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OBJECTION TO APPLICATION BY DOW AGROSCIENCES TRIPLE STACKED GM MAIZE, EVENTS, 1507 x NK603 x 59199.

TO: THE REGISTRAR: GMO ACT, DEPARTMENT OF AGRICULTURE

January 2006

The African Centre for Biosafety (ACB) has to date, lodged objections to the following applications by Dow Agrosciences for commodity import clearance:

-GM Maize event 59122
-GM Maize event 59122xTC 1507
-GM Maize event 59122x NK603

We will thus not repeat the grounds upon which we have based our comprehensive objections, but reiterate them here, and request that the Executive Council take these into account in considering this application, see further,
http://www.biosafetyafrica.net/objections

FURTHER GROUNDS FOR OUT OF HAND REJECTION

1. **GM 59122 NOT YET APPROVED IN USA/NOT BEING GROWN IN USA** We, are utterly amazed that Dow Agrosciences is persisting in seeking regulatory approval for the current GM maize event 1507x 59122 x NK 603, in the light that the cry genes Bt Cry34Ab1/Cry35Ab1 used in event 59122 have not yet been registered by the Environment Protection Authority in the USA. According to information at our disposal from our sources in the USA, the GM maize in question, containing the triple gene is thus not yet in commerical production in the USA or any where else in the world.

2. **FLAGRANT DISREGARD FOR SA GOVT'S MORATORIUM** Dow Agrosciences is keen to break into the GM seed market and is hence seeking approval for its GM maize varieties in the hope that it can convince farmers in the US to plant its GM maize in other words, that there is a market in South Africa for this GM maize. We find this application to be deeply offensive to us, as it is highly disreptful of decision by the South African Executive Council not to grant any further approvals of new GM applications until such time that the Department of Trade and Industry (DTI) has conducted its socio-economic studies of the impacts of GM imports on South African society and the economy.

3. **NEW IMPORTANT FOOD SAFETY STUDY TO BE TAKEN INTO ACCOUNT** During 2005, scientists, Prescott VE et al., 2005, published their work 'Transgenic expression of bean alpha amylase inhibitor in peas results in altered structure and immunogencity, J. Agric. Food Chem. 53:9023-9030' on GE immunogenicity which shows that even moving a gene to a closely related plant resulted in changing protein to an immunogen in mice that has properties similar to allergenicity. This resulted in the developers of the GM crop (pea) to voluntarily withdraw their crop from consideration for safety review and commercialistion.

This important study shows that the current South African regulatory system cannot adequately detect potential new allergens, especially given the moderate stability of Cry34.

What did the Study Find?

- The scientists fed mice peas that contained a gene from beans that produced a transgenic protein (alpha-amylase inhibitor, AAI) intended to control insect pests. They also fed mice non-transgenic peas, or beans from which the gene/protein originated. After several weeks, the mice where tested in several ways to see if

they had become immunogenically sensitized to the protein.[1] The mice that ate the transgenic peas showed sensitivity when later exposed to transgenic peas by injection or respiratory exposure, showing immune responses such as tissue swelling and respiratory inflammation. Beans (the source of the non-transgenic version of the gene) did not cause these or other responses that also occur during allergic reactions.

- Simultaneously feeding transgenic pea and several other food proteins increased the immunogenicity of those other proteins
- Tests used to determine the chemical structure of the original bean and transgenic pea AAI showed that in pea, the protein was modified (glycosylated) differently than in bean. The authors believe that these relatively subtle differences were probably responsible for the immunogenicity of the protein in pea (possibly along with other undetermined changes).

What is the Significance of these Findings?

- Genetically engineering this gene/protein caused changes in its structure (addition of carbohydrate molecules, called glycosylation) that made it antigenic (immunogenic) in mice. The native bean protein had low antigenicity. This demonstrates that genetic engineering can cause unexpected changes in the transgenic protein that may be harmful. This is all the more interesting, because bean and pea are relatively closely related plants (both in the legume family). So one might predict (as proponents of GE have) that a gene or protein transferred from one to the other would act in a predictable manner, and would not be altered, which was not the case.
- The changes in structure would almost certainly not have been detected by the tests for allergenicity that are currently carried out during the GE regulatory process. The mouse tests used in this study, or anything similar to them, are not required for regulatory purposes. The amino acid sequence (primary structure of the protein) was identical for the bean AAI and the transgenic bean AAI in pea. So sequencing the gene or protein (which is not required in the U.S., but is sometimes done), would not detect the differences seen in this study. In addition, both the bean AAI and the transgenic AAI were glycosylated, but the chemical details of the glycosylation differed. These differences would not be detected by the tests that are currently performed for U.S. regulatory agencies (those required by U.S. EPA, but not required by U.S. FDA). The tests typically done for EPA only look at whether the transgenic protein is, or is not, glycosylated compared to the non-transgenic version (+ or – glycosylation). That test would not detect differences in the nature of the glycosylation, as occurred in the transgenic peas. Gel electrophoresis of the proteins, which is typically performed for regulatory processes, did detect differences in size between the pea and bean AAIs. But similar differences between proteins have been dismissed by regulators in the past.
- Reports of similar mouse studies in 1998 reportedly showed accurate prediction of antigenicity in several proteins compared to the human responses, and that proteins that were stronger food allergens gave stronger antigenic responses in the mouse. However, the regulatory agencies have given little assistance to researchers trying to develop this and other animal models that may predict

[1] Because mice do not have immune reactions identical to allergy in humans, the mouse response is properly characterized as an immune response, and the protein as antigenic. But the response has several physiological and biochemical similarities to allergy and asthma.

allergenicity, despite long recognition that current *in vitro* approaches are inadequate.

- When the AAI is heated (cooked) it largely losses its ability to inhibit alpha amylase (kill insects), but retains its ability to cause an immune response. Companies have often used loss of specific activity of a protein as an argument that it is unlikely to be an allergen, even though previous studies have shown that denaturing by cooking (loss of activity) does not always lead to loss of allergenicity. This study adds to that data.
- The ability of transgenic AAI to increase the antigenicity of other proteins (act as an adjuvant) suggests the possibility that it may increase the allergenicity of other proteins in the transgenic plant.

4. **ABUSE OF SOUTH AFRICA'S REGULATORY SYSTEM.** It is becoming customary for mulitinational gene giants/agrochemical companies to abuse the South African regulatory system and seek food safety approvals (commodity clearances) for GM maize that is still undergoing field trials in the US. Monsanto has tried to obtain food safety approval in 2004 for its non-existent GM wheat, and now Dow Agrociences, and in May 2005, Syngenta sought commodity clearance for its GM maize MIR 604 which had not yet been approved in the USA.

We are thus of the opinion that the Executive Council should request that Dow Agrosciences withdraw its application with immediate effect. Valuable and indeed, scarce tax payers money should not be squandered on paying members of the Advisory Committee to assess this application.