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REPORT OF THE WORKING GROUP ON HARMONISATION OF REGULATORY OVERSIGHT IN BIOTECHNOLOGY

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EXECUTIVE SUMMARY

1. This report of OECD's *Working Group on Harmonisation of Regulatory Oversight in Biotechnology* is complementary to that of OECD's *Task Force for the Safety of Novel Foods and Feeds* [C(2000)86/ADD1]. It focuses specifically on the environmental safety implications of the use of products of modern biotechnology, including the use of genetically engineered organisms, in food production. In this context, this includes those safety considerations which have implications for the conservation of biodiversity, given that biodiversity is the ultimate source of food and genetic resources. The report has an emphasis on crop plants since this sector is currently the most developed with respect to food biotechnology. To a lesser extent, micro-organisms in food production are also considered. Commercial applications using animal biotechnology are still in development for the most part and are not considered as a priority in this report.

2. Most of the participants in OECD's Working Group work in ministries and agencies, which have a responsibility for ensuring environmental safety. Their need to make environmental risk/ safety assessments of genetically engineered organisms is not new, given that most Member countries have long had regulatory systems in place to ensure their safe use. The first field trials took place in 1986, and to date globally, there have been thousands of such events. The first commercial uses of genetically modified crops began in the mid-1990s. The vast majority of genetically engineered organisms, both in field trials and in commercial applications, have been of crop plants that are important trading commodities, such as maize, soybean, cotton, rapeseed, potato and tomato. In total, environmental risk/safety assessors have accumulated almost 15 years of experience, though the level of experience in the assessment of environmental effects and benefits varies between countries and regions.

3. The objectives of environmental safety and food safety assessments are different and in most jurisdictions, different ministries or agencies undertake them. The focus of the former is on environmental effects while that of the latter on human health effects. However, product characterisation is a common element between environmental safety and food safety assessments. There is also a commonality in the information used. For example, both environmental and food safety assessors need to know if the genetic modification of an organism produces toxic effects: the former wish to know whether it is toxic to non-target species; while the latter are concerned with its potential impact on human health. Although their objectives are distinct, they often use similar procedures to arrive at their conclusions. **The Working Group believes that while environmental and food safety assessments are separate and distinct, environmental risk/safety assessors need to continue to collaborate with food safety assessors.**

4. The experience that has been developed at the national level has also been shared in a number of intergovernmental fora including the OECD. A number of concepts and principles for use in risk/safety assessments have been agreed upon at the international level through the OECD, such as the concept of *familiarity*. There have also been a number of practical tools developed such as OECD's Consensus Documents, which include information (for example on host organisms and traits) that Member countries have agreed is important in risk/safety assessments.

5. Regulatory harmonisation has been the primary goal of the Working Group since it was established in 1995. This is the attempt to ensure that the information used in risk/safety assessments,

as well as the methods used to assess safety, are as similar as possible between countries. The benefits of harmonisation are clear. It increases mutual understanding among Member countries, which avoids duplication, and increases efficiency – which in turn improves safety and avoids unnecessary trade disputes.

6. The Working Group has identified a number of needs and future challenges. Despite the efforts taken towards harmonisation so far, more progress needs to be made if the potential benefits are to be fully realised. In particular, the document makes reference to the fact that while different authorities may use similar information and similar assessment procedures, they sometimes arrive at different conclusions. Some reasons for this are clear, for example, risk/safety assessors from different countries are dealing with different environments. On the other hand, the report identifies other possible reasons. **The Working Group believes that increased effort is needed to identify reasons for Member country differences in product approval systems.**

7. The topic of risk management is a specific area where there are differences between countries, which need to be better understood. Risk management methods are normally applied to minimise or mitigate those risks which have been identified during a risk/safety assessment. Science-based or technical procedures can, for example, include confinement of a specific crop variety, or perhaps the restriction of its use to specific geographic locations. They may also include methods to identify or monitor genetically modified products once they have been cleared for use in commercial applications. **The Working Group believes that there is a need for an increased mutual understanding among Member countries of their risk management policies.**

8. A particular difficulty, where there are strong differences among Member countries, is apparent in all discussions related to the management of scientific uncertainty. While it is clear that scientific uncertainty is a normal part of the work of risk/safety assessors and risk managers, there are clear differences between countries on whether or how *precaution*, sometimes referred to as the precautionary approach, would be applied within the context of the risk/safety assessment and risk management of GM foods. It is clear that there is a need for a continuing dialogue between countries to increase their mutual understanding on this topic.

9. Although much experience has been gained in the environmental risk/safety assessment of the *first-generation* of genetically engineered organisms, new environmental safety questions will arise as the volume and types of GM products on the global market increase. The range of organisms, the number of traits and the geographical locations of deliberate releases all might increase in the future. This will lead to challenges in the application of currently accepted concepts such as *familiarity*. In addition, the different local environmental and agricultural environments will continue to be taken into account and can lead to different conclusions in an environmental risk/safety assessment. More detailed insights into environmental interactions of organisms may reduce uncertainty but also raise new questions, for example, on long-term and indirect effects. **The Working Group believes that environmental risk/safety assessors should keep the risk/safety assessment methods under review and should continue to exchange experiences and to collaborate towards a further improvement in risk/safety assessment and monitoring methods.**

10. An additional challenge in the risk/safety assessment of genetically engineered organisms is to transfer the knowledge obtained by those countries with experience in risk/safety assessment to all those who need it, including non-member countries. In recent years, the OECD, especially the Working Group, has established information exchange mechanisms and databases. BioTrack Online, the information exchange mechanism of the OECD (developed by the Working Group) is one of the best sources of information on Member country regulations and regulatory developments, as well as

field trials and product approvals. BioTrack is also available on the World Wide Web to the public. Furthermore, BioTrack is closely linked with UNIDO's (United Nations Industrial Development Organization) BINAS (Biosafety Information Network and Advisory Service), which covers non-member countries. However, much remains to be done to facilitate the transfer of risk/safety assessment experience, especially from the G7/8 countries, to those who are still developing capacity in this area. In this context, reference is made to the initiative taken by the supervisory committee of the Working Group, (OECD's Environment Policy Committee) which has proposed a major conference on the environmental aspects of biotechnology.

11. This document makes reference to the activities of a number of other intergovernmental organisations. For example, UNIDO and the CBD (Convention on Biological Diversity) Secretariat have regularly participated in meetings of the Working Group. In addition, both of the organisations have organised input into the Consensus Documents of the Working Group by experts from non-member countries. The adoption of the Biosafety Protocol to the Convention on Biological Diversity in January 2000 is intended to lay the foundation for a global system for assessing the impact of genetically engineered organisms on biodiversity, and exchanging information though a Biosafety Clearing House. It also contains provisions to encourage capacity building in developing the environmental assessment of genetically engineered organisms. **This experience shows that interactions between intergovernmental organisations and sharing of technical documents and expertise will avoid duplication of efforts and facilitate understanding of risk/safety assessment of products of biotechnology.**

AN INTRODUCTION TO OECD'S WORKING GROUP

12. The Working Group on Harmonization of Regulatory Oversight in Biotechnology is comprised of individuals from government ministries or agencies, which have responsibility for the environmental risk/safety assessment of products of modern biotechnology (including genetically modified organisms). This report builds on OECD’s extensive experience with safety related activities dating back to the mid-1980s. Initially, much of the effort at OECD was concentrated on the environmental and agricultural implications of field trials of GM crops. This was followed by a consideration of the large-scale use, and commercialisation of crop plants. In 1995, arrangements for environmental biosafety, food safety as well as varietal registration and seed certification were reviewed, showing considerable commonality among Member countries in the information used in risk/safety assessments.

13. Since that time, the Working Group has been established and has focused on promoting harmonisation through the development of Consensus Documents. The goal is to identify common information in the risk/safety assessment of products being developed through modern biotechnology (including new varieties) in order to encourage information sharing and prevent duplication of effort among countries. The common elements fall into two general categories: the biology of the host species or crop, and traits used in genetic modifications.

