II

(Acts whose publication is not obligatory)

COMMISSION

COMMISSION DECISION

of 24 July 2002

establishing guidance notes supplementing Annex II to Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC

(notified under document number C(2002) 2715)

(Text with EEA relevance)

(2002/623/EC)

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Community,

Having regard to Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC [1], and in particular the first paragraph of Annex II thereto,

Whereas:

(1) Under Directive 2001/18/EC, Member States and, where appropriate, the Commission must ensure that potential adverse effects on human health and the environment, which may occur directly or indirectly through gene transfer from genetically modified organisms (hereinafter GMOs) to other organisms, are accurately assessed on a case-by-case basis in accordance with Annex II to that Directive.

(2) Under Article 6(2)(b) and Article 13(2)(b) of Directive 2001/18/EC, notifications for the release or placing on the market of GMOs must include an environmental risk assessment and the conclusions on the potential environmental impact of the release or the placing on the market of those GMOs in accordance with Annex II to that Directive.

(3) Annex II to Directive 2001/18/EC should be supplemented by notes providing detailed guidance on the objective, elements, general principles and methodology of the environmental risk assessment referred to in that Annex.

(4) The measures provided for in this Decision are in accordance with the opinion of the Committee established under Article 30(1) of Directive 2001/18/EC,

HAS ADOPTED THIS DECISION:

Article 1

The guidance notes set out in the Annex to this Decision shall be used as a supplement to Annex II to Directive 2001/18/EC.

Article 2

This Decision is addressed to the Member States.

Done at Brussels, 24 July 2002.

For the Commission

Margot WALLSTRÖM

Member of the Commission

[1] OJ L 106, 17.4.2001, p. 1.

ANNEX

GUIDANCE NOTES ON THE OBJECTIVE, ELEMENTS, GENERAL PRINCIPLES AND METHODOLOGY OF THE ENVIRONMENTAL RISK ASSESSMENT REFERRED TO IN ANNEX II TO DIRECTIVE 2001/18/EC

1. **INTRODUCTION**

Environmental risk assessment (ERA) is defined in Article 2(8) of Directive 2001/18/EC as 'the evaluation of risks to human health and the environment, whether direct or indirect, immediate or delayed, which the deliberate release or the placing on the market of GMOs may pose'. As one of the general obligations under the Directive, Article 4(3) requires Member States and, where appropriate, the Commission to ensure that potential adverse effects on human health and the environment, which may occur in particular directly or indirectly, are accurately assessed on a case-by-case basis taking into account the environmental impact according to the nature of the organism introduced and the receiving environment. ERA is carried out in accordance with Annex II to the Directive, and is also referred to in Parts B and C thereof. Annex II 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 ERA, taking into account the impact on human health and the environment according to the nature of the organism introduced and the receiving environment.

Notifiers must submit a notification including an ERA for deliberate release under Article 6(2) or for placing on the market under Article 13(2).

This guidance note supplements Annex II to Directive 2001/18/EC and outlines the objectives and principles as well as the methodology for the ERA, in order to assist notifiers, to facilitate the performance by the competent authorities of a comprehensive and appropriate ERA under Directive 2001/18/EC and to make the process of ERA transparent to the general public.

The six steps in the ERA are set out in Chapter 4.2.

2. **OBJECTIVE**

In accordance with Annex II to Directive 2001/18/EC, *the objective of an ERA 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 placing on the market of GMOs may have. The ERA 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* [1].

The ERA therefore covers deliberate release (Part B) and placing on the market (Part C) as referred to in Directive 2001/18/EC. Placing on the market very often, but not necessarily, includes deliberate release into the environment, but is always an intentional introduction on the market (for example, agricultural products containing or consisting of GMOs, only for the use of food, feed and processing). In these cases too an ERA has to be included in the notification process. In general there may be a difference between the ERA for deliberate release and that for placing on the market, due, for example, to the differences in existing data, time-scale and area.

In addition, these guidance notes cover all GMOs, including microorganisms, plants and animals. Although so far most GMOs deliberately released or placed on the market are higher plants, this may change in future.

The ERA will serve as the basis for identifying the need for risk management and, if so, the most appropriate methods to be used, and for focused monitoring (see Chapter 3).

