ACB's Objection to Monsanto's application for an extension permit of drought tolerant GM Maize hybrids:

MON 87460 x MON 810
MON 87460 x NK603 x MON 89034
MON 87460 x MON 89034

Supported by:

More than 25 000 people who signed a Care2 "#VoteNoToGMO!" Petition

22 June 2015

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

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

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1. INTRODUCTION

The African Centre for Biodiversity (previously 'Biosafety') was established in 2003 and registered in 2004. ACB carries out research, analysis, capacity and movement building, and advocacy, and shares information to widen awareness and catalyse collective action and influence decision-making on issues of biosafety, agricultural biodiversity and farmer-managed seed systems (FMSS) in Africa. The ACB's work both informs and amplifies the voices of social movements fighting for food justice and food sovereignty in Africa.

The ACB has played an essential watch-dog role on new GMO permits in South Africa for a decade now, adding substantially to the discourse about the scientific assessment of GMOs as well as issues of socio-economic impacts and democratic decision-making, through lodging substantive comments on at least 30 permit applications.

The ACB has been engaging with permit applications relating to MON87460 since May 2007, when it placed on record its concerns about the granting of field trial permits for MON87460 in Orania and Hopetown. In 2010 we submitted an objection to Monsanto's application for extension permits and once again reiterated our concerns in an objection to the extension permits in May 2011. In 2012 the ACB submitted comments on the application for an extension of field trials in Delareyville, Lutzville and Pretoria, for which initial approval had been given in 2009.

We are objecting to the extended trial release of the following stacked GM events, involving the drought tolerant trait of drought tolerant GM Maize hybrids: MON 87460 x MON 810; MON 87460 x NK603 x MON 89034 and MON 87460 x MON 89034. The further trials are to take place in several locations in the Western and Northern Capes, Free State and Mpumalanga. This objection is supported by a #VoteNoToGMO!" petition signed by more than 20 000 people and which is attached hereto marked annexure "A". In addition, 63 members of the public copied the objections they have submitted to the Registrar: GMO Act regarding these trials. These names can be found in Annex 1 of this document.

On 7th August 2015 the ACB lodged an appeal against the decision of the Executive Council's approving the commercial release of MON87460 and this appeal is yet to be heard and resolved. Central issues raised by the ACB in the appeal include: that the ACB was unable to meaningfully participate in the decision making process that culminated in the commercial release due to crucial information being withheld on the grounds of confidential business information (CBI); absence of peer-reviewed scientific data and evidence supporting Monsanto's claim that MON87460 will confer drought tolerance; flawed experimental design to assess the efficacy of the trait; and that potential socio-economic risks posed by MON87460 to smallholder and resource poor farmers have not been considered.

The ACB has also published a number of briefings exploring the Water Efficient Maize for Africa (WEMA) project, which is a public-private partnership including Monsanto, the Bill and Melinda Gates Foundation, USAID, the Howard Buffet Foundation, CIMMYT and several national agricultural research systems (NARs), to introduce both GM and conventional drought tolerant maize varieties to smallholder farmers in 5 African countries. We have placed on record in our previous objections our concerns with the underlying principles of the WEMA project. We have also highlighted that that drought tolerance in plants is an extremely complex phenomenon and evidence from the United States shows that this technology has made minimal impact. It is our view

that under the guise of philanthropy and fighting climate change, the WEMA project is seeking especially via the regulatory systems of South Africa, to lay the groundwork for the acceptance of GM crops on the rest of the continent[1].

MON 87460 is now being trialled in SA with insect resistant traits – MON810 and MON89034 as well as glyphosate tolerant NK603. These herbicide tolerant and insect resistant traits have already been approved for commercial release in South Africa (granted approval in 1997, 2002 and 2014 respectively) and have therefore been in use for a number of years. MON 810 has largely failed in SA and has been shown to be completely unsuitable for small-scale farmers.

2. KEY CONCERNS WITH APPLICATIONS FOR STACKED TRIALS

This submission lays out our concerns with the safety dossiers submitted by Monsanto for an extension of field trials of MON 87460 x MON 810, MON 87460 x NK603 x MON 89034 and MON 87460 x MON 89034.

1. '**Confidential business information' obstructs meaningful assessment**. The ACB was unable to conduct a meaningful and rigorous independent scientific assessment of the applications because important information was withheld relating to *inter alia* the location of the trial and the environmental conditions (including distance from nearest human settlements, weather, topographical, soil conditions; data on sequence information of the expression cassette, the flanking sequences, or evidence of genomic stability. Information on the phenotypes are non-existent, bar the claim that the phenotype of all three varieties are 'equivalent to conventional maize', 'except for the introduced traits'. It is therefore impossible to rule out known or probable risks associated with artificial genetic modification. We also note that tables on pesticide treatments appeared to have been 'cut-and-pasted' across all three of the safety dossiers, thus casting the rigour of the safety information provided in serious doubt.

2.GM drought tolerant maize is an inappropriate technological fix to a systemic problem. GM crops persist with "Green Revolution" technology while industrial agriculture has been identified as a major contributor to climate change. As we struggle through a prolonged drought, the appropriateness of an industrial farming system in the face of climate change needs to be urgently assessed with a view to transforming agricultural production to agroecological methods to ensure diversity and resilience to mitigate and adapt to climate change.

3.Best biosafety practice – case-by-case assessment – is being ignored. The stacked events are not being assessed on their own merit, rather, the parental lines are considered in isolation. This approach is inadequate in terms of our GMO Act, as the new stack events must be assessed for combinatorial effects to ensure environmental, human and animal health safety.

