GUIDANCE DOCUMENT[1]

Late stage R&D and regulatory roadmap for commercialising a GM crop in South Africa

Below follows a brief overview of the typical information and activities that are required during the late stage development and commercialisation of a GMO in South Africa. Please note that this is not an exhaustive list of all requirements - technology developers should also refer to other more comprehensive BSA guidance document and the official regulatory application forms and guidelines, for each individual type of application, available from the Registrar of the GMO Act (http://www.daff.gov.za).

Stage 1: Confirm commercial viability of the intended GM product

The difference between "a technology development/research project" and "a product" is a viable market. Confirm that you have a viable product before investing time and money in the development and commercialisation processes.

1.1 Market (potential income).

a. Current total market for product vs. possible market for GM product.
    i) Is the GM trait relevant and does it add a clear benefit for the consumer?
    ii) Is there a quantifiable demand for the new trait?
    iii) Are there alternatives and how do they compete with your product (also in terms of "soft" issues, e.g. consumer preference issues)?
    iv) Consider balance between possible gain due to GM trait and loss due to possible market perceptions (i.e. acceptability).
b. Deployment and capacity issues.
    i) How will the GM product reach the intended market?
    ii) Would the GM trait change current on-farm and/or consumer practices?

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1.2 Commercialisation constrains & costs.

a. Background IP – do you have freedom to operate with ALL the technologies used? Any GM project potentially infringes hundreds of patents.

b. A single, clear vision for commercialisation.
   i) Is there a firm and clear agreement in place between the development partners?
   ii) Do other influential stakeholders (incl. outside the development partnership, e.g. the wider industry and its clients) agree on the introduction of the GM product and do they support it?
   iii) Is there already a similar product in the market? If not, will it create additional problems?

c. Development of the regulatory dossier.
   i) Biosafety (food and feed plus environmental safety) & socio-economic data generation.
   ii) Costs directly associated with regulatory compliance are estimated at ~R10M per line.

d. Possible local regulatory risks (uncertainty re new products and moving targets).

e. Individual regulatory barriers in every export market (national & international regulations) increase regulatory costs and exposure to different interpretations in each unique framework, e.g. liability issues.

f. Transporting LMOs (living modified organisms) across international borders triggers the Cartagena Protocol on Biosafety.

Stage 2: Field trials

Field trials are designed to generate the required data to support a subsequent general release application and confirm efficacy. This is usually done with a limited number of transgenic lines that have already showed potential.

2.1 Before the trial (developing the field trial application).

a. Public notification.

b. General risk communication starts now and is important – be prepared!

c. Theoretical background on crop (biology document) & GM trait.

d. Molecular characterisation of GMO.
   i) General description of transgenic intervention, i.e. why, what & how. Protein expression vs. gene silencing, etc.
   ii) List and description of transgene and regulatory sequences, incl. their sources.
   iii) Available genomic stability data.
   iv) Sequences of integration sites.
   v) Description of detection and identification protocol.

e. Efficacy data from greenhouse trials. The transgene should clearly be able to impart the trait it is suppose to.

f. *Ex ante* biosafety risk analysis (in particular any safety aspects that may need further investigation/confirmation should be identified and, if possible, integrated into the field trial). Start doing some of the work that is not dependent on lots of fresh material, e.g. molecular and bioinformatics analyses including allergenicity assessments.
    i) Food & feed safety.
    ii) Environmental safety.
g. *Ex ante* socio-economic overview.
    i) Who are the stakeholders and how will they be impacted (positively and/or negatively) upon?
h. Field trial design.
    i) Confinement is the primary biosafety goal.
    ii) Clearly state expected goals and outcomes.
    iii) Should be able to generate data that can deliver on the requirements of the regulatory dossier.
    iv) Compile risk management plan.
i. Field trial application.

2.2 During the trial

a. Efficacy of the GM trait in the field.
b. Agronomic performance of GMO compared to control.
c. Biosafety of GMO (environmental and food & feed safety issues), which may include:
    i) Expression level of all transgenes.
    ii) Development of an event-specific PCR for the GMO.
    iii) Sequence of the T-DNA inserted into the genome as compared to the original T-DNA.
    iv) Determine number of inserted T-DNAs.
    v) Determine absence of plasmid backbone in GMO.
    vi) Sequence of left and right borders between T-DNA and genome of GMO.
    vii) Search for sequence similarities with known protein toxins.
    viii) Equivalence of expression of transgene in *E. coli* and GMO.
    ix) Possible effect of GMO on non-target organisms (field and lab).
d. Sustainability of GM product (including socio-economic issues).

2.3 After the trial

a. Complete trial report.
b. Complete post-trial monitoring and risk management activities.