The overall case-by-case assessment covers the GMO(s) concerned (GMO-by-GMO assessment) and the environment(s) in which the GMO is to be released (for example, site-by-site assessment and region-by-region assessment, if applicable).

Future developments in genetic modification may make it necessary to adapt Annex II and these guidance notes to technical progress. Further differentiation of information requirements for different types of GMOs, like single cell organisms, fish or insects, or for particular uses of GMOs, like the development of vaccines, may be possible once there is sufficient experience with notifications for the release of particular GMOs in the Community (Annex III, fourth paragraph, and Chapter 6).

Risk assessment of the use of antibiotic resistance marker genes is a very specific issue and further guidance on this item may be recommended.

[1] The text in italics is taken directly from Annex II to Directive 2001/18/EC.

Different 'effect categories' of GMOs on human health or the environment are described in Annex II to Directive 2001/18/EC. In the interests of a common interpretation, the definitions given in the Directive of the following terms are illustrated as follows:

— *'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* (for example, the direct effect of the Bt toxin on target organisms, or the pathogenic effect of a GM microorganism on human health),

— *'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* (for example, where reducing the target population of insects affects the population of other insects, or where the development of multiple resistance or systemic effects will require assessment of long-term interaction; however, some indirect effects such as reductions in usage of pesticides could be immediate),

— *'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* (for example, death of insects foraging on transgenic plants that have pest-resistant traits, or the induction of allergies in susceptible humans due to exposure to a particular GMO),

— *'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* (for example, establishment or invasive behaviour of a GMO after several generations following deliberate release, which is very important if the GMO lives for a long time, for example, genetically modified tree species; or hybrids of close relatives of a transgenic crop becoming invasive in natural ecosystems).

The delayed effects in particular may be difficult to determine, especially if they become apparent only in the long term. Appropriate measures such as monitoring (see below) can help in detecting these effects.

3. **GENERAL PRINCIPLES**

In accordance with the precautionary principle, the ERA should be based on the following general principles:

— *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.*

A baseline of the receiving environment, including its organisms and their interactions and their known variations, should be determined before any (harmful) characteristics of the GMO can be identified. The baseline serves as a point of reference against which future changes can be compared. For example, in the case of vegetatively propagated crops, comparative analysis should include the parental species used to generate the transgenic lines. In the case of crops that reproduce sexually, comparators would include appropriate isogenic lines. If crops are developed using back-crossing, it is important that in such cases substantial equivalence testing uses the most appropriate controls and does not simply rely on comparisons with original parental material.

If the existing data are not sufficient, a baseline has to be defined on other references to allow a comparison. The baseline will depend to a considerable extent on the receiving environment, including biotic and abiotic factors (for example, natural preserved habitats, agricultural farmland or contaminated land) or a combination of different environments.

— *The ERA should be carried out in a scientifically sound and transparent manner based on available scientific and technical data.*

Evaluation of potential adverse effects should be based on scientific and technical data and on common methodology for the identification, gathering and interpretation of the relevant data. Data, measurements and tests should be clearly described. In addition, the use of scientifically sound modelling procedures could provide missing data useful for ERA.

ERA has to take into account uncertainty at various levels. Scientific uncertainty results usually from five characteristics of the scientific method: the variable chosen, the measurements made, the samples taken, the models used and the causal relationships employed. Scientific uncertainty may also arise from a controversy on existing data or lack of some relevant data. Uncertainty may relate to qualitative or quantitative elements of the analysis. The level of knowledge or data for a baseline is reflected by the level of uncertainty, which has to be provided by the notifier (assessment of uncertainty, including lack of data, knowledge gaps, standard deviation, complexity, etc.) in comparison with the scientific uncertainties in current practice.

The ERA may not always result in definitive answers to all the questions considered because of lack of data. For potential long-term effects, in particular, the availability of data may be very low. In these cases in particular appropriate risk management (safeguards) has to be considered in accordance with the precautionary principle in order to prevent adverse effects on human health and the environment.

As a general principle, the ERA should include the results of adequate research into the potential risks involved in the deliberate release or placing on the market of GMOs, along with any clearly documented comparable experience.

Use of the step-by-step approach (i.e. all the steps beginning with experiments in the contained use system through deliberate release up to placing on the market) can be useful. Data from each step should be collected as early as possible during the procedure. Simulated environmental conditions in a contained system could give results of relevance to deliberate release (for example, the behaviour of microorganisms can be simulated in microcosms, or the behaviour of plants can be simulated in greenhouses to a certain extent).

