

REPORT TO THE OILSEEDS ADVISORY COMMITTEE:
BRIEF OVERVIEW OF THE ISBGMO SYMPOSIUM ON GMO IMPACT
ON THE ENVIRONMENT: ENVIRONMENTAL RISK ASSESSMENT

CAPE TOWN, 9 – 14 NOVEMBER 2014

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1. INTRODUCTION

The 13th International Symposium on the Biosafety of Genetically Modified Organisms (GMO), organized by the International Society for Biosafety Research (ISBR), was held at the Westin Hotel, Cape Town, on 9 – 13 November 2014. The lead organizer was Dr Morven McLean, President of ISBR, USA, assisted by the local co-organizer Dr Hennie Groenewald, Head of Biosafety SA, and supported by some 20 committee members. Some 270 participants attended of which 100 were from Africa. Though the overall mandate covered GMO impact on the environment, the specific focus was on Environmental Risk Assessment (ERA). The programme generally started each day with a plenary session, followed by three sessions running concurrently (22 sessions in total).

ISBR is the leading scientific society of scientists, risk assessors, regulators, policy makers, students, and others, with the objective of promoting science in agricultural biotech and environmental risk assessment by way of international symposia on biosafety. In South Africa, the Department of Science & Technology is the custodian and coordinator of the national system of innovation and the 10-year innovation plan, also the science-based National Bio-economy Strategy.

The concurrent sessions meant that I could only attend one-third of the sessions. Some 147 abstracts were contained in the symposium booklet but quite a number of presenters did not submit abstracts on time. My synthesis on information conveyed at the event is, therefore, based on notes taken on one third of sessions, relevant but not all abstracts, and personal discussions with various speakers. I followed up by email the issue of canola gene flow with Dr Linda Hall of Canada and she kindly responded by sending several articles and a range of references. Several of these articles were used to add more information, especially on pollen flow studies in canola. Dr Marc Ghislain of the International Centre for Potatoes unit in Kenya, subsequently provided details of his cost analysis applicable for moving a GM potato application through the biosafety regulatory framework. This can indicate costs for other GM crops as well. However, his draft article is still confidential and I can only use the key outcome. Email contact with some other speakers still awaits their responses.

This overview deals with main elements of ERA individually, and some technical presentations separately, key points from published scientific articles, followed by my personal comments and impressions. ERA information has been included as this will show what awaits South African applications for approval of GM crops.

2. ERA PRESENTATIONS

2.1 Objectives of Symposium

Wendy Craig of the International Centre on Genetic Engineering and Biotechnology (ICGEB) presented the historic time line for GM/biotech innovation:

- 1983: First GM tobacco developed
- 1986: First field trials of GM tobacco
- 1987: Field trials GM tomato and tobacco
- 1992: Flavour Saver tomato released
- 1992: Convention on Biological Diversity
- 1993: OECD considers biotech scale-up
- 2000: Cartagena Protocol on Biosafety drafted
- 2013: 178 million additional hectares GM crops planted by 27 countries

The matter of assessing GMOs and, specifically, GM crops, originated from the 1992 Convention on Biological Diversity which stated that modalities may be considered to handle potential impact of GM crops on biodiversity. The subsequent Cartagena Protocol on Biotechnology, adopted in 2002, set standards and requirements for member states for managing Transboundary Movement of Live Modified Organisms (LMOs) that may have adverse effects on biodiversity and human health. The protocol has three addenda, one of which stipulates detailed biosafety assessments prior to shipment. From the scope of LMOs, transboundary movement and adverse effects, biosafety assessments soon moved to all GMOs and GM crops. The Protocol then established an Ad Hoc Technical Expert Group and will now update its risk assessment guidance document.

The basic objective of the symposium was to expose participants to status of ERA and the need to improve and harmonize guidelines, building upon lessons learned and experiences over 20 years. The first session dealt with practical ERA approaches and the need to have proper Problem Formulation as starting point. The second session dealt with RNAi, a natural genetic system for inhibiting expression of a specific gene, adapted for use in biotechnology to silence genes that determine harmful traits. Quite a number of presentations covered the slow progress in approval of GM trees in Session 3. Other focal areas covered quality

of scientific studies, science communication, synthesis of evidence from GMO impact assessments, insect resistance management, and addressing public inputs.