Note that a number of successive trials may be required before all the necessary information needed for a general release is available.

Gate 2

Stage 3: General release / commercialisation

The South African regulatory system does not “deregulate” GMOs – general release is always conditional. A comprehensive regulatory dossier forms the basis of the general release application.

3.1 Regulatory dossier development:

a. Detailed description of GMO.
b. Field trial report.
c. Food and feed safety.
d. Environmental safety.
e. Socio-economic issues.

(refer to other guidelines for detailed discussions on the various sections)

3.2 Communication strategy (risk communication).

3.3 Comply with permit conditions once general release status has been granted.

a. Compliance and stewardship including risk mitigation plans and monitoring

The above can also be summarised in the following diagram, which highlights the multi-disciplinary and integrated nature of all these issues.

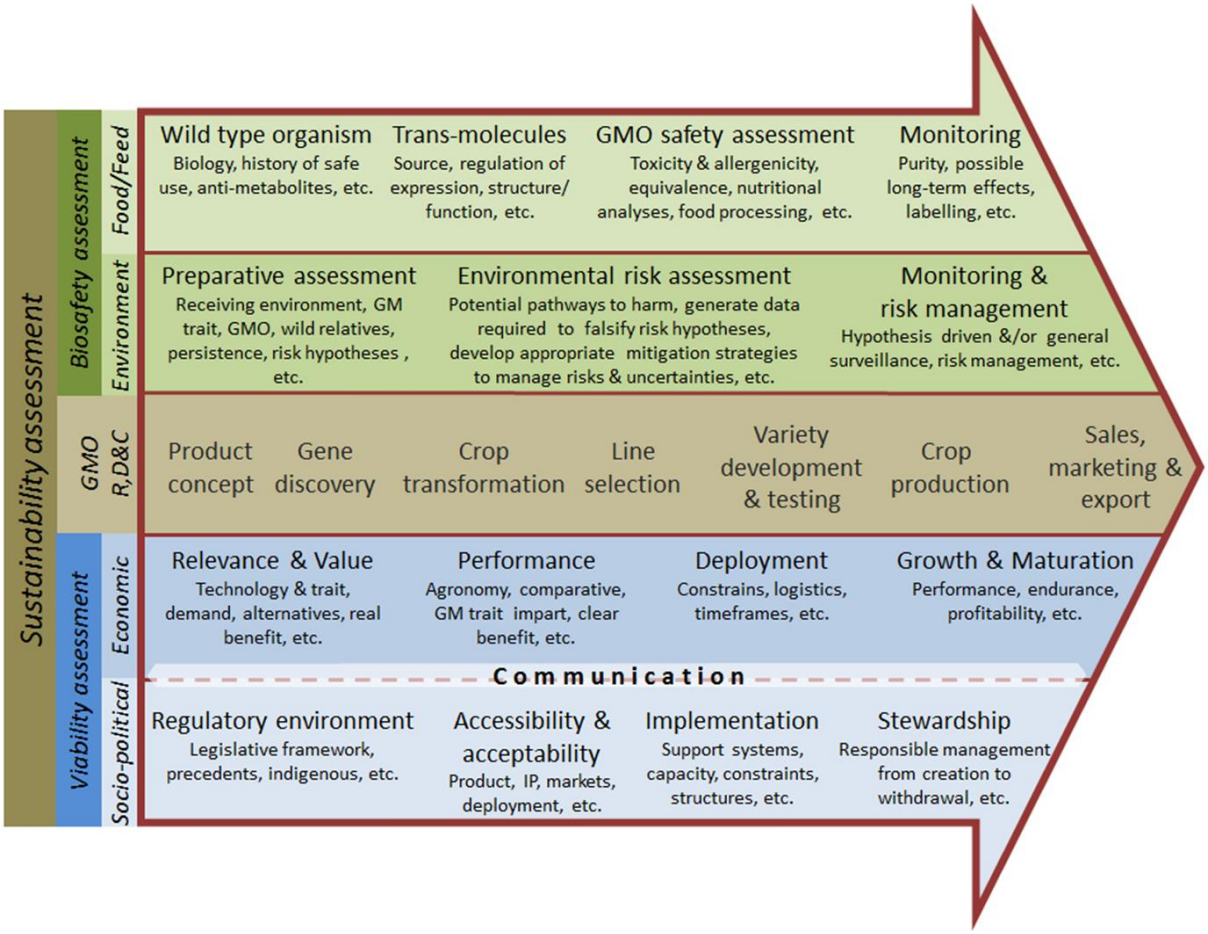

Figure 1. Integrated, conceptual framework for the development and commercialisation of a GM crop.