For GMOs to be placed on the market, relevant and available data from deliberate releases should be provided from the types of environment where the GMO will be used.

— *The ERA 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,* inter alia*, GMOs already in the environment*.

The ERA should use the case-by-case principle because of the broad range of individual characteristics of different organisms (GMO by GMO) and different environments (site by site and region by region).

There may be a huge variety in the environmental effects of genetically modified microorganisms (because of their small size and their often unknown interactions), plants (for example, higher plants used for food and feed, or trees because of their potential longevity), and animals (for example, insects because of their small size and their high potential for overcoming barriers; or saltwater fish because of their high distribution potential).

Moreover, there may be a broad range of environmental characteristics (site-specific or regional-specific) to be taken into account. To support a case-by-case assessment, it may be useful to classify regional data by habitat area, reflecting aspects of the receiving environment relevant to GMOs (for example, botanical data on the occurrence of wild relatives of GMO plants in different agricultural or natural habitats of Europe).

The notifier must also take into account potentially harmful interactions of the GMO with any relevant GMOs that may have been deliberately released or placed on the market in the past, including repeated releases of the same GMO, such as the use of plant protection products. Repeated releases, as compared to occasional releases, might in time cause a high background level of the GMO to become permanent in the environment.

If new information on the GMO and its effects on human health or the environment becomes available, the ERA may need to be re-addressed in order to:

— determine whether the risk has changed,

— determine whether there it is necessary to amend the risk management accordingly.

In the case of new information, irrespective of whether immediate measures need to be taken, there may have to be a new ERA to assess the need to change the terms of authorisation for the GMO's release or placing on the market, or to adjust risk management measures (see also Chapter 6). New information can arise from research or from monitoring plans, or from relevant experience elsewhere.

ERA and monitoring are closely linked. The ERA provides the basis for the monitoring plans, which focus on adverse effects on human health and the environment. The requirements for the monitoring plans for the deliberate release of GMOs (Part B in accordance with the relevant parts of Annex III) and the placing on the market of GMOs (Part C in accordance with Annex VII) are different. The Part C monitoring, including general surveillance, may also play an important role in providing data for long-term, potentially adverse effects of GMOs. Monitoring results may confirm the ERA or may lead to re-evaluation of the ERA.

— *A general principle for ERA 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 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.*

In considering the potential cumulative long-term effects, the ERA should take into account issues such as:

— the long-term interactions of the GMO and the receiving environment,

— the characteristics of a GMO which become important on a long-term basis,

— repeated deliberate releases or placings on the market over a long period,

— the GMOs deliberately released or placed on the market in the past.

Further information may be required on long-term effects in particular (for instance, multiple herbicide resistances) and there must be adequate research, partly within the framework of the monitoring plans, which can provide important data for assessing cumulative long-term effects. Further guidance on this item may be recommended.

4. **METHODOLOGY**

4.1. **Characteristics of GMOs and releases**

The ERA 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 ERA.

Prior to deliberate release of a GMO or a combination of GMOs under Part B or to the placing on the market under Part C of the Directive, a notification including the information set out in Annexes IIIA and IIIB to the Directive (information on the GMO, the donor, the recipient, the vector, the conditions of the release and the environment, the interactions between the GMOs and the environment and of monitoring GMOs) should be submitted to the competent authority of the Member State where the release or the placing on the market is to take place for the first time.

Those notifications should contain a technical dossier of information including a full ERA in accordance with Article 6(2) and Article 13(2) of the Directive, the amount of detail needed to substantiate any point depending on its importance in the ERA. Notifiers shall provide bibliographic references and indicate the methods used.