14. Regulatory harmonisation has been the primary goal of the working Group since it was established in 1995. It is the attempt to ensure that the information used in risk/safety assessment, as well as the methods used, are as similar as possible. It could lead to countries recognising or even accepting information from one another’s assessments. The benefits of harmonisation are clear. It increases mutual understanding among Member countries, which avoids duplication and increases efficiency, which in turn improves safety.

15. The Working Group is also focusing on outreach activities, particularly through its information exchange mechanism, BioTrack Online. This mechanism includes information on regulatory developments in OECD Member countries, including details of laws, regulations and the contact points of the responsible ministries and agencies. It also has a database of field trials in OECD Member countries, as well as a database of products that have been commercialised.

16. The Working Group is currently making the next steps towards harmonisation. It is working to identify the differences among Member countries in their regulatory decision making as well as delineating specific information requirements that countries have in common. It will also focus on scientific and technical aspects of risk management issues.

HOW THE WORKING GROUP DRAFTED THIS REPORT

17. This report was drafted by the delegations of OECD Member countries to the Working Group. In drafting the report, the Working Group had a period of 6 months, which is a relatively short period of time, to fully address the large number of issues relevant to the topic, some of which are controversial. Nevertheless, it does represent a good overview of the topic that the Working Group may use when further developing its future work programme.

A NOTE ON THE USE OF TERMINOLOGY

18. Different Member countries have different preferences for terms which describe *products of modern biotechnology*. In this document the term *genetically engineered organism* is used most frequently. For the purposes of this text, it is (for practical purposes) equivalent to the term *genetically modified organism (GMO)* or *transgenic organism*. A similar term, *living modified organism (LMO)* is also used in certain sections of this report. This is the term that is used in the Cartagena Protocol on Biosafety.

19. Different Member countries also have different preferences for the terms *risk assessment* or *safety assessment*, and *risk assessor* or *safety assessor*. In this report, therefore, the terms *risk/safety assessment*, and *risk/safety assessor* are used. The term risk management is used to describe measures taken to minimise hazards identified in a risk/safety assessment. A related term, *risk/safety analysis* is also used, mainly when quoting other texts where this term is employed. Where it is used in this document, this term is (for practical purposes) equivalent to risk/safety assessment.

CHAPTER I - ENVIRONMENTAL RISK/SAFETY ASSESSMENT OF BIOTECHNOLOGY PRODUCTS

A. THE ENVIRONMENTAL CONSEQUENCES OF BIOTECHNOLOGY IN FOOD PRODUCTION

20. This is a companion report to that of the **Task Force for the Safety of Novel Foods and Feeds** [C(2000)86/ADD1]. The report of the **Task Force** includes an extensive description of biotechnology and its impact on the food supply, so it is possible to refer to that document for a comprehensive description.

21. Whereas the Task Force report covers food safety assessment, this report deals with the environmental aspects associated with the production of GM foods and is based on the work of the OECD and its Member countries since the mid-1980s. This coincided with the first field trials involving genetically engineered organisms in 1986, and to date there have been thousands of such events globally. The first commercialised plantings of GM crops took place in the mid-1990s. The vast majority of genetically engineered organisms, both in field trials and in commercialised applications, have been of important crop plants that are international trading commodities, such as maize, soybean, cotton, rapeseed, potato and tomato. There have also been a number of GM micro-organisms used in food production. Although these field trials and commercial applications have not occurred uniformly across the OECD Member countries, many governments have accumulated experience in environmental risk/safety assessments, having reviewed these products from an environmental perspective as well as for food safety.

B. THE BIOLOGY OF PLANTS AND MICRO-ORGANISMS AND THEIR INTERACTIONS WITH THE ENVIRONMENT

22. In considering the potential environmental impacts of genetically engineered organisms, risk/safety assessors require a sound understanding of the biology of an organism as well as its relationship with the environment in which it is to be released. Therefore, this section sets the scene by focusing on the basic biology of plants and micro-organisms, and their interactions with the environment.

B.1. Plants

B.1.1. OECD Plant Consensus Documents

23. The OECD Working Group has produced a series of Consensus Documents on the biology of several crop plant species (as well as on trees, and micro-organisms) that focus on those biological attributes that are important in evaluating the safety of a genetically engineered organism. These documents deal with some of the important issues in evaluating safety, including genetic characteristics, reproductive biology, the "centre of origin" and biodiversity, pests, diseases and ecological characteristics. The information in the Consensus Documents is intended to be mutually recognised among OECD Member countries for use in risk/safety assessments.

24. The following section is a general background on plant biology. It is fundamental biological knowledge understood by most biological scientists.

B.1.2. General biology

25. Living organisms constantly need energy to perform their life functions. Many organisms obtain this energy by eating other organisms. Plants, however, form the base of all life on Earth because they are able to capture the energy of the sun, in a process called "photosynthesis", to perform their life functions. All plant biomass production depends on photosynthesis (Foyer et al., 1996). Photosynthesis, which occurs in the green cells of plants, is the single energy-trapping process capable of converting large quantities of light energy into chemical energy (Levitt, 1969), that can be used by other organisms. Plants use this energy to produce a number of substances:

- **starch**, an end product of photosynthesis, is a molecule which the plant uses to capture excess energy for future use. A large amount of starch is accumulated as a carbon reserve in potato tubers (Moorby et al, 1975), sweet potato roots and cereal grains (Evance et al., 1996).
- **proteins**, are formed by building blocks, called "amino acids" (Levitt, 1969). Proteins are the substances through which the various enzymatic reactions that characterise the life processes of cells are formed.
- **lipids** are a diverse group of chemicals which perform several major functions in plants as well as being the major component of membranes (organic layers that exist in membranes enclosing both the cell itself and structures within cells such as nucleus, plastids, mitochondria).

All of these substances are good sources of nutrition for other organisms, as well as being useful to the plant itself.

26. Plants also produce other substances that are known as "secondary metabolites". Frequently these substances are the by-products, or waste products, of the plant cell, although the plant may use such waste products for other useful functions, for example, to repel pests and herbivores. Some of these secondary metabolites attract pollinating insects or seed-dispersing animals. The major secondary metabolites include the alkaloids (secondary metabolites derived from amino acids), terpenes (essential oils, resins, rubber), many phenolic substances (e.g., tannins), and glycosides (Levitt, 1969). The Task Force report discusses this group of plant constituents in some detail.

27. Plants therefore play a critical role in life on Earth as they are the base of the food chain. Most animals eat plant material as food, although some animals are carnivores, dependent on plant-eating animals. As discussed in this report in the following sections, micro-organisms can also make a living from either living or decaying plants. Plants also have complex interactions with each other as they compete for light, space and other nutrients (Raven, 1992). As mentioned above, they also have complex interactions with pests and herbivores, as well as with pollinating insects or seed-dispersing animals (Raven, 1992). In some relationships, they provide habitat for other living organisms (Raven, 1992). Pathogenic micro-organisms may also induce in plants a Hypersensitive Reaction (HR), a systemically acquired resistance to pathogens (Baker et al., 1997; Seo et al., 1997). Plants also play an important role in determining the relative amounts of oxygen and carbon dioxide in the atmosphere. Recently, evidence has been accumulating showing that the amount of these substances in the atmosphere plays an important role in climate.

28. Plants play a number of roles in the environment and may affect other organisms through a number of direct and indirect mechanisms. The risk/safety assessor in considering the safety of transgenic plants will evaluate the potential for disruption of these interactions.

B.2. Micro-organisms

B.2.1. The approach of the Working Group to micro-organisms

29. The OECD has been considering GM micro-organisms for a number of years. Initially, the focus was on their contained use, and recently more emphasis was placed on releases into the environment. Although environmental releases of GM micro-organisms are less common than transgenic plants, the Working Group has developed consensus documents on some species of micro-organisms (for example OECD, 1996). They are comprehensive, compiling much knowledge relevant to regulators. As with the plant consensus documents, they include information on the biology of those micro-organisms which are, or are likely to be, the subject of genetic engineering. However, compiling this type of information is inherently more difficult with micro-organisms for a number of scientific reasons, and the relevance of certain safety issues is still under debate. The Working Group currently is reviewing how best to deal with the risk/safety assessments of GM micro-organisms.

