacy of the experimental design being used by developers in studies provided to decision-makers attesting to the wholesomeness and safety of GMOs as food. The authors found that the "results of the survey of the literature showed, in general, low power of statistical tests for feeding experiments involving non-GM grains or in those cases when GM and non-GM grains were compared in poultry feeding experiments. These results suggest that care needs to be taken when designing experiments for bioequivalence of grains fed to poultry."[15]

In the present application, reference to the animal feeding experiment is lacking even the most basic information, including: the length of the feeding trial, the size of the study group and control groups, the diet of the control groups (which should be the conventional comparator of the GMO which was produced simultaneously and under identical conditions (e.g., grown side by side if a GM plant).[16] One simply has to take Dow's word at face value, without any recourse for independent verification.

Natural Bt is not necessarily equivalent to Bt expressed in plants

Dow claims that "the Cry1A.105, Cry2Ab2 and Cry1F proteins are functionally and structurally similar to Cry proteins that have a demonstrated history of safe use. Cry proteins have been used as components of microbial pesticides derived from Bt for over 45 years. They are generally recognized as non-toxic to humans and other mammalian species". (p. 19)

Though no risk assessment dossier would be complete without bioinformatics analysis, they are not validated and their use is not harmonized. In silico approaches are limited to identified proteins and to epitopes that are not influenced by post-translational modification (PTM).[17] Bioinformatics of this

type also cannot provide insight into unanticipated or unintended changes that introduce new allergens. Moreover, the databases are limited to those proteins known to be allergens.[18] These databases are growing rapidly, but it cannot be concluded that they are comprehensive. In the case of toxins, the search results are dependent upon those annotating the databases to recognize that the proteins are toxins. These methods also heavily rely on the algorithm used and guesses about protein folding, which are far from strong.[19]

Natural Bt toxin is not necessarily the same as the Bt toxin expressed in GM plants; the Bt toxin in GM plants may be truncated or otherwise modified. For example, there is a 40% difference between the toxin in Bt176 maize and the natural Bt toxin.[20] Further research into the safety of genetically engineered Bt is necessary as it cannot be assumed safe based on the safe use of pesticides derived from naturally occurring Bt.

Hematotoxicity of Bt

Published studies carried out on Swiss mice showed that the "Bt spore-crystals genetically modified to express individually Cry1Aa, Cry1Ab, Cry1Ac or Cry2A can cause some hematological risks to vertebrates, increasing their toxic effects with long-term exposure". The researchers concluded, "taking into account the increased risk of human and animal exposures to significant levels of these toxins, especially through diet, our results suggest that further studies are required to clarify the mechanism involved in the hematotoxicity found in mice, and to establish the toxicological risks to non-target organisms, especially mammals, before concluding that these microbiological control agents are safe for mammals.[21]

Immune effects

"MON 89034 × 1507 × NK603 maize does not introduce any new allergens and the inherent characteristics of maize regarding its allergenic potential have not been altered; hence increase in allergenicity is not a concern." (p. 21)

In Genoks assessment of MON 8903x1507 x NK603, they point out that:

> "Published mouse experiments have demonstrated that Cry1Ac raises specific immune reactions, and also possesses adjuvant properties by increasing the immunogenicity of proteins intermixed with feed products (Moreno-Fierros et al. 2003; Vazquez et al. 1999; Vazquez-Padron et al. 1999; Vazquez-Padron et al. 2000), (Rojas-Hernandez et al. 2004).
>
> This may result in increased immunological and allergic responses. In other words, the likelihood of immunological and allergic responses increases if Cry1Ac is administered together with a dietary antigen/allergen. Published data also suggest that Cry proteins may inhibit development of mucosally induced suppressive immune mechanisms referred to as "oral tolerance" against innocuous food proteins (Brandtzaeg 2007). In investigations with Cry1Ab protein, (Guimaraes et al. 2008) did not find a similar type of adjuvant effect elicited against peanut proteins as with Cry1Ac, yet instead found evidence of Cry1Ab acting as an adjuvant leading to early phase production of leukotrienes and increased Th2 and Th17-cytokine production in branchoalveolar lavage fluids after airway exposure. The

implication of possible effects of Cry1Ab to produce allergen-induced cytokine responses is an area of investigation warranting further inquiry."[22]

It is as yet unknown if the risk of food allergy increases with the presence of intestinal localized Cry proteins. The use of maize containing multiple Cry proteins, brings up a concern whether there will be a higher incidence rate for food allergy, especially when eaten as a staple by infants, adults, the sick and elderly. In addition, "since the Cry proteins possess adjuvant activity there may be enhanced inflammatory processes. Combinatorial or synergistic effects of recombinant proteins acting as adjuvants to immunostimulatory effects, or as potential allergens are areas of important coming scientific inquiry"[23].

We are anxious to remind the Executive Council that maize is not consumed by the general population as a staple anywhere else in the world. Consideration of our local eating habits must be taken into account. We note that a Codex Alimentarius task team has developed a decision making model to assist in allergenicity risk assessment. The team concluded that while the decision-making model improved risk assessment procedures, "due to the wide genetic variability in the human population and different geographical dietary intake, further evaluation for adverse effects of the genetically modified food should be considered once the product has reached the market"[24]. They found that further research into allergernicity is still needed and that "further studies are needed to determine the amount of allergen that sensitises and elicits allergic events"[25]. With regard to allergies in general, they noted that "Severe reactions can take place after intake of minute amounts of the offending food, and a safe threshold level below which reaction will not occur has not been defined"[26].

