agriculture, land reform & rural development
Department:
Agriculture, Land Reform and Rural Development
REPUBLIC OF SOUTH AFRICA

DIRECTORATE GENETIC RESOURCES
Private Bag X973, Pretoria, 0001
Harvest House, 30 Hamilton Street,
Arcadia, Pretoria, 0002
Tel: 012 319 6382, Fax: 012 319 6298,
E-mail: NompumeleloM@dalrrd.gov.za

APPLICATION FOR GENERAL RELEASE OF GENETICALLY MODIFIED ORGANISMS (GMOs) IN SOUTH AFRICA

Notes:

1. Host or unmodified organism refers to an organism prior to the genetic modification(s) that results in the organism being classified as a GMO.
2. Although this application form is to be used for all general release applications, it is primarily intended for applications dealing with genetically modified (GM) plants.
3. Applicants should substantiate “yes” or “no” answers and provide answers that are detailed enough to enable thorough risk assessment by regulatory bodies. Answers may, where appropriate, be summaries that are based on relevant, peer-reviewed literature.
4. Applications with superficial answers may result in significant delays in the review and decision-making process.
5. All the data required to assess the application should be included in the application dossier. Applicants should not refer to in-house generated results or data that are not part of the application dossier. Applicants should include substantiating data and reports with the application dossier.
6. The application is structured in two tiers:
    a. Tier 1. Part I to III of Tier 1 must be completed for all GMOs.
    b. Tier 2. Sections in Part IV only need to be completed if the applicant is referred to these sections based on the applicant’s responses in Tier 1. In Part V, only the section relevant to the GMO should be completed.
7. Part VI must be completed for all GMOs.
8. Figure 1 on page 2 shows a graphical overview of the key parts of the application template, with colour coding used to assist applicants in understanding which parts of the application template they need to complete.
9. Complete the affidavit. The affidavit is an inseparable part of the application form.