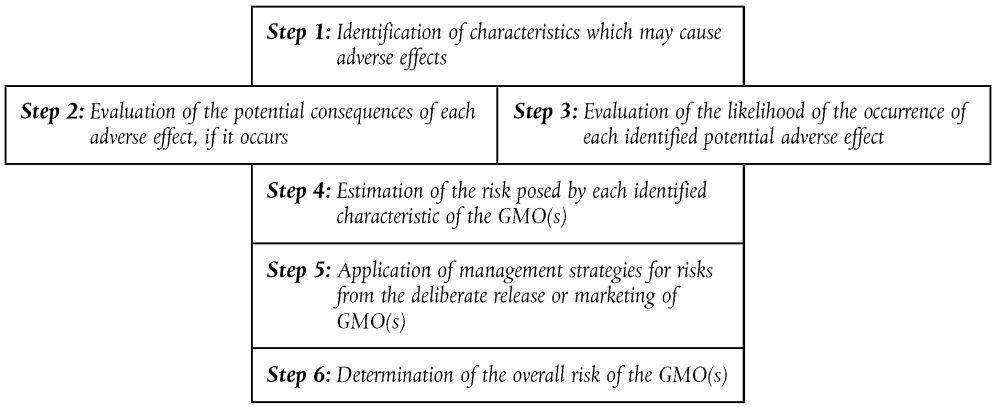
The information on recipient, donor, vector, genetic modification and the GMO, on the basis of information requested in Annexes IIIA and IIIB to the Directive, is independent of the environment in which the GMO is to be experimentally released or placed on the market, and the conditions under which it will be experimentally released or marketed. This information is the basis for identifying any potential harmful characteristics (potential hazards) of the GMO. Knowledge and experience gained in releases of the same or similar GMOs may provide important information on the potential hazards of the release in question.

Information on intended release, receiving environment and interaction between these, as requested in Annexes IIIA and IIIB to the Directive relates to the particular environment into which the GMO will be released, and the conditions, including the scale of the release. This information will determine the extent of any potentially harmful characteristics of the GMO.

4.2. **Steps in the analysis of ERA**

In drawing conclusions for the ERA referred to in Articles 4, 6, 7 and 13 of Directive 2001/18/EC, the following points should be addressed as main steps in the ERA.

Diagram 1: The six steps in the analysis of ERA



A 'hazard' (harmful characteristics) is defined as the potential of an organism to cause harm to or adverse effects on human health and/or the environment.

A 'risk' is the combination of the magnitude of the consequences of a hazard, if it occurs, and the likelihood that the consequences occur.

4.2.1. *Step 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 must 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 in the GMO. 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,*

— *disease to animals and plants including toxic, and where appropriate, allergenic effects,*

— *effects on the dynamics of populations of species in the receiving environment and the genetic diversity of each of these populations,*

— *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,*

— *effects on biogeochemistry (biogeochemical cycles), particularly carbon and nitrogen recycling through changes in soil decomposition of organic material.*

Examples of the above potential adverse effects are given in Annexes IIIA and IIIB to Directive 2001/18/EC.

Most of the identifiable hazards (harmful characteristics) which may cause adverse effects will be related to the gene or genes of interest, deliberately introduced into the GMO and the corresponding protein(s) being expressed from these genes. Additional adverse effects, for example, pleiotropic effects, might have been generated as a result of the method used to create the transgenes, and of the location of the construction in the genome of the GMO where the transgenes were inserted. Where more than one transgene is transferred into a recipient or where a transgene is transferred into a GMO, the potential interaction of the different transgenes has to be taken into account considering potentially epigenetic or regulatory effects.

While it is important to define the hazard as accurately as possible, it will, in many cases, be useful to consider hazards under the headings set out below, and then to specify the particular hazard identified for the purposes of ERA (for example, if in a specific case a potential for adverse effects on human health — allergenicity and toxigenicity — were identified, these should be considered separately in the ERA).

If a hazard is present in the GMO, it is always present and it can be regarded as an inherent property. Hazards can give rise — with a given likelihood (step 3) — to negative consequences and these consequences in turn can have different orders of magnitude (step 2). Finally, the individual hazards have to be summarised for the GMO.

At this stage of the ERA, however, it is only necessary to consider the hazards introduced as a result of genetic modification that could cause adverse effects. Step 1 provides the scientific basis for the following steps in the ERA. Even at this stage, it is critical to identify, for each potential hazard, the specific level of scientific uncertainty so that it can be taken into account at a later stage.

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

— *The spread of the GMO(s) in the environment*

Distribution pathways show the potential pathways of distribution of the GMO or of the potential hazard into and within the environment (for example, human toxicity: inhalation of toxic microorganisms or toxic proteins).