2.2 Problem Formulation

One cannot plunge into safety assessments without defining and analysing the issues around potential risks and then formulate what the perceived problem is.

Problem formulation must deal with the GM trait, pollen and gene flow, non-target organisms, weediness, genetic diversity, etc. Wendy Craig of ICGEB stated that the first ERA approaches came from regulators familiar only with non-GM agriculture which led to lack of international consensus on practicalities and identification of potential harm for GMOs. There needs to be a baseline for comparative risk assessment. Z. Barbara reported how they developed framing questions on GM weevil resistant sweetpotato in Uganda and designed an analysis plan for assessment. R. Layton of DuPont, USA, explained that high quality data beginning with an ERA framework, problem formulation, getting data to address uncertainties and to test hypotheses, including quality of exposure and hazard estimates. These organized steps will also help to identify gaps in data.

2.3 Fit-for-Use Requirements

An ERA will have to deal with a wide range of scenarios of different crop species, genetic modifications, environments, target and non-target pests or weeds, and each approach must be tailor-made for specific situations. Layton of DuPont Pioneer stated that the main purpose of ERA is to provide risk managers with the best data; therefore, explicit problem formulation must focus on protection goals that are most important. Hazard and exposure are combined for the potential risk to be communicated to risk managers. L. Ramatha from Malaysia gave a review of fit-for-use approach in the limited release (Mark-Release-Capture trial) of GM mosquitoes that had the dominant lethal gene to reduce mosquito increase. Their approach made use of data from the Cayman Island mosquito release, USDA-APHIS, CSIRO, applicant documents, and public inputs, all used to compile the final risk assessment process. The government Biosafety Board had 180 days in which to make a decision.

2.4 Uncertainties in ERA results

Most endeavours have elements of uncertainty such as GMO detection in products for which a lowest level of detection standard has been set, as one example. One common mistake in environmental risk assessment is to keep on posing questions, known elsewhere as the bucket approach (until the bucket runs over). Paul Keese of the office of the Gene Regulator in Australia cautioned that all risk assessments contain uncertainties and generating more data often leads to more uncertainty. The first tier in ERA is uncertainty analysis. Assessors should separate need-to-know from nice-to-know. It is useful to differentiate harm from significant harm, use more simple indicators of risk, more simple forms, use conservative estimates,

set parameters for quality and sufficiency of data, set upper and lower boundaries for risk likelihood. Also apply second tier uncertainty analysis. Anne Myhr stated that release of GMOs into the environment presents uncertainties of expected benefits and adverse effects. The complex relationship between economic development and ecological systems must be taken into account. She recommended that the precautionary principle must be used to achieve full certainty on expected benefits and adverse impact before full-scale release is approved.

During question time I posed the comment to Keese that while we are dealing with reducing uncertainties, anti-biotech groups are creating more uncertainties. (See the Annexure for a case in point).

2.5 Science-based Evidence Reporting

Not all scientists or institutions use a common way of drafting reports on outcome of studies. Several speakers offered guidance on doing evidence-based reporting. Jeremy Sweet from the UK reported that there are numerous field studies on cultivated GM crops and their impact on target and non-target organisms. A comprehensive synthesis of all the data by reviewers is underway on the major GM crops: insect resistant and herbicide tolerant traits. The full review will be published in 2015. N. B. Haddaway of the UK provided an overview of evidence synthesis, systematic maps and reviews, including quality appraisal of methods and different approaches by other sciences such as social and health. The potential impact of evidence synthesis on decision making is being studied. R. Wilhelm of Germany highlighted elements of the GRACE and Cadama projects (more in 2.7 and 2.8).