[1] For further information, please see:
May 2011. Water efficient maize for Africa: pushing GMO crops onto Africa.
http://acbio.org.za/wp-content/uploads/2015/02/WEMA-Pushing-GMO-crops.pdf

May 2015 Profiting from the Climate Crisis, undermining resilience in Africa: Gates and Monsanto's Water Efficient Maize for Africa (WEMA) Project
http://acbio.org.za/wp-content/uploads/2015/05/WEMA_report_may2015.pdf

4.Controversies also surround the already approved parental lines, which have not been taken into account. These include the following:

4.1 The approval for commercial release of Monsanto's drought tolerant trait, MON87460, is currently under appeal. The ACB has appealed on a number of grounds, including that a single gene (*cspB*) is highly unlikely to confer efficacious drought tolerance while risking the introduction of yet another novel and controversial gene into our staple food chain. This represents no benefits while introducing new risk.

4.2 MON810 has been replaced by the stacked Bt event, MON89034, in South Africa due to the development of pest resistance and resultant product failure. Expert opinion predicts that MON89034 is likely to develop similar resistance.

4.3 NK603 confers tolerance to the herbicide glyphosate. This chemical is deeply controversial since the WHO International Association for Research into Cancer (IARC) categorised it as a class 2A carcinogen in May 2015. The ACB also wrote to the Minister of Health as far back as 2012 asking him to launch an investigation into the toxicity of glyphosate and the lack of capacity for monitoring its use and impacts in South Africa, as well as asking for a review of risk assessment procedures to include chemicals associated with GMO crops. The South African public has since then called once again for similar actions and in 2016 almost 2000 people signed a "Glyphosate Must Fall" petition, which is attached hereto marked "B".

5.Questionable safety data presented by Monsanto – it appears that Monsanto has simply copied and pasted tables regarding insecticide treatments across all 3 previous trial data reports, as identical treatments are reported for all. Bt was applied to crops that should have been expressing Bt toxins. Insecticide treatments were also identical to the field trial data for MON87460 x NK603, which unlike the other lines, does not express Bt toxins. Herbicide treatments, bar the additional use of glyphosate on the glyphosate tolerant line, were also identical. The rigorousness of these safety dossiers is therefore seriously brought into question.

6. Failure to demonstrate safety – the dossiers submitted by Monsanto in the application for these trials did not provide sufficient evidence to demonstrate safety. Our submission points to a number of areas of scientific uncertainty that pose serious risks and require further research. The Precautionary Principle enshrined in the GMO Act and the Biosafety Protocol to which SA is a Party, obliges the Executive Council to refuse to grant the extension permits being sought by Monsanto.

3. BACKGROUND

South Africa is in the grip of the worst drought experienced since 1992, with many parts of the country experiencing record temperatures and little to no rain. The total maize crop for the year is estimated at just 4.7-million tonnes, far less than half the industry average of about 11.5-million tonnes a year for 2011-15, and falling far short of SA's average consumption of 9.6-million tonnes a year (Agriportal, June 2016). This leaves us in the alarming position of having only 8 months of our staple food – white maize – available, and leaving the stocks bare for the next season. The Bureau for Food and Agricultural Policy (BFAP) notes that maize meal prices have already increased by 20% and will increase by a further 10% in the first quarter of this year, hitting poor consumers hard (Agriportal, 2016).

It is against this backdrop that Monsanto is offering a potential solution to the intense drought periods we are expecting as climate change becomes a reality in South Africa and other African countries – its GM drought tolerant maize. However, the ACB has consistently raised concerns about the complex nature of drought and the extreme unlikelihood of a single gene providing a solution. In addition we have noted that industrial agriculture, which is responsible for the lion's share of global greenhouse gases and therefore a prime cause of climate change (Elver, H. 2015), cannot provide a solution to climate change related problems.

Instead of entrenching industrial agriculture with new technological fixes such as GM DT maize varieties, we submit that our government needs to bring about real agrarian reform and transition to agroecology in order to safeguard our food supply and environment as we move into a dry future. This position is gaining traction at international levels; in her interim report presented to the United Nations in August 2015 on the adverse impacts of climate change and the right to food, the Special Rapporteur on the Right to Food, Hilal Elver, stated that global agriculture policy urgently needs to "focus on ensuring the right to food for both present and future generations through sustainable agricultural practices. This implies moving away from industrialized agricultural practices". The report went on further to say that "Agroecology is an ecological approach that integrates agricultural development with relevant ecosystems. It focuses on maintaining productive agriculture that sustains yields and optimizes the use of local resources while minimizing the negative environmental and socioeconomic impacts of modern technologies". (Elver, H. 2015)

However, MON87460 has been approved in South Africa and as mentioned above, has been subject to field trials with insect resistant traits – MON810 and MON89034 as well as glyphosate tolerant NK603 and new extension permits are being sought for the continuation of the trials. These herbicide tolerant and insect resistant traits have already been approved for commercial release in South Africa (granted approval in 1997, 2002 and 2014 respectively) and have therefore been in use for a number of years. Mon810 was discontinued after the 2012 season due to the widespread development of pest resistance and replaced by MON89034 (Van den Berg, et al. 2013), it is therefore unclear why there is an application for trials with this event in South Africa.