30. In considering its future work, the Working Group will take into account efforts which are underway to establish databases of micro-organisms, vector constructs and marker genes, as well as traits and functional genes. It will also take into account efforts to improve the taxonomic understanding of important groups of micro-organisms. In the same vein, information is needed on the relevance of clonal structure and horizontal gene transfer. Sampling, detection and identification methods for the monitoring of micro-organisms continue to be developed, and will be evaluated by the Working Group when planning its future work. This could contribute to the goal of a further development of criteria for the environment risk/safety assessment of GM micro-organisms.

31. It is also important to take into account information generated through reviews of micro-organisms used in related applications, such as their use as biopesticides.

B.2.2. General biology

32. Micro-organisms are ubiquitous. They make up 90% of the soil biomass. All living macro-organisms have their associated micro-organisms, called commensals. There are as many micro-organisms on a single human body as there are human cells. Micro-organisms are also found in water, air, rocks and thousands of feet into the earth's mantle. Some are adapted to the most extreme conditions and can be found in hot springs, at extremely low temperatures, at high pressure and in environments that would kill most other living things.

33. Micro-organisms re-cycle key elements such as carbon, nitrogen, phosphorus, sulphur and oxygen, so they are essential to maintaining the balance for life on Earth.

34. Humans and animals rely on micro-organisms for certain essential functions. Micro-organisms in the human gastrointestinal tract, are necessary to the process of digestion and the acquisition of certain vitamins. Micro-organisms on the skin surface protect the body against pathogens and disease. However, micro-organisms can also be the cause of diseases of humans, animals and plants.

35. Humans have used micro-organisms to produce foods for millennia. Micro-organisms are also important in feed production, such as silage, and in industrial applications (e.g. creation of speciality or commodity chemicals). These applications take place under special conditions and surveillance in a more or less contained environment. In contrast, it is more difficult to get a new micro-organism to become established in a more open environment like soil. Nevertheless, special micro-organisms are used in agriculture to fix nitrogen which frequently is a limiting element in plant growth.

36. Micro-organisms play numerous roles in the environment and may affect other organisms through a number of direct or indirect mechanisms. Many of these mechanisms remain subject to research, and the role of only a relatively small fraction of all micro-organisms in a given ecosystem is known. Although micro-organisms can have impacts on the environment, it remains difficult to detect alterations in a very complex system of microbial interactions that may vary in the short as well as long term. Often the assessor, in considering the safety of GM micro-organisms, has to evaluate the potential for a disruption of key environmental interactions from inference from previous findings or based on the knowledge of a safe history of use.

B.3. Animals

37. No transgenic animals have yet been commercialised but a number of applications involving animals are under development. In particular, there is interest world-wide in applying genetic engineering to aquaculture (e.g. Chen & Powers, 1990) and genetically modified salmon are close to commercialisation. Although genetic modification of animals is not yet a priority for the Working Group, the OECD has made an initial study on the environmental impacts of aquaculture (OECD, 1996) which could be a basis for future activities in this field.

C. ENVIRONMENTAL SAFETY ISSUES

38. Most OECD Member countries have a system for the environmental risk/safety assessment for evaluating the growth or production of GM foods. For example, most OECD Member countries

have a system for performing environmental assessments of plants used to grow food, or micro-organisms used in the production of foods. An environmental risk/safety assessment takes into account the biological properties of the host organism. It also includes information on the source of the gene(s) introduced, how the gene(s) is (are) expressed in the genetically engineered organism and the nature of the gene product. The characteristics of the organism are taken into account, as well as its likely performance and impact in the environment where it is to be released. For example exposure and toxicity data are used to examine potential ecological effects to resident wildlife and biodiversity (for example, plants with pesticidal genes may impact non-target species of insects). In addition, information on the eventual use of the product is necessary to ensure a complete assessment. The kinds of information risk/safety assessors use have been developed, in part, from experience with traditional organisms. The general issues assessed for transgenic plants were developed by OECD and include the following: gene transfer, weediness, trait or non-target effects, genetic or phenotypic variability, and the use of vectors and genes from pathogens. The following describes some of the issues addressed by risk/safety assessors, section C.1. focuses on transgenic plants and section C.2. on transgenic micro-organisms.

C.1. Plants

C.1.1. Gene transfer to related plants

39. An issue for risk/safety assessors, is the possibility that genes may be transferred by pollen to populations of the same crop species or to sexually compatible wild relatives that grow in the surrounding area. For this to happen, a number of factors must be in place. The most important is the occurrence of sexually compatible plant populations within range of the movement of the transgenic pollen. However, for a successful fertilisation to occur, there must also be the formation of receptive flowers at the same time of pollination. For a population with the transferred gene to persist, a variety of circumstances must occur, including the production of viable seeds and the germination and growth of the seeds. Finally, it depends on the fertility of the resulting plant and its progeny. Therefore the chances for outcrossing are low to nil for maize having no known relatives in Europe as compared to oilseed rape, where several related species are found. Another important aspect for a successful cross is the genetic compatibility. Compatibility often depends on which plant species is the pollen donor. Data on compatibility are usually based on crosses with the cultivated crop plant as the female part (Dietz, 1993), but there are studies for both combinations in Brassicas (Downey and Kirkland, 1997). The new introduced trait may be similar to mutations (e.g. herbicide tolerance) but can also be completely new (e.g. B.t toxin in plants) for the species. Repeated pollination would increase the probability of the integration of the trait into the wild population.

40. The establishment of the trait in a wild population depends, not only on the frequency of the transfer, but also on chance effects and selection pressure. It has been suggested that if the gene confers selective advantage under the existing environmental or agricultural conditions (i.e. herbicide tolerance, insecticide tolerance, or greater tolerance to environmental stresses) the plants or transgene may spread and could change species composition (Lupi, 1995). On the other hand, genes which do not reduce the fitness have a higher probability to be maintained in wild plant populations. Under natural conditions, crop plant characteristics usually cause a decreased fitness of the hybrids. In general, on a long-term basis, gene transfer to related wild plants cannot be excluded in certain cases and, therefore, beyond considering the impact on biodiversity, it may be important to find out the effects of the gene introduced in the genomic background of another plant species (Dietz, 1993). It

may also be important to consider whether similar traits from traditional breeding have had an effect on wild relatives.

C.1.2. Gene transfer to unrelated organisms

41. Horizontal gene transfer is the exchange of genetic material between unrelated organisms, for example between plants and micro-organisms. In the case of micro-organism to micro-organism transfer, various mechanisms are well documented, for example, conjugation, transduction and transformation, which allow the transfer of genetic material.

42. There are specific cases where plants are the recipients for natural gene transfer from micro-organisms. For example, *Agrobacterium tumefaciens* is a pathogenic bacterium which causes abnormal swelling, or galls, in certain plants (dicotyledons). Part of the bacterial DNA (located on a plasmid) is transferred to the plant cell and incorporated into a plant chromosome. Although scientists have looked for many years for the transfer of genetic material from the plant to *Agrobacterium tumefaciends*, it has not been detected.

43. A hypothetical mechanism for horizontal gene transfer from plants to micro-organisms, is the uptake of DNA, released by decaying plants, by micro-organisms. The Task Force report [C(2000)86/ADD1] discusses the potential for this to occur in some detail.

C.1.3. Establishment and persistence of populations of transgenic organisms: Weediness in the agricultural setting

44. When considering transgenic crop plants, one issue that risk/safety assessors address is whether a new plant variety has an increased tendency to persist, invade, compete or disperse in the environment. The introduction of herbicide resistance genes, for example, could create problems in controlling emerging herbicide resistant plants in crop rotations in agricultural settings.