2.6 Minimizing Bias in Assessments and Reporting

Scientists with practical expertise in biosafety assessments can never be devoid of interests due to own personal projects, corporate or institutional interests. The possibility of bias may occur unintentionally or, theoretically, by design, mind sets, or also being influenced by background such as social science, health, farming, DNA diagnostics, historical backgrounds. Therefore, it is the responsibility of reviewing teams to make sure that potential biases do not affect quality of science. Bias may occur in five cases: (a) landscape non-homogeneity due to low levels of non-target organisms or Bt test fields not having had the same historic farm management; (b) performance bias with plots' statistical design not good enough, plots not exposed to same pesticides or not large enough to show adequate taxa numbers; (c) detection bias with measurements not objective, methods used not appropriate, sampling over replications insufficient; (d) attrition bias when non-uniform flooding or drought stress occurs; and (e) reporting bias when project is funded or executed by party with vested interests.

2.7 The European GRACE Project

The EU is funding a project called GMO Risk Assessment and Communication of Evidence (GRACE). W Ralf from Germany reported that GRACE aims to create greater transparency and traceability of information on potential risks and benefits with release of GMOs into the environment. To this end, an internet open-access database will be established. Grace comprises a very large number of scientists who will review studies or repeat such studies. Assessment of MON 810 Bt insect resistant maize data since October 2014 found that there is no evidence that this GM modification has led to any toxicologically negative impact. This finding was immediately challenged and rejected by a GMO testing party who, to date, has refused to discuss their allegations with GRACE staff. (See attached Annexure).

2.8 The CADIMA Project

The Central Access Database for Impact Assessment for Crop Genetic Improvement Technologies will not be time bound though it links to GRACE. Their collaboration for Environmental Evidence focus, operates in three areas: a central access information source, informatics tools for core steps of a systematic review, and an open-access database on animal feeding trials. It is intended as open- access primarily for review teams.

2.9 Communication and Public Awareness

Paul Keese covered the Australian efforts to be seen by its public as open, transparent and consultative. However, this is subject to challenges: the variation within the public on values, perceptions and expectations on GM technology; tension between narrow focus of legislation and wide public concerns; maintaining neutrality and integrity while addressing misconceptions; open for consultation but limiting role in decision making; declaring some information as confidential. Australia is now partly guided by its Gene Technology Ethics and Community Consultative Committee, and experience from other countries.

2.10 Cost of GM biosafety framework process

We do not have much information on the cost of successfully passing the strict biosafety regulatory process due to lack of local experience. To date, all commercially released GM crops have made use of foreign MNC data in applications, supplemented by some local investigations, as may have been required. Tentative estimates have been around R14 million to R20 million per application. These do not include the impact of delays due to back-referral to the applicant or to farmers not having the benefit of improved crop protection during the delays. It may be that the regulatory process may be more costly than R & D to develop the GM product. Marc Ghislain of the International Potato Centre in Kenya presented an analysis of moving a late blight resistant GM potato through the biosafety system. He concluded that the cost of US\$1.4 million (R16 million) to US\$2.3 million (R26 million) over 8 – 9 years will be less for a non-profit

institution than for a private company. It will even be much less if only differences due to the novel GM trait between the GM potato and its conventional counterpart are subject to risk assessments. A representative from an international company indicated privately that their costs are higher as they usually also apply for release in neighbouring countries, as often considered necessary.

3. OTHER RELATED TECHNICAL PRESENTATIONS

3.1 **Canola** outcrossing with wild relatives.

Melody McGeogh of Stellenbosch University has published several articles on possible pollen flow/gene flow from canola to wild relatives such as *Sinapsis arvensis* (wild mustard) in South Africa. Linda Hall of Canada in her presentation at the ISBGMO symposium, stated that pollen flow does not equal gene flow. For genetic impact there has to be sexual compatibility, fertilization to produce a hybrid plant with fertile pollen to produce fertile offspring, termed fecundity. The hybrid must have fitness, growth vigour, produce viable seed that can also persist in the soil to germinate later. Interspecies crosses usually have low fitness. There are 13 traits that determine whether a plant will become weedy. Two other questions are relevant: Will the GM trait persist in the wild population and, if so, what will the effect be, such as selective advantage over wild relatives? I have made e-mail contact with Dr Hall who provided five research articles as well as a list of related articles, and she offered her assistance if we have other questions. (Excerpts from these articles are covered below in 3.3 to 3.5).