The potential of a GMO to spread into the environment will depend, for example, on:

— its biological fitness (GMOs designed for better performance in the environment of interest by the expression of traits leading to increased competitiveness in natural environments, or qualitative and quantitative change in composition of ingredients, or GMOs with resistance to natural selection pressure like disease, or abiotic stress like heat, cold, salt, or production of anti-microbial substances in microorganisms),

— the conditions of the deliberate release or placing on the market (particularly the area of release and the scale, that is to say, the number of GMOs released),

— the likelihood of a deliberate release or placing on the market, or unintentional releases into the environment (for example, GMOs for processing),

— pathways of dispersal of viable material (for example, seeds, spores and so on) by wind, water, animals, etc.,

— particular environmental considerations (site-specific or regional-specific): to allow a site-by-site or a region-by-region assessment it may be useful to classify data by habitat area, reflecting aspects of the receiving environment relevant to the GMO (for example, botanical data on the occurrence of crossable wild relatives of GMO plants in different agricultural or natural habitats of Europe).

It is also important to assess the length of time an individual GMO or a specific number of GMOs of a certain species is generally likely to survive, and the readiness with which it can be disseminated and become established in a variety of habitats. Consideration will need to be given to reproductive, survival and dormant forms, including, for example:

— for plants: the viability of pollen, seeds and vegetative structures,

— for microorganisms: the viability of spores as survival forms, or the potential of the microorganisms to enter the viable but not cultivable state.

The overall spread potential may vary considerably, depending on the species, the genetic modification and the receiving environment, for example plant cultivation in the desert or fish cultivation in the sea.

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

A hazard could result in adverse effects through gene transfer within the same species or to other species (vertical and horizontal gene transfer). The speed and extent of gene transfer to other species (usually sexually compatible in the case of higher organisms) will depend, for example, on:

— the reproductive properties of the GMO itself, including the modified sequences,

— the conditions of release, and particular environmental considerations such as climate (for example, wind),

— differences in reproduction biology,

— agricultural practices,

— the availability of potential crossing partners,

— transport and pollinating vectors (for example, insects or birds, animals in general),

— the availability of hosts for parasites.

The occurrence of specific adverse effects through gene transfer may be linked to the number of GMOs released. Large fields of transgenic plants may have a completely different potential for gene transfer from small fields, even on a proportional basis. Moreover, qualitative and quantitative information about the existence of potential crossing partners or recipients (for plants within relevant distances) is very important.

For higher plants and animals, further distinctions should be made regarding possible gene transfer to the same, closely related, distantly related and unrelated species.

In the case of microorganisms, horizontal gene transfer plays a more important role. Certain genetic material can be easy transferred between more closely related organisms, for example, via plasmids or phages. The potential rapid growth rate of microorganisms can enable gene transfer at relatively high levels compared to higher organisms.

Transfer of transgenes may lead to a mixed population of GMOs or to different gene-plant combinations after a time, which can then give rise to complex patterns of especially long-term adverse effects. These will become more complex as more transgenic material is transferred into a population (for example, gene stacking).

In some cases, the method of genetic modification may change the potential for gene transfer, such as in the case of non-integrating plasmids or viral vectors. The method of genetic modification may also decrease the potential for gene transfer, for example, chloroplast transformation.

Gene transfer may result in persistence of the introduced genetic material in natural populations. If a GMO has the potential for gene transfer, this does not necessarily mean intrinsic risk, or a change in the capacity to survive, to become established or cause adverse effects. This will depend on the genetic material inserted, the species and the receiving environment, including the potential recipients.

— *Phenotypic and genetic instability*

The extent to which genetic (in)stability might lead to phenotypic (in)stability and result in a hazard should be considered. Instability of the genetic modification may in certain cases result in reversion into the wild type phenotype. Other cases should be considered, for example:

— if in a transgenic plant line that contains more than one transgene, the subsequent segregation process results in these transgenes being divided up in the progeny, there could be plants with less transgenes but new phenotypes,

— if attenuated mutants may, due to instability (because of the construction of the particular mutation) revert to virulence,

— if duplication of transgenes leads to gene silencing,

— if copy numbers are very high,

— if re-insertion of transposable elements results in new phenotypes, due to inactivation of the transgene by the insertion of mobile genetic elements,

— if the level of transgene expression is important (for example, a very low expression of a toxic substance), the genetic instability of the regulatory element(s) may result in a higher transgene expression.