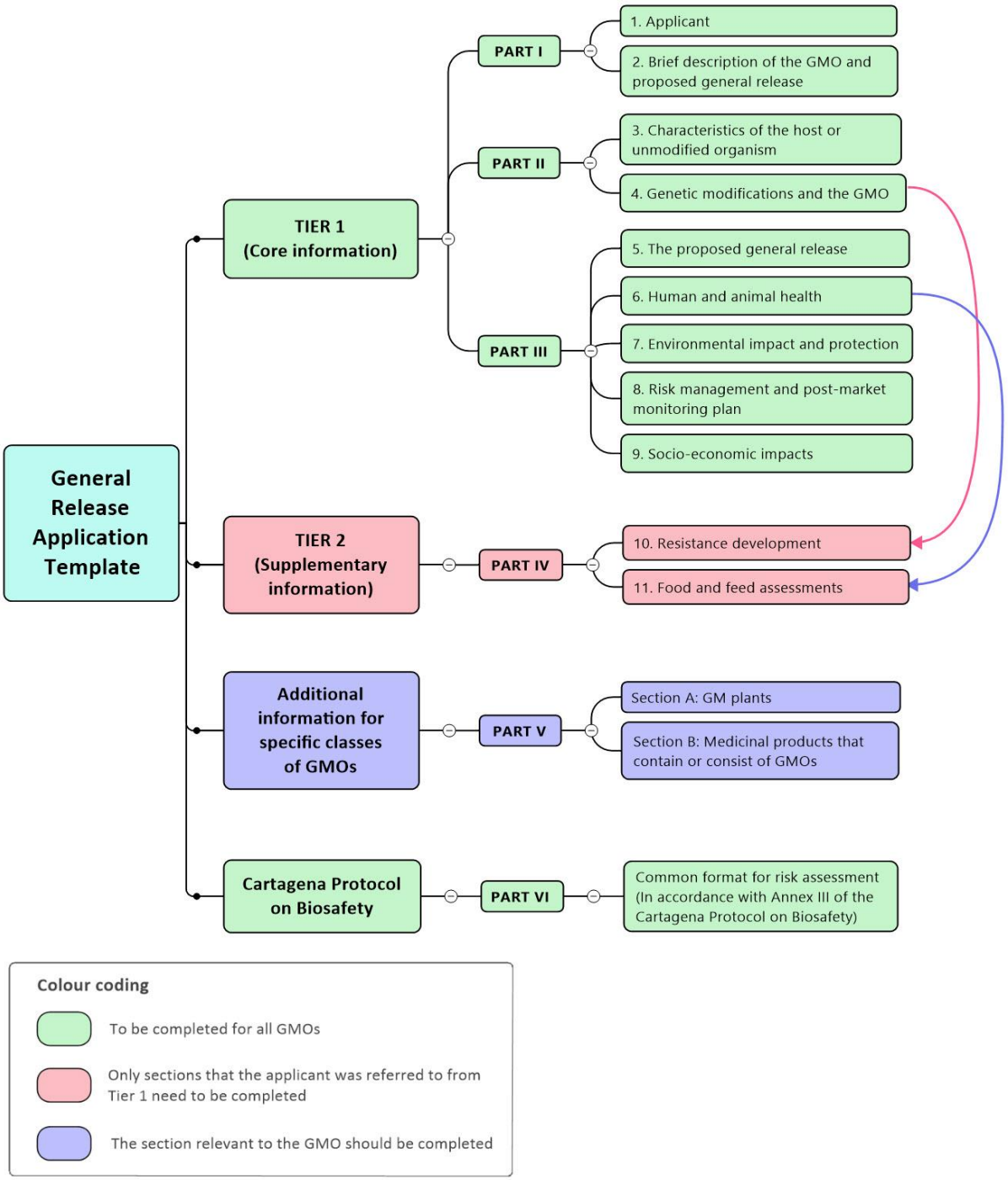

Figure 1. Graphical overview of the two-tier general release application template. The colour coding shows which parts need to be completed by the applicant: (1) Tier 1 and the Cartagena Protocol on Biosafety sections need to be completed for all GMOs, (2) for Tier 2, sections in Part IV only need to be completed if the applicant is referred to these sections based on the applicant's responses in Tier 1, and (3) in the "Additional information for specific classes of GMOs" part of the template, only the section relevant to the GMO should be completed. The arrows show where in the application template an applicant may be referred from Tier 1 (core information) to Tier 2 (supplementary information).

TIER 1 (Core Information)

PART I (to be completed for all GMOs)

1. APPLICANT

1.1 Name of applicant

1.2 Address of applicant

2. BRIEF DESCRIPTION OF THE GMO AND PROPOSED GENERAL RELEASE

2.1 Provide a unique identifier and brief description of the GMO, the intended function(s) of the genetic modification(s), and the genetically modified trait(s) of the GMO.

2.2 Provide a brief description of the proposed general release.

2.3 Is the unmodified organism indigenous to South Africa or does it have a history of safe use in South Africa?

PART II (to be completed for all GMOs)

3. CHARACTERISTICS OF THE HOST OR UNMODIFIED ORGANISM

3.1 Specific and common names of the unmodified organism (recipient or parental organism).

3.2 Describe the natural habitat, geographic distribution, geographic origin, and centres for diversity of the unmodified organism. Also, provide details on the type of environment and the geographical areas for which the unmodified organism is suited.

3.3 Comment on whether or not the unmodified organism has any adverse effect on:

- 3.3.1 Humans
- 3.3.2 Animals
- 3.3.3 Plants
- 3.3.4 Agricultural production
- 3.3.5 Any other aspect of the environment

3.4 Reproduction of the unmodified organism:

- 3.4.1 Provide detailed information on the mode(s) of reproduction.
- 3.4.2 Provide detailed information on specific factors affecting reproduction.
- 3.4.3 For pollen spread, identify pollinating agents and the distances to which pollen is known to spread.

3.4.4 Provide detailed information on the generation time.

3.5 Sexually compatible species:

3.5.1 Provide information on cultivated species, their distribution, and proximity to the general release areas.

3.5.2 Give details of wild species and their distribution and proximity to general release areas.

3.5.3 Identify any plants in the area of the general release that may become cross-pollinated with the host plant.

3.6 Survivability in the environment of the unmodified organism:

3.6.1 Provide details on structures produced by the unmodified organism for survival or dormancy.

3.6.2 Provide information on specific factors affecting survivability of the unmodified organism in the environment.

3.7 Dissemination of the unmodified organism in the environment:

3.7.1 Provide details on how the unmodified organism may disseminate in the environment.

3.7.2 Provide information on specific factors affecting dissemination of the unmodified organism in the environment.

3.8 Provide information on how the unmodified organism is usually utilised in agriculture, forestry, medicine, or other areas.