3.2 **Canola** outcrossing in Italy.

An Italian study was reported by Anna Buonamici. Pollen dispersal from canola was detected 30 and 34 m away from the canola field in two test fields. Some 25% of seedlings were genetically tested and found to be hybrids with wild mustard (*Sinapsis*). Spatial separation of canola is recommended but will differ according to the geography of the field and wind directions.

3.3 **Canola** pollen-mediated gene flow (Beckey & Hall article, 2008): Canola has an out-crossing character that may be as high as 30% in the field. Such outcrossing may make it difficult to maintain compliance with the EU level of 0.9% presence maximum of GM in adjacent non-GM. They assessed four studies and statistical models used from other researchers who used glyphosate tolerant pollen donor varieties with the following outcome:

- Interplant outcrossing is variable due to mix of natural and insect-mediated pollen flow

- Outcrossing rate depended less on size of field than length of gap or no gap between pollen donor and non-GM recipient rows
- The hybrid from the outcross seems to be more sensitive to glyphosate spray than the resistant pollinator, therefore, may have less survival
- Isolation distance will be more efficient in reducing outcrossing than using a pollinator barrier
- Three other studies used a male-sterile recipient for measuring pollen flow; one test being 0 – 50m with no gap between donor and recipient and another 50 – 5 000m with no adjacent fields. The former showed probability of 0.75 at about 5 – 8m, declining to negligible towards 130m. The second set for long distance flow started at 0.006 probability to very few plants towards 3 000m.
- The recommendation was that impure seed and volunteers may contribute equal to or more than outcrossing; therefore, certified seed and removal of volunteers through integrated herbicide and non-herbicide practices are required. Non-GM should not be planted on fields that had GM crop in the previous season.

3.4 GM **Canola** persistence in Canada. A review article (Harker et al, 2006) showed that canola at 6 plants per m² in wheat fields will depress yields by over 6%, at 52 plants over 50%. Presence of wild mustard (here stated as *Brassica kaber*) with similar growth habit as canola, can depress yields between 15 and 75 %. Yet, despite the high level of spilled canola seed after harvesting, such volunteer plants in the next season are minimal after weed management practices.

3.5 Glyphosate resistant **Canola** gene flow (article by C. Mallory-Smith and M-Zapiola, 2008) has been reported as being a weed in Manitoba, Canada. Canola may also grow along roads although seed retained in soil quickly loses viability. Most studies have not yet assessed canola impact on vegetable species such as Brussel sprouts and kale (*B.oleracea*) or Chinese cabbage and turnip (*B. rapa*). Such crosses are rare and have little impact as these vegetables are harvested before flowering but it may occur in seed production.

3.6 New breeding techniques and biosafety

Rene Custers of Belgium covered EU regulations that are both process- and product- based. By definition, non-biotech breeding in the EU and elsewhere does not fall within the GM regulations. However, new breeding techniques that use natural, but adapted procedures, such as site directed mutations, DNA editing, stacking natural genes into the same species, conventional scion grafted onto GM root stock, etc., have caused re-thinking with anti-biotech groups' position that all genetic changes are GMOs and must be regulated. Mutation breeding, natural or induced, is a standard way of changing genetics and is, by definition, not GM

technology. (NOTE: This issue is highlighted by an article by Dr Huw Jones of Rothamsted Research institution, UK, in *Nature Plants*, 2015).

3.6 Development of a harmonized biosafety framework and assessment in Africa.

The COMESA trade block of 19 countries started on this project more than eight years ago by establishing a panel of 10 biotech experts and a drafting team to assist (I served on the panel and my associate on the drafting team for two years). The process then stalled due to interaction of COMESA Secretariat with each of the member states. This was followed by a biotech desk under Getashew Belay in the ACTESA trade office. The Association for Strengthening Agricultural Research in Eastern and Southern Africa (ASARECA) played a prominent role in these processes. Michael Waithaka of ASARECA presented the following key developments:

- COMESA members raised concerns about increase of GM crops in 2001 and biosafety became one of the issues discussed in their trade harmonization meetings
- In 2006, the focus moved to commercial GM planting, commercial trade, and emergency food aid that may contain GM.
- Ministerial meetings took place in 2008, 2009, 2010, 2013, and 2014
- Note was taken of increasing contained field trials with GM varieties
- The framework developed comprises: application for GM variety testing and/or release goes from the national competent authority to the COMESA secretariat; the panel of biotech experts at COMESA will use their Genetic Risk Assessment Committee for assessment and the outcome of recommending rejection or approval for use as food, feed or processing will be forwarded to the Secretariat. The decision will be applicable to the COMESA region, subject to country subsidiarity for accepting or rejecting the decision, taking into account benefits and risks associated with GMOs.
- In February 2014 the COMESA Council of Ministers adopted this policy for the region.
- I posed the question of implementation to Waithaka after his presentation. His response was that implementation starts when the first 2 or 3 countries approve the policy and other member countries can come in when they are ready.

4. COMMENTS, CRITIQUE AND RECOMMENDATIONS

4.1 Participation in the ISBGMO Symposium was a valuable experience in broadening my understanding of environmental risk assessment approaches and requirements, as well as what awaits South Africa in terms of both re-assessments

of approved GM crops and national R & D innovation that will need to go through biosafety assessments that include ERA.

- 4.2 The Symposium was built around ERA with a few other technical presentations on the side, thus the event was not a holistic view on GM crop impacts.
- 4.3 The event was dominated by European and some Scandinavian presentations. My rough analysis showed the following: Europe and Scandinavia 38% of presentations, 32% of posters; USA plus Canada 29% of presentations and 13% of posters; Asia 5% of presentations and 11% of posters; Latin America 5% of presentations and 11% of posters; Africa 30% of presentations and 8% of posters; Australia 5% of presentations and 8% of posters; South Africa 8% of presentations and 11% of posters. I shall leave interpretation to the reader.
- 4.4 The ERA point of departure is based on working from the Cartagena Protocol on Biosafety, i.e. GM crops may be hazardous to biodiversity and the environment and, therefore, should be biosafety assessed.
- 4.5 The new technical approaches to ERA, combined with the short term GRACE and the longer term CADIMA projects will not silence critics (Annexure below) but will hopefully improve decision making by regulators.
- 4.6 It is doubtful that South African ERA application in the past, complied with standards, especially as regards the defined objectives and problem formulation are concerned.
- 4.7 How will South Africa adopt the new requirements: blindly just following or assessing applications on a case-by-case basis, and do we have the national human resources to do that? I put the latter part of the question in private to two South African scientists. One said no problem to comply, the second said difficult as the non-target insect population differs from one on-farm sample to the next on the same field.
- 4.8 Will government properly fund projects through the Department of Environment for research and capacity building? Acceptance of a US\$2 million donation from Norway, a non-GM country, through their Genok institute, raises questions.
- 4.9 What South Africa needs is urgent capacity building in human resources from scientists and drafters of applications, GMO advisory committee, reviewers, to the Executive Council where decisions are made. Approaches should be based on South African conditions, target and non-target organisms, farming practices, on a crop-by-crop species basis. Applications for research funding must include an estimate of costs associated with regulatory biosafety requirements, as well as registering plant breeders' rights and/or patents.
- 4.10 Industry stakeholders must engage in their own capacity building so that they can help to guide government in the biosafety process as regards practical and effective regulations.
- 4.11 Biotechnology and plant breeding experts must get involved in advising government on what is inside GMO regulations and what is outside.
- 4.12 The six government departments represented on the Executive Council need to accept that they are compelled to engage in proper public awareness: all six of them.

ANNEXURE: GRACE PRESS RELEASE, 14 Jan 2015

Testbiotech refuses to join public scientific debate

In October 2014, the EU-funded research project GRACE invited experts and interested members of the public to take part in a scientific discussion of the results of its 90-day feeding studies with genetically modified MON810 maize, which were published the same month. A public discussion forum was set up for this purpose, hosted by the scientific journal Archives of Toxicology. Testbiotech e.V. has been criticising the study in public ever since, but refuses to take part in the open discussion on the forum. In addition, in its key criticisms of the study, Testbiotech refers to an analysis by an anonymous toxicologist. Under these circumstances, GRACE no longer sees any basis for continuing the debate with Testbiotech.