Despite more than a decade of assurances that GM maize would be a boon to consumers in South Africa and address food security in the country, we can now see that this has not been borne out in reality. The South African National Health and Nutrition Examination Survey (SANHANES_1) published at the end of 2012 released the shocking findings that 46% of South African households are hungry and 1 in 4 children are stunted as a result of undernourishment. The survey also revealed high levels of obesity and a lack of micronutrients. (Shisana, O. et al. 2013) The promotion of maize mono-diets was identified as one of the causes of undernourishment in South Africa.

To add insult to injury to South African consumers, they have been forced to eat genetically modified maize for more than a decade without their knowledge or consent, either through the formal markets or as a result of the contamination of the national grain storage system with GM maize. It is disturbing that our regulatory authorities are considering burdening consumers with yet another novel and controversial gene in their staple food as well as novel stacks of genes, which they will have no choice but to consume.

SUMMARY OF APPLICATIONS

Approval of Monsanto South Africa's field trials with: MON87460 x MON810 (permit, 39.4(4/14/400)(DAFF. 2014), MON87460 x MON89034 (permit, 39.4(4/14/394)(DAFF, 2014) and MON 87460 x MON89034 x NK603 (permit, 39.4(4/14/396)(DAFF, 2014) at four locations (Lutzville, Orania, Hopetown and Melelane) was first granted in 2014, and an extension of this activity was approved in 2015 (DAFF, 2014).

The current applications are for an extension of the above trials for a third season for MON87460 x MON89034 and MON 87460 x MON89034 x NK603, and a second season for MON87460 x MON810. These crop events are summarised in Table 1.

Table 1

Crop Event	**Trait/s of interest**	**Gene/s Introduced***
MON87460 x MON810	Drought tolerance, insecticidal activity	*cspB*, *Cry1Ab*
MON87460 x MON89034	Drought tolerance, insecticidal activity	*cspB*, *Cry2Ab2*, *Cry1A.105*
MON87460 x NK603 x MON89034	Drought tolerance, insecticidal activity, Glyphosate tolerance	*cspB*, *Cry2Ab2* and *Cry1A.105*, *CS-cp4 epsps*

* only the transgene conferring the trait of interest are included. Additional genes/genetic elements not described here have also been introduced

All three maize products are 'stacked varieties' where two or more GM varieties are combined from traditionally cross breeding GM the parental lines. The parental lines for the three maize products are described below:

MON87460 contains the bacterial cold shock protein B (*CspB*), derived from the common soil bacterium *Bacillus subtilis*. According to Monsanto's general release application for MON87460, the *cspB* gene helps to preserve cellular functions during certain stresses' and 'reduces yield loss, primarily through increasing kernel numbers per ear'. It also contains the antibiotic resistance marker *nptII*, conferring resistance to neomycin and kanamycin antibiotics.

MON87460, or 'Droughtgard', was first commercialised in the US from 2011. Its introduction into South Africa for trials stems from a Monsanto/Gates Foundation project, Water Efficient Maize for Africa (WEMA). The project is being implemented in South Africa, Kenya, Uganda, Tanzania and Mozambique, and purports to offer the GM drought tolerant maize to smallholder farmers in Africa as a 'Climate Smart' solution to abiotic stresses such as drought.

The first field trials took place in 2007 in Hopetown and Orania in Northern Cape. In 2009, they took place in a further three locations, Delareyvile, Lutzville and Pretoria. The ACB has previously submitted objections to these trials (ACB, 2007; 2010; 2012). On 7th August 2015, the ACB launched an appeal to Agriculture, Water Affairs and Forestry Minister Senzeni Zokwana against the general approval of MON87460 granted by the Executive Council (EC): GMO Act (ACB, 2015). Such approval means that Monsanto can sell the GM maize seed, MON87460, to farmers in South Africa for cultivation.

MON810 contains an insecticidal Bt protein, Cry1Ab that targets certain members of the lepidopteran family (moths and butterflies). Bt insecticidal toxins were isolated from the bacterium *Bacillus thuringiensis* subsp. *kurstaki* Strain HD-1.

MON89034 is a stacked Bt crop, containing two Bt toxins, Cry2Ab2 and Cry1A.105. Cry1A.105 (also known as CS-cry1A.105 3.53) is not one Bt toxin, but a protein comprised of naturally occurring Cry1Ab, Cry1F, and Cry1Ac proteins. The gene cry1A.105 is a chimeric gene comprising of 4 domains from other cry genes previously used in transgenic plants. Bt insecticidal toxins were isolated from the bacterium *Bacillus thuringiensis* subsp. *kurstaki* Strain HD-1 and *Bacillus thuringiensis* subsp. *kumamotoensis*

NK603 contains the *CS-cp4 epsps* gene from the bacterium *Agrobacterium tumefaciens* CP4, for glyphosate herbicide tolerance.

4. COMMENTS ON THE APPLICATIONS FOR FIELD TRIALS

GENETIC MODIFICATION

MOLECULAR CHARACTERISATION

Monsanto does not provide any sequence information on the transgene constructs, the flanking sequences to the transgene insertion, or of the wider genome as a whole in any of the applications. It is therefore impossible to corroborate Monsanto's claims in their applications that "except for the introduced traits" each crop is "equivalent to conventional maize". There is no mention of molecular techniques routinely performed e.g. PCR or Southern blotting to confirm the presence and stability of all the stacked traits in each line.

Evidence of whole-genome analyses of the GM crop varieties (e.g. global genomic, transcriptomic or proteomic profile analyses) to be trialled have not been performed or are not publically available.

