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DEPARTMENT OF AGRICULTURE

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GUIDELINE DOCUMENT FOR USE BY THE ADVISORY COMMITTEE WHEN CONSIDERING PROPOSALS/APPLICATIONS FOR ACTIVITIES WITH GENETICALLY MODIFIED ORGANISMS

Genetically Modified Organisms Act, 1997 (Act No. 15 of 1997)

May 2004

Foreword by Ms Thoko Didiza, MP and Minister for Agriculture and Land Affairs

According to the National Biotechnology Strategy, South Africa can be summarised as follows: "South Africa has a solid history of engagement with traditional biotechnology. It has produced one of the largest brewing companies in the world; it makes wines that compare with the best; it has developed many new animal breeds and plant varieties, some of which are used commercially all over the world and it has competitive industries in the manufacture of dairy products such as cheese, yogurt, baker's yeast and other fermentation products".

However, in spite of the achievements from traditional biotechnology, South Africa has failed to extract value from the more recent advances of the technology, such as genomics, bioinformatics and proteomics. The majority of South Africans have not benefited from recent advances in biotechnology, largely due to the political history of the country where large sectors of the population could not access services and technologies in order to respond to agricultural challenges.

The National Biotechnology Strategy is designed to stimulate growth of biotechnology industries within South Africa to enable us to take full advantage of this technology and in turn maintain sustainable development. In order to achieve this successfully, a governmental agency will champion biotechnology, built human resources proactively and develop scientific and technological capabilities in this field. In addition, successful commercialisation of public sector-supported research and development (R&D) will require strong linkages between institutions within the National System of Innovation and a vibrant culture of innovation and entrepreneurship, assisted by incubators, supply-side measures and other supporting programmes and institutions.

Government has identified agriculture as one of the sectors of the economy that require special attention because of its potential to contribute to the objectives of higher growth rates and job creation, but also for its potential in addressing other national imperatives such as improved access to and affordable health care, sufficient nutrition at low cost and the protection of our rich environment. With the vision of a united and prosperous agricultural sector, the Department of Agriculture acknowledges the diversity of the agricultural sector and aims to ensure a place and role for all farmers in a united sector. This includes sectors taking advantage of genetic engineering, provided that the technology is applied in a regulated manner.

All activities with genetically modified organisms in South Africa are regulated under the Genetically Modified Organisms Act, 1997 (Act No. 15 of 1997). This Act provides for measures to promote the responsible development, production, use and application of genetically modified organisms to ensure that all activities involving the use of genetically modified organisms are carried out in such a way as to limit possible harmful consequences to the environment. The Act also makes provision for the determination of requirements and criteria for risk assessments that will ensure that genetically modified organisms are appropriate and do not present a hazard to the environment or human and animal health.

The GMO Act is administered by the Directorate Genetic Resources within the national Department of Agriculture and makes provision for a Registrar, two regulatory bodies, i.e. the Advisory Committee and Executive Council, and inspectors. The Registrar is responsible for administration of the Act, the Advisory Committee for evaluation of risk assessment data within every application and the Executive Council for taking a decision on whether a specific activity should be authorised or not. Inspectors appointed in terms of the Act monitors authorised activities with GMO's across the country.

Sections 4 and 5 of the Act stipulate the objectives, powers and duties of the Executive Council. One provision made in Section 5 is the development and publication of guidelines for all uses of GMO's. It is in accordance with this provision, as well as the aim to establish appropriate procedures for the notification of specific activities involving the use of genetically modified

organisms, that the Department of Agriculture has, through the assistance and recommendations of the Advisory Committee and Executive Council, produced the guidelines provided for in this document.

These guidelines aim to provide general information on the provisions of the Act, functioning of the bodies appointed in terms of the Act, how applications are processed and provide assistance to the applicant on how to apply for a permit. The guidelines will aid in public understanding of the administration of the Act and increase transparency towards the regulation of GMO's in SA. I therefore want to express my sincere gratitude and appreciation to the Advisory Committee and Executive Council, and the Registrar for GMO's, for their commitment in developing these guidelines.

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1. SCOPE

1.1 The Advisory Committee for Genetically Modified Organisms as constituted in accordance with Section 10 of the Genetically Modified Organisms Act, 1997 (GMO Act No. 15 of 1997), hereafter, referred to as the Act, is expected to perform all functions as stipulated in Section 11 of the Act.

1.2 Membership of the Advisory Committee as stipulated within the Act, is limited to persons "knowledgeable in those fields of science applicable to the development and release of genetically modified organisms, including knowledge of ecological matters". For example, the fields of science applicable, inter alia, are:

- animal health
- human medicine
- biochemistry
- molecular biology
- ecology
- entomology
- plant pathology
- biotechnology
- virology

1.3. Rationale for the Guidelines

There are several concerns about the consequences of development and deployment of genetically modified organisms, with particular reference to transgenic herbicide-resistant (HR) and insect-resistant (IR) crops. Objections to the use of these transgenic crops rest on several issues related to the associated risks, such as:

- the potential transfer of genes from herbicide resistant crops (HRC) to wild relatives thus creating super weeds;
- possibility of HRC volunteers to become weeds in subsequent crops;
- development of resistance by insect pests to crops with *Bacillus thuringiensis* (Bt) toxin;
- adverse effects on ecological processes and non-target organisms due to massive use of Bt toxin in crops.

All these concerns show the importance of assessment of possible hazards from the use of transgenic HR and IR crops. Assessment is required to decide whether these crops may be introduced and will not pose any hazard to the environment bringing expected benefits to the farmers.

The guidelines describe the process of analysis and assessment of ecological risks associated with the introduction of herbicide resistant crops (HRC) or genetically modified insect resistant (e.g. with genes coding for endotoxins from *Bacillus thuringiensi*s) crops (IRC). Furthermore, the guidelines list the responsibilities of governmental authorities, applicant or permit holders and farmers growing HRC and IRC. **The main aim of the guidelines is to provide a framework, in alignment with the GMO Act and the associated regulations, on assessing the ecological risks of HRC/IRCs.**

1.4 Functions of the Committee

1.4.1 In terms of the Act, The Committee shall-

1.4.1.1 act as the national advisory body on all matters concerning or related to genetic modification of organisms;

1.4.1.2 advise, on request or of its own accord, the Minister, the Council, other Ministries and appropriate bodies, on matters concerning GMO's and *inter alia* advise them-

a) on all aspects relating to the introduction of GMO's into the environment
b) on proposals for specific activities or projects concerning the genetic modification of organisms
c) on all aspects concerning the contained use of GMO's
d) on the importation and exportation of GMO's, and
e) on proposed regulations and written guidelines.

