ANNEX II

PRINCIPLES FOR THE ENVIRONMENTAL RISK ASSESSMENT

[F1C.**Methodology**

Guidance issued by the European Food Safety Authority is available for the implementation of this section for Part C notifications.

C.1. *General and specific considerations for the e.r.a.*

1. *Intended and unintended changes*

As part of the identification and evaluation of the potential adverse effects referred to in Section A, the e.r.a shall identify the intended and unintended changes resulting from the genetic modification and shall evaluate their potential to cause adverse effects on human health and on the environment.

Intended changes resulting from the genetic modification are changes that are designed to occur and which fulfil the original objectives of the genetic modification.

Unintended changes resulting from the genetic modification are consistent changes which go beyond the intended change(s) resulting from the genetic modification.

Intended and unintended changes can have either direct or indirect, and either immediate or delayed effects on human health and on the environment.

2. *Long-term adverse effects and cumulative long-term adverse effects in the e.r.a. of Part C notifications*

Long-term effects of a GMO are effects resulting either from a delayed response by organisms or their progeny to long-term or chronic exposure to a GMO or from an extensive use of a GMO in time and space.

The identification and evaluation of the potential long-term adverse effects of a GMO on human health and on the environment shall take into account the following:

(a) the long-term interactions of the GMO and the receiving environment;

(b) the characteristics of the GMO which become important on a long-term basis;

(c) data obtained from repeated deliberate releases or placings on the market of the GMO over a long period.

The identification and evaluation of the potential cumulative long-term adverse effects referred to in the introductory part of Annex II shall also take into account the GMOs deliberately released or placed on the market in the past.

3. *Quality of the data*

In order to carry out an e.r.a. for a notification under Part C of this Directive, the notifier shall collate already available data from scientific literature or from other sources, including monitoring reports, and shall generate the necessary data by performing, where possible, appropriate studies. Where applicable, the notifier shall justify in the e.r.a. why generating data by studies is not possible.

The e.r.a. for notifications under Part B of the Directive shall be based at least on already available data from scientific literature or from other sources and may be supplemented by additional data generated by the notifier.

Where data generated outside Europe is provided in the e.r.a., its relevance to receiving environment(s) in the Union shall be justified.

Data provided in the e.r.a for notifications under part C of this Directive shall comply with the following requirements:

(a) where toxicological studies carried out to assess risk to human or animal health are provided in the e.ra., the notifier shall provide evidence to demonstrate that they were conducted in facilities which comply with:

  (i) the requirements of Directive 2004/10/EC; or

  (ii) the 'OECD Principles on Good Laboratory Practice' (GLP), if carried out outside the Union;

(b) where studies other than toxicological studies are provided in the e.r.a., they shall:

  (i) comply with the principles of Good Laboratory Practice (GLP) laid down in Directive 2004/10/EC, where relevant; or

  (ii) be conducted by organisations accredited under the relevant ISO standard; or

  (iii) in the absence of a relevant ISO standard, be conducted in accordance with internationally recognised standards;

(c) information on the results obtained from the studies referred to in points (a) and (b) and on the study protocols used shall be reliable and comprehensive and shall include the raw data in an electronic format suitable for carrying out statistical or other analysis;

(d) the notifier shall specify, where possible, the size of effect that each study performed intends to detect and justify it;

(e) the selection of sites for field studies shall be based on relevant receiving environments in view of the potential exposure and impact that would be observed where the GMO may be released. The selection shall be justified in the e.r.a.;

(f) the non-genetically modified comparator shall be appropriate for the relevant receiving environment(s) and shall have a genetic background comparable to the GMO. The choice of the comparator shall be justified in the e.r.a.

4. *Stacked transformation events in Part C notifications*

The following shall apply to the e.r.a. of a GMO containing stacked transformation events in Part C notifications:

(a) the notifier shall provide an e.r.a. for each single transformation event in the GMO or refer to already submitted notifications for those single transformation events;

(b) the notifier shall provide an assessment of the following aspects:

  (i) the stability of the transformation events;

  (ii) the expression of the transformation events;

  (iii) the potential additive, synergistic or antagonistic effects resulting from the combination of the transformation events;

(c) where the progeny of the GMO can contain various subcombinations of the stacked transformation events, the notifier shall provide a scientific rationale justifying that

there is no need to provide experimental data for the concerned subcombinations, independently of their origin, or, in the absence of such scientific rationale, shall provide the relevant experimental data.

C.2. *Characteristics of the GMO and of the releases*

The e.r.a. shall take into account the relevant technical and scientific details regarding characteristics of:

— the recipient or parental organism(s),
— the genetic modification(s), be it insertion 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(s) into which the GMO will be released and into which the transgene may spread, and
— the interaction(s) between these characteristics.