Protein digestibility

Dow states that the PAT protein's 'Rapid digestibility in simulated digestive fluids' (p.20) provides additional assurance of safety.

The correlation between resistance to digestion by pepsin and a protein's potential to be an allergen is in doubt because some allergens are readily digested and some non-allergens are resistant to digestion. Industry-independent observers note that "[l]ater work, however, cast some doubt on the usefulness of this test since few of all known food allergens demonstrate resistance to simulated gastric fluid (SGF-containing pepsin) or to simulated intestinal fluid (SIF) comprising pancreatin (a mixture of five enzymes: amylase, trypsin, lipase, ribonuclease, and protease). An explanation for the lack of correlation between SGF digestability and nonallergenicity may be that both children and adults may have naturally or iatrogenically increased ventricular pH for extended periods."[27]

Criticism also arises from the apparent lack of correlation between digestibility and percentage of allergenicity (i.e. major allergens are not more stable than minor ones). Furthermore, digestibility of a protein in SGF does not seem to correlate with digestibility in SIF. (Note though, that the digestibility of the vast majority of allergens (there are more than 1000 in databases), has not been determined.[28]

Apart from questions about the validity of the assumption that stability and allergenicity are linked, several experimental factors are of concern, mainly arising from the fact that the assay is not

standardized. First of all, the interpretation of obtained data can vary greatly between different studies as there is no agreed on definition of "stability". Astwood et al[29], for example, defined "labile" as digested after 30 sec, while "stable" proteins were detectable for more than 30 sec and up to 60 min, the maximum time of the experiment. Other studies used different frames, e.g. defining a protein detectable for 30 min as stable or discounting fragments that were stable for the maximum time of the assay, even though the whole protein was not (reviewed e.g. in Bannon, G. A. & Ogawa, T., 2006). Different studies have shown that a variety of factors can profoundly influence the result of the assay, leading to false negative results (that is, suggesting that the protein is less stable than it actually is). Factors that can influence the results include: the enzyme to test protein ratio, pH, purity of the test protein used, and the detection method.

New Evidence of stomach inflammation in pigs fed GM maize and soya

A thorough, long-term toxicology study (for 22.7 weeks, being the normal lifespan of a commercial pig from weaning to slaughter) on pigs in a USA commercial piggery was carried out in order to compare the effects of eating either a mixed GM soya and GM maize diet, or an equivalent diet with non-GM ingredients. The maize used in the study contained 90% DK 42-88 RR YG PL (a triple stack of NK603, MON863 and MON810 genes) with the remainder being equal quantities of Pannar 5E-900RR (containing NK603), Pannar 4E-705RR/Bt (a double stack of NK603 and MON810) and Producers 5152 RR (containing NK603) [30].

The results showed that the GM diet caused gastric and uterine differences in pigs. GM-fed pigs had uteri that were 25% heavier than non-GM fed pigs. GM-fed pigs had a higher rate of severe stomach inflammation with a rate of 32% of GM-fed pigs compared to 12% of non-GM-fed pigs. The severe stomach inflammation was worse in GM-fed males compared to non-GM fed males by a factor of 4.0, and GM-fed females compared to non-GM fed females by a factor of 2.2.[31]

The researchers highlight the importance of this study, saying that,

> "Our findings are noteworthy for several reasons. First, we found these results in real on-farm conditions, not in a laboratory, but with the added benefit of strict scientific controls that are not normally present on farms.
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> "Second, we used pigs. Pigs with these health problems end up in our food supply. We eat them.
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> "Third, pigs have a similar digestive system to people, so we need to investigate if people are also getting digestive problems from eating GM crops.
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> "Fourth, we found these adverse effects when we fed the animals a mixture of crops containing three GM genes and the GM proteins that these genes produce. Yet no food regulator anywhere in the world requires a safety assessment for the possible toxic effects of mixtures. Regulators simply assume that they can't happen.
>
> "Our results provide clear evidence that regulators need to safety assess GM crops containing mixtures of GM genes, regardless of whether those genes occur in the one

GM plant or in a mixture of GM plants eaten in the same meal, even if regulators have already assessed GM plants containing single GM genes in the mixture."[32]

This study is of extreme concern to us due to the fact that GM maize, and increasingly stacked varieties of GM maize, are the staple diet of our nation. No monitoring has been carried out to understand the effects this diet may be having on our health. We believe that 90 day studies carried out on rats and non-mammals are not sufficient to ascertain the long term effects of consuming GM maize and we cite numerous studies in this objection to support our concerns. We are baffled why our regulators continue to have faith in non-peer reviewed, producer generated safety data that shows safety, while turning a blind eye to an ever-mounting body of independent peer-reviewed science that is raising red flags. Our trust in the regulatory process is further eroded when a vast amount of information is not made available for independent oversight, due to protection of business information. Consumers are being kept in the dark about the safety of their staple food and to make matters worse, have no choice but to eat it because there is no alternative on the market. Something has gone horribly wrong when corporate interests are allowed to trump the rights of citizens, especially in a matter as intimate as the food we put into our bodies.