1.4.2 liase, through relevant national departments, with international groups or organisations concerned with biosafety; and

1.4.3 invite written comments from knowledgeable persons on any aspect of the genetic modification, which lies within the Committee's brief.

1.4.4 The Committee may appoint subcommittees to deal with specific matters as required.

1.4.5 The Committee shall meet at a minimum on a quarterly basis, and where necessary, schedule other meetings; such meetings shall consist of a quorum based on the majority of members attending.

1.5 Conflict of interest

As stipulated in the Act, a person appointed to the Committee shall immediately recuse himself or herself as a member of the Committee if a subject matter is in issue in which he or she has any direct or indirect interest or if, for any other reason, there is or there is likely to be a conflict of interest as a result of his or her participation in the proceedings of the Committee.

2. PROCEDURE FOR PROCESSING OF APPLICATIONS

All applications received by the Registrar for GMO's within the Department of Agriculture are reviewed according to the following procedure:

2.1 Registrar does a first hand review of the application to determine compliance with the provisions of the Act. If the application is not compliant, the application is referred back to the applicant.

2.2 Once compliant, the application is forwarded to a review committee (expertise nominated by AC chairperson) formed under the Advisory Committee to conduct a review of the proposed activity. The evaluation (assessment) of the review committee includes an evaluation of the risk assessment data, including food safety (if applicable) submitted in the application. The sub-committees conduct these assessments. Conclusions of the assessment are captured in a recommendation report, which is sent to the Registrar on completion of the review.

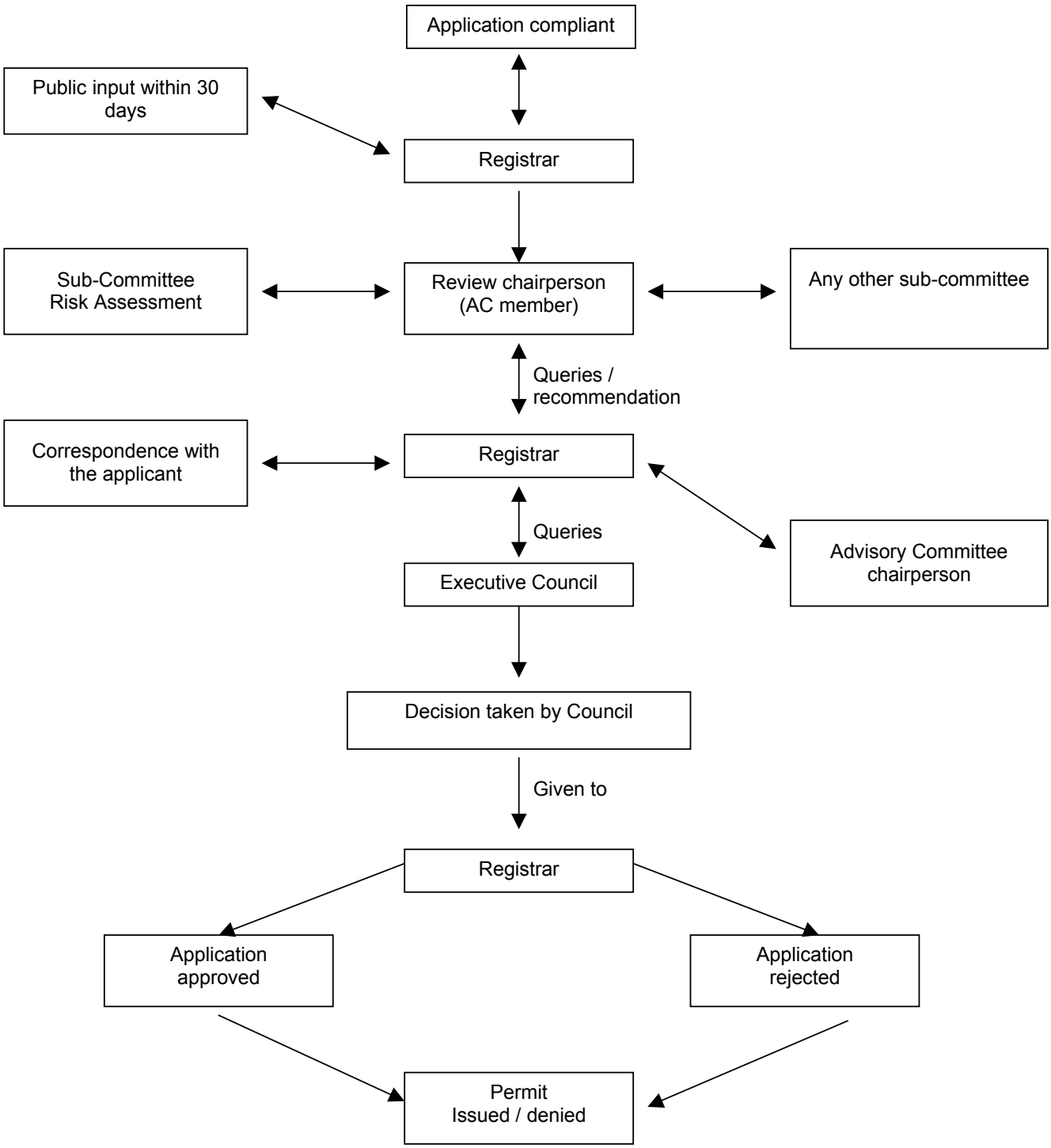
2.3 This phase is only applicable if the review committee raised concerns with regard to the application, or if additional information is requested. The application is referred back to the applicant to address the concerns raised or to supply additional information. The response from the applicant is returned to the Committee. Once all concerns have been addressed, the Committee makes a recommendation on the application to the Executive Council.

2.4 The recommendation document, public input and a copy of the application is forwarded to the Executive Council. The Council considers the application based on the information supplied by the Registrar, but also takes into account the socio-economical impact that the GMO may have. The Council submits its decision in writing prior to, or at a meeting, to the Registrar.

2.5 This phase is only applicable if the Council raised concerns in addition to the concerns raised by the Committee. The Registrar will once again refer the application back to the applicant for clarification. Based on the information received from the applicant and the assessment done by the Council, the application will be approved or rejected.

2.6 If the application is approved, the Council authorises the Registrar to issue a permit to the applicant. This permit will be accompanied by specific containment conditions as prescribed by the Council. If the application was rejected, the Registrar will communicate the decision back to the applicant with reasons for the rejection.