4. GENETIC MODIFICATIONS AND THE GMO

4.1 Was a donor organism(s) used as a source of the nucleic acid sequences used in the genetic modification(s)? If yes, provide:

4.1.1 Scientific and common names of the donor organism(s).

4.1.2 Provide details of the natural habitat, geographic distribution, geographic origin, and centres for diversity of the donor organism(s).

4.2 Provide a detailed description of the methods used for the genetic modification(s) and, in cases where vectors were used, describe the nature and source of the vectors used.

4.3 Provide detailed information on the genetic construct that enacts the genetic modification in the unmodified organism, including the source of donor DNA and the size and intended function of each constituent fragment that is inserted in the host's genome or that plays a role in making the genetic modification(s). Use maps and tables as appropriate.

4.4 Provide detailed information on the genetic modification(s) (e.g., base edits, inserted or deleted sequences) and phenotypic trait(s) and characteristics associated with the genetic modifications.

All information provided must be substantiated with appropriate empirical evidence and a description of the methodology used to generate the evidence.

There is no prescribed way for presenting the information, but information should be presented in a way that facilitates thorough review and must include the following:

(a) Identification and location of all inserted sequences (including short indels) and genes, including the copy numbers for all inserts, both complete and partial. The organisation of the inserted genetic material at the insertion site.

(b) Identification and location of all deleted sequence(s), the size of the deleted region(s), and the gene(s) and function(s) that are impacted upon by the deletion(s).

(c) The identification and location of all nucleotide base edits that are part of the planned genetic modification(s).

(d) The molecular methods used for determination of the location(s) of the genetic modification(s) and copy number determinations. The location(s) of genetic modification(s) information should indicate if the modification(s) is in the nucleus, chloroplasts, mitochondria, or maintained in a non-integrated form.

(e) The genetic stability of the modification(s) and the methods used to assess the stability.

(f) The biological activity, trait and phenotypic outcome associated with each genetic modification in the GMO.

(g) The biological activities, traits and phenotypic outcomes that results from the combination of genetic modifications in the GMO.

(h) The phenotypic stability of the GMO.

4.5 Expression of inserted sequences or genes:

4.5.1 Provide information on the expression of inserted sequences or genes.

4.5.2 State whether expression is constitutive or inducible. In the case of inducible expression, discuss the induction conditions.

4.5.3 Provide information on the rate and level of expression of the products of the inserted sequences or inserted genes and the sensitivity of the measurement of the rate and level.

4.5.4 In the case of GM plants, provide information on the expression of the products of the inserted sequences or inserted genes in different plant tissues. For stacked events, provide data on the expression of the inserted sequences relative to that in the parental GM events.

4.6 Changes in the expression of endogenous genes:

4.6.1 Provide information on the expression of previously inactive genes or changes in the expression of endogenous genes intentionally brought about by genetic modification(s) in the GMO.

4.6.2 Provide information on the rate and level of expression of previously inactive genes or genes that the levels of expression were intentionally changed by genetic modification(s) in the GMO. State the sensitivity of the measurement of the rate and level.

4.7 Provide information on how the GMO differs, or is expected to differ, from the unmodified organism with regard to:

4.7.1 General traits (including agronomic traits were relevant).

4.7.2 Natural habitat and geographic distribution.

4.7.3 Reproduction.

4.7.4 Dissemination/dispersion, including persistence and invasiveness.

4.7.5 Survivability, especially in the spectrum of conditions which are likely to be found in the general release areas.

4.7.6 The ability to transfer genetic material to other organisms, including bacteria and plants.

4.7.7 Adverse effects on:

4.7.7.1 Humans

4.7.7.2 Animals

4.7.7.3 Plants

4.7.7.4 Agricultural production

4.7.7.5 Any other aspect of the environment

4.7.7.6 Other.

4.8 Unintended effects:

4.8.1 Provide information on the assessment of unintended effects in the GMO (e.g., off-target effects, unintended DNA insertions, and chromosomal rearrangements). Include details of the assessment methods.

4.8.2 If unintended effects were observed, provide comprehensive information on the unintended effects and the impact of the unintended effects on the traits and characteristics of the GMO, especially in the context of section 4.7.

4.9 Can any organism or component of the environment develop resistance to any gene product, especially foreign gene product, that is produced as a result of the genetic modification(s) in the GMO? If yes, complete section 10 of Part IV.

4.10 Provide detailed, implementable protocols or standard operating procedures (SOPs) for:

4.10.1 The detection in the environment/other organisms of the genetically modified nucleic acid sequences that define the organism as a GMO.

