EU Directive on the Deliberate Release into the Environment of Genetically Modified Microorganisms

Get involved – The AMI Policy Team intends to submit a response to the European Commission's public consultation on the Biotech Act, specifically the amendments to Directive 2001/18/EC, which regulates the deliberate release into the environment of genetically modified organisms (GMOs) and introduces new provisions specifically for genetically modified micro-organisms (GMMs).

Context – The European Commission has proposed a European Biotech Act to strengthen the competitiveness of the biotechnology sector. Its main objectives relate to safeguarding high standards for the protection of human health, animal health, patients and consumers, and the environment, while strengthening the competitiveness of the biotechnology sector.

As part of this new Act, the European Commission has proposed amendments to Directive 2001/18/EC which relates to Genetically Modified Organisms (GMOs). Although Directive 2001/18/EC applies to all GMOs, much of its framework was developed with genetically modified plants in mind. The proposed amendments introduce provisions specifically for genetically modified microorganisms (GMMs), as or in products other than food or feed. The aim is to create a regulatory system better suited to GMMs, making the approval process more efficient whilst maintaining safety.

The proposal introduces changes in several key areas:

- **Environmental risk assessment:** The information that companies must provide as part of the environmental risk assessment (currently set out in Annex III of Directive 2001/18/EC) could be adapted in the future to better reflect the specific characteristics of GMMs. These changes would be made by the European Commission through delegated acts but would still have to follow the general environmental risk assessment principles set out in Annex II of the Directive.
- **Duration of approvals:** Unlike the current system, where marketing consents are granted for a limited period, approvals for GMMs would become valid indefinitely. Existing obligations to report new information and measures to protect human health and the environment would continue to apply.
- **Detection methods:** The proposal also updates the requirements for detecting GMMs. Where it is not technically possible to provide a method that can detect, identify and quantify a GMM, alternative arrangements would be allowed.
- **Simplified authorisation:** The proposal introduces a new category of "low-risk GMMs" and establishes a framework for a “proportionate authorisation process” for these organisms. It sets out scientific criteria that a GMM must meet to be

considered low risk and establishes a framework for a simplified authorisation process for these GMMs. The European Commission would be given the power, through delegated acts, to:
    - further develop the criteria for determining whether a GMM is low risk;
    - adapt the information required for environmental risk assessments (Annex III) for low-risk GMMs; and
    - simplify certain parts of the authorisation procedure for these GMMs
- **Post-market environmental monitoring:** Finally, the proposal would also modify the requirements for post-market environmental monitoring of low-risk GMMs. Under certain conditions, applicants could propose that post-market environmental monitoring is not required for a low-risk GMM.

The European Commission is inviting feedback on the proposed legislative amendments rather than asking stakeholders to answer a fixed set of consultation questions. As such, the AMI policy team have pulled out several questions we'd value input on below but also welcome **any** thoughts in regard to this new directive.

Please share input by Wednesday 29 July.

If you have any questions about how to get involved, get in touch – policy@appliedmicrobiology.org

To note: the PDF pertaining specifically to Directive 2001/18/EC and its amendments can be found at the bottom of the consultation page. This document also covers a separate proposal relating to amendments around the processing of human organs intended for transplantation. AMI's response will focus only on the proposed amendments relating to genetically modified microorganisms.

Expert review questions on the proposed EU Biotech Act (GMM provisions)

1. Definition of microorganisms

The proposal would add definitions of "micro-organism" and "genetically modified micro-organism" (GMM) to Directive 2001/18/EC, based on the definitions in Directive 2009/41/EC but excluding animal and plant cells in culture.

Directive 2009/41/EC defines a micro-organism as "any microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, including viruses, viroids and animal and plant cells in culture". Under the proposal, the new GMM-specific provisions would cover micro-organisms in the biological sense, including Archaea, Bacteria, unicellular species and life stages of Protozoa, Chromista and Fungi,

filamentous fungi and viruses. Animal and plant cells in culture would remain subject to the general GMO rules rather than the new GMM-specific provisions.

Question: Do you consider the proposed definition of "micro-organism" to be scientifically accurate, sufficiently clear and appropriate for current and emerging biotechnology?

2. Environmental risk assessment

The proposal would allow the European Commission to amend Annex III of Directive 2001/18/EC to introduce information requirements specifically adapted to GMMs and to scientific and technical progress. Environmental risk assessments would continue to follow the general principles in Annex II of the Directive.