Figure 1: PROCESSING OF HANDLING GMO APPLICATIONS



3. ASSESSMENTS CONDUCTED BY THE ADVISORY COMMITTEE

3.1 Types of applications

In accordance with the scope/objectives stipulated in section 1 above, the Committee shall advise on:

a) Applications to import genetically modified organisms into South Africa;
b) Applications to export genetically modified organisms from South Africa;
c) Applications for contained use (including development, production, distribution, transport) of genetically modified organisms;
d) Applications to deliberately release genetically modified organisms into the environment (trial and general release); and
e) Applications to obtain commodity clearance of genetically modified organisms in South Africa.

Activities with GMO's for research and academic purposes, conducted at containment levels 1 and 2 (determined through a risk assessment conducted by the officer in charge) within a laboratory or growth room in an academic or research facility, are exempted from the requirement of a contained use permit in terms of Regulation 2(2). A contained use permit is required once the research is scaled up from basic research to product development, or when conducting the activities in a greenhouse or when the containment level is 3 and above.

3.2 The review committee

The review committee is a sub-committee established under by the Advisory Committee, and is responsible for the evaluation (risk assessment data) of proposed activities with genetically modified organisms. A review committee shall consists of the following:

- Review chairperson;
- Risk assessment sub-committee, and
- Any other assessment sub-committee (if applicable) required.

3.2.1 The review chairperson

The review chairperson refers to the chairperson appointed to chair the evaluation/assessment of a particular proposal/application for activities with genetically modified organisms. The Registrar selects this chairperson. The review chairperson is therefore any member of the Committee, including the chairperson of the Committee.

The review chairperson consolidates the findings and recommendations of the risk assessment sub-committee into a final recommendation document, which will be copied to members of the sub-committee and to other members of the Committee. The final recommendation document will be accompanied by any other assessment report (if applicable or not incorporated into the risk assessment report). Once the review committee is in consensus about the application, these documents will be forwarded to the Registrar.

It is the responsibility of the review chairperson to ensure that -

(a) the review committee contains the expertise required to enable a good assessment of all safety aspects of the application;
(b) if the committee is lacking certain expertise, inform the Registrar and nominate an appropriate individual with the required expertise;

(c) that every individual on the committee will treat the information submitted to him or her as “confidential business information”;
(d) the review is conducted within the time frame allocated by the Registrar.
(e) The recommendation document makes mention of every concern raised by the committee and gives an indication to the Registrar, based on the concerns raised by the committee, on the questions/concerns that should be raised to the applicant.

3.2.2 Risk assessment sub-committee

All proposals/applications for activities with genetically modified organisms shall be evaluated on a case by case basis. Such evaluations shall be scientific and will include an evaluation of the risk assessment submitted in the application, as stipulated by the Act.

Members of this sub-committee shall consist of three individuals with knowledge in the fields of science related to the proposed activity. The review chairperson appoints these individuals, and is responsible for dissemination of the relevant documentation to them.

Each member of the sub-committee must submit a report to the review chairperson within a period of three weeks. This report shall be in the format to enable the review chairperson to compile a recommendation document. The sub-committee may make use of the reviewer’s checklist (Annexure A) for recording the conclusions made during their assessment.

3.2.3 Any other sub-committee

Proposals for activities with genetically modified organisms shall be subject to an additional assessment, in addition to the general risk assessment evaluation in paragraph 3.2.2, if deemed necessary by the Advisory Committee and/or Executive Council.

The sub-committee shall be, in collaboration with the Registrar, appointed and supervised by the Advisory Committee or Executive Council. Members of this sub-committee shall receive all documentation regarding the proposed activities from the review chairperson.

4. DEFINITIONS AND ABBREVIATIONS

Applicant/notifier	The party (e.g. seed producer or importer, agro-chemical company or farmers' organization) that requests permission to experimentally release or commercially introduce an HRC/IRC in a country.
Authority	A governmental institution, organization or entity officially designated by the government to deal with matters arising from the responsibilities set forth in the Guidelines.
Bacillus thuringiensis (Bt)	Bacterium species currently used as a microbiological agent to control larvae of *Lepidoptera*, *Diptera* or *Coleoptera*.
Competitiveness	A plant’s ability to exploit essential elements such as light, water and plant nutrients at the expense of other plants.

Congeners	Refers to species belonging to the same genus.
Conspecific	Refers to individuals or populations of the same species.
Crop production system	A particular agricultural scheme, including monocultures, rotations and polycultures, and their associated practices such as tillage plant protection and harvesting.
Ecosystem	A complex of organisms and their environment, interacting as a coherent unit (natural or modified by human activity, e.g. agro-ecosystem), irrespective of political boundaries, to maintain a flow of energy and to acquire, store and recycle nutrients.
Fitness	Reproductive success or the proportion of genes an individual leaves in the gene pool of a population.
Gene flow	The transfer of genes (specifically, alleles) from one population to another by way of interbreeding of individuals in the two populations.
Gene pool	All of the alleles available among the reproductive members of a population from which gametes can be drawn.
Genetic engineering	Altering the genetic material of cells or organisms to make them capable of making new substances or performing new functions.
Genetically modified (GM) plant	A plant whose genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination.
Hazard	Intrinsic property of a physical situation (or dangerous substance) which can cause damage to human, animal and/or plant life or health and/or the environment.
Herbicide	A chemical substance or mixture of substances designed to control weeds.
Herbicide resistant crop (HRC)	A crop plant that by genetic modification(s) or breeding has acquired resistance towards a herbicide it would otherwise be sensitive to.

Insect resistant crop (IRC)	A crop that by genetic engineering has become protected from damage by one or more harmful insects.
Insecticide	A chemical substance or mixture of substances that controls insects that harm crop production or prevents their damage.
Introgression	The transfer of genes from one population to another by backcrossing.
Marketing	Supplying or making available to third parties.
Maternal inheritance	The transmission of nuclear and extra-nuclear genes from the mother usually referred to extra-nuclear genes.
Pest	Organisms which are capable of transmitting disease or unwanted species of plants or animals causing harm during or otherwise interfering with the production, processing, storage transport or marketing of food, agricultural commodities, wood and wood products or animal feedstuffs.
Pesticide	Refers to any substance or mixture of substances intended to prevent, destroy or control any pest, including substances intended for use as a plant growth regulator, defoliant, desiccant, or agent for thinning fruit or preventing the premature fall of fruit, and substances applied to crops either before or after harvest or protect the commodity from deterioration during storage and transport.
Release	Introduction into the environment of a genetically modified organism (GMO) with or without provisions for containment. Release can be deliberate, experimental, accidental or commercial.
Resistance	In the case of plant populations, their inherited ability to grow and reproduce normally when exposed to high doses or levels of a specific agent (e.g. herbicide or insect attacks), which normally would harm plants.
Risk	The probability of occurrence of a hazard which can cause damage to human, animal and/or plant life or health and/or the environment and its potential economic implications.