Glyphosate/Glufosinate safety

No data is given on the safety of the two herbicides that will be used on this crop. In fact, Dow gives the false impression (p.18-19) that the use of this stacked event will enable farmers to cultivate without any poisonous chemicals and hence they will no longer need safety gear or to take safety measures. In addition they claim that the problem of the re-use of chemical containers for drinking water will be "effectively negated". They make the bizarre claim that MON 8903 x 1507 x NK603 will reduce the risk from insecticide and herbicide use to humans and the environment.

Research carried out in the United States has found that genetically engineered crops have led to an increase in overall pesticide use, by 404 million pounds (7%) from the time they were introduced in 1996 through 2011. Of that total, herbicide use increased over the 16-year period by 527 million pounds while insecticide use decreased by 123 million pounds[33]. Similar increases have been observed in Latin America. For example, between 1996 and 2011 the amount of glyphosate used in Argentina increased 11 fold, to 237 million litres. The volume of pesticides sold in Brazil increased by 360% between 2000 and 2009.[34] In South Africa, annual glyphosate use has increased from 12 million litres in 2005 to 20 million litres, while from 2007 to 2011 glyphosate imports increased by 177%. Over a similar period, herbicide tolerant soya cultivation rose from 165,000 ha in 2008 to 472,000 ha in 2012.[35]

The development of resistant weeds has played a large role in this massive increase in use of herbicides in the USA. The fact that Monsanto and the University of Pretoria have a collaborative research programme into glyphosate resistant weeds indicates that this issue is anticipated in South Africa.[36] The omission of any information regarding the problem of weed resistance in this application and plans on mitigating the risk is disturbing. Instead, Dow intends to fix a problem they have created with yet another of their products, which will in turn create further problems for them to fix, all at the expense of our health and environment.

Glufosinate

Studies have shown that this chemical negatively affects the cardiovascular, nervous and reproductive systems in rodents and mammals[37]. In 2009 the European Parliament voted to ban glufosinate, along with 21 other pesticides classified as carcinogenic, mutagenic or toxic to reproduction. It has further been shown that the metabolite of glufosinate (NAG) produced by the transgenic plant can be reconverted into the pesticide itself by gut bacteria, leading to increased health risks for animals and consumers. The use of glufosinate will be completely phased out in the European Union by 2017.[38]

Glyphosate

Glyphosate is one of the world's most ubiquitous agro-chemicals, and is the most traded active ingredient in the global herbicide market. It is a broad spectrum herbicide that works by inhibiting the enzyme enolpyruvylshikimate-phosphate-synthase (EPSPS), which is a catalyst for the production of three essential amino acids: phenylalanine, tyrosine, and tryptophan. Though Dow's application states that there is 'a history of consumption of related EPSPS enzymes found naturally in plant material of commonly consumed foods, there is no reference at all to the safety of glyphosate or glyphosate based herbicides. The agro-chemicals industry has claimed glyphosate is benign to humans and animals, a plethora of studies have shown otherwise:

- Glyphosate formations can induce cell death in human umbilical, embryonic and placental cells. The same study further added that 'adjuvants in Roundup are not inert'.[39]
- In order to improve the efficacy of glyphosate as a herbicide, it is combined with other chemicals (called adjuvants) when sold commercially (such as under Monsanto's Roundup brand). These adjuvants are claimed to be benign, and not always listed on the packaging of the herbicide (under the guise of commercial confidentiality). However, research carried out on nine commercial formulations of glyphosate based herbicides revealed that one of these adjuvants, POE-15, was actually more toxic to human cells than glyphosate itself.[40]
- Cell exposure to glyphosate can trigger programmed cell death (to prevent the growth of tumours, for example). Research has revealed that Bt toxins (produced by the other significant GM trait on the commercial market[41]) can impair this process in human embryonic kidney cells.[42] This could have severe implications, as 'stacked' GM crops, which contain both traits, are becoming more and more prevalent.
- In Ontario, Canada, glyphosate use has been associated with an increased risk of spontaneous and late abortions among farm-workers[43]. Similar evidence has emerged from Argentina.[44]

In addition, a growing number of studies have shown the environmental impacts of glyphosate, including negative impacts on aquatic systems (see section 7 under 'environmental impacts').

7. Environmental impacts

Impact of Bt proteins on biodiversity and non-target organisms

Dow's application claims that the "Cry1A.105, Cry2Ab2 and Cry1F proteins exhibit toxicity towards certain lepidopteran insects and but not against other insect orders," (p.25), is rapidly degraded in

the soil and therefore shows no 'deleterious effects' on soil-dwelling organisms (p. 26) and aquatic species (p. 25).