Annex II sets out the principles and methodology for environmental risk assessment. Annex III sets out the information that must accompany a notification, including information on the recipient and donor organisms, the genetic modification, the resulting GMO, the intended use, the receiving environment, potential environmental interactions, monitoring, control and emergency measures.

For GMMs, Annex IIIA is the relevant section. Annex IIIB applies to genetically modified higher plants.

A delegated act allows the Commission to supplement or amend specified non-essential elements of legislation. Under the proposal, delegated acts would be used to establish GMM-specific information requirements in Annex III.

Annex II and III can be found towards the bottom of this webpage, and at the bottom of this document.

Question: Do you consider the current information requirements in Annex IIIA and the environmental risk-assessment principles in Annex II appropriate for assessing GMMs? Are there any requirements or principles that should be added, removed or adapted, and why?

3. Unlimited duration of consents

Under the existing Directive, a consent to place a GMO on the market is time limited and may be renewed. The renewal process allows updated information, monitoring results and new evidence to be considered.

The proposal would provide that consents for placing GMMs on the market are valid for an unlimited period and that the existing renewal procedure in Article 17 would not apply. This would not remove the existing provisions allowing action to be taken when new information affects the assessment of risk or when a Member State has justified reasons to consider that an authorised GMO presents a risk.

The Commission's rationale is that:

- GMM product cycles are often short;
- new GMM products may build on experience gained from earlier products, including risk-assessment experience;
- periodic renewal creates burdens for operators and competent authorities;
- notifiers must already provide relevant new information; and
- safeguard measures are available if new risks are identified.

The proposal argues that time-limited consents provide limited additional safety value where the commercial lifetime of a GMM product is short.

Question: Do you consider the proposed move to unlimited-duration market consents for genetically modified microorganisms to be scientifically justified?

4. Detection methods

Notifications under Directive 2001/18/EC normally include a method for detecting, identifying and quantifying the relevant transformation event.

The proposal recognises that, for some GMMs, particularly some produced using new genomic techniques, it may not be feasible to provide such a method. Where this is duly justified by the notifier, adapted arrangements for meeting analytical-method performance requirements would be established through implementing acts. The competent authority would assess whether the notifier has adequately justified the use of those adapted arrangements.

An implementing act is used to establish uniform conditions for applying EU legislation across Member States.

Question: Do you consider the proposed approach to detection methods appropriate, where it is not technically feasible to provide analytical methods capable of detecting, identifying and quantifying the transformation event?

5. Simplified authorisation and 'low risk' GMMs

The proposal would introduce a category of “low-risk GMMs”. A GMM would have to meet all three of the following criteria:

1. it is taxonomically and molecularly well characterised;
2. it belongs to a taxonomic unit with Qualified Presumption of Safety status; and
3. it does not contain genes of concern that are not naturally present in the parental organism, particularly acquired antimicrobial-resistance genes.

Qualified Presumption of Safety is a status assigned by the European Food Safety Authority to selected groups of micro-organisms following an assessment indicating no safety concerns.

The Commission would be empowered through delegated acts to:

- further specify these criteria;
- establish additional criteria where necessary;
- introduce specific Annex III information requirements for low-risk GMMs; and
- establish adapted risk-assessment procedures for low-risk GMMs.

The proposal states that the assessment and authorisation process should be adapted to the characteristics of low-risk GMMs, streamline certain procedural elements and shorten timelines, while maintaining protection of human health and the environment and the necessary consultation of competent authorities and the public. The exact reduced information requirements and procedural changes are not set out in the proposal and would be established later.

Question: Do you support the proposal to introduce a category of "low-risk GMMs"? If so, are the proposed criteria sufficient? Are there additional scientific criteria or safeguards that should be included?

6. Post-market environmental monitoring

Under the proposal, a notifier of a low-risk GMM could propose not to submit a post-market environmental monitoring plan. This would have to be justified by:

- evidence from any previous notified release;
- the findings of the environmental risk assessment;
- the characteristics of the GMM;
- the characteristics and scale of its expected use; and
- the characteristics of the receiving environment.

The absence of monitoring would not be automatic. The written consent would either specify the monitoring requirements or state that monitoring is not required.

The proposal explains that monitoring might be waived where the environmental risk assessment does not identify concerns requiring monitoring, including possible indirect, delayed or unanticipated effects on human health or the environment.

Question: Do you consider it appropriate to allow post-market environmental monitoring to be omitted for certain low-risk GMMs? Under what circumstances, if any, would this be scientifically justified?