C.1.4. Instability of the genetic modification

45. Generally, genes are stably inherited. Instabilities in the inheritance and expression of an introduced gene may be possible for several reasons. The novel characteristic can be lost if the inserted gene is not expressed by the recipient organism, or inhibited by interactions with other genes. It can also be lost through the segregation of genetic material during further breeding. This may not change the risk assessment of the genetically modified organism regarding the potential effects on human health or the environment. In other cases, however, it may be an important issue for risk/safety assessors. For example, where the aim of the genetic modification is to remove a specific adverse characteristic of the recipient organism (e.g. toxic or allergenic compounds).

C.1.5. Secondary and non-target adverse effects

46. The potential impact of a transgenic crop on organisms in the surrounding communities is an important consideration in risk/safety assessment. Important points to consider are: a) which species feed on, or otherwise come in contact with, the transgenic plant; b) whether the pollen of the transgenic plant contains the new gene product; if so, what the potential effects maybe on non-target organisms such as bees, butterflies or aquatic organisms, since plant pollen has the potential to enter

adjacent environments through wind dispersal; c) whether the new gene product is expressed in seed or fruit; and if so, whether animals eat these fruits and/or seeds; d) whether the new gene product is present in roots or plant tissue at senescence and is then tilled into the soil, or left in the field to decompose, following harvest; whether the new gene product is stable and bioavailable in the soil, and what the potential effects on soil dwelling organisms may be; and e) if the new gene product is sufficiently stable to digestion such that species feeding on the transgenic plant would accumulate enough of the new gene product to affect predatory species feeding on them.

47. Relevant for risk/safety assessment are especially toxic or harmful effects on the environment, as well as secondary and indirect effects which might occur, for example, on the food web. Potential adverse effects could include effects on biogeochemistry, such as changes in nitrogen and/or carbon metabolism in the soil through genetically engineered organisms affecting organisms of the micro- and/or meso-fauna that are important in decomposition processes. The expression of environmentally interactive traits in modified plants and micro-organisms may cause ecotoxicity problems. Expression of insecticidal toxins and of some plant viral genes have also been identified as examples of critical traits when considering possible unintended adverse effects on the environment.

C.2. Micro-organisms

C.2.1. Micro-organisms used in food production - environmental risk/safety considerations

48. Micro-organisms used in “contained” conditions have been selected to minimise the potential for the production of toxins, and are usually debilitated. The debilitation occurs either by design or because micro-organisms repeatedly grown in specific conditions become adapted to those conditions and often lose the ability to survive outside. In this case, they pose limited or no environmental risk. However, the fitness of the micro-organisms to survive outside of the contained conditions, should be assessed on a case-by-case basis.

49. The experience gained from the use of micro-organisms in containment over the years provides scientists with considerable familiarity. However, as described above, the use of micro-organisms in containment may differ considerably from requirements that micro-organisms must meet if they should compete successfully in the environment. Nevertheless, experience shows, for example, that many micro-organisms can be used safely even if their precise roles in the microbial community or ecosystem are unknown, although this cannot be assumed for all micro-organisms. Because we lack perfect knowledge of the roles of micro-organisms, we must base our assessment on inference from previous scientific findings and the availability of a record of safety. Unfamiliar micro-organisms or instances of significant uncertainty about the interaction of the micro-organism and the environment into which it is to be introduced require careful evaluation prior to release. Issues that may have ecological significance include the following: the functional role or niche of the micro-organism in the microbial community and ecosystem; the potential for gene exchange between micro-organisms; the ability to monitor persistence and spread of the micro-organism; and, most important, the potential ecological consequences of persistence and spread, and the potential measures to control, if necessary, the effects of introduced micro-organisms.

50. Although human health aspects are paramount in the application of micro-organisms in food production, there are also environmental factors to be taken into account since micro-organisms (or genetically engineered micro-organisms) may be accidentally or routinely released into the

environment. The potential environmental interactions of micro-organisms could be (but is not necessarily) considerable, since a new strain in an ecosystem also leads to the introduction of new genes into the gene pool (Tiedje et al., 1989). In addition, newly introduced micro-organisms could replace others and take over their functions in an ecosystem. This can entail an alteration of such functions, and have effects on the ecosystem at large (Cairns and Orvos, 1992). The natural microbial community can counteract the introduction of new micro-organisms by competition (Tiedje et al., 1989; Tiedje et al., 1999). It is also believed that there is a great deal of redundancy of function in the microbial world and the introduction of a function or trait by genetic engineering of one micro-organism is not likely to upset ecological balances in a microbial community (Tiedje et al., 1999). The large number of complex interactions in which micro-organisms are involved makes it difficult to give a comprehensive description in a brief review. This section thus focuses on three examples of environmental safety issues involved in food and food production.

51. First, risk/safety assessors often focus on the use of antibiotic resistance markers. The concern is that a GM micro-organism introduced into food, or into the environment for some other purpose, might be a source of antibiotic resistance for the commensals (normal resident flora) on the body of humans or other animals, or for pathogens of humans or other animals. Similarly, human commensals can be sources of antibiotic resistance potentially affecting the relationships between and among other macro-and micro-organisms in the environment.

52. A second risk consideration in a risk/safety assessment is whether a micro-organism is able to produce a toxin that can have a deleterious effect on humans or other animals. The individual need not ingest the bacterium to be affected if the toxin is secreted. Some organisms used in food production are related to micro-organisms that produce such toxins (e.g., *Aspergillus oryzae* used for hundreds of years to produce soy sauce, miso and sake). One risk assessment question posed is whether a micro-organism that grows symbiotically in an human or animal (e.g., *Escherichia coli*) could acquire such a toxin from a transgenic bacterium (genetically modified or not), or whether a toxin contaminant from a transgenic micro-organism could be in food or feed or otherwise consumed by an animal.

53. A third consideration relates to transgenic micro-organisms (e.g., *Sinorhizobium meliloti*) in a symbiotic relationship with leguminous plants to extract nitrogen from the atmosphere and fix it in soil. Again, these applications must be assessed on a case-by-case basis. There have been several series of field tests and a commercial application over the past several years involving such micro-organisms.

CHAPTER II - CURRENT APPROACHES AND EXPERIENCES IN ENVIRONMENTAL RISK/SAFETY ASSESSMENT

A. INTERNATIONALLY ESTABLISHED SCIENTIFIC PRINCIPLES

A.1. Risk/safety assessment and risk management

54. Risk/safety assessment involves the identification of potential environmental adverse effects or hazards, and determining, when a hazard is identified, the probability of it occurring. If a potential hazard or adverse affect is identified, measures may be taken to minimise or mitigate it. This is risk management. Absolute certainty or zero risk in a safety assessment is not achievable, so uncertainty is an inescapable aspect of all risk assessment and risk management (OECD, 1993). For example, there is uncertainty in extrapolating the results of testing in one species to identify potential effects in another. Risk assessors and risk managers thus spend considerable effort to address uncertainty. Many of the activities in intergovernmental organisations, such as the OECD, address ways to handle uncertainty.

A.2. Efforts within the OECD

55. Since the 1980s the OECD has been developing harmonised approaches to the risk/safety assessment of products of modern biotechnology. To date, OECD has published a number of expert reports on safety considerations, concepts and principles for risk/safety assessment as well as information on field releases of transgenic crops, and a consideration of traditional crop breeding practices. Currently the OECD is publishing Consensus Documents on information used in the assessment of environmental applications of specific organisms and traits.

A.2.1. Underlying scientific principles

56. In 1986, OECD published its first safety considerations for genetically engineered organisms (OECD, 1986). These included the issues (relevant to human health, the environment and agriculture) which might be considered in a risk/safety assessment. In its recommendations for agricultural and environmental applications, it suggested that risk/safety assessors:

- “use the considerable data on the environmental and human health effects of living organisms to guide risk assessments;
- ensure that recombinant DNA organisms are evaluated for potential risk, prior to application in agriculture and the environment by means of an independent review of potential risks on a case-by-case basis;

- conduct the development of recombinant DNA organisms for agricultural and environmental applications in a stepwise fashion, moving, where appropriate, from the laboratory to the growth chamber and greenhouse, to limited field testing and finally to large-scale field testing;
- encourage further research to improve the prediction, evaluation, and monitoring of the outcome of applications of recombinant DNA organisms."