4.10.2 Identification and detection of the GMO in the environment and for distinguishing between the GMO and the unmodified organism.

The responses for 4.10.1 and 4.10.2 should include information on the sensitivity, reliability and specificity of the techniques.

The detailed protocols should be included as annexures to the application.

PART III (to be completed for all GMOs)

5. THE PROPOSED GENERAL RELEASE

5.1 Who will undertake the general release?

5.2 Why is general release being requested?

5.3 When and where will general release be implemented?

5.4 Provide details of the environment and the geographical areas for which the GMO is suited.

5.5 Estimate the amount of production of the GMO within South Africa per annum.

5.6 Give a description of the intended use of the GMO and/or derived product. Indicate if the derived products are for food/feed or industrial use.

5.7 Identify the parts of the GMO to be used for the product, the type of product, and the use of the product as well as the market sector in which the product may be marketed.

5.8 Provide information on the proposed labelling of the product for marketing. Please refer also to the Consumer Act, 2008 (No. 68 of 2008) and other relevant Acts for guidance on labelling requirements.

5.9 State whether the benefits of the product are available in any other non-GM form. If so, state why the GM form should be approved for general release when other, non-GM products are available.

6. HUMAN AND ANIMAL HEALTH

6.1 Provide information on the anticipated extent of exposure to the GMO or its products for humans and animals.

6.2 Toxicology:

6.2.1 Provide details of experiments undertaken to determine the toxicity to humans and animals of the newly expressed proteins (including antibiotic markers) or new constituents other than proteins.

6.3 Allergenicity:

6.3.1 What are the common/major allergens present in the unmodified organism?

6.3.2 Provide details of experiments undertaken to determine the allergenicity of the newly expressed gene products (including antibiotic markers) to humans and animals.

6.3.3 What evidence is there that the genetic modification described in this application did not result in over-expression of the possible allergens indicated in 6.3.1, i.e., is the expression of the possible allergens in the non-GM counterpart substantially equivalent to that in the GM organism?

6.3.4 Provide details of any experiments undertaken to determine the allergenicity of whole GM food or GM feed.

6.4 If the newly expressed gene products are toxic or allergenic in any way, detail how the general release will be managed to prevent contact with animals or humans that will lead to discomfort or toxicity.

6.5 Can the GMO or its products be used for food or feed? If yes, please complete section 11 of Part IV.

6.6 What are the implications of the proposed activity (general release) with regard to the health and safety of the workers, cleaning personnel and any other person that will be directly or indirectly involved in the activity? Please take into consideration the provisions of the Occupational Health and Safety Act, 1993 (Act No. 85 of 1993 as amended by Act No. 181 of 1993) (and accompanying regulations) and indicate the proposed health and safety measures that would be applied.

7. ENVIRONMENTAL IMPACT AND PROTECTION

7.1 Submit a comprehensive evaluation of the foreseeable or likely impacts, especially long-term, that the general release of the GMO is likely to have on the environment. The impact assessment should consider abiotic and biotic components of the environment, including but not limited to impacts on non-target organisms, biodiversity and ecosystems.

7.2 If the genetic modification(s) give rise to GM plants that are tolerant to agrochemicals, provide information on the registered agrochemicals that the GM plant will be tolerant to.

8. RISK MANAGEMENT AND POST-MARKET MONITORING PLAN

8.1 Please indicate any risk management measures that users of this GMO will have to adhere to with regard to commercial planting and/or use.

8.2 Please specify an environmental monitoring plan (approach, strategy, method and analysis) which encompasses but is not limited to the following:

(i) Spread of the GMO.

(ii) Environmental impact and protection (focusing on issues such as pathogenic and ecological impacts, weed and insect resistance management, and direct and indirect impacts on non-target organisms).

(iii) Effects on human and animal health.

(iv) In the case of GM plants, impacts of the cultivation, management and harvesting techniques specific to the GMO.

(v) Also refer to requirements in terms of the Environmental Risk Assessment Framework for Genetically Modified Organisms.