Risk assessment	The qualitative or quantitative evaluation of risks resulting from the release of genetically modified plants or products containing GM plants.
Spread	Expansion of the geographical distribution of plants containing a genetically modified gene.
Tolerance	Referred to plants, it is an increased ability of a biotype to endure damage, survive and reproduce after a limited exposure to a specific stress factor (in this context, herbicide applications or insect attack) compared to other biotypes of the species. Tolerance is often a polygenetic inherited trait.
Transgene	A gene or DNA fragment from one organism that has been stably incorporated into the genome of a plant of interest.
Transgenic	See genetically modified (GM) plant.
Vector	A plasmid that can be used to transfer DNA sequences from one organism to another.
Volunteer	A crop plant regenerated from seed or propagules left after a previous harvest and which can act as a weed in the present crop.
Weed	A plant that is growing where it is not wanted by humans.

5. DELIMITATIONS

These guidelines are currently confined to deal with the ecological hazard assessment of HRC and IRCs based on a strictly scientific and technical approach. The hazard assessment must be performed on a case-by-case basis and adapted to the local conditions and agricultural production system. Other relevant aspects related to HRC/IRCs such as food safety, pleiotropic effects associated with transgenes, ethical concerns and socio-economic consequences are not considered in these guidelines.

6. RESPONSIBILITIES

6.1 Responsibilities of applicant/permit holder

a) To comply with all the regulations established by the country where the HRC/IRC will be introduced or grown.
b) To prepare a dossier for submission to the authority with each application for experimental release or commercial production including all pertinent and required information on the HRC/IRC to be released.
c) Ensure that persons involved in distribution of their HRC or IRC product are adequately trained, such that they are capable of providing a user with advice on efficient and safe use.

d) Notify the authorities and voluntarily take corrective action and, when requested by authorities, help to find solutions to any problem related to the release and use of the HRC/IRCs.

6.2 Responsibilities of users (e.g. farmers) growing HRC/IRC

Determination of risks and liability shall be as stipulated in section 17 of the Act. The responsibilities of the cultivator/farmer as the final user of a technology are those stated in the binding labels of HRC/IRC products and any contractual agreement signed with an importer, distributor or supplier of seed and by the regulations associated with the use of pesticides.

6.2.1 Farmers should:

- Maintain appropriate records of HRC/IRC varieties and area planted and pesticide use.
- Respect and obey indications and requirements related to refugia and other agronomic practices intended to prevent or delay the evolution of resistance in pests.
- Comply with any signed agreement regulating the production, saving and distribution of seed from HRC/IRCs.
- When growing HRC/IRCs, which involve the use of a pesticide, follow the regulatory rules for the particular pesticide and specific use.

7. RISK IDENTIFICATION

- The assessment of potential hazards of growing HRC/IRC crops concerns both the crop itself and its impact on the wild flora. Consequently, understanding the interaction between the transgenic crops and all compatible relatives is crucial for a realistic hazard assessment. Consideration may also be necessary to the fauna associated with the crop, especially both insect pests and beneficial organisms.
- The HRC/IRC itself may establish beyond its agricultural boundaries and growing season and become a weed in the succeeding crops.
- The HRC/IRC may pollute the gene pool of non-transgenic relatives growing in the same or adjacent areas, depending on cross pollination characteristics and agents such as wind or by insects. In some instances where the population size of native relatives is low, genes from the transgenic crop may come to dominate the native population and lead to their extinction. The compatibility between the HRC/IRC and non-target species is of utmost importance in this regard.
- The HRC/IRC may have botanical identical or closely related species that can hybridize with the crop, either in the adjacent ecosystems or in the agro-ecosystem. Hybridization could lead to pollution of non-transgenic crops, gene stacking in volunteer plants and transfer of the resistance trait to weedy or wild species.
- The continuous use of HRCs with their associated herbicide over large areas for several years may unintentionally change the composition of the weed flora by selecting for naturally tolerant weeds. This is particularly important in monocultures or in cropping systems with limited crop rotation or **minimum tillage**.
- Intensive use of HRC/IRC may have a detrimental effect on the populations of non-target organisms (i.e. birds, beneficial insects)
- In case of IRC the engineered traits may increase fitness of volunteers or weedy hybrids, thus making a crop turn into a weed that can interfere with future crop

production or aggravating the negative impact of existing weed species. The incorporation of resistance into a non-target species may also alter its competitive ability and displace other native species.

- Intensive use of IRC may select insect strains resistant to the toxins produced by the plant as a result of the genetic alteration.

7.1 The process of risk assessment

- The main objective of an ecological risk assessment of HRC/IRCs is to identify possible adverse effects on the environment from growing these crops. Risk identification is only the first step in a conventional risk assessment, the other steps being risk characterization (magnitude of the risk), exposure assessment (in this context an estimate of likelihood or frequency of identified risks) and finally risk characterization.
- Risk characterization takes into account the results of the previous three steps to provide an estimation of the likelihood by which the adverse effects occur combined with their magnitude. This risk assessment may be quantitative or qualitative. The latter has prevailed in previous cases with approval of genetically modified organisms, because the complexity of biological systems makes it difficult to pursue a quantitative approach. Much of the needed information for a risk assessment can be obtained from practical experience with traditional crops growing in the same environment, but in some cases further experimentation is needed particularly regarding gene flow and fitness.
- In established regulations of HRC/IRCs, the applicant is required to deliver the relevant information and the authorities may then base the evaluation upon this information combined with expert opinions and, sometimes, public hearings of scientific institutions, consumer organizations, NGO's and the general public. The objective of the following guideline is, however, only to identify potential adverse ecological risks to the environment by using simple decision keys.