7. Scientific input into future technical requirements

The proposal would give the European Commission the power to develop several technical aspects of the framework after the Directive is adopted. These include:

- adapting the information required for environmental risk assessments of GMMs;
- further developing the criteria for classifying GMMs as "low risk";
- adapting the risk assessment process for low-risk GMMs; and
- developing the technical requirements relating to detection methods.

These technical requirements would be developed in the future as scientific knowledge and experience evolve.

Question: What scientific expertise should inform these future technical requirements? Which areas of microbiology expertise should be involved? Are there particular topics where wider scientific consultation would be especially important?

8. Overall regulatory framework

Question: Overall, do you consider that the proposed amendments provide an appropriate balance between facilitating innovation and maintaining a high level of protection of human health and the environment?

Annex III of Directive 2001/18/EC, relating to the risk assessment of GMM's

ANNEX III A

INFORMATION REQUIRED IN NOTIFICATIONS CONCERNING RELEASES OF GENETICALLY MODIFIED ORGANISMS OTHER THAN HIGHER PLANTS

I. GENERAL INFORMATION

A. Name and address of the notifier (company or institute)

B. Name, qualifications and experience of the responsible scientist(s)

C. Title of the project

II. INFORMATION RELATING TO THE GMO

A. Characteristics of (a) the donor, (b) the recipient or (c) (where appropriate) parental organism(s):

1. scientific name,

2. taxonomy,

3. other names (usual name, strain name, etc.),

4. phenotypic and genetic markers,

5. degree of relatedness between donor and recipient or between parental organisms,

6. description of identification and detection techniques,

7. sensitivity, reliability (in quantitative terms) and specificity of detection and identification techniques,

8. description of the geographic distribution and of the natural habitat of the organism including information on natural predators, preys, parasites and competitors, symbionts and hosts,

9. organisms with which transfer of genetic material is known to occur under natural conditions,

10. verification of the genetic stability of the organisms and factors affecting it,

11. pathological, ecological and physiological traits:

(a) classification of hazard according to existing Community rules concerning the protection of human health and/or the environment;

(b) generation time in natural ecosystems, sexual and asexual reproductive cycle;

(c) information on survival, including seasonability and the ability to form survival structures;

(d) pathogenicity: infectivity, toxigenicity, virulence, allergenicity, carrier (vector) of pathogen, possible vectors, host range including non-target organism. Possible activation of latent viruses (proviruses). Ability to colonise other organisms;

(e) antibiotic resistance, and potential use of these antibiotics in humans and domestic organisms for prophylaxis and therapy;

(f) involvement in environmental processes: primary production, nutrient turnover, decomposition of organic matter, respiration, etc.

12. Nature of indigenous vectors:

(a) sequence;

(b) frequency of mobilisation;

(c) specificity;

(d) presence of genes which confer resistance.

13. History of previous genetic modifications.

B. Characteristics of the vector

1. nature and source of the vector,

2. sequence of transposons, vectors and other non-coding genetic segments used to construct the GMO and to make the introduced vector and insert function in the GMO,

3. frequency of mobilisation of inserted vector and/or genetic transfer capabilities and methods of determination,

4. information on the degree to which the vector is limited to the DNA required to perform the intended function.

C. Characteristics of the modified organism

1. Information relating to the genetic modification:

(a) methods used for the modification;

(b) methods used to construct and introduce the insert(s) into the recipient or to delete a sequence;

(c) description of the insert and/or vector construction;

(d) purity of the insert from any unknown sequence and information on the degree to which the inserted sequence is limited to the DNA required to perform the intended function;

(e) methods and criteria used for selection;

(f) sequence, functional identity and location of the altered/inserted/deleted nucleic acid segment(s) in question with particular reference to any known harmful sequence.