Various meta-analysis studies dispute this: Lövei, G L, Arpaia, S, (2005) documented that 30% of studies on predators and 57% of studies on parasitoids display negative effects to Cry1Ab transgenic insecticidal proteins[45]. Another review (Hilbeck & Schmidt, 2006) on various Bt-plants found 50% of studies documenting negative effects on tested invertebrates. Further meta-analysis of 42 field experiments has found GM Bt producing crops to have toxic effects on non-target insect populations,[46] including butterflies[47] [48] [49] and beneficial predators such as ladybirds[50] [51] and lacewings.[52] Bt toxin has also been found to impact bee's learning behaviour, interfering with bee's ability to find nectare sources for food.[53]

More recent research on aquatic environments has sparked intense interest in the impact of Bt-crops on aquatic invertebrates Daphnia magna[54] and caddisflies.[55] These publications warrant future study, given the potential load of novel target proteins that may end up in agricultural runoff and end up in aquatic environments. Douville et al (2007) present evidence of the persistence of the transgenic insecticidal protein Cry1Ab in aquatic environments and suggest that that sustained release of this potently bioactive compound from Bt maize production could result in negative impact on aquatic biodiversity.[56]

Impacts on soil microflora and fauna, including earthworms,[57] mychorizzal fungi[58] and microarthropods in response to Cry endotoxins have also been reported. [59] [60]

Environmental impacts of glyphosate

Again, Dow does not deem it necessary to consider the potential impacts of glyphosate on the environment. This is in keeping with the biotechnology industry's very narrow definition of potential 'stressors' in GM plants; that only the novel 'trait' (e.g. the CP4 ESPS enzyme) is to be assessed, and not the chemical that the trait has been expressly created to be used with.[61] A more holistic approach to biosafety should consider the impacts of glyphosate (and glyphosate based herbicides) in addition to the CP4 ESPS enzyme, which could include the following:

- Research analyzing the impact of Roundup formulations and glyphosate itself, has shown it to have an inhibitory effect on microbial growth at lower concentrations than those recommended in agriculture. The toxic effect of glyphosate was amplified by its formulation adjuvants.[62]
- Glyphosate is generally considered to rapidly 'bind' to soil particles following application in the field, therefore minimising the risk of it leaching from the soil into nearby water. However, glyphosate's ability to bind to soil particles can vary depending upon specific chemical properties (such as soil Ph levels). It is also known that phosphate (which is used extensively in chemical agriculture as a fertiliser) plays a particularly important role in this, though further study will be needed.[63] This could be of particular relevance to South Africa, as phosphate use is expected to increase in accordance with increased grain production within the Republic.[64]
- Various studies have found glyphosate to: impair water intake and use efficiency, and biomass production in plants[65]; interfere with the uptake of calcium, magnesium, iron and

manganese in non HT soybeans[66]; and contribute significantly to incidences of fungal disease.[67]

- Glyphosate weed control programmes have been linked to increased incidences of over thirty plant diseases, in crops as diverse as apples, barley, canola, citrus, cotton, soybeans, tomatoes and wheat.[68]
- Greenhouse studies have shown that glyphosate interferes with iron uptake even in glyphosate tolerant soybean plants.[69] A three year field study in the USA indicated that, at rates of 2.52kg/ha, glyphosate inhibits nitrogen fixation and or simulation in glyphosate resistant soybeans.[70]
- In greenhouse and growth chamber experiments, conventional and glyphosate tolerant soybeans were treated with glyphosate doses of 0.28 kg/ha, 1.12 kg/ha and 2.24 kg/ha. A dose of 2.24kg/ha reduced the dry shoot and root weight of glyphosate tolerant soybeans by 25-30%. A repeated dosage reduced root growth, and reduced the nodule number by between 30% and 39%.[71]
- Glyphosate is toxic to earthworms.[72]
- Glyphosate's impact on plant (weed) diversity in areas it is used has knock-on effects further up the food-chain: The rapid spread of GM HT crops in the USA has contributed significantly to 'the potential collapse' of the 'unique migration and overwintering biology of the eastern North American monarch butterfly'.[73] Studies from the USA have also linked its use to declining bird populations (similar results were observed in the UK – see below).[74]

Glyphosate in Water

A study conducted by the US geological survey from 2001 – 2006 detected glyphosate and AMPA in 32% of 608 surface water samples collected. In areas with near continual applications (common in areas with HT crops), glyphosate and AMPA were detected 'in almost every sample'.[75]

- Other studies from the Mississippi river basin in the USA, revealed glyphosate and AMPA detection rates ranged from 60 – 100%. Its concentration in rain was found to be higher than any other high use herbicides in the area.[76]
- In Catalonia, Spain, 140 ground water samples were analyzed from 2007 – 2010. Glyphosate was present above limits of quantification levels in 41% of samples, with the highest recorded sample at 2.5ug/L in one location (25 times the European Unions' maximum level of pesticides permitted in water).[77]
- A recent study carried out by Friends of the Earth Europe, in which volunteers in 18 European countries gave urine samples, found traces of glyphosate in people in every country represented. In Great Britain, Germany and Poland 70% of participants were found to have glyphosate traces in their urine. Disturbingly, all of the volunteers in the study lived in cities, and none had handled or used glyphosate products in the run up to the tests.[78]

Glyphosate is highly soluble in water, giving it the capacity to be highly mobile in aquatic systems.[79] There is mounting evidence that, once glyphosate, GBHs and AMPA have entered surface water courses, they can cause considerable damage:

- Western chorus tadpoles exposed to the glyphosate product Roundup WeatherMax at 572 µg/L glyphosate acid equivalents (a.e.) resulted in 80% mortality, which the authors

suggestedresulted from a unique surfactant formulation. Exposure to WeatherMax or Roundup OriginalMax at 572 µg/L a.e. also lengthened the larval period for American toads.[80]