Phenotypic instability could result from interaction with the environment during cultivation, so the effects of environmental and agronomic factors on expression of transgenes should be considered in the ERA.

If transgene expression is limited to a certain compartment in the GMO (such as a certain plant tissue), instability of regulation could result in expression of the transgene in the entire organism. In this context regulatory signals (such as promoters) play an important role and should be considered.

Also the expression of the transgene at a certain time in the life cycle of the organism or under specific environmental conditions should be considered.

Specific infertility transgenes may have been introduced into the GMO to make it infertile (for example, to prevent transfer and spread of certain transgenes). Instability of the infertility transgenes could result in reactivation of the fertility of the plant allowing the spread of the transgenes, which could have adverse affects.

The stability of the different transgene(s) not only in the primary GMO but also in its progeny is of importance for long-term effects in particular.

— *Interactions with other organisms (other than exchange of genetic material/pollen)*

Possible interactions with other organisms, including other GMOs, have to be carefully assessed, taking into account the complexity of multitrophic interactions. Directly hazardous interactions which could cause adverse effects might include:

— exposure to humans (such as farmers, consumers),

— exposure to animals,

— competition for natural resources like soil, area, water, light,

— displacement of natural populations of other organisms,

— delivery of toxic substances,

— different growth patterns.

In general, if biological fitness is enhanced by the genetic modification, the GMO may invade new environments and replace existing species. Often the occurrence of specific adverse effects is proportionally linked to scale of release.

— *Changes in management, including, where applicable, in agricultural practices*

The relevance of changes in management procedures as an unavoidable consequence of the deliberate release of the GMO has to be assessed on the basis of existing procedures. Changes in farm management could, for example, relate to:

— sowing, planting, growing, harvesting or transporting crops (for example, planting in small or large fields), timing,

— crop rotation (for example, cultivating the same plant species every year or every fourth year),

— disease and pest control (for example, type and dose of insecticide for plants, or antibiotics for animals, or alternative measures),

— resistance management (for example, type and dose of herbicide for herbicide-tolerant plants, or change in use of biological control via Bt proteins, or impact of viruses),

— isolation in land agricultural and aquatic agricultural systems (for example, isolation distances in plant cultivation or quality of isolation in fish farms),

— agricultural practices (farming GMOs and non transgenic farming, including organic farming),

— management in non-agricultural systems (for example, isolation distances of natural habitats from GMO planting areas).

4.2.2. *Step 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.

Apart from the likelihood that the potential harmful characteristics will occur (see Chapter 4.2.3, step 3), evaluating the magnitude of the consequences is an important part of risk assessment. The magnitude is the extent to which the consequences of any potential hazards of the GMOs to be deliberately released or placed on the market will be realised.

The magnitude is to be seen in relation to the baseline and likely to be influenced by:

— genetic construction,

— each adverse effect identified,

— the number of GMOs released (scale),

— the environment into which the GMO(s) is (are) to be released,

— the conditions of the release, including control measures,

— combinations of the above.

For each adverse effect identified, the consequences for other organisms, populations, species or ecosystems exposed to the GMO have to be evaluated. This requires detailed knowledge of the environment into which the GMO is to be released (site, region) and the method of release. Consequences will range from 'negligible' or insignificant and self-limiting to 'high' or significant, either having an immediate and serious adverse effect or possibly leading to long-term, permanent adverse effects.

In quantitative terms the magnitude should, if possible, be expressed as 'high', 'moderate', 'low' or 'negligible'. In some cases, it is not possible to identify an adverse effect in a particular environment. In such cases, the risk associated with that particular adverse effect could be assessed as 'negligible' or insignificant.