Studies have shown that many of the genetic elements introduced into the crops are genetically unstable and prone to rearrangements. This has led to the view by the geneticist the late Dr. MW Ho (2013) that artificial modification is inherently hazardous, with 'uncontrollable, unpredictable impacts on safety due to the genetic modification process. Agrobacterium-mediated transformation is associated with genomic rearrangements. Unintended effects that are not detected in the lab and that may only become apparent in the long term cannot be ruled out.

PARENTAL LINES SHOW GENOMIC INSTABILITY & NON-EQUIVALENCE

MON810 (used in this trial as a parental line) has been shown in several studies to have re-arranged on several independent occasions, as have other GM crops. Furthermore, it has been shown to have significant differences in nutritional content when compared to conventional, near isogenic varieties (Sirinathsinghji, 2013).

In 2010 SANBI published the results of a joint research project, carried out with the Norwegian government on the environmental impact of MON810. This is the first and only study published to date in fulfilment of their mandate under the National Environmental Biodiversity Management Act (NEMBA), requiring them to monitor the post-commercialisation impact of GMOs.

The SANBI study found MON810 to be not substantially equivalent to conventional varieties, finding 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". The study showed that some proteins have different expression levels (i.e. they are present at different amounts) in the GM and the non-GM comparator, even though both plant types are grown in the same field. The researchers recommended that further research is needed to identify what effects these have on the environment and if these differences also are present in other growing environments in South Africa (SANBI. 2011).

'STACKED' VARIETIES UNTESTED FOR RISK ASSESSMENT

Evidence of safety pertaining to the new-stacked lines is lacking. 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.' (Genok Centre for Biosafety. 2010)

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.'[5] The South African GMO Act stipulates that each single variety in a stacked event must be subjected to a safety assessment[6]. 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 are concerned about the possibility of pleiotropic effects occurring in the three-stacked maize varieties. Indeed, a recent study detected 22 proteins that were differentially expressed between single trait events and stacked GM events on the same genetic background, as detected by global profiling technologies (Agapito-Tenfen *et al.*, 2014). Monsanto have failed to provide evidence for equivalence or long-term stability of any of the three maize products.

QUESTIONABLE RELIABILITY OF DATA FROM PREVIOUS TRIAL REPORTS

The reliability of tabulated data of pesticide use in three previous trial reports for the maize products is questionable. There was identical pesticide treatments for MON87460 x NK603 (permit 39.4(4/14/398) (not to be re-tested in the proposed trials), as MON87460 x NK603 x MON89304 (39.4(4/14/396) Similarly, the tables for pesticide use for the crops MON 87460 x MON 810

(39.4(4/14/400) and MON 87460 x MON 89034 (39.4(4/14/394) were identical. Indeed, the only difference in pesticide treatment across all four field trial data is the additional application of glyphosate to MON87460 x NK603 x MON8904 and MON87460 x NK603. It raises questions regarding either the reliability of data, or alternatively, the efficacy or uniqueness of each line, if all has to be treated in near identical fashion with regards to weed and insect control.

Similarly, the insecticide data shows that identical quantities of the insecticide *Bt sprays* was used across all four trial reports. The Bt pesticide strain *Bacillus thuringiensis* subsp. *kustaki* (H-3a, 3b HD-1) contains the following toxins: Cry1Ac, Cry1Ab, Cry1Ac and Cry2Aa. MON89034 and MON810 already contain Cry1Ab, while MON89034 additionally contains Cry1Ac. Pyrethroids and benfuracarb insecticides were also applied, which are advertised as effective against maize borers. If the Bt toxins expressed in MON 89034 and MON810 are effective, it remains to be understood why application of Bt toxins and other insecticides, was necessary.

It is difficult to be confident in this data when it shows that Monsanto are not even testing the GM traits such as pest control conferred by Bt transgenes. It also calls into question the efficacy of Bt transgenes in MON 89034 and MON810 as well as the reliability of their pesticide data at all.

Further, the trial release reports have entire sections completely omitted, including both the results and discussion section. It is therefore impossible to independently assess the efficacy of the crops, the success/failure of the trials, or the confusion over their pesticide use. There is no mention of control lines being used. Evidence for ecological monitoring is also lacking, making it impossible to verify the claim that Monsanto 'have been conducting field trials in South Africa for two decades with no ecologically disruptive impacts recorded as a results of this trial'.

RISK ASSESSMENT OF MON87460 INADEQUATE

As emphasized by the ACB's appeal to the trial release of MON87460, the hazard identification and risk assessment for this crop is inadequate. (ACB's appeal documents are a matter of public record and in the possession of the South African GMO regulators.) It is particularly true in the context of the South African diet where maize is a staple food. Monsanto claim that the CSPB protein has a 'history of safe use' and can be designated as 'Generally Recognised As Safe' (GRAS) due to the fact that the CSPB protein is present in bacterium *B. subtilis*, found in the Japanese fermented food 'natto' and probiotics. The designation of GRAS and a 'history of safe use' make products exempt from regulatory testing. However the designation of GRAS has been misused in this context, as it can only be applied to extracted enzymes.