A.2.2. The role of confinement in small scale testing

57. In 1992, OECD published its Good Developmental Principles (GDP) (OECD, 1992) for the design of small-scale field research involving GM plants and GM micro-organisms. This document, amongst other things, describes the use of *confinement* in field tests. Confinement includes measures, to avoid the dissemination or establishment of organisms from a field trial, for example, the use of physical, temporal, or biological isolation (such as the use of sterility).

A.2.3. Scale-up of crop-plants – "risk/safety analysis"

58. By 1993, the focus of attention had switched to the *scale-up* of crop plants as plant breeders began to move to larger-scale production and commercialisation of GM plants. OECD published general principles for, *scale-up* (OECD, 1993) which re-affirmed that, "*safety in biotechnology is achieved by the appropriate application of risk/safety analysis and risk management. Risk/safety analysis comprises hazard identification and, if a hazard has been identified, risk assessment. Risk/safety analysis is based on the characteristics of the organism, the introduced trait, the environment into which the organism is introduced, the interaction between these, and the intended application. Risk/safety analysis is conducted prior to an intended action and is typically a routine component of research, development and testing of new organisms, whether performed in a laboratory or a field setting. Risk/safety analysis is a scientific procedure which does not imply or exclude regulatory oversight or imply that every case will necessarily be reviewed by a national or other authority*" (OECD, 1993).

A.2.4. The role of familiarity in risk/safety assessment

59. The issue of *scale-up* also led to an important concept, *familiarity*, which is one key approach that has been used subsequently to address the environmental safety of transgenic plants.

60. The concept of familiarity is based on the fact that most genetically engineered organisms are developed from organisms such as crop plants whose biology is well understood. It is not a risk/safety assessment in itself (NAS, 1989). However, the concept facilitates risk/safety assessments, because to be familiar, means having enough information to be able to make a judgement of safety or risk (U.S. NAS, 1989). Familiarity can also be used to indicate appropriate management practices including whether standard agricultural practices are adequate or whether other management practices are needed to manage the risk (OECD, 1993). Familiarity allows the risk assessor to draw on previous knowledge and experience with the introduction of plants and micro-organisms into the environment and this indicates appropriate management practices. As familiarity depends also on the knowledge

about the environment and its interaction with introduced organisms, the risk/safety assessment in one country may not be applicable in another country. However, as field tests are performed, information will accumulate about the organisms involved, and their interactions with a number of environments.

61. Familiarity comes from the knowledge and experience available for conducting a risk/safety analysis prior to scale-up of any new plant line or crop cultivar in a particular environment. For plants, for example, familiarity takes account of, but need not be restricted to, knowledge and experience with:

- "the crop plant, including its flowering/reproductive characteristics, ecological requirements, and past breeding experiences;
- the agricultural and surrounding environment of the trial site;
- specific trait(s) transferred to the plant line(s);
- results from previous basic research including greenhouse/glasshouse and small-scale field research with the new plant line or with other plant lines having the same trait;
- the scale-up of lines of the plant crop varieties developed by more traditional techniques of plant breeding;
- the scale-up of other plant lines developed by the same technique
- the presence of related (and sexually compatible) plants in the surrounding natural environment, and knowledge of the potential for gene transfer between crop plant and the relative; and
- interactions between/among the crop plant, environment and trait." (OECD, 1993)

A.2.5. Regulatory harmonisation

62. The Working Group was established in 1995 at a time when a number of GM foods were being commercialised in some OECD Member countries. One of the aims of the Working Group is to promote international harmonisation in biotechnology among Member countries building on the previous principles and concepts developed at OECD. Its work is designed to ensure that environmental health and safety aspects are properly evaluated.

63. The Working Group is currently developing Consensus Documents that address plants, micro-organisms and traits of products that have already entered in international trade or are expected to in the near future. The Documents which have been published so far address crop plants (e.g., oilseed rape, potato, bread wheat, rice), tree species (Norway spruce, White spruce) and micro-organisms (*Pseudomonas*). A number of documents also address genetically modified traits (e.g., virus resistance and herbicide tolerance). Currently, the Working Group has around 15 additional Consensus Documents in preparation.

64. Consensus Documents are intended to be a "snapshot" of current information, for use during the regulatory assessment of products of biotechnology, which are intended to be mutually recognised among OECD Member countries. The Consensus Documents are not intended to be a substitute for a

risk/safety assessment. However, they encourage information sharing on key safety issues and prevent duplication of effort among countries. The documents are being used: a) by applicants as information for the applications to regulators; b) by regulators as a general guide and reference source in their reviews; and c) by governments for information sharing, research reference and public information.

65. Another important aspect of the work of the Working Group is its outreach activities. In particular, BioTrack Online on the World Wide Web, http://www.oecd.org/ehs/service.htm (OECD Web Site, a), includes information on the regulatory oversight of products of biotechnology that is used by governments and industry, in preparing notifications and assessments. BioTrack fosters international co-ordination by sharing information on regulatory developments in Member countries (OECD Web Site, d) and providing a database on field trials (OECD Web Site, c) and approved products (OECD Web Site, b). To aid regulators in product identification as well as to improve the databases, the concept of a unique identifier of products will be further developed at a workshop in October 2000. The use of a unique identifier will allow for the identification of the same product in different countries by regulators. BioTrack Online provides information on OECD’s past work, has joint web sites as well as links to other relevant sites; in particular, it has a joint web site with UNIDO, i.e., BINAS site. Other outreach activities have resulted in integrating input from non-member countries, especially with respect to “centres of origin and diversity”.

A.3. Other intergovernmental activities

66. A number of other intergovernmental activities have a bearing on the risk/safety assessment of genetically engineered organisms.

67. There are various documents from international organisations relevant to harmonisation which are intended to be mutually supportive. UNIDO, UNEP, FAO and other international bodies have published reports, recommendations and/or guidelines on the safety of environmental release of genetically engineered organisms. The UNEP guidelines (UNEP, 1995) are an example of a voluntary agreement. The Cartagena Protocol on Biosafety which was recently adopted (29 January 2000, in Montreal) defines obligations for the transboundary movements of LMOs (living modified organisms), international exchange of genetically engineered organisms and includes an annex on risk assessment that addresses objectives, general principles and methodology in that area. The revised 1997 International Plant Protection Convention (IPPC) has reference to measuring environment impacts in risk analysis, which are being spelt out in a draft International Standard for Phytosanitary Measures (ISPM) for risk analysis. The IPPC ISPMs are referenced in the SPS Agreement (Sanitary and Phytosanitary Agreement) as standards that members shall use when assessing risks. The International Commission for Phytosanitary Measures (ICPM), under the IPPC, has established a working group which is examining the need for a specific ISPM on risk analysis for genetically engineered organisms. Another relevant instrument is the WTO Agreement on Sanitary and Phytosanitary Measures (WTO, 1995), which specifies the conditions where trade restrictions may be imposed if there is a concern that a disease agent or other pest may be spread.

68. There are a number of regional harmonisation efforts, based on either mandatory or voluntary agreements, to further international harmonisation of regulatory oversight. For example, the EC Directives (Council of the EU, 1990) establish a common framework on how to deal with genetically modified organisms. Directive 90/220 is currently under revision, and the amendments are intended to promote further harmonisation among Member States.

69. In addition, there are bilateral discussions to promote the harmonisation of data requirements and risk assessment procedures. They include discussions on the development of molecular characterisation standards as an important part of environmental risk/safety assessment, based on projects between the US/USDA and Canada, between the EU and Canada, as well as the EU and US/USDA (the so called Transatlantic Economic Partnership or TEP Pilot Project).

B. REGIONAL AND NATIONAL EXPERIENCES

70. Regulatory oversight of biotechnology had its origins in the mid- to late 1970s, when guidelines were developed for laboratory experiments using recombinant DNA techniques. In the mid-1980s, when it became clear that environmental releases or field tests of transgenic plants and micro-organisms were imminent (especially field tests of transgenic crop plants), Member countries began to develop systems for regulatory oversight to ensure adequate risk/safety assessments. In some countries, existing laws were adapted whilst in others new legislation was created. Concomitant with the development of regulatory oversight was the development of risk/safety assessment methods.