The aim of the feeding study was to test the added scientific value of feeding trials for risk assessments of GM plants. The results showed that food containing up to 33 per cent MON810 maize did not have any negative effects on male or female Wistar Han RCC rats following subchronic exposure (90-day feeding trial). In response, Testbiotech e.V. (Executive Director Dr Christoph Then) published press releases and critical background reports on the results of the GRACE study. Among other things, Testbiotech accused the research project of having drawn the wrong conclusions from the trial data. Suspected manipulation of the results was also mentioned. In addition, Testbiotech claimed that some of the scientists involved in the study had links to industry and were therefore not independent, and called for the paper to be withdrawn.

GRACE opens forum for public discussion of its research

Since then, the GRACE project has responded in detail to Testbiotech's accusations in a number of open letters and statements ([correspondence between GRACE, Testbiotech e.V. and the EU Commission](#)). In December 2014, the Editor-in-Chief of Archives of Toxicology, Prof. Jan Hengstler, launched the open scientific forum with a [leading article](#). In another contribution on the forum, Prof. Pablo Steinberg, one of the main authors of the GRACE paper, [responded in detail](#) to Testbiotech's criticisms of the study. GRACE has repeatedly invited Testbiotech to take part in the forum and to share its arguments and discuss them in a scientific manner with interested experts and members of the public, but without success.

GRACE has attached great importance to transparency and ongoing, public, scientific discussion of its work since the project planning phase. Throughout the project, GRACE has encouraged, and continues to encourage, debate with stakeholders and external experts in the forums set up for this purpose. Both when it came to drawing up the study plans and discussing the interim results, more than 700 stakeholders and scientists were invited to take part in workshops and to submit

written comments (including Testbiotech). The European Commission has now also confirmed, in response to an enquiry from Testbiotech, that GRACE has successfully implemented this transparency principle and the involvement of stakeholders in the analysis of the 90-day feeding trials and that it has therefore put in place the necessary conditions for a constructive public debate of the results. Testbiotech has published the response from the European Commission.

Testbiotech opts for media performance instead of scientific debate

Instead of taking part in this debate, Testbiotech and some media outlets are pursuing a one-sided representation of the GRACE project. A new background report from Testbiotech and a television programme supported by Christoph Then and shown on Bavarian television in January this year, shorten statements made by the GRACE consortium and present them out of context, which distorts the meaning. They fail to mention the project's responses to the accusations concerning a lack of independence of some of the project scientists and alleged errors in evaluating the study data. The unabridged statements from GRACE and from the European Commission in response to Testbiotech's accusations and in answer to Bavarian television's enquiry can be found on the [GRACE project website](#).

In its criticisms of the feeding studies, Testbiotech refers to analyses carried out by an anonymous toxicologist. The reasons for concealing the toxicologist's identity are not clear and raise more questions. In the interests of a constructive evaluation of the study results, GRACE would greatly appreciate it if this anonymous toxicologist would take part in the public discussion forum. He interpreted some of the study data as indications of potential harmful health effects. Scientists involved in the GRACE study [responded to his assessment](#) in detail in November and disagreed with most of it. Unfortunately however, further transparent, scientific discussion with the anonymous expert does not appear practicable in the circumstances.

Following its experience with Testbiotech, the GRACE consortium has decided to restrict further discussion of the published feeding studies to scientific, transparent platforms. GRACE has worked with Archives of Toxicology to set up a discussion forum on the subject, where specialist comments on the feeding studies are discussed openly and scientifically by as broad a range of experts and other interested parties as possible.

EU research project GRACE (GMO Risk Assessment and Communication of Evidence)

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The EU's GRACE research project is investigating methods for assessing the risk of genetically modified plants. They include animal feeding trials and in vitro methods. The project is part of the

European Commission's 7th Framework Programme and runs from July 2012 to February 2016. 18 research institutions from 13 countries are involved in the project.

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