Relying on GRAS and 'history of safe use' designation is inadequate for risk assessment. Certain forms of toxicity that would not be detected under these guidelines could otherwise be revealed by case-by-case risk assessments. The guidelines rely on the assumption that a protein that is safely consumed in its natural context is automatically safe in a new, artificial context i.e. under the control of a synthetic transgene, in a new location of a genome, within the genome of a different species. Predictions of safety based on the similarity between protein sequences are not sufficient to determine the lack of allergenicity/toxicity of a transprotein. This is highlighted by a study that took a gene from one edible species of bean and transferred it to an edible pea species, resulting in post-translational modifications that elicited immunogenic, inflammatory responses in mice

(Prescott *et al*., 2005). Despite the 'history of safe use', the gene when expressed as a transgene out of context, produced a highly allergenic protein to mice. As Heinemann pointed out, even very subtle changes in a genetic sequence that do not alter the protein sequence (synonymous mutations), can alter the behaviour of a protein. Single nucleotide changes have also been shown to alter allergenicity of proteins. Indeed Monsanto state that there is a single amino acid substitution in the N-terminus of the protein. How this affects the allergenicity and/or behaviour of the protein unknown, such as the nucleic acid binding activity of CSPB, making their claim that "there is no reason to believe CSPB: nucleic acid complexes would behave differently" unfounded without experimental validation.

As outlined in the appeal, limitations in terms of assessing *CspB* toxicity include:

- A failure to identify hazards or perform risk assessment for all relevant-exposure routes including inhalation of pollen & effects of processing e.g. home cooking on CSPB protein. *CspB* expression is highest in pollen so exposure via pollen should be included in risk assessment
- There is no 'history of safe' use in the context of *cspB* expression in maize or at comparable concentrations. 'History of safe use' does not take into account the quantity of maize eaten in South Africa.
- 'History of safe use' should not be applied to a fermented food. Fermentation is a specific process and rarely represents how South Africans will consume maize. There is no evidence that expression of *CspB* is similar between natto, where fermentation results in the digestion of proteins, and maize.
- Recent *in vivo* evidence shows that nucleic acids (both DNA and RNA) as well as proteins can survive the digestive tract. A study showed that Bt toxins from GM foods were found to be circulating in blood of pregnant mothers' and their foetuses in Canada (*Aris* et al., 2011). Claiming that there are biological barriers preventing the survival of transgenes and transproteins is no longer in agreement with scientific literature and cannot be used as a presumptive safety claim for GM food consumption.
- MON87460 has not been grown long enough to be able to identify all hazards.

DROUGHT TOLERANCE

Drought tolerance is understood to be a highly complex trait in plants, involving an estimated 60 genes, all-interacting in a subtle and complex way. The successful manipulation of such a large number of genes without side effects, to adapt to a number of conditions, is a long way off current scientific knowledge. Conventional breeding on the other hand is also being performed to generate drought resistant crops, including the Drought Tolerant Maize for Africa (DTMA) project that includes developing open pollinated varieties alongside hybrids.

Conventional breeding has recently seen increased yields of drought-tolerant varieties by as much as 30 % (La Rovere *et al*., 2014). As stated in a *Nature* piece in 2014, the race to develop drought-tolerant varieties has been clearly won by conventional breeding over GM techniques to date [42, 43]. The development of hybrid varieties has its own socio-economic and sustainability problems, but these results offer the proof-of-principle concept that developing genetically complex traits can be achieved much more efficiently through cross-breeding than single-gene transgenic insertions.

Scientific evidence of yield improvement MON87460 is lacking. Previous trial data have the results and discussion deleted and peer-reviewed data is also lacking. As far as ACB is aware, there is only one published study on yield data. This study, conducted by Monsanto, found an average of 6% yield increase under water-limited conditions over 3 years of trials. It is instructive to note that one of those years saw a 0% increase in yield (Nemali *et al*., 2015).

FAILURE OF BT CROPS TO CONTROL PESTS

The use of Bt crops thus far has proven to be a failure in South Africa. Pest resistance to MON810 first officially reported only 9 years after its first season of commercial release in 1998/1999, though evidence of pest damage was observed only 2 seasons into cultivation. By 2010, some regions experienced over 50% infestations, forcing Monsanto to withdraw it from the market. Other global regions have suffered similar fates with Bt crop resistance. MON87460 x MON810 trials therefore raise alarm bells. Any repeat of crop infestations will only hurt smallholder farmers in South Africa.

The biotech industry was quick to scapegoat South African farmers for the spread of resistance, claiming that it was their fault for not implementing the recommended pest strategies such as the "high dose/refuge strategy". This involves 5-10 % of the total maize area is planted with non-Bt crop varieties. The practice theoretically requires doses of Bt toxin expressed at 25 times the level required to kill 99 percent of susceptible pests. This high dose is designed to kill any heterozygote insects (with one copy of resistance gene) that have partial resistance, thereby making the resistant trait functionally recessive. The success of the high-dose/refuge strategy depends on the size of the refuge and most critically, the resistant gene being recessive. If dominant resistance develops, then a refuge is ineffective in delaying it from spreading, as heterozygotes will be resistant and therefore the trait will spread more rapidly through the population. One may even argue that a refuge is counter-effective with dominant resistance, as the refuge may provide more potential breeding mates when initial numbers of resistant insects is low in the population. It is hard to determine the soundness of this strategy, as little long-term field studies have been performed to test the hypothesis.

Experiments have also revealed that the dose of the Cry1Ab in MON810 maize is low (Tabashnik *et al*., 2009) and variable between different parts of the plant, in different genetic backgrounds and under different environmental conditions, with hot/dry conditions reducing Bt protein levels (Trtikova *et al*., 2015). Low levels of expression allow partially resistant insects to survive. Bt crops also have prolonged expression of the Bt transgene, which increases selection pressure on pests to adapt, unlike Bt sprays, which degrade in the sun.