2. Information on the final GMO:

(a) description of genetic trait(s) or phenotypic characteristics and in particular any new traits and characteristics which may be expressed or no longer expressed;

(b) structure and amount of any vector and/or donor nucleic acid remaining in the final construction of the modified organism;

(c) stability of the organism in terms of genetic traits;

(d) rate and level of expression of the new genetic material. Method and sensitivity of measurement;

(e) activity of the expressed protein(s);

(f) description of identification and detection techniques including techniques for the identification and detection of the inserted sequence and vector;

(g) sensitivity, reliability (in quantitative terms) and specificity of detection and identification techniques;

(h) history of previous releases or uses of the GMO;

(i) considerations for human health and animal health, as well as plant health:

(i) toxic or allergenic effects of the GMOs and/or their metabolic products;

(ii) comparison of the modified organism to the donor, recipient or (where appropriate) parental organism regarding pathogenicity;

(iii) capacity for colonisation;

(iv) if the organism is pathogenic to humans who are immunocompetent:

- diseases caused and mechanism of pathogenicity including invasiveness and virulence,

- communicability,

- infective dose,

- host range, possibility of alteration,

- possibility of survival outside of human host,

- presence of vectors or means of dissemination,

- biological stability,

- antibiotic resistance patterns,

- allergenicity,

- availability of appropriate therapies.

(v) other product hazards.

III. INFORMATION RELATING TO THE CONDITIONS OF RELEASE AND THE RECEIVING ENVIRONMENT

A. Information on the release

1. description of the proposed deliberate release, including the purpose(s) and foreseen products,

2. foreseen dates of the release and time planning of the experiment including frequency and duration of releases,

3. preparation of the site previous to the release,

4. size of the site,

5. method(s) to be used for the release,

6. quantities of GMOs to be released,

7. disturbance on the site (type and method of cultivation, mining, irrigation, or other activities),

8. worker protection measures taken during the release,

9. post-release treatment of the site,

10. techniques foreseen for elimination or inactivation of the GMOs at the end of the experiment,

11. information on, and results of, previous releases of the GMOs, especially at different scales and in different ecosystems.

B. Information on the environment (both on the site and in the wider environment):

1. geographical location and grid reference of the site(s) (in case of notifications under part C the site(s) of release will be the foreseen areas of use of the product),

2. physical or biological proximity to humans and other significant biota,

3. proximity to significant biotopes, protected areas, or drinking water supplies,

4. climatic characteristics of the region(s) likely to be affected,

5. geographical, geological and pedological characteristics,

6. flora and fauna, including crops, livestock and migratory species,

7. description of target and non-target ecosystems likely to be affected,

8. a comparison of the natural habitat of the recipient organism with the proposed site(s) of release,

9. any known planned developments or changes in land use in the region which could influence the environmental impact of the release.

IV. INFORMATION RELATING TO THE INTERACTIONS BETWEEN THE GMOs AND THE ENVIRONMENT

A. Characteristics affecting survival, multiplication and dissemination

1. biological features which affect survival, multiplication and dispersal,

2. known or predicted environmental conditions which may affect survival, multiplication and dissemination (wind, water, soil, temperature, pH, etc.),

3. sensitivity to specific agents.

B. Interactions with the environment

1. predicted habitat of the GMOs,

2. studies of the behaviour and characteristics of the GMOs and their ecological impact carried out in simulated natural environments, such as microcosms, growth rooms, greenhouses,

3. genetic transfer capability

(a) postrelease transfer of genetic material from GMOs into organisms in affected ecosystems;

(b) postrelease transfer of genetic material from indigenous organisms to the GMOs;

4. likelihood of postrelease selection leading to the expression of unexpected and/or undesirable traits in the modified organism,

5. measures employed to ensure and to verify genetic stability. Description of genetic traits which may prevent or minimise dispersal of genetic material. Methods to verify genetic stability,

6. routes of biological dispersal, known or potential modes of interaction with the disseminating agent, including inhalation, ingestion, surface contact, burrowing, etc.,

7. description of ecosystems to which the GMOs could be disseminated,

8. potential for excessive population increase in the environment,

9. competitive advantage of the GMOs in relation to the unmodified recipient or parental organism(s),

10. identification and description of the target organisms if applicable,

11. anticipated mechanism and result of interaction between the released GMOs and the target organism(s) if applicable,

12. identification and description of non-target organisms which may be adversely affected by the release of the GMO, and the anticipated mechanisms of any identified adverse interaction,

13. likelihood of postrelease shifts in biological interactions or in host range,

14. known or predicted interactions with non-target organisms in the environment, including competitors, preys, hosts, symbionts, predators, parasites and pathogens,

15. known or predicted involvement in biogeochemical processes,

16. other potential interactions with the environment.

V. INFORMATION ON MONITORING, CONTROL, WASTE TREATMENT AND EMERGENCY RESPONSE PLANS

A. Monitoring techniques

1. methods for tracing the GMOs, and for monitoring their effects,

2. specificity (to identify the GMOs, and to distinguish them from the donor, recipient or, where appropriate, the parental organisms), sensitivity and reliability of the monitoring techniques,

3. techniques for detecting transfer of the donated genetic material to other organisms,

4. duration and frequency of the monitoring.