Relevant information from previous releases of the same or similar GMOs and organisms with similar traits and their biotic and abiotic interaction with similar receiving environments, including information resulting from the monitoring of such organisms, shall be considered in the e.r.a., subject to Article 6(3) or Article 13(4).

C.3. *Steps in the e.r.a.*

The e.r.a. referred to in Articles 4, 6, 7 and 13 shall be conducted for each relevant area of risk referred to in Section D1 or in Section D2 in accordance with the following six steps:

1. *Problem formulation including hazard identification*

The problem formulation shall:

(a) identify any changes in the characteristics of the organism, linked to the genetic modification, by comparing the characteristics of the GMO with those of the chosen non-genetically modified comparator under corresponding conditions of release or use;

(b) identify potential adverse effects on human health or the environment which are linked to the changes that have been identified under point (a) above;

Potential adverse effects shall not be discounted on the basis that they are unlikely to occur.

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

— effects on the dynamics of populations of species in the receiving environment and the genetic diversity of each of these populations leading to a potential decline in biodiversity,
— altered susceptibility to pathogens facilitating the dissemination of infectious diseases 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,
— effects on biogeochemistry (biogeochemical cycles), including carbon and nitrogen recycling through changes in soil decomposition of organic material,
— disease affecting humans, including allergenic or toxic reactions,

— disease affecting animals and plants, including toxic, and, in the case of animals, allergenic reactions, where appropriate.

Where potential long-term adverse effects of a GMO are identified, they shall be assessed in the form of desk based studies using, where possible, one or more of the following:

(i) evidence from previous experiences;

(ii) available data sets or literature;

(iii) mathematical modelling;

(c) identify relevant assessment endpoints.

Those potential adverse effects that could impact the identified assessment endpoints shall be considered in the next steps of the risk assessment;

(d) identify and describe the exposure pathways or other mechanisms through which adverse effects may occur.

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

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

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

— phenotypic and genetic instability,

— interactions with other organisms,

— changes in management, including, where applicable, in agricultural practices;

(e) formulate testable hypotheses, and define relevant measurement endpoints, to allow, where possible, a quantitative evaluation of the potential adverse effect(s);

(f) consider possible uncertainties, including knowledge gaps and methodological limitations.

2. *Hazard characterisation*

The magnitude of each potential adverse effect shall be evaluated. This evaluation shall assume that such an adverse effect will occur. The e.r.a shall consider that the magnitude is likely to be influenced by the receiving environment(s) into which the GMO is intended to be released and by the scale and conditions of the release.

Where possible, the evaluation shall be expressed in quantitative terms.

Where the evaluation is expressed in qualitative terms, a categorical description (‘high’, ‘moderate’, ‘low’ or ‘negligible’) shall be used and an explanation of the scale of effect represented by each category shall be provided.

3. *Exposure characterisation*

The likelihood or probability of each identified potential adverse effect occurring shall be evaluated to provide, where possible, a quantitative assessment of the exposure as a relative measure of probability, or otherwise a qualitative assessment of the exposure. The characteristics of the receiving environment(s) and the scope of the notification shall be taken into consideration.

Where the evaluation is expressed in qualitative terms, a categorical description ('high', 'moderate', 'low' or 'negligible') of the exposure shall be used and an explanation of the scale of effect represented by each category shall be provided.

4. *Risk characterisation*

The risk shall be characterised by combining, for each potential adverse effect, the magnitude with the likelihood of that adverse effect occurring to provide a quantitative or semi quantitative estimation of the risk.

Where a quantitative or semi quantitative estimation is not possible, a qualitative estimation of the risk shall be provided. In that case, a categorical description ('high', 'moderate', 'low' or 'negligible') of the risk shall be used and an explanation of the scale of effect represented by each category shall be provided.

Where relevant, the uncertainty for each identified risk shall be described and, where possible, expressed in quantitative terms.

5. *Risk management strategies*

Where risks are identified that require, on the basis of their characterisation, measures to manage them, a risk management strategy shall be proposed.

The risk management strategies shall be described in terms of reducing the hazard or the exposure, or both, and shall be proportionate to the intended reduction of the risk, the scale and conditions of the release and the levels of uncertainty identified in the e.r.a.

The consequent reduction in overall risk shall be quantified where possible.

6. *Overall risk evaluation and conclusions*

A qualitative and, where possible, quantitative evaluation of the overall risk of the GMO shall be made taking into account the results of the risk characterisation, the proposed risk management strategies and the associated levels of uncertainty.

The overall risk evaluation shall include, where applicable, the risk management strategies proposed for each identified risk.

The overall risk evaluation and conclusions shall also propose specific requirements for the monitoring plan of the GMO and, where appropriate, the monitoring of the efficacy of the proposed risk management measures.

For notifications under Part C of the Directive, the overall risk evaluation shall also include an explanation of the assumptions made during the e.r.a. and of the nature and magnitude of uncertainties associated with the risks, and a justification of the risk management measures proposed.**]**