The following are suggested as illustrative and qualitative examples in a very broad sense. They are not intended to be definitive or exclusive, but to give an indication of the considerations that might be taken into account when weighing up the consequences:

— 'high level consequences' might be significant changes in the numbers of one or more species of other organisms, including endangered and beneficial species in the short or long term. Such changes might include a reduction in or complete eradication of a species leading to a negative effect on the functioning of the ecosystem and/or other connected ecosystems. Such changes would probably not be readily reversible and any recovery of the ecosystem that did take place would probably be slow,

— 'moderate consequences' might be significant changes in population densities of other organisms, but not a change which could result in the total eradication of a species or any significant effect on endangered or beneficial species. Transient and substantial changes in populations might be included if likely to be reversible. There could be long-term effects, provided there are no serious negative effects on the functioning of the ecosystem,

— 'low level consequences' might be non-significant changes in population densities of other organisms, which do not result in the total eradication of any population or species of other organisms and have no negative effects on functioning of the ecosystem. The only organisms that might be affected would be non-endangered, non-beneficial species in the short or long term,

— 'negligible consequences' would mean that no significant changes had been caused in any of the populations in the environment or in any ecosystems.

The above examples reflect the potential adverse effects of GMOs on populations, although in some cases, it may be more appropriate to consider the likely effects on individual organisms. One single hazard could have more than one adverse effect, and in fact the magnitudes of the individual adverse effects could be different. The adverse effects of one single hazard on human health, and agricultural and natural habitats could vary.

The potential consequences could be summarised in such a way as to cover all the ecological entities which could be affected (such as species, populations, trophic levels, ecosystems) including the potential effect and the level of uncertainty.

4.2.3. *Step 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.

Besides the magnitude of the consequences of the hazards (see Chapter 4.2.2, step 2) evaluating the likelihood of adverse effects occurring is another important part in assessing risks. This step is to estimate how likely it is that adverse effects will actually occur. In some cases both the likelihood and the frequency should be addressed. As in step 2 (evaluate the potential consequences of each adverse effect if it occurs), besides the hazard itself, the number of GMOs, the receiving environment and the conditions of the release are important for defining the likelihood. Climatic, geographical, soil and demographic conditions, and the types of flora and fauna in the potential receiving environment are some of the important considerations.

For capability of survival, therefore, it is appropriate to assess the proportion of GMOs that are likely to survive, outside the intended risk management measures proposed for the deliberate release or placing on the market. Where gene transfer is likely, the probable number of such events or the extent to which transfer will occur should be considered. If the GMO has pathogenic or toxic characteristics, the proportion of target organisms in the environment likely to be affected should be assessed.

Moreover, the likelihood of the occurrence of an effect will depend on the specific risk management measures that may prevent that risk from occurring (for example, if pollen dispersal is impossible due to the destruction of the inflorescences).

For each adverse effect identified, the relative likelihood of the consequence can probably not be assessed quantitatively, but it can be expressed in terms of 'high', 'moderate', 'low' or 'negligible'.

The above examples reflect the potential adverse effect of the GMO on populations, although in some cases, it may be more appropriate to consider the likely effects on individual organisms. One single hazard could have more than one adverse effect, so the likelihood of individual adverse effects could also be different. The adverse effects of one single hazard on human health, agricultural and natural habitats could vary.

Likelihood could be summarised in a way which covers all the ecological entities which could be affected (such as species, populations, trophic levels, ecosystems) including measures about the potential effect as well as the level of uncertainty.

4.2.4. *Step 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.

On the basis of the conclusions reached in steps 2 and 3, an estimate of the risk of adverse effects should be made for each hazard identified in step 1. Again quantitative evaluation is unlikely to be possible. The evaluation for each hazard should consider:

— the magnitude of the consequences ('high', 'moderate', 'low' or 'negligible'),

— the likelihood of the adverse effect ('high', 'moderate', 'low' or 'negligible'),

— if a hazard has more than one adverse effect, the magnitude and likelihood of each individual adverse effect.

Each GMO has to be considered on a case-by-case basis. Any general attempt to quantify what has been described before has to be made very carefully. For example, in one case the high magnitude of the consequences of an adverse effect may be combined with a negligible likelihood of it occurring, resulting in the whole range from high risk down to negligible risk. The result will depend on the circumstances of the case and the weighting of certain factors by the notifier, all of which should be set out clearly and justified in the recorded ERA.

The overall uncertainty for each identified risk has to be described, possibly including documentation relating to:

— assumptions and extrapolations made at various levels in the ERA,

— different scientific assessments and viewpoints,

— uncertainties,

— the known limits of mitigation measures,

— conclusions that can be derived from the data.