- A study published this year revealed that Roundup actually induced morphological changes in tadpoles. The author concluded that to his knowledge 'this is the first study to show that a pesticide can induce morphological changes in a vertebrate.'[81]
- Scientists in Argentina exposed embryos of Xenopus laevis (African Clawed Frog) to commercial formulations of GBHs. The embryos exhibited 'highly abnormal with marked alternations in cephalic and neural crest development', which are vital processes in cranial development.[82]
- Rotifer (Brachionus calyciflorus) (microscopic aquatic animals) exposed to different concentrations of glyphosate had longer embryonic developmental time, longer durations of juvenile and reproductive periods, shorter average lifespan, a reduced net reproductive rate and reductions in the intrinsic population growth rates.[83]

At Rhodes University, research has been taking place into the impact of Roundup formulations on aquatic ecosystems, using Freshwater Shrimp (Caridina Nilotica) as a biomarker. Roundup's toxicity was tested in new born (up to 7 days after hatching), juvenile (7-20 days) and adult (over 40 days) Freshwater shrimps. Though newborns were the most sensitive to Roundup formulations, all three age groups exhibited slow and erratic movements. The study concluded that even low levels of Roundup may adversely affect Caridina Nilotica health and survival.[84] A study to assess oxidative tissue damage was assessed by determining lipid peroxidation (LPx). The results suggested that Roundup 'exerts toxic effects related to oxidative stress.'[85] (In human's oxidative stress is thought to be involved in the development of many diseases or may exacerbate their symptoms, including cancer, Parkinson's and Alzheimer's disease).[86]

The spread of Herbicide resistance and resistance of insects to Bt

Insect resistance

On page 19 Dow states that, "Multiple gene strategy in addition to the continued maintenance of the refuge system will further enhance the prevention of insect resistance development in South African maize production areas". The assumptions about multiple gene stacking to arrest resistance need to be interrogated. In addition, the lack of compliance of refuges by farmers is well known and well documented, as are instances of insect resistance caused by this.

In June 2007, Van Rensburg published a paper entitled "First report of field resistance by the stem borer, Busseola fusca (Fuller) to Bt-transgenic maize"[87]. Two reasons were cited for the development of this resistance: 1) the lack of refugia inside irrigated plantings with farmers opting to use susceptible plantings provided under rain fed conditions in the immediate vicinity of irrigated plantings as refugia; and 2) continuous exposure of larvae of the second seasonal moth flight to sub-lethal levels of the toxin at late plant growth stages. In SANBI's report on MON810, they found that differing levels of bt toxin in different parts of the maize plant could be providing sub-lethal doses of bt that in effect vaccinate target pests against the toxin. SANBI also reported non-compliance of farmers in terms of planting refugia as a cause of resistance. The report suggested that in areas where resistance has set in, even current refugia requirements will not arrest the problem[88]. Lack of

compliance by farmers is rife and Dow should acknowledge this reality and lay out their strategy to deal with it, at the very least they should bring it to the attention of regulators in their application.

Professor Cummins, Emeritus of Genetics at the University of Western Ontario, has pointed to resistance monitoring data from five continents, reported in 41 studies that evaluate responses of field populations of 11 lepidopteran pests to four Bt toxins produced by Bt corn and cotton. "After more than a decade since initial commercialization of Bt crops, most target pest populations remain susceptible, whereas field-evolved resistance has been documented in some populations of three noctuid moth species: Spodoptera frugiperda (J. E. Smith) to Bt corn in Puerto Rico, Busseola fusca (Fuller) to Cry1Ab in Bt corn in South Africa, and Helicoverpa zea (Boddie) to Cry1Ac and Cry2Ab in Bt cotton in the southeastern United States" [89].

Studies have now also shown that increased resistance was observed in pest populations exposed to the concurrent use of pyramid plants (where two dissimilar Bt toxins are inserted to reduce the risk of resistance development) and single Bt events, as 'exposed populations were given a "stepping stone" to develop resistance to both toxins'.[90] Indeed, the multi-gene strategy might be responsible for increasing the pace of resistance rather than effectively dealing with it.

Herbicide resistant weeds

GMOs, expressing herbicide resistance and producing Bt-insecticidal toxins may have impacts in terms of non-target effects, the generation of multiple herbicide-resistant weeds and changes in soil biodiversity and function[91]. The overreliance on glyphosate herbicide in genetically modified (GM) glyphosate-resistant cropping systems has created an outbreak of glyphosate-resistant weeds, the severity of which has been enough to motivate hearings in the US Congress to assess the problem. Biotechnology companies are now promoting second generation GMO crops resistant to additional herbicides as a solution to glyphosate-resistant weed problems. This approach will create new resistant-weed challenges, will increase risks to environmental quality, and will lead to a decline in the science and practice of integrated weed management[92].

There is a dramatic rise in the number and extent of weed species resistant to glyphosate (Heap 2011), and a concomitant decline in the effectiveness of glyphosate as a weed management tool (Duke and Powles 2009, NRC 2010). The number and extent of weed species resistant to glyphosate has increased rapidly since 1996, with 21 species now confirmed globally (Heap 2011).