B. Control of the release

1. methods and procedures to avoid and/or minimise the spread of the GMOs beyond the site of release or the designated area for use,

2. methods and procedures to protect the site from intrusion by unauthorised individuals,

3. methods and procedures to prevent other organisms from entering the site.

C. Waste treatment

1. type of waste generated,

2. expected amount of waste,

3. description of treatment envisaged.

D. Emergency response plans

1. methods and procedures for controlling the GMOs in case of unexpected spread,

2. methods for decontamination of the areas affected, for example eradication of the GMOs,

3. methods for disposal or sanitation of plants, animals, soils, etc., that were exposed during or after the spread,

4. methods for the isolation of the area affected by the spread,

5 plans for protecting human health and the environment in case of the occurrence of an undesirable effect.

Annex II of Directive 2001/18/EC, relating to the principles for undertaking an environmental risk assessment for GMMs

ANNEX II

PRINCIPLES FOR THE ENVIRONMENTAL RISK ASSESSMENT

This Annex describes in general terms the objective to be achieved, the elements to be considered and the general principles and methodology to be followed to perform the environmental risk assessment (e.r.a.).

- "direct effects" refers to primary effects on human health or the environment which are a result of the GMO itself and which do not occur through a causal chain of events;

- "indirect effects" refers to effects on human health or the environment occurring through a causal chain of events, through mechanisms such as interactions with other organisms, transfer of genetic material, or changes in use or management.

Observations of indirect effects are likely to be delayed;

- "immediate effects" refers to effects on human health or the environment which are observed during the period of the release of the GMO. Immediate effects may be direct or indirect;

- "delayed effects" refers to effects on human health or the environment which may not be observed during the period of the release of the GMO, but become apparent as a direct or indirect effect either at a later stage or after termination of the release.

A general principle for environmental risk assessment is also that an analysis of the "cumulative long-term effects" relevant to the release and the placing on the market is to be carried out. "Cumulative long-term effects" refers to the accumulated effects of consents on human health and the environment, including inter alia flora and fauna, soil fertility, soil degradation of organic material, the feed/ food chain, biological diversity, animal health and resistance problems in relation to antibiotics.

A. Objective

The objective of an e.r.a. is, on a case by case basis, to identify and evaluate potential adverse effects of the GMO, either direct and indirect, immediate or delayed, on human health and the environment which the deliberate release or the placing on the market of GMOs may have. The e.r.a. should be conducted with a view to identifying if there is a need for risk management and if so, the most appropriate methods to be used.

B. General Principles

In accordance with the precautionary principle, the following general principles should be followed when performing the e.r.a.:

- identified characteristics of the GMO and its use which have the potential to cause adverse effects should be compared to those presented by the non-modified organism from which it is derived and its use under corresponding situations;

- the e.r.a. should be carried out in a scientifically sound and transparent manner based on available scientific and technical data;

- the e.r.a. should be carried out on a case by case basis, meaning that the required information may vary depending on the type of the GMOs concerned, their intended use and the potential receiving environment, taking into account, i.a., GMOs already in the environment;

- if new information on the GMO and its effects on human health or the environment becomes available, the e.r.a. may need to be readdressed in order to:

- determine whether the risk has changed;

- determine whether there is a need for amending the risk management accordingly.

C. Methodology

C.1. Characteristics of GMOs and releases

Depending on the case the e.r.a. has to take into account the relevant technical and scientific details regarding characteristics of:

- the recipient or parental organism(s);

- the genetic modification(s), be it inclusion or deletion of genetic material, and relevant information on the vector and the donor;

- the GMO;

- the intended release or use including its scale;

- the potential receiving environment; and

- the interaction between these.

Information from releases of similar organisms and organisms with similar traits and their interaction with similar environments can assist the e.r.a.

C.2. Steps in the e.r.a.

In drawing conclusions for the e.r.a. the following points should be addressed:

1. Identification of characteristics which may cause adverse effects:

Any characteristics of the GMOs linked to the genetic modification that may result in adverse effects on human health or the environment shall be identified. A comparison of the characteristics of the GMO(s) with those of the non-modified organism under corresponding conditions of the release or use, will assist in identifying the particular potential adverse effects arising from the genetic modification. It is important not to discount any potential adverse effect on the basis that it is unlikely to occur.