Although the ERA should be based on quantifiable outcomes, it is likely that many of the results of the ERA will have to be qualitative. But it is necessary, wherever possible, to have ERA results which are relative (compared with a non-GM reference, for instance), even if they are qualitative.

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

The ERA may identify risks that require measures to manage them, and a risk management strategy should be defined.

Before applying risk management, consideration should be given, with a view to prevention, to modifying the release, preferably until the risk is negligible. For example, genetic elements, which may cause adverse effects or are undefined, should be avoided in the gene construction process. If this is not possible, these genetic elements should preferably be removed from the GMO at a later stage, prior to its deliberate release or placing on the market.

This should be taken into account in steps 1 to 4. Risk management should control an identified risk and cover the uncertainties. Safeguard measures should be proportionate to the level of risk and to the level of uncertainty. When relevant data becomes available at a later stage, risk management should be adapted in line with that new data.

To reduce the risk by management, the measures should clearly achieve that end. For example, if there is a risk of a gene toxic to insects inserted into a crop plant being transferred to related plant species, suitable control measures might include spatial or temporal isolation from those related species or perhaps changing the release site to an area where there is no exposure to a specific risk (such as plant species).

Management strategies can include isolation measures at every relevant stage of the handling and use of GMOs. They can also include a wide range of measures, including various means to isolate reproduction, physical or biological barriers, and cleaning machines or containers in contact with GMOs, and so on.

Detailed risk management procedures will depend on:

— the use of the GMO (type and scale of deliberate release or placing on the market),

— the type of GMO (for example, genetically modified microorganisms, higher annual plant, higher long-life plant or animal, GMO with single or multiple modification, one or different kinds of GMOs),

— the general type of habitat (for example, biogeochemical status, climate, availability of inter- and interspecific crossing partners, centres of origin, connection of different habitats),

— the type of agricultural habitat (for example, agriculture, forestry, aquatic culture, rural areas, size of sites, number of different GMOs),

— the type of natural habitat (for example, status of preserved areas).

There should be a clear statement of the implications of risk management in terms of the necessary adjustments to experiments, conditions for placing on the market, and so on, and the consequent reduction in risk likely to be achieved.

4.2.6. *Step 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.

On the basis of step 4 and, if appropriate, step 5, a final evaluation should be made of the overall risk, including the magnitude and likelihood of the adverse effects of the GMO, based on the combination of the risks from each individual adverse effect, including cumulative effects from other GMOs. This final evaluation should be expressed in the form of a summary of the overall risks from deliberate release or placing on the market, including the overall uncertainties.

5. CONCLUSIONS ON THE POTENTIAL ENVIRONMENTAL IMPACT FROM THE RELEASE OR THE PLACING ON THE MARKET OF GMOs

On the basis of an ERA, carried out in accordance with the general principles and methodology outlined in sections 3 and 4, information on the points listed in sections D1 or D2 of Annex II to Directive 2001/18/EC 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.

Future developments, especially in the non-plant area, may give further guidance on the information to be included in the notifications.

6. REVIEW AND ADAPTATION

6.1. Review and adaptation of an ERA

An ERA should not be viewed as static. It should be regularly reviewed and updated or perhaps changed to take account of relevant new data (in accordance with Articles 8 or 20 of Directive 2001/18/EC). Any reviews should consider the effectiveness, efficiency and accuracy of the ERA and risk management, taking account of data from research, other deliberate releases and monitoring data. This will also depend on the level of uncertainty determined by the ERA.

Following any such reviews, the ERA and risk management should be adapted or upgraded as appropriate.

6.2. Review and adaptation of the ERA guidance

Future developments in genetic modification may make it necessary to adapt to technical progress Annex II and these guidance notes. Further differentiation of information requirements for different types of GMOs, like single cell organisms, fish or insects, or for particular use of GMOs, like the development of vaccines, may be possible once there is sufficient experience with notifications for the release of particular GMOs in the Community (Annex III, fourth paragraph).

The review and adaptation of the ERA guidance should also take into account, where appropriate, the need to adapt to technical progress and the need to develop further guidance based on experience — where sufficient — with releases of certain GMOs into certain ecosystems, in accordance with the criteria set out in Annex V (Article 7(1)) of the Directive, as well as experience and scientific evidence relating to the safety of human health and the environment in connection with the placing on the market of certain GMOs (Article 16(2)).