Although several of these species first appeared in cropping systems where glyphosate was being used without a resistant cultivar, the most severe outbreaks have occurred in regions where glyphosate-resistant crops have facilitated the continued overuse of this herbicide. The list includes many of the most problematic agronomic weeds, such as Palmer amaranth (Amaranthus palmeri), horseweed (Conyza canadensis), and Johnsongrass (Sorghum halepense), several of which infest millions of hectares (Heap 2011).

The result of the extensive use of these herbicides over vastly expanded areas will likely create interrelated challenges for sustainable weed management. First, crops with stacked herbicide resistance are likely to increase the severity of resistant weeds. Second, these crops will facilitate a

significant increase in herbicide use, with potential negative consequences for environmental quality. Finally, the short-term fix provided by the new traits will encourage continued neglect of public research and extension in integrated weed management.

8. Gene flow in maize

As these locations have been deleted, it is impossible for farmers or other interested parties adjacent to the trials to participate in decision making, a crucial aspect of risk assessment. There could, for instance, be farmers growing non-GM maize for niche markets, organic maize farmers or farmers using traditional varieties that suit their particular needs. Even farmers growing approved GM varieties are at risk of contamination from an unapproved variety. The arrangements for transport to trial sites has also been *deleted as confidential business information.*

Dow does not adequately describe measures to prevent cross-pollination, other than to say that adequate temporal and/or spatial isolation measures will be provided and that the trial sites will be fenced in. What isolation distances will be used? What temporal measures will be provided? How will fencing prevent pollen movement? *These crucial details are deleted as confidential business information.*

According to Professor Viljoen of the University of the Free State, "There are no published data regarding the extent of cross-pollination for maize in South Africa, even after a decade of commercialization of GM. … Despite a requirement for non-GM food, especially for export, there is no system for coexistence of GM and non-GM crop. Gene flow is a major contributor to commingling …"[93]. His research showed that "the use of mean values of cross-pollination over distance may result in an underestimation of gene flow" and suggest that, "where stringent control of gene flow is required, for example, for non-GM seed production or for GM field trials under contained use, the high values of cross-pollination should be used to determine isolation distance. However, this may not be practical in terms of the isolation distance required. We therefore suggest that temporal and distance isolations be combined, taking into account the GM maize pollen sources within the radius of the most stringent isolation distance required"[94].

According to Viljoen, "based on the logarithmic equations of cross-pollination over distance, 45 m is sufficient to minimize cross-pollination to between <1.0% and 0.1%, 145 m for <0.1% to 0.01% and 473 m for <0.01% to 0.001%. However, compared to this, a theoretical isolation distance of 135 m is required to ensure a minimum level of cross-pollination between <1.0% and 0.1%, 503 m for <0.1% to 0.01% and 1.8 km for <0.01% to 0.001% based on high values of cross-pollination[95]".

The loose assurances of Dow on this issue cannot simply be accepted. In May 2013 the United States Department of agriculture confirmed that instances of volunteer wheat, from trials that were discontinued in 2005, had been detected in farmer fields. This has resulted in the temporary loss of wheat exports to Japan, Korea and the European Union, threatening the US$8 billion wheat market[96]. In addition, it has cast grave doubts on the control methods currently employed to control open field trials of GMOs. It also begs the question of liability and redress; should farmers suffer financial losses due to such trials, how will they be compensated?

In recent weeks several food manufacturers have publicly pledged to source GM-free maize and soya due to public demand. FutureLife explained that they have to set up their own silos and

contract farmers to produce for them at great cost. They are willing to bear this cost because the use GM ingredients threaten their bottom line[97]. Consumer demand for GM-free maize already exists internationally and is now growing in South Africa, all efforts must be made to ensure that these markets are protected and that consumer choice is respected and protected. People living in the vicinity of the trials or businesses in the vicinity should be apprised of the trials and their opinions solicited.

9. Socio-economic issues

Benefits for small-scale farmers

On page 18 Dow states that, "People working in a rural setting generally do not have access to suitable sites to store pesticides, or the correct spray and safety clothing to protect them when they apply the pesticides. This often leads to poisonings in the fields, at mixing sites and in the home, where family members may be exposed because of inadequate storage facilities." On page 19, they continue that "the problem of container management, that is, the re-use of chemical containers for drinking water transportation and the persistent pollution of the plastic containers in the environment, is effectively negated." We have looked at this claim under the human and animal health section, where we argue that far from decreasing use of chemicals, this event will increase use. We also note that glufosinate is a banned substance in Europe due to health and environmental safety problems.

Dow cites extensive benefits to small-scale farmers with no socio-economic studies referenced to support their claims. On page 18 Dow claims that "excess production can be sold to fund other essential costs or even increased plantings. The increased planting area changes the status from subsistence to small scale commercial farming. This results in the farmer becoming a supplier in the community and creates an opportunity for secondary business development e.g. small milling industry to process the excess maize". No reference is given to socio-economic studies where they have found this to be the case.