Introducing MON89304, which also contains Cry1Ab that is present in MON810, means that one of the four Cry toxins is already futile. Cross-resistance is also documented between certain Cry toxins. It is only a matter of time before industry will need to introduce yet more stacked events, likely adding to the spread of Bt resistance, repeating short-term strategies to delay the inevitable.

BIOSAFETY CONCERNS OF PESTICIDE USE

GLYPHOSATE

It is important to focus on glyphosate toxicity as one of the proposed maize products carries a transgene conferring tolerance to glyphosate (MON 87460 x MON 89034 x NK 603). Glyphosate is used in conjunction with glyphosate-tolerant (GR) crop cultivation, exemplified by the finding that

its use has risen sharply since the development of GR crops, which make up the vast majority of GM crops cultivated globally (Dill *et al.*, 2008).

The purported claim by Monsanto that it is safe to humans and the environment has been discredited by the recent WHO declaration that it is a "Category 2A probable human carcinogen". This analysis is not only corroborated by clinical reports, (Dill GM, et al. 2008) research findings but also industry data itself. Documents from the US Environmental Protection Agency (EPA) show evidence of carcinogenicity in Monsanto data from as far back as the 1980s. (Reduas, 2015)

Since the IARC finding, new evidence on carcinogenicity have emerged from Argentina, where a team of researchers at Universidad Nacional de Rio Cuarto found that children living within 500 m of spraying areas have over 66 % more cells with DNA damage than those living more than 3 000 m away (Bernari *et al.*, 2015). In addition, 40 % of the exposed children suffer from persistent conditions that may be associated with chronic pesticide exposure including respiratory symptoms, with and without additional symptoms such skin itching or stains, nose itching or bleeding, lacrimation, eye and ear burning or itching.

Glyphosate has also been linked to birth defects, neurological disease, kidney and liver damage amongst other illnesses (for a review see Sirinathsinghji et al., 2015). Over 200 published peer-reviewed papers link glyphosate to human and/or environmental toxicity, an overwhelming depth of evidence to support banning its use under the precautionary principle. (Isis.org)

Sri Lanka and El Salvador have already initiated complete or partial bans due to the rise in chronic kidney disease that is associated with glyphosate exposure. The EU is currently in a deadlock over its re-approval, which has been blocked for the third time and is set to result in the withdrawal of glyphosate from the shelves at the end of June 2016.

There is considerable resistance in SA to the use of glyphosate in our food systems and in this regard, 1932 people have signed a petition, which is submitted with this petition demanding that the South African government:

- Ban and remove glyphosate from our food and farming systems;
- Establish an independent review panel to assess the toxicity and health impacts of glyphosate on farmers and farm workers—both full time and seasonal—and consumers, especially consumers of Genetically Modified (GM) maize; and
- Commit to the transformation of our corporate controlled, chemical-laden food systems to systems that support previously disadvantaged producers and locally controlled smallholder food production systems, based on agro-ecological and food sovereignty principles.

The spread of glyphosate resistant weeds questions the long-term viability of glyphosate tolerant crops such as NK603. Over 32 species of weeds have developed resistance to glyphosate in recent years mainly in the US and Argentina. (ISHRW). This has led to farmers having to use additional, alternative herbicides and is threatening the farming industry in GM cultivation regions such as the US. A recent report shows that US farmers now spend 88% more on pesticides than they did only 6 years ago. (Weedscience.org) As has occurred with Bt crops in South Africa, the evolution of herbicide resistance is to be expected and serves to put farmers on a pesticide treadmill, increasing costs and increasing environmental contamination.

With no information on the proximity of trials to human settlements, it is impossible to guarantee the non-exposure of the public to glyphosate.

BT CROPS

Bt insecticidal toxins have been introduced into both MON 89034 and MON810 maize products. Bt toxins have been associated with the following health and environmental risks (see Ho & Sirinathsinghji, 2013 for review):

- Toxicity to non-target insects
- Lethality to amphibians
- Allergenicity in farm workers
- Stomach inflammation in livestock
- Toxicity to human kidney cells *in vitro*
- Abnormal immune response in lab animals
- Rapid spread of Bt resistance in target pests
- Rise of secondary pest infestation
- Bt sprays have been linked to allergenic skin sensitisation in farm workers

The use of a chemical cocktail on the GM trial is a health and environmental concern. Additional pesticides used in the trial such as atrazine has been banned in the EU due to its endocrine toxicity. With deletion of data on the location of the trials and their proximity to residential areas/farm workers, it is impossible to guarantee safety to humans and environment during the trials.

BIOSAFETY CONCERNS REGARDING GENE FLOW

Despite the reassurances by Monsanto that they have adequate measures in place to prevent genetic contamination from the three GM maize products, current evidence suggests that containment of transgenic DNA is impossible to guarantee. This is corroborated by the documentation of over 396 incidents of GM contamination across the globe (1997-2013) (Price *et al.*, 2014). These findings come in spite of a chronic lack of monitoring by regulatory agencies and industry as a whole.

South Africa has not escaped the issue. A study recently showed that small farmers' maize fields were contaminated with MON810 maize, while 25 % of seed stocks were positive for transgenic DNA (Iversen *et al.*, 2014). In the context of South African farming systems where seed saving and exchange is still practiced, the issue of contaminated seed spreading is a major concern. The issue is compounded by the implementation of government development projects that promote the use of GM varieties, such as the Massive Food Production Programme in the Eastern Cape, through handouts and subsidies. In light of the fact that MON87460 is being promoted through the public/private WEMA project, we must ask what mechanisms will be put in place to ensure that beneficiaries are aware of the special precautions and prohibitions related to genetically modified seeds and what safeguards are implemented to prevent the contamination of farmers' varieties?