Potential adverse effects of GMOs will vary from case to case, and may include:

- disease to humans including allergenic or toxic effects (see for example items II.A.11. and II.C.2(i) in Annex III A, and B 7 in Annex III B);

- disease to animals and plants including toxic, and where appropriate, allergenic effects (see for example items II.A.11. and II.C.2(i) in Annex III A, and B 7 and D 8 in Annex III B);

- effects on the dynamics of populations of species in the receiving environment and the genetic diversity of each of these populations (see for example items IV B 8, 9 and 12 in Annex III A);

- altered susceptibility to pathogens facilitating the dissemination of infectious diseases and/or creating new reservoirs or vectors;

- compromising prophylactic or therapeutic medical, veterinary, or plant protection treatments, for example by transfer of genes conferring resistance to antibiotics used in

human or veterinary medicine (see for example items II.A.11(e) and II.C.2(i)(iv) in Annex III A);

- effects on biogeochemistry(biogeochemical cycles), particularly carbon and nitrogen recycling through changes in soil decomposition of organic material (see for example items II.A.11(f) and IV.B.15 in Annex III A, and D 11 in Annex III B).

Adverse effects may occur directly or indirectly through mechanisms which may include:

- the spread of the GMO(s) in the environment,

- the transfer of the inserted genetic material to other organisms, or the same organism whether genetically modified or not,

- phenotypic and genetic instability,

- interactions with other organisms,

- changes in management, including, where applicable, in agricultural practices.

2. Evaluation of the potential consequences of each adverse effect, if it occurs

The magnitude of the consequences of each potential adverse effect should be evaluated.

This evaluation should assume that such an adverse effect will occur. The magnitude of the consequences is likely to be influenced by the environment into which the GMO(s) is (are) intended to be released and the manner of the release.

3. Evaluation of the likelihood of the occurrence of each identified potential adverse effect

A major factor in evaluating the likelihood or probability of adverse effects occurring is the characteristics of the environment into which the GMO(s) is intended to be released, and the manner of the release.

4. Estimation of the risk posed by each identified characteristic of the GMO(s)

An estimation of the risk to human health or the environment posed by each identified characteristic of the GMO which has the potential to cause adverse effects should be made as far as possible, given the state of the art, by combining the likelihood of the adverse effect occurring and the magnitude of the consequences, if it occurs.

5. Application of management strategies for risks from the deliberate release or marketing of GMO(s)

The risk assessment may identify risks that require management and how best to manage them, and a risk management strategy should be defined.

6. Determination of the overall risk of the GMO(s)

An evaluation of the overall risk of the GMO(s) should be made taking into account any risk management strategies which are proposed.

D. Conclusions on the potential environmental impact from the release or the placing on the market of GMOs

On the basis of an e.r.a. carried out in accordance with the principles and methodology outlined in sections B and C, information on the points listed in sections D1 or D2 should be included, as appropriate, in notifications with a view to assisting in drawing conclusions on the potential environmental impact from the release or the placing on the market of GMOs:

D.1. In the case of GMOs other than higher plants

1. Likelihood of the GMO to become persistent and invasive in natural habitats under the conditions of the proposed release(s).

2. Any selective advantage or disadvantage conferred to the GMO and the likelihood of this becoming realised under the conditions of the proposed release(s).

3. Potential for gene transfer to other species under conditions of the proposed release of the GMO and any selective advantage or disadvantage conferred to those species.

4. Potential immediate and/or delayed environmental impact of the direct and indirect interactions between the GMO and target organisms (if applicable).

5. Potential immediate and/or delayed environmental impact of the direct and indirect interactions between the GMO with non-target organisms, including impact on population levels of competitors, prey, hosts, symbionts, predators, parasites and pathogens.

6. Possible immediate and/or delayed effects on human health resulting from potential direct and indirect interactions of the GMO and persons working with, coming into contact with or in the vicinity of the GMO release(s).

7. Possible immediate and/or delayed effects on animal health and consequences for the feed/food chain resulting from consumption of the GMO and any product derived from it, if it is intended to be used as animal feed.

8. Possible immediate and/or delayed effects on biogeochemical processes resulting from potential direct and indirect interactions of the GMO and target and non-target organisms in the vicinity of the GMO release(s).

9. Possible immediate and/or delayed, direct and indirect environmental impacts of the specific techniques used for the management of the GMO where these are different from those used for non-GMOs.