Research into the Massive Food Production Programme (MFPP) operating in the Amathole District of the Eastern Cape as part of the provincial government's Growth and Development Plan (PGDP) showed exactly the opposite. Through this programme farmers were encouraged to shift away from traditional agriculture and adopt technology packages of GM cotton, maize and soya; purchase of expensive equipment and access to credit. The research found that switching to cash crops did not improve household livelihoods. One problem among many, was that farmers could not get good prices as they have very little bargaining power[98]. These farmers have very little margin for risk, such as taking out credit to farm a hi-tech capital intensive crop for a competitive market while abandoning diverse cropping systems that can provide diverse household nutrition, foraging crops for livestock, soil management crops and medicinal plants. These farmers insisted that political, not technological interventions were necessary for them to thrive; access to land tenure, water, markets and appropriate extension and research services in support of the systems currently in use.

The famous adoption by small-scale farmers in Makhathini of GM cotton from 1997 onwards also came to a disastrous end, despite enormous extension, financial and infrastructural support by industry and government. By 2002 farmers owed R22 million in debt and Vunisa cotton, which supplied the loans, folded[99]. At the height of Makhathini's success, in 2001/2002, there were over

3000 small scale-cotton farmers in KwaZulu Natal. By 2009/2010, most of them had abandoned cotton, there are now less than 300 left in operation[100].

Increased profit and farmer choice

"By combining comprehensive protection against a variety of lepidpoteran maize pests and two distinct modes of herbicide tolerance, glufosinate-ammonium and glyphosate tolerance, in hybrids developed across diverse breeding platforms, MON 89034 × 1507 × NK603 maximizes grower choice, production efficiency, Bt maize durability, and grower profit potential while at the same time reducing the risk from insecticide and herbicide use to humans and the environment". (p. 19)

Costs of stacked GM seeds

It has been well documented that the prices South African farmers pay for inputs, including seeds, has been outstripping the prices they receive for their produce. For example, between June 2008 and June 2009 the average price received by local farmers rose by 6.2%, while the prices paid by farmers for inputs rose by an average of 23.2%. In 2004/05 a South African maize farmer would, on average, have spent roughly 6% of their overall costs on seed. By the 2010/11 season this figure had more than doubled, to 13%.[101] The situation has not gone unnoticed within organised commercial agriculture. Grain SA, an organisation that represents and supports South African grain producers, has held regular meetings with various seed companies over the last year 'to address producers' concern about the extent to which seed prices are increasing on a continuous basis in relation to the price of the different commodities.'[102]

Stacked GM maize seed varieties, such as MON89034 x 1507 x NK603, are typically more expensive than their single trait counterparts. The table below, showing the collated average maize seed list prices[103] from Monsanto, Pannar seed and Pioneer Hi-Bred, the three largest seed companies operating in South Africa (though Pioneer was granted approval to purchase Pannar in 2012, the list prices supplied by Grain SA still show them as separate entities). It can be seen that during 2012 white and yellow stacked seed varieties were, on average, R306 and R373 more expensive respectively. More striking is the difference between the lowest and highest priced seed varieties. Monsanto's most expensive stacked yellow variety is R1,064 more than its cheapest yellow GM seed varieties. Pioneer Hi-Bred charges R900 more for its most expensive stacked yellow variety than its cheapest, and R950 more for its highest priced white stacked seed varieties over its cheapest.

Also noteworthy is the fact that all of the major seed companies appear to be increasing the prices of their single Bt varieties quicker than for their stacked varieties. The ACB has previously documented this phenomenon: from 2008 to 2011 the average price of single gene Bt white and yellow varieties increased by 42% and 43% respectively, compared to increases of 28% and 23% for yellow and white stacked varieties respectively. This is a common tactic that has been used elsewhere to 'encourage' farmers to stop purchasing the older varieties and start purchasing their latest products. This tactic appears to be bearing fruit, as stacked varieties accounted for 41% of all GM maize cultivated in 2011/12, up from just 5% of GM maize plantings in 2007/08.[104]

Rising farm input and energy prices, the removal of price support and huge subsidies given to farmers in the USA and European Union are some of the reasons why the number of commercial farmers in South Africa has fallen from 60,000 in 1996 to less than 40,000 today.[105] For South Africa's

200,000 small scale commercial farmers and approximately 1 million households who carry out subsistence farming, the ever increasing price of seed could be catastrophic. In December 2010 Pionner Hi-Bred applied to the Competition Commission for approval of their proposed acquisition of Pannar Seed, the largest remaining South African seed company. The Competition Commission rejected the merger, partly over fears of higher maize seed prices that would arise from a situation where only 2 companies controlled the market. Pioneer and Pannar Seed both appealed to the decision to the Competition Tribunal, which heard the case during September 2011. At the hearings an expert witness led evidence, on behalf of the ACB, in which he testified that any seed price increases resulting from the merger would make it impossible for small scale famers and subsistence farmers to continue farming.[106] The Competition Tribunal concurred, stating in its judgement that the 'likely' seed price increases would affect maize farmers in South Africa, including small scale commercial and subsistence farmers'.[107]

Variety	**2010**	**2012**	**% change 2010 - 2012**
Yellow Bt	1,941	2,310	19
Yellow RR	1,981	2,225	12
Yellow Stacked	2,364	2,683	13
White Bt	2,081	2,393	15
White RR	2,112	2,379	13
White Stacked	2,434	2,699	11

Source: Grain SA

Land

It has been noted several times that the locations of these field trials have been kept confidential. We would like to point out that small-holder farmers in the Lutzville area have reported that Monsanto's drought tolerant maize field trials are taking place on State land, while they, the farmers, struggle for secure tenure to subsist and make a livelihood. Whose land will Dow's field trials be carried out on, private or State land? It is objectionable that foreign corporations should receive State land for experimental purposes while so many people in the country are struggling for right of land tenure in order to grow food for sustenance and livelihoods.