7.2 Information desirable for risk assessment

a) Information related to the HRC/IRC:
   - Taxonomic description and scientific name
   - Cultivar's name
   - Diagnostic phenotypic and genetic markers
   - Description of geographic distribution and of the natural habitat of the plant
   - Potential for gene flow and exchange with other plants
   - Ecological and physiological traits:
     - Generation time in natural ecosystems, sexual and asexual reproductive cycle
     - Information on survival, including the incidence of volunteers and the ability to form perenniating structures (propagules)
   - Information related to the genetic modification process
     - Methods used for the modification
     - Description of the inserted genetic material and vector construction
     - Sequence, functional identity and location of the altered/inserted/deleted nucleic acid segment(s) in question
   - Information on the inserted genetic material in the HRC/IRC
     - Description of genetic trait(s) or phenotypic characteristics, particularly new traits and characteristics which may be expressed or no longer expressed
     - Characteristics of the vector

- Stability of the genetic trait(s)
- Cumulative effects if the event is a combination of two or more traits (e.g. stacked event such as MON810 x NK603)
- Rate and level of expression of the new genetic material
- Description of identification and detection techniques
- History of previous releases or uses of the HRC/IRC

b) Information on the receiving environment:
   - Geographical location of the site
   - Proximity to protected habitats or areas
   - Proximity to compatible, related species
   - Climatic characteristics and flora and fauna of the region
   - Description of target and non-target ecosystems likely to be affected
   - Any known planned developments or changes in land use in the region which could influence the environmental impact of the released crop
   - Description of ecosystems to which the HRC/IRC could be disseminated

c) Information related to the interactions between the HRC/IRC and the environment:
   - Characteristics affecting survival, multiplication and dissemination
   - Studies of the behavior and characteristics of the HRC/IRC and their ecological impact
   - Post release genetic transfer capability from the HRC/IRC into organisms in the affected ecosystems
   - Likelihood of post-release selection leading to the expression of unexpected and/or undesirable traits in the HRC or IRC
   - Description of genetic traits, which may prevent or minimize dispersal of genetic material.
   - Routes of biological dispersal and known or potential modes of interaction with the dissemination agent.

d) Potential environmental impact:
   - Potential for excessive population increase in the environment
   - Competitive advantage of the HRC/IRC in relation to the unmodified recipient
   - Anticipated mechanism and result of interaction between the released plant and wild and weedy relatives
   - Known or predicted effects of non-target organisms on the environment, impact on population levels of all potential competitors.

7.3 Information on the conditions of experimental release:

a) Description of the proposed release including the purposes and foreseen products
b) Foreseen dates of the release and time planning of experiment including frequency and duration of release
c) Size of the site
d) Method to be used for the release
e) Quantities of HRC/IRC to be released
f) Method of cultivation and description of general agricultural practices
g) Post-release treatment of the site
h) Techniques which will be applied for the elimination or inactivation of the HRC/IRC upon experiment completion
i) Information on and results of previous releases of the HRC/IRC, especially at different scales in different ecosystems.

7.4 Information required in the case of notification for placing in the market:

a) Name of product and names of HRC/IRC contained therein
b) Name and address of manufacturer in country of origin
c) Specificity of the product including the appropriate environment and geographical area of the country for which the product is suited
d) Estimated production or import to the country
e) Proposed packaging (to prevent unintended release during storage or at a later stage)
f) Proposed labeling in the official language(s) of the country including information on handling and agricultural use.

7.5 Information on monitoring and control of release:

a) Methods for tracing the HRC/IRC and monitoring its effects
b) Specificity, sensitivity and reliability of monitoring techniques
c) Techniques for detecting transgenes introgressed into non-target plants
d) Methods and procedures to avoid and minimize the spread of the HRC/IRC beyond the site of release or the designated area for use
e) Methods and procedures for controlling the HRC/IRC in case of unexpected spread.

8. Risk assessment

- In assessing potential risks associated with the introduction or planting HRC/IRCs in a particular area or country, a starting point will be to identify the scenarios (agro-ecosystems) under which the crop will be released and select the appropriate procedure to assess the specific risk associated with it.

- Whatever approach is used to identify risks, care should be taken to consider risks to both agronomic and natural ecosystems. As indicated before, any assessment of risk requires a case-by-case study and is location-specific.

- Specific local conditions would determine the relative importance of each type of risk. For example, cropping patterns and landscape could have an important role in the possible escape transgenes, a process that involves hybridization followed by the subsequent establishment and persistence of the hybrid. The likelihood of GM crops and wild relatives forming hybrids is particularly pertinent in the centers of origin and diversity of crops, thus hazards derived from gene flow should be the priority in assessing the overall risk of release of GM crops in these areas. Another special case is that of a crop that has con-specific weeds, which increases the risk of gene movement from the GM-crop.

- An important aspect, besides those mentioned above, that should be considered is the possible impact of HRC/IRCs on non-target organisms (e.g. pollinators, soil fauna or other organisms associated with the crop plant). Planting HRCs, especially over large areas, allowing the application of herbicides not previously used in the conventional crop could impose new selection pressure on weeds leading to the evolution of herbicide resistance. Similarly, exposure to insecticidal toxins from IRCs over long periods could also select for resistance in the target pests and affect predators, parasitoids and other non-target organisms. Side effects of IRCs producing insecticidal toxins are difficult to assess because of lack

of knowledge thus scientific experts should be consulted regarding this on a case-by-case basis.

- The final decision on releasing HRCs and IRCs is ultimately a balance between science, economics, ethics and values, local benefits and public interest. Consequently, the perceived risk sometimes reflects conflicts of interests.

- The use of assessment keys should facilitate arriving to a decision based on scientific knowledge rather than on perceptions, although a quantitative approach is yet to be developed. The keys presented below were designed only as a guide in assessing the ecological risks based on the most likely relevant scenarios. They have limitations and should be considered carefully according to local conditions and experience. It is important to take into account that cropping practices and local environmental conditions and characteristics can affect the risks and how they are assessed or perceived. For example, inter-planting an IRC with unmodified crop plants would affect the rate at which resistant individual could be selected in the target pest population. Also, the level of expression of the toxin in the crop plant can affect the likelihood of survival of slightly resistant individuals.

- The keys are a useful method to begin the process of the risk identification and assessment for IRC/HRCs, but do not in themselves provide the user with a conclusive description of the risks of planting IRC/HRCs. The questions in the keys have been arranged according to increasing magnitude of the risks. Two main possible simplified scenarios are considered:

8.1 *Scenario 1*

The HRC/IRC is to be released in an agricultural system where there are compatible wild relatives or **weed species**.

When a HRC is to be released into an area where there are compatible wild or weedy relatives there is a possibility that the transgenes will escape and introgress into those compatible species. As a result, the wild or weedy relatives (congeneric or conspecific) could become resistant to the herbicide, making them a more noxious agricultural or environmental pest. There is also the possibility that the competitive ability of wild relatives might be altered especially if IR-genes become established in native populations. This possibility is of particular concern when the IRC is to be released into its wild progenitor's center of origin or diversity, which serve as a particularly valuable source of genes for plant breeding. Useful genes might be lost if introgression with transgenic crops results in the replacement of native genes. Under these conditions, assessment should consider all the corresponding keys below:

8.2 Scenario 2

The HRC/IRC is to be released in an agricultural system where there is no risk of gene flow to other species.

