How effective and safe is *Bt*-maize in South Africa?

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The South African National Biodiversity Institute (SANBI) recently released the outcome of the South Africa–Norway bio-safety cooperation project 'Monitoring the environmental impacts of GM maize in South Africa'. This project studied possible impacts of commercial genetically modified (GM) maize (MON810 maize), containing the Cry1Ab protein (*Bt*-protein), on the South African environment.[1] The report addresses concerns about *Bt*-technology in GM maize in South Africa, in particular the development of possible resistance of target insects to the *Bt*-toxin and of unintended effects of GM maize on non-target organisms.

Bt-protein is produced by a common soil bacterium first isolated in the Thuringia region of Germany. When eaten by an insect, the digestive system activates a toxic form of the *Bt*-protein killing the target insect within a few days. The ability to transform plants with the gene sequence of the *Bt*-protein provided the opportunity to produce the protein inside the plant, instead of a *Bt*-spray application commonly used by organic farmers. Production inside the plant created the first generation of *Bt*-crops, which were investigated by the South African–Norwegian project team. Over the last 20 years, there has been a reduction in the amount of chemical insecticides used for insect control on these *Bt*-crops. In addition, as outlined in a recent report by the Academy of Science of South Africa (ASSAf), *GMOs for African agriculture*, these crops might offer benefits.[2,3] However, relatively little research has been carried out in our country regarding their environmental impact even though the *Bt*-crops have been grown for several years.

One of the key outcomes of the project was the observation of varying levels of the expression of the *Bt*-toxin that was interpreted as likely to contribute to the development of insect resistance to the *Bt*-toxin in South Africa. However, development of such resistance against the *Bt*-toxin is not different to the development of resistance to any other chemical used in insect control. The finding of the project team is therefore not entirely new. When *Bt*-technology was introduced almost 20 years ago using GM plants, scientists projected a rapid increase in the resistance level against the *Bt*-toxin. Worst-case scenarios even predicted that pests would become resistant to such GM *Bt*-plants in a very short time period. This prediction was further supported by a study indicating that the frequency of a resistant gene in the pink bollworm was about 1 in 10, about 100 times higher than estimated when compared to other pests of *Bt*-crops. However, a rapid build-up of resistance has not occurred, despite the fact that *Bt*-crops have been grown since 1996 on more than 162 million hectares worldwide. Growing *Bt*-crops on millions of hectares has generated a selection process for insects never experienced before and most insect pests are still susceptible to the *Bt*-toxin. However, there is evidence that frequency of resistance alleles in insects has recently increased against the first generation of *Bt*-crops.[4,5]

The introduction of the refuge strategy, in which a non-*Bt*-crop is grown near a *Bt*-crop to provide a source of non-resistant target species to prevent domination by a resistant population, has helped tremendously to delay resistance build-up against nearly all targeted pest populations. Therefore, non-compliance of South African farmers to the refuge strategy when *Bt*-maize was introduced in South Africa might ultimately contribute to an accelerated resistance development that is not experienced in other countries that strictly apply the refuge strategy. The report also mentioned possible resistance development in target pests as a result of variation in the insecticidal *Bt*-protein content in GM plants, depending on the local environmental conditions. Indeed, the refuge strategy requires a large amount of the *Bt*-protein to be continuously produced in a *Bt*-plant to limit larval growth and the possible build-up of resistance. Therefore, continuous feeding of insects on plants producing only a sub-lethal dose might seriously compromise the refuge strategy. A sub-lethal dose may also be produced by contamination of refuges or non-*Bt* fields by *Bt*-toxin genes from *Bt*-maize, as mentioned in the report and also reported by other researchers.[6] Studies have already shown such variability for the *Bt*-protein produced in individual plants. But this variability in *Bt*-protein amounts is not surprising and has also been found with other non-*Bt* GM plants.[7] Both plant maturation and photosynthesis have been identified as possible factors controlling *Bt*-protein production in GM plants. From our own research, we have further evidence that moderate water deficits decrease *Bt*-protein production but, surprisingly, these water deficits cause little decrease in *Bt*-efficacy; secondary metabolites produced under drought possibly support *Bt*-toxin action. Stabilising *Bt*-protein expression in individual plants to prevent resistance development may therefore be a worthwhile future research topic. In addition, the introduction of a new generation of more efficient *Bt*-proteins and applying gene pyramiding approaches by combining two types of *Bt*-proteins, or two different types of toxins, can be considered as strategies to prevent possible resistance development.[8] Knowledge gained from the introduction of the first generation of GM crops should help to minimise the risks involved in introducing this new type of *Bt*-crop.

The project team also investigated environmental concerns including the unintended *Bt*-effects of non-target insects and gene flow to non-*Bt* fields. Such gene flow can certainly be a major commercial concern when both non-*Bt* and *Bt*-crops are grown in close proximity and a non-*Bt* crop is polluted by *Bt*-pollen. Although studies have been previously carried out to determine 'safe' distances, local environmental conditions may vary greatly, necessitating a more detailed study about pollen pollution in South Africa.

The importance of unintended *Bt*-effects on non-target insects is a continuing concern. Although the recent ASSAf report indicates that non-target studies have demonstrated that *Bt*-crops do not have any unexpected toxic effects on natural enemy species of agricultural pests,[3] studying insect diversity in a *Bt*-crop growing country should always be a vital procedure, as any direct unintended effect on non-target insects cannot be excluded *de facto*. This recommendation was also highlighted in the SANBI report. Development of *Bt*-resistance of a non-target lepidopteran insect, the African bollworm, as a result of exposure to *Bt*-maize could be considered as an example of the preferential, but non-exclusive, action of the *Bt*-toxin against a specific target pest. Because *Bt*-maize had no effect on African bollworm survival, the team expressed the concern that the insect might become an important secondary pest. This further demonstrates that diversity has to be studied case by case. A transfer of data from one growth area of a *Bt*-crop to another might simply not be sufficient.

The project team also focused on possible structural changes of the *Bt*-protein when expressed in a plant as well as changes in both micro-RNA and protein profiles in a *Bt*-plant. These are interesting and worthwhile future research topics to be studied in more detail but should not be used at this stage as an argument for an existing risk. In particular, protein profiling using a proteomics approach, but also metabolite profiling, are becoming increasingly important in risk studies.[9] Such profiling techniques might ultimately provide a rigorous scientific basis for the identification of any possible unintended health effect, such as allergen production. The project team used a 2D gel approach which compares two gels with protein spots of various intensities, but without demonstration of reproducibility. With only a limited number of protein spots detected (400) and without any clear identification and quantification of changed spots, in particular detection of the *Bt*-protein spot, this would hardly satisfy current international standards. A major further challenge of the proteomics approach will be the analysis and interpretation of the amount of data generated with many proteins still unknown. Cost and technical skills might also be limiting factors in South Africa.

No technology is without risk. In addition, some people have a basic fear of new technology and take time to become accustomed to a new technological idea and using products derived from it. The project team suggests establishing a research institute in South Africa to evaluate the current and future risk of GM crops. I personally would support a possible variation of this idea – a virtual institute (which is open-minded and science-based) could be established with participants from both the sciences and social sciences. Such an institute should not be viewed as an entity to erect impenetrable barriers to any introduction of transgenic crops or food derived from these crops. An institute developed to collect data to provide a sound judgement on the risks associated with GM crops may also greatly help to overcome the current fear of GM crops. Such an institute may further limit misinformation about GM technology by educating the public about the advantages and limitations of and risks involved in the technology. Initial interaction between the project team and an independent centre concerned with GMOs in Norway to understand better the type of research being conducted by them was an excellent start to catch up with global trends.

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