9. SOCIO-ECONOMIC IMPACTS

9.1 Specify what, if any, positive or negative socio-economic impacts the general release of the GMO and its products will have on South Africa and its people. The information may include but is not limited to information on the impact on the following:

9.1.1 Income, competitiveness or economic markets.

9.1.2 Food security.

9.1.3 The continued existence and range of diversity of biological resources.

9.1.4 Access to genetics and other natural resources previously available.

9.1.5 Cultural traditions, knowledge and practices.

TIER 2 (Supplementary Information)

PART IV (only sections that the applicant was referred to from Tier 1 need to be completed)

10. RESISTANCE DEVELOPMENT

(To be completed if you answered yes to the question in section 4.9)

10.1 Provide details on any component of the environment that can develop resistance to any gene product, especially foreign gene product, that is produced as a result of the genetic modification(s) in the GMO.

10.2 Highlight the occurrence of resistance in previous trial releases or general releases or in the literature for GMOs containing the same or similar genes or genetic modifications.

10.3 Provide details on the methods that are available and that could/will be implemented to minimise the risk of resistance developing in the environment to any gene product, especially foreign gene product, that is produced as a result of the genetic modification(s) in the GMO.

11. FOOD AND FEED ASSESSMENTS

(To be completed if you answered yes to the question in section 6.5)

11.1 Provide information on the anticipated intake of the GMO or its products for humans and animals.

11.2 Compositional analysis and feeding studies:

Compositional analyses and feeding studies should be done using widely-accepted industry standards or guidelines (e.g., OECD or WHO guidelines) and appropriate statistical methods.

The Appendix contains guidance for the completion of section 11.2 for general release applications of GM plants.

11.2.1 Compositional analysis:

Provide the results of compositional analyses, and highlight any changes in natural food and feed constituents, including toxicants, metabolites and anti-nutritional factors.

Discuss the significance or biological relevance of any statistically significant differences between the GMO and appropriate comparators.

11.2.2 Feeding studies:

(a) Provide the results of nutritional performance or comparison studies.

(b) Provide the results of toxicological studies undertaken with the GMO or GM plant (e.g., whole GM food and/or GM feed).

For both (a) and (b), discuss the significance or biological relevance of statistically significant differences between the GMO and appropriate comparators.

Additional information for specific classes of GMOs

PART V (the section relevant to the GMO should be completed)

SECTION A: GM plants

1. Trial releases

1.1 Submit a list of previously authorised activities undertaken by the applicant with the GMO in:

(a) South Africa

(b) Other countries.

Your answers to (a) and (b) should include information on the country, year, location and the authority from which permission was obtained to run the trial releases.

1.2 Provide a scientific summary of the field performance of the GM plants, including a scientific explanation of the efficacy of the introduced trait(s) for each of the previously authorised activities listed in 1.1 (of Section A).

For South African trial releases, in depth discussions of the performance of the GMO is required, and detailed trial release reports should be included with the application dossier.

SECTION B: Medicinal products that contain or consist of GMOs

1. Trial releases

1.1 Submit a list of previously authorised activities undertaken by the applicant with the GMO in:

(a) South Africa

(b) Other countries.

Your answers to (a) and (b) should include information on the country, year, location and the authority from which permission was obtained to run the trial releases.

1.2 Provide a scientific summary of the results for each of the previously authorised activities listed in 1.1 (of Section B)

For South African trial releases, in depth discussions of the performance of the GMO is required, and detailed trial release reports should be included with the application dossier.

Cartagena Protocol on Biosafety

PART VI

COMMON FORMAT FOR RISK ASSESSMENT

(In accordance with Annex III of the Cartagena Protocol on Biosafety)

	Risk assessment details	
1.	Country Taking Decision:	South Africa
2.	Title:	<Text entry>
3.	Contact details:	<Standard contact address details: name, function (job title/designation), organization, address, phone, fax, email, website>
	LMO information	
4.	Name and identity of the living modified organism:	<Text entry – Identity of the living modified organism, and the differences between the biological characteristic of living modified organism and those of the recipient organism or parental organisms>
5.	Unique identification of the living modified organism:	<Text entry>
6.	Transformation event:	<Text entry>