71. Today, a significant number of plant varieties and some microbial products have gone through the regulatory review process in most OECD Member countries. While many of these have been for experimental field trials, others have been approved for commercial use. Today, millions of acres in some countries are being planted with transgenic crops such as potato, cotton, maize, soybean or oil seed rape (canola). In other Member countries, some applications are still pending.

72. Assessments are conducted in a variety of ways. In some Member countries, committees of scientific experts are appointed to review information and make recommendations to decision-making authorities. In other countries, the assessors are government employees trained in the necessary scientific disciplines. Specific information regarding a GM product, its use and distribution, is then coupled to the current state of scientific knowledge to determine whether there are risks to releasing the organism to the environment and if so whether they are acceptable. Where there is uncertainty regarding the level of risk this may be addressed by additional research or monitoring. In such cases some countries consider the application of precaution as an adequate measure of risk management. A great deal of information may be derived throughout the development of biotechnology products step by step, especially that regarding specific traits and how they are presented in a variety of environments (OECD, 1992).

73. An important part of the risk/safety assessment process is providing information to the public. In many OECD countries, specific measures are taken to inform the public when applications are received, what they are and their intended use. Often there is the possibility for members of the public to comment. In order to ensure transparency, many countries publish the outcome of risk/safety assessments, together with documents describing regulatory decisions. Historically, much of this information was disseminated through official journals. However, the Internet is an increasingly important tool in this respect.

74. Annex 1 describes national and regional approaches in certain Member countries.

CHAPTER III CURRENT NEEDS AND FUTURE CHALLENGES

75. Although much progress has been made on the environmental risk/safety assessment of genetically engineered organisms, both at the national and international level, much work remains to be done. This chapter identifies a number of the current needs and future challenges.

A. HARMONISATION: THE NEXT STEPS

76. Regulatory harmonisation, while ensuring a high level of safety, has been the primary goal of the Working Group since it was established in 1995. It is the attempt to ensure that the information used in risk/safety assessment, as well as the methods used, are as similar as possible between different countries. This could lead to harmonised data requirements, countries accepting information from one another's assessments or mutual recognition of assessments. The ultimate ambitious goal of harmonisation is to reach mutual acceptance of decisions though this is far in the future. The benefits of harmonisation are clear. Harmonisation increases mutual understanding among Member countries, which avoids duplication and increases efficiency, which in turn improves safety.

77. In the area of modern biotechnology the OECD has undertaken a number of studies which investigate national policies with respect to regulatory oversight, as well as data requirements for use in risk/safety assessment. These studies showed a high level of commonality in the information used in risk/safety assessments. In spite of this commonality, it is obvious that Member countries have arrived at different decisions for product approval.

78. One of the main reasons for these different conclusions is that there are environmental differences between Member countries which need to be taken into account in a risk/safety assessment. Differences in national or regional procedures also play a role. While all countries rely on the results of scientific-based risk/safety assessment, different authorities may place different weight on different scientific disciplines, for example, molecular biology as compared to ecological studies. Some countries, however, address additional factors, for example, socio-economic impacts in their product approval process. Many countries believe that a precautionary approach has an explicit place in risk management, and this, together with different interpretations of precaution, can also lead to different decisions from one country to another.

79. In order to obtain a better understanding of what Member countries currently consider to be essential information elements in risk/safety assessment, and which considerations affect the decision making process, the Working Group is considering activities which could be undertaken in the future at the OECD.

80. For example, it will be useful to analyse the key issues addressed by Member countries in national risk/safety assessments. As an illustration of how this study might be structured, a model questionnaire was circulated to Member countries inviting them to identify three key scientific issues in the fields of health, environment and agriculture, which applicants are asked to address during the

national risk or safety assessment procedures. A number of Member countries have responded and the results are compiled in Annex 2.

81. Coming back to the continuum of harmonisation, the obvious choice is to proceed step-wise and to evaluate the experiences gained at every step in order to properly design the next. Thus, as a first step, countries could harmonise the scientific data quality and the choice of data-generating methods could be specified. The next step could be a mutual understanding about data needs and validity. The acceptance of the entire assessment finally demands an agreement on the relevance and interpretation of the data.

82. It is important to note that most Member countries, and most participants in the Working Group are also engaged in other intergovernmental activities. For this reason, it is important to identify ways to reduce duplication and increase co-operation. The Working Group believes that it is important for an interaction to be maintained among intergovernmental organisations, to ensure the sharing of technical documents and expertise. This should lead to an improvement in risk/safety assessment, and avoid duplication of effort.

B. IMPROVEMENTS IN RISK/SAFETY ASSESSMENT APPROACHES

83. Although there has been considerable experience in environmental risk/safety assessment in many OECD countries (especially the G7/G8 countries), and the principles developed at OECD have gained world-wide acceptance, there is a need for further progress in specific areas.

- **Capacity building** is needed in many countries as they lack the infrastructure to do an environmental risk/safety assessment specific for the local environment.
- **New scientific and technical developments** giving rise to new varieties of genetically engineered organisms will lead to new issues and challenges for risk/safety assessment.
- Since technological developments should be compatible with **broader policy objectives**, risk/safety assessments will have to operate within a broader policy context.

B.1. Capacity building

84. Over the years, all OECD Member countries have established a system to assess the environmental safety of genetically engineered organisms. However, this is not true globally. If the products of biotechnology are cultivated globally, risk/safety assessments will have to be carried out by many countries, so there is a need for capacity building where there is a lack of the necessary infrastructure for performing assessments. Such assessments may have to take into account the geographical variation, especially with respect to naturally occurring relatives, climate and soil. It would be beneficial to the goal of harmonisation for countries that already have gained experience with risk/safety assessments of genetically engineered organisms to assist in the development of such infrastructure. This is recognised in the Biosafety Protocol through the establishment of mechanisms such as the Biosafety Clearing House which will give countries lacking experience and without domestic frameworks the ability to take informed decisions, such as on the import of LMOs.

85. This is a vital issue in respect of the “centres of origin” and biodiversity of crop plant species. The “centres of origin” are those regions where it is believed that the wild ancestors of crop plants originated. Typically, populations of “wild ancestral relatives” still exist in those regions. A

good example from a Member country are the “teosinte” populations (*Zea diploperennis, Z. luxurians, Z. perennis, Z. mays subsp. mexicana, Z. mays subsp. Perviglumis*), wild relatives of maize, which grow in Mexico. Another example is rape seed, where the centre of origin is located within a number of Member countries. The location of these populations is important for two reasons. First they are often a source of genetic resources to plant breeders. Second, they could hybridise with commercial crop varieties, if they are grown in the area. However, for a number of important crop plants, the “centres of origin” are not found in OECD Member countries.

B.2. New scientific and technical developments

86. It is known that many novel applications of biotechnology are under development, and in the future regulators will have to undertake more sophisticated risk/safety assessments. Where experience in evaluating certain products indicates little or no concern, there is a demand by some regulators to streamline existing environmental risk/safety assessment procedures in order to focus their resources on these newer types of products. In order to enhance their ability to take decisions about genetically engineered organism safety issues, assessment procedures must be ready to manage such developments. In particular, there are these areas of concern, already being addressed in some Member countries:

- The range of modified organisms will increase. In the near future, not only transgenic plants will have to be assessed, but also micro-organisms and animals including fish. This may present a challenge to established concepts such as *familiarity*, which have worked well for specific crop plants. Methods to assess and monitor environmental impacts may have to be further developed.
- The number of traits involved in genetic modification will increase. Until recently most genetically engineered organisms only had one or a few genes altered, but in the future many will carry multiple or “stacked genes”. Also, genes from new sources or in new combinations might be introduced (for example leading to higher tolerance to stress, drought, temperature, or to increased nitrogen fixation capabilities) which could lead to new challenges in environmental risk/safety assessment.
- While direct, short-term effects often can be assessed with sufficient accuracy, this may not be the case for long-term and indirect influences, whose assessment frequently makes use of ecological models (for example, Sukopp and Sukopp, 1994).