Genetic contamination has not only occurred with commercialised crops, but also un-approved varieties, highlighting the failures of containment measures used in previous GM trials (Price *et al.*, 2014). This is exemplified by the fact that the highest numbers of contamination have been recorded in rice, despite there never having been a commercialised GM rice product anywhere in the world.

Monsanto states in the applications that it has been conducting field trials in South Africa for two decades "with no ecologically disruptive impacts recorded as a result", but there is no evidence in their applications or trial reports that they have assessed gene flow into the environment. Furthermore, to date, experience and scientific evidence (summarised below), suggests that the stringency measures they have in place are insufficient in preventing gene flow.

POLLEN AND SEED FLOW

As outlined in ACBs objection to MON87460 trials, maize is an outbreeding species that produces high levels of pollen that are spread via wind. Though the majority of cross-pollination occurs at short distances, distances as far as 300 meters are predicted to be insufficient to ensure 0 % contamination. A study of South African maize, performed by testing field trials of GM maize surrounded by non-GM maize concluded that isolation distances of above 135 m are needed to ensure contamination below 1 %, 503 m for below 0.1 % and 1.8 km for ensuring contamination below 0.01 %. Maximum isolation distances proposed in the trials by Monsanto are only 500 m.

Comprehensive analysis of maize pollination also reveals huge variation in the degree of cross-pollination, dependent on many factors including wind speed, wind direction and the presence of swirling winds[34]. Being downwind of a GM-trial was shown to significantly increase cross-pollination. Current guidelines do not consider wind-speed or direction when calculating isolation distances.

Monsanto fails to include environmental data that is necessary to estimate the levels of gene flow. Information on locations of the trials, a map of adjacent plants, as well as climactic factors such as prevailing winds (Section 8 (i), (ii), (iii) and (iv)) have been deleted from all three applications.

The previous trial reports for the same maize products used various isolation distances of:

125 m with a 4-week temporal isolation (Hopetown district)

70 m with 6-week temporal isolation (Malelane)

500 m, with no temporal isolation (Oriana)

Whether or not the temporal isolation of 4-6 weeks is sufficient to prevent gene flow is unproven in the scientific literature, especially when isolation distances are as low as 70 m. The rationale for the different isolation differences between trial sites is also unexplained by Monsanto. No data from these previous trial reports have shown experimentally that gene flow did not occur.

HORIZONTAL GENE TRANSFER

Horizontal gene transfer (HGT) is the movement of genetic material between organisms, outside of the context of parent to offspring reproduction. It offers another route for transgenic DNA to escape from genetically modified organisms into the environment, presenting a serious biosafety risk to both human and environmental health.

Monsanto dismisses the risks of HGT as an "extremely rare event" which is "only significant on an evolutionary time-scale". But, HGT frequency is more common than initially thought. It allows for the rapid acquisition of genes from other organisms with a substantial fraction of bacterial genes have been horizontally transferred. A relevant example of this is the acquisition of antibiotic resistance to survive the ecological niche of agricultural animals and humans treated with antibiotics.

The spread of antibiotic resistance genes or other genetic elements via HGT is a biosafety concern, with each of the maize products carrying antibiotic resistance genes (*nptII* gene which encodes resistance to neomycin and kanamycin) within their transgenic constructs. NptII inactivates kanamycin and neomycin - both recently classified as critically important antibiotics for humans and animals by the WHO (WHO, 2012) – and paromomycin, ribostamycin, lividomycin, butirosin, gentamicin B and isepamicin. Neomycin has also been shown to cross-react with other therapeutic antibiotics. Any release of this gene into the environment undeniably increases the chances that pathogenic bacteria are exposed to the resistance gene. Plants once degraded release their DNA into the soil where it can remain stable for at least a year (Lerat *et al*., 2007). This provides a potential HGT route from GM plants to soil bacteria. Incidentally, soil bacteria have been suggested to be a major reservoir for HGT to human pathogens (Robinson *et al*., 2013).

Examples of HGT to the environment include:

A 2012 study analysed 6 rivers in China, detecting bacteria with synthetically derived DNA sequences that included the antibiotic resistance *bla* gene. (Chen *et al*., 2012).

A study found that under conditions found in nature, *A. tumefaciens* introduced DNA into a species of disease-causing fungi that is known to infect plants. The study also found that GM DNA sequences in the *A. tumefaciens* were incorporated into the DNA of the fungi, showing that the *A. tumefaciens* was genetically engineering the fungi (Knight *et al*., 2010).

HGT between prokaryotes and multicellular eukaryotes (including plants, birds and insects) has also been documented. The rate of transfer of genes from bacteria to animal genomes is now thought to be higher than previously estimated. Evidence of HGT to animal species:

A study found that the intestinal bacteria of a person whose diet included soy carried sequences unique to the GM soy that was part of their diet (Netherwood et al., 2004).

A 2015 paper showing the presence of transgenic DNA in the genomes of rats fed GM rat feed. The study detected CaMV35S DNA in genomic DNA extracted from various tissue including brain and liver as well as blood (Oraby *et al*., 2014; Ho, 2015).

Monsanto claim that HGT can only take place when there is high sequence homology between the transgenic DNA and the host genome it is inserting into. This is based on the incorrect understanding that:

The only mechanism by which HGT can occur is via homologous recombination (a type of genetic recombination which nucleotide sequences are exchanged between two similar or identical molecules of DNA). However, HGT has been shown to occur via other mechanisms including illegitimate recombination, relying on short anchor sequences of homology between transgenic and host sequences that can then be used to introduce long stretches of novel DNA sequences (De Vries *et al*., 2004).