7.	Introduced or Modified Traits:	Choose the trait from the following list: <u>A. Abiotic environmental tolerance</u> - Altered photoperiod sensitivity - Cold or heat tolerance - Drought or water tolerance - Other abiotic environmental tolerance <u>B. Altered growth, development and product quality</u> - Altered ripening or flowering - Colouration - Fertility restoration - Growth rate or yield - Male sterility - Nutritional composition (incl. allergenicity) - Other growth, development and product quality - Selectable marker genes and reporter genes - Uptake or degradation of environmental pollutants **Chemical tolerance** - Herbicide tolerance - Other chemical tolerance **Medical products** - Animal vaccines - Development of transplant organs - Other medical products - Production of pharmaceuticals **Pest resistance** - Bacterial resistance - Fungus resistance - Insect resistance - Nematode resistance - Other pest resistance - Virus resistance and <text entry for other, not on the list>
8.	Techniques used for modification:	<Controlled vocabulary for common techniques - Please select techniques used for the transformation: plasmid carried by *Agrobacterium tumefaciens*, biolistic methods, breeding, electric shock (poration), osmotic shock> *and* <text entry – for other, not on the list>
9.	Description of gene modification:	<Text entry>
		Characteristics of modification
10.	Vector characteristics (Annex III.9(c)):	<Text entry - Characteristics of the vector, should include its identity, if any, and its source or origin, and its host range >
11.	Insert or inserts (Annex III.9(d)):	<Text entry - Genetic characteristics of the inserted nucleic acid and the function it specifies, and/or characteristics of the modification introduced>

Recipient organism or parental organisms (Annex III.9(a)):	
12. Taxonomic name/status of recipient organism or parental organisms:	<Controlled vocabulary: agreed international standards> *and* <text entry – for other, not on the list>
13. Common name of recipient organism or parental organisms:	<Controlled vocabulary with thesaurus> *and* <text entry – for other, not on the list>
14. Point of collection or acquisition of recipient or parental organisms:	<Text entry >
15. Characteristics of recipient organism or parental organisms related to biosafety:	<Text entry >
16. Centre(s) of origin of recipient organism or parental organisms:	<Text entry - Describe the exact location and give geographical coordinates>
17. Centres of genetic diversity, if known, of recipient organism or parental organisms:	<Text entry - Describe the exact location and give geographical coordinates>
18. Habitats where the recipient organism or parental organisms may persist or proliferate:	<Text entry - Description of the habitat where the organisms may persist or proliferate>
Donor organism or organisms (Annex III.9(b)):	
19. Taxonomic name/status of donor organism(s)	<Controlled vocabulary: agreed international standards> and <text entry for other, not on the list>
20. Common name of donor organism(s):	<Controlled vocabulary with thesaurus> and <text entry for other, not on the list>
21. Point of collection or acquisition of donor organism(s):	<Text entry - the exact location and geographical coordinates>
22. Characteristics of donor organism(s) related to biosafety:	<Text entry - Relevant biological characteristics of donor organisms>

Intended use and receiving environment	
23. Intended use of the LMO (Annex III 9(g)):	<Text entry - Information relating to the intended use of the living modified organism, including new or changed use compared to the recipient organism or parental organisms>
24. Receiving environment (Annex III.9(h)):	<Text entry - Information on the location, geographical, climatic and ecological characteristics, including relevant information on biological diversity and centres of origin of the likely potential receiving environment>
Risk assessment summary	
25. Detection/Identification method of the LMO (Annex III.9(f)):	<Text entry - Suggested detection and identification methods and their specificity, sensitivity and reliability>
26. Evaluation of the likelihood of adverse effects (Annex III.8(b)):	<Text entry - An evaluation of the likelihood of these adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism>
27. Evaluation of the consequences (Annex III.8(c)):	<Text entry - An evaluation of the consequences should these adverse effects be realized>
28. Overall risk (Annex III.8(d)):	<Text entry - An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized>
29. Recommendation (Annex III.8(e)):	<Text entry - A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks>
30. Actions to address uncertainty regarding the level of risk (Annex III.8(f)):	<Text entry - details about any further information that has been requested where there is uncertainty regarding the level of risk, as well as any information on risk management strategies and/or monitoring of the LMO in the receiving environment>
Additional information	
31. Availability of detailed risk assessment information:	<Text entry - Please indicate whether more details on the risk assessment are available and how they can be accessed>
32. Any other relevant information:	< Text entry - any other information that is relevant to the risk assessment. e.g. information of non CBI nature that was included in the original application but is not included in this form>
33. Attach document:	*Not applicable to applicant*<Specific types of entry: option to choose a file from the local source and 'upload' a copy to the BCH server>
34. Notes:	<Text entry>

AFFIDAVIT/STATEMENT

(to be completed in the presence of a Commissioner of Oaths)

I…….

ID Number……. Age ……..

Working address ……..