10. Lack of State capacity

According to the SANBI research on MON810, State capacity for research and monitoring lags behind corporate research and development and is hampered by lack of resources and available expertise[108]. To date only one state study has been carried out on the environmental impacts of a single trait variety – MON810. The State should set the pace for the introduction of GMOs into the environment and the food chain, not the producers of the technology; the Precautionary Principle allows for this.

The same report also highlights the difficulty of research and monitoring in the face of corporate protectionism, stating, "It is also important to note that when planning to use existing monitoring programmes and data it is necessary to clarify the availability of the data. Hugo and co-workers

pointed out that in the UK, Defra may have to negotiate for the use of/purchase the raw data from the owners; and/or obtain specific authorization for the use of data. A similar experience in Germany was found by Wilhelm, et.al. (2010) related to a German research project by the Federal Ministry of Education and Research. Such issues may make the attempt to link existing monitoring programmes to GMO monitoring programmes more challenging"[109]. Why should the public accept a technology under these circumstances? Where monitoring and safety is hampered by corporate protectionism?

Coupled with lack of capacity for the health and environmental monitoring of GM crops, there is also a noticeable lack of public capacity for the monitoring of pesticide use in South Africa's food chain and the environment. In 2012, research from the ACB revealed that there was no testing for glyphosate residues in maize and soya products within South Africa, and no laboratories that could do this. There is also a barely believable eleven 'food inspectors' among the 3,264 environmental health practitioners registered with the Health Professions Council of South Africa (HPCSA).[110] The Minister of Health, Dr Aaron Motsoaledi, appears to have recognised the severe potential risks of this, and informed us in October 2012 that the Department of Health was planning to undertake sampling runs to test for glyphosate residues in maize and soya meal products during 2012/13.[111]

There is also a distinct lack of environmental monitoring of pesticides (including glyphosate) in South Africa. The right to a healthy environment and to sufficient and safe water is enshrined in the South African Constitution. Further, the National Water Act (Act.36 of 1998) requires the Minister of Water Affairs to establish systems to monitor the health of our nation's water resources. It is staggering to note that there are no water quality standards to protect the country's freshwater systems, or indigenous freshwater organisms, from glyphosate based herbicides (GBHs). Neither is there a national maximum residue level (MRL) set for glyphosate in water sources. The Department of Water Affairs (DWA) and the Council for Scientific and Industrial Research (CSIR) have both conducted water monitoring projects for pesticides. Regrettably, neither of them focused on glyphosate or GBHs. Researchers at Rhodes University have been attempting to fill this knowledge gap by using Fresh-water Shrimp (*Caridina nilotica*) as a biomarker for the potential impact of GBHs in aquatic systems. Initial studies have concluded that even low levels of Roundup may adversely affect this species. (see above)

The Department of Agriculture, Forestry and fisheries (DAFF) recognises that the current legislation regulating pesticides in South Africa[112] is hopelessly outdated and in need of a substantial overhaul. In 2010 it published a Pesticide Management Policy which recognised, among other issues, that current legislation does not provide adequate measures to monitor the environmental impact of pesticides; neither does it provide for the protection of non-target areas (such as residential areas or schools). Experts who commented on the policy noted that the policy paid scant attention to the protection of water sources.[113]

SANBI is in the very early stages of formulating an environmental monitoring project for glyphosate tolerant genetically modified (GM) crops. However, the project's lead person has subsequently left SANBI, leaving the fate of such a study uncertain. In 1999 the UK government conducted a similar study, which highlighted a number of impacts that glyphosate tolerant crops could have on biodiversity.[114]

11. Conclusion

This application has failed to adequately show that MON89034 x 1507 x NK603 is safe for human, animal and environmental health. Our submission points to a number of areas of scientific uncertainty that pose serious risks and require further research. The Precautionary Principle requires commitment to the idea that full scientific proof of a causal link between a potentially damaging operation and a long term environmental impact is not required to take action in order to avoid negative effects on health and the environment. The Precautionary Principle supplies the EC with a tool to halt further introduction of genetically modified crops, and especially stacked varieties, due to the lack of information available in the scientific literature on genetic stability, expression of inserted proteins or immune effects as well as the stacked event of the MON 89034 x 1507 x NK603. In addition, the EC needs to review its decision to allow commodity clearance of this event. It is incumbent on the EC to ensure the integrity of South Africa's maize, which is a staple food of the nation.

In addition, we do not believe that stacking genes to deal with insect and herbicide resistance is a reasonable response to these problems. It is clear that this strategy will lead to a cycle of further stacking, further resistance and increased use of agro-chemicals to deal with the problem. Alternative weed and insect management systems exist and are proving to be effective while in no way undermining agricultural yield.

Lastly, consumers are becoming more vocal in their rejection of GM maize as it benefits them in no way while creating uncertainty about health and environmental impacts. The complete saturation of the maize market with GM maize and the utter lack of choice for consumers, for whom maize is a staple, is an unacceptable situation that undermines consumer rights and indeed, human rights.

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