Under this scenario, there are three main concerns to consider. Weeds could evolve resistance to the herbicide that the HRC withstands because of the selection pressure imposed by its use. Secondly, management of HRC volunteers in succeeding plantings of the conventional crop or in rotation crops could become increasingly difficult. Third, there is the possibility that insects could evolve resistance to the insecticidal toxin produced by the

IRC, due to increased selection pressure. Initiate the assessment by considering key no. 3 (assessing of volunteers' control) and 4 or 5 (build up of resistance).

When using a key, if you reach a point where you cannot continue any further or there is an indication of "stop", it means that you need to make a decision about a particular risk.

Key 1: Likelihood that the competitive abilities of wild relatives occurring in undisturbed wild-lands will be altered by hybridization with transgenic crops

1. Is the crop only self-pollinating?
If no: Go to No. 2 If yes: Stop, and go to key 3.

2. *Can viable hybrids form between the crop and wild relatives?*
If yes: Go to No. 3 If no: Stop, and go to key 2.

3. *Do these wild relatives occur in the proximity of the crop?*
If yes: Go to No. 4 If no: Stop, and go to key 2.

4. *Do the crop and the wild relatives overlap in flowering periods?*
If yes: Go to No. 5 If no: Stop, and go to key 2.

5. *Do hybrids survive and reproduce in the native habitat*
If yes: Go to No. 6 If no: Stop, and go to key 2.

6. *Does HR/IR trait give hybrids or introgressants a fitness advantage in wild habitats?*
If yes: Go to No. 7 If no: Stop, and go to key 2.

7. *Is the resistance trait maternally inherited?*
If yes: Likelihood of producing If no: Likelihood of producing
new, more competitive native new, more competitive native
species. species rapidly.

Key 2: Likelihood that a new type of arable weed will be produced by gene flow between the transgenic crop and its relatives:

1. *Do hybrids occur between the crop and any weedy/wild relative?*
If yes: Go to No. 2 If no: Stop, and go to key 3.

2. *Do these weedy/wild relatives occur in the proximity of the crop?*
If yes: Go to No. 3 If no: Stop, and go to key 3.

3. Do the crop and the weedy/wild relatives overlap in flowering periods?
If yes: Go to No. 4 If no: Stop, and go to key 3.

4. *Are the hybrids and/or introgressants highly competitive in arable environments?*
If yes: Go to No. 5 If no: Stop, and go to key 3.

5. *Are hybrids or introgressants herbicide resistant or insect resistant?*
If HR: Go to No. 6 If IR: Go to No. 8.

6. *Can HR hybrids or introgressants easily be controlled by other means besides the herbicides associated with the HRC?*

If yes: Likelihood of losing If no: Go to No. 7
one herbicide.

7. *Is the same herbicide used in succeeding crops?*
If yes: Likelihood of losing If no: Stop and go to key 3.
the only weed control option.
.
8. *Does the IR trait confer an increased fitness in the wild/weedy relative compared to non-IR relative?*
If yes: Likelihood of increased If no: Stop and go to key 3.
weed problems

Key 3: Likelihood that the transgenic crop will become a volunteer problem on arable land or wild areas:

1. *Is the crop known to leave volunteers in succeeding crops?*
If yes: Go to No. 2 If no: Stop. There should
not be a volunteer problem. Assess hazard of evolution of herbicide or insecticide resistance (keys 4 and 5).

2. *Does the crop have weedy traits?*
If yes: Go to No. 3 If no: Stop, and go to key 4.

3. *Is the volunteer plant expected to be herbicide resistant or insect resistant?*
If HR: Go to No. 4 If IR: Go to No. 6.

4. *Can the HR-volunteer easily be controlled by other means but the herbicides associated with HRC?*
If yes: likelihood of losing If no: Go to No. 5
use of a herbicide.

5. *Is the herbicide used for control of non-transgenic volunteers in succeeding crops?*
If yes: likelihood of losing If no: Stop, and go to key 4
the weed control option (herbicide)

6. *Is the IR-volunteer crop able to establish itself in the wild?*
If yes: likelihood of escapes If no: Go to No. 7
into wild habitats

7. *Can the IR volunteer easily be controlled in succeeding crops?*
If no: Go to No. 8 If yes: Stop, and go to key 5

8. *Does the IR trait confer an increased fitness in the volunteer compared to non-transgenic volunteers?*
If yes: Likelihood of increased If no: Stop, and go to key 5
weed problems

Key 4: Likelihood of build-up of HR-resistant weeds:

1. *Are resistance cases to the herbicide that the HRC withstands or herbicides belonging to the same chemical family or having the same mode of action (MOA) or degradation known*

to occur, or is gene flow possible from HRC to related weedy species, or is the herbicide a new chemical?
If yes: Go to No. 2 If no: Stop. There should be a low hazard of evolution of herbicide resistant weeds, especially if integrated weed management is used.

2. *Is the cropping system primarily a monoculture or the HRC is or will be fully rotated with other crops?*
If monoculture: Go to No. 5 If fully rotated: Go to No. 3.

3. *Is weed management primarily based on an integrated strategy or on chemical control?*
If chemical control: Go to No. 4. If integrated strategy: Stop. Very limited hazard of Herbicide resistance evolution.

4. *Is the MOA of the herbicide used in HRC crop similar or different to that used in the other rotational crops?*
If same: consider likelihood of selection for resistant weeds If other: Stop. Very limited hazard of herbicide resistance evolution.

5. *Is weed management under the monoculture system primarily dependent on herbicides?*
If yes: Go to No. 6 If no: Stop. Very limited hazard of herbicide resistance evolution.

6. *Is the herbicide to be used in the HRC a new persistent compound or a chemical to be used twice or more in cropping cycle?*
If yes: consider the likelihood of selecting new resistant weeds. If no: Go to No. 7

7. *Does the herbicide used in HRC share MOA with others in use?*
If yes: Risk of aggravating or speeding resistance problems If no: Stop. Limited hazard of herbicide resistance evolution.

Key 5: Likelihood of build-up of resistant insects:

1. *Does the IRC comprise a major proportion of the local area planted with non-transgenic varieties of that crop?*
If yes: Go to No. 2 If no: Stop. Limited hazard of insecticide resistance evolution.

2. *Does the IRC express only a single or few insecticidal-toxin(s) active against the harmful insect?*
If yes: Go to No. 3 If no: Stop. Limited hazard of insecticide resistance evolution.

3. *Is expression of the IR trait confined to a short lasting selected growth stage of the crop?*
If no: Go to No. 4 If yes: Stop. Limited hazard of insecticide resistance evolution.