Tel ……..(w) ……(h) ……(cell)

Declare under oath in English / confirm in English –

……
……
……
……

I am familiar with, and understand the contents of this declaration. I have no objection/have objection to taking the prescribed oath. I consider the prescribed oath as binding to my conscience.

Place: …….. Date: ……..

Time: ……

Signature: ……

I certify that the above statement was taken from me and that the deponent has acknowledged that he/she knows and understands the contents of the statement. The statement was sworn to/affirmed before me and deponents signature/mark/thumb print was placed thereon in my presence.

At: …… on …… at …….

……..
Commissioner of Oaths
(details to be provided on physical and postal address e.g., stamp of police station)

……
Force number/Rank/Name – print

Directions for the applicant:

(This page must be excluded from the documents submitted to the Registrar's office)

- Please complete all relevant sections of the questionnaire CLEARLY.
- Please provide 1 original and 15 copies (9 additional copies if application for a crop with no previous general release approval) of the application with confidential information for use by the regulatory bodies appointed in terms of the Genetically Modified Organisms Act, 1997 (Act No. 15 of 1997).

  Please confirm with the Office of the Registrar with regard to submission of electronic applications
- Please provide an additional hard copy and electronic version of the application containing no confidential information. Non-Confidential Business Information (Non-CBI) copy - this is your application where you have deleted any information that you regard as confidential business information. Please take note that you must make reference to the specific section of the Promotion of Access to Information Act, 2000 whenever you "delete" information in this application. This copy must be clearly marked NON-CONFIDENTIAL, and will be made available for public scrutiny and placed on the website of the Department. This copy of the application must be submitted to the Registrar one day after the placing of the public notices.
- Please provide an electronic and hard copy of a risk assessment conducted in accordance with Annex III of the Cartagena Protocol on Biosafety and in the format prescribed below.
- Please conduct a public notification in accordance with Regulation 9 of the GMO Act, and making use of the guideline document available on the website of the department. Copies of the public notification must be submitted with the application.
- Please submit all relevant documentation to the Registrar at the address indicated in the application form.
- The appropriate fee stipulated under the GMO Act must accompany the application. Please note that the Registrar's office does not accept cash.

APPENDIX

Guidance for section 11.2 (compositional analysis and feeding studies)

1. Compositional data should be provided for the GM crop (including stacked events) under consideration in the application.
2. For both compositional analyses and feeding studies, provide clear information on:
    a. the choice of non-GM comparators,
    b. the production of material for the comparative assessments, including locations, replicates and growing seasons, and
    c. the baselines used for consideration of natural variations.
3. For all stacked event applications that include a complete, stand-alone risk assessment package for the stacked event, there is no expectation that data will be provided for the parental GM events.
4. For stacked events that contain RSA-approved parental GM events and a parental GM event that has not yet been approved in the RSA, the safety assessment of the stacked event may take into consideration the demonstrated safety of the parental GM events (i.e., a data bridging approach may be used); however, detailed safety assessments, including feeding and toxicological studies, would be expected for the unapproved GM event in the stack. Alternatively, a full risk assessment package may be submitted for the stacked event under consideration. For either approach, agronomic/phenotypic, expression and compositional data for the stacked event are expected. The expression levels of the inserted sequences relative to those in the parental GM events need to be taken into consideration (see also 7.5.3).
5. For all stacked event applications that do not include a complete risk assessment package for the stacked event (e.g., prior RSA approval for parental GM events is used to argue that feeding studies are not required; see point 4 above), the full safety assessment package for each parental GM event needs to be included in the application dossier.
6. For stacked events in general: in the event that the compositional analyses show that there are statistically significant differences of biological relevance between the stacked event and the non-GM comparators, further safety assessments, including feeding and toxicological studies, of the stacked event under consideration would be expected.

7. Lower-level stack applications: in the event that compositional analyses show that there are not statistically significant differences of biological relevance between a lower-level stack (e.g., AxBxC) and both a previously RSA-approved higher-level stack (e.g., AxBxCxD) and non-GM comparators, then the need for further safety assessments should be considered on a case-by-case basis. However, in all such applications, the full risk assessment package (including expression and feeding studies) for each parental GM event needs to be included in the application dossier. In these types of applications, the expression levels of the inserted sequences relative to those in the parental GM events need to be taken into consideration (see also 7.5.3).

8. For all newly assessed single events: besides compositional data, further detailed safety assessments, including feeding and toxicological studies, for the GM crop under consideration are expected.