B.3. Linking risk/safety assessment to broader policy objectives

87. The most important aspect of any risk/safety assessment is to ensure human health or to avoid or minimise adverse effects on the environment. However, once mechanisms are in place to address these issues, it may be important in a number of countries to put risk/safety assessment in a broader policy context.

88. For example, agriculture in general may have detrimental impacts on air, water resources, landscape, flora and fauna (U.K DETR, 1998) from the use of pesticides, energy and water or from a loss of biological diversity. For this reason, many countries have taken measures to enhance the environmental benefits of agriculture (OECD, 1997b) and to reduce negative effects, to balance ecological and economic objectives and to promote sustainable development. Many countries believe

that the use of genetically engineered organisms should be compatible with, or even promote, such policies.

89. Although there is a lot of knowledge about new crop plant varieties from plant breeders' agronomic assessments, this is usually not sufficient to cover all potential indirect or long-term influences on agriculture or the environment. Hence, it may become necessary to use assessment procedures which will allow the balancing of ecological benefits against disadvantages. Recent examples are life cycle assessments where an attempt to assess the environmental effects of specific GM crop plant “from the cradle to the grave” has been made (UBA, 1999).

C. RELATIONSHIP BETWEEN FOOD AND ENVIRONMENTAL RISK/SAFETY ASSESSMENTS

C.1. Introduction

90. A GM product may be the subject of both a food risk/safety assessment and an environmental risk/safety assessment. In most Member countries, these two different procedures are the responsibility of different ministries or agencies. In many cases the same or similar information is used in both types of assessment, such as information on the biology of the host organism, the molecular characterisation of the inserted gene(s) and the properties of the modified organism. Even though the different ministries usually perform their assessments independently, a better understanding of the way similar considerations can be used in the two assessments, may lead to a better understanding of the effectiveness of the overall risk assessment of the product.

C.1.1. Plants

91. A specific example where a food risk/safety assessment might share information with environmental safety is the level of natural toxicants in plants. Many plants produce compounds, such as alkaloids, glycosides and phenolics, which are toxic at a certain level to humans and other animals.

92. Classical plant breeding has led to crop varieties which contain levels of such toxicants accepted as safe for human consumption. Occasionally, plant breeding can lead to varieties with elevated levels of toxicants which are then discarded for use as human foods. Similarly, genetic engineering has the potential to create varieties with elevated levels of toxicants. This is a recognised safety issue with certain GM foods. Transgenic plant varieties may also contain proteins, new to the variety (such as Bt endotoxins), which are considered by both food safety and environmental risk/safety assessors.

93. Elevated toxicant levels could also represent an environmental risk to any toxicant-sensitive non-target herbivores that feed directly on the crop or on crop debris. In addition, the trait might introgress into compatible wild relatives. In this situation, the impacts on the herbivores that feed on the wild relatives and the potential for increased invasiveness of the plant due to decreased herbivory could both be considered. Therefore, the same data on toxicant levels in a transgenic plant may be used in both the human and non-target organism risk/safety assessments.

94. Another link between food and environmental risk/safety assessment is shown in a recent research report showing an association between Bt-maize and mycotoxin in which the decreased

insect damage of the Bt-maize resulted in decreased infection by a mycotoxin-producing *Fusarium* strain. The *Fusarium* fungus is an opportunist on maize, whose mycotoxins can be found in the kernels. Mycotoxins are known human and animal health hazards (e.g. they are acute toxicants). Therefore, the insecticidal properties of Bt-maize may have a positive impact on food safety by reducing the level of exposure to mycotoxins.

95. An important set of information relevant to food and environmental risk/safety assessment is the information gathered by the plant breeders during the development of new crop varieties. In evaluating new varieties of any crop, the breeder generally follows a well-established process. Whether a new trait has been introduced through traditional breeding or genetic engineering, the breeder needs to know that the new variety meets a high standard for general agronomic performance and efficacy. In doing this, the breeder makes quantitative and qualitative observations, to ensure acceptable plant performance. These observations are often carried out over a number of years and in a number of environments. Aberrant types are eliminated before lines are chosen for development and eventual evaluation by regulatory officials.

96. While characteristics measured by plant breeders are not conducted for risk/safety assessment purposes, they form part of the knowledge base for risk/safety assessments for both food and the environment. They provide background information and the assurance that there are no obvious, unanticipated phenotypes associated with the new variety. The role of the risk/safety assessor is to build on this information, to identify specific risks especially with respect to the environment which may not have been fully assessed by the breeder, and to further assess the safety of the crop, by identifying risks in relation to the introduced trait.

C.1.2. Micro-organisms

97. Genetically modified micro-organisms that are used to produce food-related enzymes or used in food itself are typically grown in containment vessels (or fermentors) in which the primary concern is keeping the organism free from contamination with other micro-organisms. Food safety assessors need to be sure that the resulting product is safe to eat. However, environmental risk/safety assessors need to be sure that there are no potential hazards associated with the release of such organisms from containment. On the other hand the industrial fermentation micro-organisms are usually poorly adapted to environmental survival and a long history and experience of safe use of micro-organisms should be recognised.

D. RISK MANAGEMENT – TECHNICAL APPROACHES

98. The OECD report, *Safety Considerations for Biotechnology: Scale-up of Crop Plants* (1993) is a detailed examination of how the concepts of risk/safety assessment and risk management can be applied to transgenic plants. The report describes the relationship between risk identification and risk management, and identifies and discusses risk considerations for transgenic crops. Many of the concepts that the report deals with also apply to transgenic micro-organisms.

99. Risk management refers to the way methods are applied in order to minimise those potential hazards or adverse effects which have been identified during a scientifically based risk assessment. It does not encompass additional factors such as socio-economic values, or ethical issues, which may be part of the overall decision making process (see chapter II.A.). Management actions should be based on, and in proportion to, the results of the risk assessment.

100. Depending upon the case, farm-scale experiments may identify the need for risk mitigation measures as part of risk management related to the use of genetically engineered organisms. Farm-scale experiments may provide additional information to laboratory and small-scale field trials and therefore may contribute to increasing knowledge and experience (for example see Farm Scale Evaluations in the UK in Annex 1).

101. The practices used to manage hazards or adverse effects identified in a risk/safety assessment may be:

- Confinement - The use of biological, chemical, physical, spatial, environmental, temporal or other isolation conditions to provide barriers to minimise the dissemination and impacts of organisms or the genetic material outside the area of application.

- Restricted use - Geographic or physical restriction may be placed on the transgenic organism. For example, a restriction could be placed on a micro-organism such that it could only be used in a contained industrial setting, e.g. production of the enzyme rennin, used in making cheese, in large-scale fermentation systems. Alternatively, restrictions could be placed on where a crop plant could be grown; for example, the US EPA does not allow Bt-cotton to be grown in Florida or Hawaii as wild/feral relatives of cotton grow in these states.

- Monitoring – [see section E]

- Guidance, technical support, advice - may be provided to users (such as farmers) on the best practices for using these products. Often this is provided by companies, but in certain cases may be part of governmental management programmes, or may be based on a partnership between government and companies.

- Record keeping - In some countries, the use of documentation is an important part of a technical approach to managing risks. This might include records kept by the manufacturer or seller, and if appropriate, these might be available for other uses later in the distribution chain.

102. The following paragraphs are examples of risk management procedures which have been applied to certain categories of transgenic crops. Some of the considerations are also relevant to transgenic micro-organisms.

D.1. Insect resistance management

103. It has been long known that populations of insect pests develop resistance to control agents, such as pesticides. Strategies to delay or avoid the development of insect resistance to important genetic resources, such as the Bt *delta*-endotoxins, have been developed. The elements of a successful programme to manage the development of resistance includes monitoring, the collection of data on the biology and behaviour of the insect(s) pest, farmer education programmes, remedial plans should resistant pest populations be detected, the establishment and management of refugia by growers, and the use of appropriate doses of the GM trait. Also restricted expression (e.g. by use of vegetation period or tissue specific or of wound induced promotors) may reduce the risk of resistance development. Resistance management programmes are currently being, developed and applied in the USA, Australia and the EU.