Genetic elements incorporated into transgenes may increase the propensity for HGT (Ho, 2013):

The CaMV35S promoter used in all three products contains within it a recombination hotspot (regions in a genome that exhibit elevated rates of recombination relative to a neutral expectation), a concern first raised by independent scientists over a decade ago.

The vector used to introduce the transgenes derives from the bacterial species *Agrobacterium tumefaciens*. This is one of the best-known examples of naturally occurring HGT, and the very reason it has become a biotechnology tool to introduce transgenic DNA into plants. *Agrobacterium* vectors may be reactivated once they have integrated into host genomic DNA. This raises a major health concern as *Agrobacterium* vectors have the ability to infect not only other plant cells, but have been shown to infect human cell lines, and have also been proposed to retrotranspose back to *Agrobacterium* (Kado, 2002). Despite scientists' warnings about the clear potential route for HGT via *Agrobacterium*, the possibility that *Agrobacterium* is a vehicle for horizontal spread of transgenic DNA and the dangers of creating new pathogens remains unresolved to this day. It is astonishing that thorough, long-term testing of HGT is not performed on a case-by-case basis.

Conceding to the possibility of HGT, Monsanto diminish the potential consequences in their response to ACB's objection of MON87460, stating it poses "no meaningful risk" as antibiotic resistance genes are "widespread in the environment". This claim is based on single study looking at various environments, though South African soil was not tested (Nesme *et al.*, 2015). As far as the ACB is aware, there has never been a study on the levels of antibiotic resistance genes in South Africa. The background presence of *nptII* or other antibiotic resistance genes in South African soil remains unknown.

5. CONCLUSION

The three applications and previous trial reports have failed to adequately show that the 3 maize varieties are an effective strategy to tackle unpredictable climate change such as drought in South Africa. It also fails to adequately provide scientific evidence that each crop is safe for human, animal and environmental health. Our submission points to a number of scientific uncertainties and risks that pose serious risks and should not be accepted by regulators and passed onto consumers and the receiving 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 nature of all three varieties. Conversely, independent literature has already provided evidence to the contrary, with parental line MON810 being detected on several occasions to be genomically unstable.

The South African experience with MON810 is the most important indicator of the limitations of single-gene approaches to tackle complex agricultural issues such as pest control. GM technologies at best, provide a short-term relief for such problems, but at a high cost to human health, environment, consumer choice, the economy and the livelihoods of South Africa's farmers. There is little use in continuing this path with yet more of the same. We support the implementation of cheaper, sustainable methods that support the rights of farmers protect the future biodiversity of our crops and protect the safety of a major staple of the South African diet.

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Annex 1: List of objections sent to government

The following objections were submitted to the Registrar: GMO Act and copied to the ACB:

Date	Name
24/05/2016	Liana Dippenaar
24/05/2016	Melanie Carstens
24/05/2016	Arther Kerr-Sheppard
24/05/2016	Carol Shaw
24/05/2016	Dumizani Zulu

24/05/2016	Rilla Maher
24/05/2016	Daniella Maher
24/05/2016	Catherine Hofmeyr
24/05/2016	Nadia Geldenhuys
24/05/2016	Emma Hedley
24/05/2016	Isabel Porzio
24/05/2016	Michael Julie
25/05/2016	Marsha Botes
25/05/2016	Roche Burgers
25/05/2016	Alani Keiser
25/05/2016	Theresa Zgerski
25/05/2016	Erica Inches
25/05/2016	Franck De Saint Simon
25/05/2016	Deborah Paterson
25/05/2016	Jeremy Van Der Want
25/05/2016	Melanie Steyn
25/05/2016	Reza Salie
25/05/2016	Zak Swartz
25/05/2016	Carola Meyer
25/05/2016	Adrian Phipps
25/05/2016	Jennifer Cherry
25/05/2016	Anthony Cunnington
25/05/2016	Nina McDonough
25/05/2016	Natasha Johnson
25/05/2016	Helen Behm
25/05/2016	Lesley Chorn
25/05/2016	Kyle Thomson
25/05/2016	Jeanine Bendzulla
26/05/2016	Charlotte Amery
26/05/2016	Marthinus Steyn
26/05/2016	Lionel Dick
26/05/2016	Caroline Hurry
26/05/2016	Jane Burger
26/05/2016	Tandi Kitching
26/05/2016	Hetty Zantman
26/05/2016	Nathalie Strassburg
27/05/2016	Dr. Marilize Burger
27/05/2016	Caroline Hurry
27/05/2016	Lara Burn
27/05/2016	Leanne Reeve
27/05/2016	Peter Visser
27/05/2016	Maria Mostert
28/06/2016	Johanet Kriel
29/06/2016	Jo Van Zyl
30/05/2016	Andre Langeveldt

30/05/2016	Lisa Sherwin
31/05/2016	Tina Slater
31/05/2016	Karen James
31/05/2016	Dawn Schmoor
31/05/2016	Suzanne Cadman
01/06/2016	Charles Oertel
01/06/2016	Ina Stofberg
02/03/2016	Carol Coney
03/03/2016	Michelle Downey
06/03/2016	Priya (Sandton Seven Point Five)
09/06/2016	Piet Bosman
16/06/2016	Grant Rahme
20/06/2016	Mischa Capazario