4. *If resistance in insects occurs, is expression of the IR trait associated with a significant fitness penalty for the resistant insect?*
If no: Go to No. 5 If yes: Stop.

5. *Are resistant insects easily controlled by other control measures?*
If yes: likelihood of losing If no: likelihood of
effect of the IR trait losing the IR trait and specific-toxin based **biological pesticides.**

8.3 Recommendation document

A recommendation document outlining the conclusions made by members of the risk assessment sub-committee shall consist of:

a) *Details of the review committee*
Provide full names, institutions and expertise involved in the review committee.

b) *Summary of the application*
Particulars of the applicant's request:
(i) Name of the applicant
(ii) Title of the application
(iii) Reference number given by the Registrar's office
(iv) Short description of the applicant's request
- The intended use
- Purpose of the use
- Scale of the use

(v) Short description of the genetic modification
- What it is?
- How developed?
- Stability of integration?

c) *Procedures followed during the evaluation of the application*
Stipulate all dates and actions involved during the evaluation process from the moment that the review chairperson receives the application.

d) *Safety issues assessed*
(i) Food and feed
- Toxicological studies
- Allergenicity studies
- Compositional analysis
- Nutritional analysis
- Pathogenicity
- Feeding trials
- Any other

(ii) Environmental
- Weediness/invaseness
- Gene flow
- Altered plant pest potential
- Non-target organisms
- Impact on biodiversity
- Any other

e) *Non-safety issues*
- Experimental design
- Sociological factors
- Any other

f) Risk management
Indicate required risk management measures required.

g) Recommendation
Note comments from reviewers that were overruled by the review chairperson and the reasons attached thereto.
Make a final recommendation to the Registrar on this application.
Sign the document and indicate the date on which the document is submitted to the Registrar.

h) Appendix
Attach review reports of each individual within the review committee.
Any other assessment report (if applicable).

8.4 Any other assessment report

The report of the sub-committee responsible for evaluation of any other aspect related to GMO's, will be included in the conclusions of the recommendation document, as an attachment to the recommendation document or as an additional report to the recommendation document.

This report will be based on an assessment conducted according to the principles and guidelines relevant to the field being investigated.

9. FAST TRACKING (EXTENDED PERMIT) APPLICATIONS

The Registrar may, at his own discretion, fast track any application for an activity involving genetically modified organisms for which a permit had previously been issued under the GMO Act (Regulation 5(12) of the GMO Act). To obtain a permit via the fast track system, the applicant must complete the application form for an extended permit.

An application for an extended permit (fast track) can only be submitted in cases where the particular activity with the GMO concerned has been authorised by the Executive Council on a previous occasion.

10. GRANTING AUTHORISATIONS

The Advisory Committee has no authority to issue, amend or withdraw any permit under the GMO Act. This Committee is purely an advisory body to the Registrar and Executive Council.

Once the Committee is satisfied that the GMO will pose no harm to the environment or lead to a health risk, a recommendation letter, accompanied by the final recommendation document, must be submitted to the Registrar.

The Registrar submits the application with the Committee's recommendations to the Executive Council for final consideration and decision.

ANNEXURE A: REVIEWERS' CHECKLISTS

This checklist may be used by any member of the sub-committee with the necessary expertise, and may be attached to the report submitted by the reviewer.
These checklists are intended to assist the reviewers, but take note that (a) a particular application may not contain all types of data listed and (b) there may be additional data provided by the applicant, or required by the reviewer, that is not included in this list.

SECTION I – CHECKLIST FOR NORTHERN BLOT DATA

	YES	NO	COMMENT
Does the Northern blot have a figure number and title?			
Are lanes labelled on the blot?			
Does the figure legend describe each lane of the blot, including a description of the following for the RNA that was loaded: What type of material was loaded (e.g. total purified RNA, poly-A RNA, crude prep, total plant extract)? Source of the material loaded (e.g. transformation event, tissue, development stage, any prior treatments to induce gene expression, etc.)? Quantity of material loaded in each lane? Quality of material loaded in each lane?			
Does the text or figure legend describe how RNA was extracted prior to electrophoresis?			
Does the blot have appropriate positive and negative control lanes - Positive control consisting of a dilution series of control RNA complemented with wild type RNA of the same tissue (this control is especially relevant for blots used to substantiate the absence of expression); Positive control purified RNA; Negative control - the unmodified parental line or variety; Check for loading differences using a probe for a "constitutive" mRNA.			
Is the gel system and Northern hybridisation protocol described in the text or in the cited literature reference? Are any modifications of the cited protocols described in the petition (application) text?			
Is the position of molecular size standards on the gel indicated, and do they cover an appropriate size range for the fragments that are expected to be detected on the blot?			
Is there a description of the probe that was used for the hybridisation? If so, is the description adequate (in the text on in the figure) to enable one to interpret the results?			
If quantitative analysis is performed, has the methodology or citation to such been provided, and have a sufficient number of replicates or samples been tested to determine whether there are differences between samples or treatments?			
Are any superfluous bands or background signals properly explained?			

SECTION II – CHECKLIST FOR SOUTHERN BLOT DAT

	YES	NO	COMMENT
Does the Southern blot have a figure number and title?			
Are lanes labelled on the blot?			
Does the figure legend describe each lane of the blot, including a description of the following for			

	YES	NO	COMMENT
the DNA that was loaded on the gel: ▪ Type of DNA loaded (e.g. entire plasmid, restriction fragment)? ▪ Source of DNA loaded (e.g. transformation event, tissue, etc.)? ▪ Restriction digestions of DNA prior to loading gel? ▪ Quantity of material loaded in each gel? ▪ Quality of the material loaded in each gel?			
Does the gel have appropriate positive and negative control lanes – Positive control consisting of a dilution of a series of control DNA complemented by wild type DNA of the same tissue; Positive control purified transformation vector; Negative control – the unmodified parental line or variety.			
Is the gel system and Southern hybridisation protocol described in the text or in the cited literature referenced? Are any modifications of the cited protocols described in the petition (application) text?			
Is the position of the molecular size standards indicated, and do they cover an appropriate size range for the fragments that are expected to the detected on the blot?			
Was an entire plasmid used as the probe for the hybridisation? If so, is the plasmid described adequately in the text or in a figure to enable one to interpret the results?			
Was a restriction fragment used as the probe for the hybridisation? If so, is the restriction fragment described adequately in the text or in a figure to enable one to interpret the results?			
Are any superfluous bands or background signals properly explained?			

SECTION III – CHECKLIST FOR RNA DOT BLOT DATA

	YES	NO	COMMENT
Does the Dot blot have a figure number and title?			
Are lanes labelled on the blot?			
Does the figure legend describe each lane of the blot, including a description of the following for the RNA that was loaded: ▪ What type of material was loaded (e.g. total purified RNA, poly-A RNA, crude prep, total plant extract)? ▪ Source of the material loaded (e.g. transformation event, tissue, development stage, any prior treatments to induce gene expression, etc.)? ▪ Quantity of material loaded in each lane? ▪ Quality of the material loaded in each lane?			
Does the text or figure legend describe how RNA was extracted prior to blotting onto the solid support?			
Does the blot have appropriate positive and negative control lanes – Positive control consisting of a dilution series of control RNA complemented with wild type RNA of the same tissue (this control is especially relevant for blots used to substantiate the absence of expression); Positive control of purified RNA			

	YES	NO	COMMENT
Negative control – the unmodified parental line or variety.			
Is the blot system and hybridisation protocol described in the text or in the cited literature reference? Are any modifications of the cited protocols described in the submitted text?			
Is there a description of the probe that was used for the hybridisation? If so, is the description adequate (in the text on in the figure) to enable one to interpret the results?			
If quantitative analysis is performed, has the methodology or citation to such been provided, and have a sufficient number of replicates or samples been tested to determine whether there are differences between samples or treatments?			

SECTION IV – CHECKLIST FOR WESTERN BLOT DATA

	YES	NO	COMMENT
Does the blot have a figure number and title?			
Are lanes clearly labelled?			
Does the figure legend describe each lane of the blot, including a description of the following for the protein that was loaded: ▪ What type of material was loaded (e.g. pure, crude, total plant extract)? ▪ Source of the material loaded (e.g. transformation event, tissue, development stage, any prior treatments to induce gene expression, etc.)? ▪ Quantity of material loaded? ▪ Quality of the material loaded?			
Is the protein extraction method adequately described in either the text or the legend?			
Is the antibody or antiserum preparation protocol adequately described in the text, including an adequate description of the antigen and its purity? Has the specificity of the antibody or antiserum been determined and described in the text or in a cited literature reference?			
Is the gel system and blotting protocol adequately described in the text or in a cited literature reference?			
Is the position of the molecular weight standards indicated, and do they cover the appropriate range for the proteins expected to be detected on the blot?			
Does the blot include appropriate positive and negative controls – Positive control consisting of a dilution series of control protein complemented with wild type material of the same tissue (this control is especially relevant for blots used to substantiate the absence of expression); Positive control of purified protein; Negative control – the unmodified parental line or variety.			
Was a normal serum control conducted?			
Are any superfluous bands or background signal properly explained?			
If quantitative analysis is performed, has the methodology or citation to such been provided, and have a sufficient number of replicates or samples been tested to determine whether there are differences between samples or treatments?			

SECTION V – CHECKLIST FOR PCR DATA

	YES	NO	COMMENT
Does the PCR gel have a figure number and title?			
Are lanes labelled on the gel?			
Does the figure legend describe each lane of the gel, including a description of the following for the DNA that was loaded: ▪ What type of material was loaded (e.g. plasmid fragment, amplified DNA)? ▪ Source of the material used in each reaction loaded (e.g. transformation event, tissue, development stage, any prior treatments to induce gene expression, etc.)? ▪ Quantity of material loaded? ▪ Quality of material loaded?			
Is the position of the molecular weight standards indicated, and do they cover an appropriate size range for the fragments that are expected to be detected on gel?			
Does the text or figure legend describe how PCR amplification was performed prior to electrophoresis?			
Is there a description of the primers used for amplification in the text or in the figure sufficient to enable one to interpret the results?			
Does the gel have appropriate positive and negative control lanes - Positive control might demonstrate specificity of the primers and the ability to amplify the appropriate size band; Negative controls might include amplification with DNA from the unmodified parental line or variety, and amplification in absence of DNA template; Check for amplification of a control fragment from the plant sample (to show that PCR is working, especially if it is intended to show absence of a specific DNA); Mix plant DNA with plasmid DNA (I copy control) to demonstrate that the PCR is working properly.			
Was an entire plasmid or a restriction fragment used as the positive control template and is it adequately described in the text or in the figure legend for interpretation of the PCR results?			
Is the gel system and PCR protocol described in the text or in a cited literature reference? Are modifications of a cited protocol described in the text?			

SECTION VI – CHECKLIST FOR ELISA DATA

	YES	NO	COMMENT
Does the table have a number and a title?			
Are all entries clearly identified in the table and described in the text or table legend?			
Is the sample preparation described?			
Is the antibody or antiserum preparation protocol adequately described in the text, including a description of the antigen and its purity? Has the specificity of the antibody or antiserum been demonstrated and described in the text or in a cited literature reference?			
Is the ELISA protocol used described in the text or cited in the scientific literature? Any modifications to a cited protocol must be described.			
Were appropriate positive controls (e.g. purified protein) and negative controls (e.g. normal or			

	YES	NO	COMMENT
preimmune serum, non-transformed plant material) used?			
When ELISA is being used to quantify protein expression in transformed tissues: ▪ Was a method for the determination of protein concentration in tissue samples presented in the text or in a cited literature reference? ▪ Were a standard curve prepared and the limit of detection indicated? ▪ Have a sufficient number of replicates or samples been tested to determine whether there are significant differences between samples or treatments? Was statistical analysis performed?			

SECTION VII – CHECKLIST FOR ENZYME ASSAYS

	YES	NO	COMMENT
Does the figure (or table) have a number and title?			
For graphical representations or tables, are the axis or columns labelled and the units indicated?			
Does the scale of the figure accurately represent and allow interpretation of the data?			
Does the legend or text describe: ▪ The substrate and amount used for the reaction? ▪ The quantity and origin of the enzyme? ▪ The temperature and pH?			
Does the text or legend describe the extraction and purification of the enzyme and the degree of purification achieved?			
If the enzyme used in the assay has not been isolated from the transformed plant but is derived from an expression system, has adequate data been presented to demonstrate its substantial equivalence to the plant expressed enzyme?			
Have the assay method and relevant information concerning the enzyme been provided in the text or in a cited literature reference?			
Are appropriate controls included in the assay?			
Has the stability of the enzyme and possible presence of enzyme inhibitors in different tissue extracts been taken into account in the design of the assay or the interpretation of the data?			
When relevant to the safety assessment, have the kinetics of the enzyme been calculated and where possible compared to published data?			
When quantitative analysis is performed, have a sufficient number of replicates or samples been tested to determine whether there are significant differences between samples or treatments? Was statistical analysis performed?			