D.2. Weediness

104. Weeds are plants that grow where humans do not want them to grow. This includes volunteer plants, crop plants remaining from the previous year's growing season, either through over wintering or by seed set. Volunteers of transgenic crops can present an agronomic problem when not properly controlled. Growers need to be especially careful to avoid the inadvertent gene stacking that can arise either by planting the same crop bearing different traits in subsequent years, or by planting crops bearing different traits close enough together that pollen flow can occur. As an example, planting canola with glyphosate herbicide tolerance in year one, followed by canola with imidazolonone herbicide tolerance in year two, can result in the appearance of canola volunteer plants bearing both herbicide tolerance traits, if gene flow is allowed to occur between the current years crop and the previous years volunteers. The presence of multiple herbicide tolerant volunteer plants may reduce the agronomic control strategies that growers can use for this type of weed. Growers need to be encouraged to apply sound agronomic practices including weed control and crop rotation. For some transgenic plants, it is important to consider whether a “wild” relative of a transgenic plant could acquire the GM trait through cross-pollination. The question is whether the wild relative could become a weed if the acquired GM trait endowed it with an ability to escape an environmental constraint, such as herbivore damage. In making this evaluation, it should be noted that “weediness” is a constellation of biological traits. It depends on the existence of a selection pressure, and would not necessarily result from a wild relative acquiring a single trait from a transgenic plant.

105. In considering potential for transfer of a trait to wild relatives, possible management procedures are taken into account. These include pollen barriers, separation distances and removal of flowers. There is also the potential for developing transgenic crops where cross-pollination is unlikely to occur by, for example, using male sterility traits or chloroplast transformation.

D.3. New viruses or new viral diseases of plants

106. Like other organisms, plant species are susceptible to infection by viruses. Modern biotechnology applied to viral disease control has been developed in which a component of the virus, normally a gene for viral coat proteins (VCP), is engineered into a crop plant to prevent the virus from infecting the plant. The risk considerations are: a) whether the VCP from the modified crop plant could be acquired by wild relatives and lead to their increased viral resistance and weediness; b) whether new viral strains may emerge through process such as recombination, transcapsidation and synergy; and c) whether changes in host range may evolve by recombination.

107. Should a potential for weediness be identified, it can be managed through methods described above. Several studies, including a Consensus Document prepared by the Working Group entitled, *Consensus Document on General Information Concerning the Biosafety of Crop Plants Made Virus Resistant through Coat Protein Gene-Mediated Protection* (OECD, 1996a), have concluded that the potential for new viral diseases to arise through use of this technology is extremely low.

D.4. Use of antibiotic resistance traits as selection markers in GM plants

108. The development of pathogen resistance to antibiotics has become a growing problem world-wide and has major implications for human health. Environmental reservoirs of pathogens resistant to antibiotics are created mainly through the misuse of antibiotics in animal feed, in

veterinary science or human healthcare. To effectively deal with the development of antibiotic resistance in pathogen populations, those items must be addressed.

109. Certain antibiotics have been used as screening agents to create and select genetically engineered organisms, such as transgenic plant varieties. Although there is no evidence that the use of antibiotic resistance traits in transgenic plants contributes to the development of resistant pathogen populations, their use has been criticised as potentially adding to the problem where alternative solutions could be devised. The use of antibiotic resistant marker genes within transgenic plants is one of the important points which are discussed, in some countries, in connection with risk assessment and precaution. It is difficult to distinguish the relative risks associated with these various practices and this may not always be appropriately reflected in public discussion. Issues associated with the use of antibiotic resistance markers have been detailed in a US FDA guidance document (1997), in an opinion by the Scientific Steering Committee on Antimicrobial Resistance (European Commission, 1999), and on the Belgian Biosafety Server (http://biosafety.ihe.be/ARGMO/ARGMOmenu.html).

110. To address these concerns and as a matter of precaution, alternatives to antibiotic resistance traits are currently assessed as to their feasibility to reduce experimental dependence on their use as selective markers, for example, the use of secondary selection markers (e.g. green fluorescent protein). The alternatives also need to be subject to a risk assessment and compared with the risks of antibiotic resistance markers. Other technologies may allow for the elimination of antibiotic resistant markers from the transgenic plant. For plants, other resistance traits, such as resistance to herbicides, may be used instead of resistance to antibiotics.

E. MONITORING ENVIRONMENTAL EFFECTS OF GENETICALLY MODIFIED (GM) PRODUCTS

111. Monitoring is a specific risk management measure which has been an important aspect of small field releases (OECD, 1992). Some Member countries have undertaken extended programmes to assess the long-term risk from releases of GM crops into the environment. However, it is a topic where there is a need for a greater understanding of the different priorities and practices of Member countries. The paragraphs below exemplify the range of factors which may be taken into account by Member countries in monitoring programmes, though the actual requirements will vary from case to case.

112. The monitoring of genetically engineered organisms in the environment may be undertaken following an experimental release or commercial use to identify either a) a predicted effect, or b) unforeseen effects, following an experimental release or commercial use. Specific monitoring is designed to detect effects predicted in the risk/safety assessment. General monitoring attempts to detect unpredicted effects.

113. If undertaken in a statistically valid way, monitoring broadens the knowledge base for future risk/safety assessment. However, the usefulness of the programme must be weighed against the costs and size of the programme, the importance of the crop as well as the potential risks to the environment. Monitoring can be a feasible safety measure when experience with a genetically engineered organism is lacking or the possibility of unknown adverse effects exists. Some countries also believe that it is an important precautionary measure. In addition to testing the conclusions of a risk assessment, specific monitoring can serve as an early warning system to alert risk/safety assessors that counter-measures against adverse effects should be implemented. Three essential

aspects of specific environmental monitoring are: (1) what to look for; (2) how to look for it, and (3) how to implement a monitoring programme.

E.1. What to look for

114. For specific monitoring what to look for is limited by what we know. Thus, we can specifically monitor effects based on the knowledge from a risk assessment. Because, by definition, general monitoring is to detect effects we have not foreseen, developing a general monitoring system is much more difficult than developing a specific monitoring system. If by general monitoring an unexpected effect is detected, the possibility that factors other than the genetically engineered organism have caused the effect must also be taken into consideration. However, since our ability to develop specific monitoring is limited by what we know, general monitoring is an important complement to specific monitoring.

E.2. How to look for it

115. Having identified a potential impact, the next challenge is to devise a monitoring system to detect it. Specific monitoring on the behaviour of transgenic plants requires a whole range of statistical and ecological tools. Basic considerations for successful monitoring include the quality and selection of methods and parameters, as well as a continuous flow of information. The data must be relevant, comparable, reliable and representative. Generally, the following considerations must be taken into account in developing a monitoring programme: a) establishing the "baseline"; b) choosing the number and location of sampling sites; c) developing a timetable for sampling; d) developing a standard approach to collecting/handling specimens; e) developing, standardising and validating testing conditions; and f) duration of monitoring. Because of the complexity of environmental monitoring, expertise from a number of scientific disciplines - e.g., ecology, entomology, and plant breeding – are likely to be involved in developing a monitoring programme, depending on the identified effect and the monitoring plan. To illustrate each of the above considerations, a brief description of how these considerations might be taken into account in creating a system to monitor for insect resistance and/or weediness is provided below.

(a) Establishing the baseline

116. In order to observe any change in the behaviour of a population of organisms, a "baseline" must be established. That is, the facet of the environment most likely to be affected must be described prior to the introduction of a genetically engineered organism. This baseline usually includes the environment containing the unmodified organism. The behaviour of the environment subsequent to introduction of the genetically engineered organism can then be measured against the "baseline" description. For monitoring of insect resistance to a pesticide, for example, the susceptibility of the moth populations to the toxin over large areas/different insect populations prior to planting large acreage of transgenic crops has to be obtained. For weediness, knowledge of the frequency of appearance of the weed or wild relative in the various areas where concerns might arise must exist or be developed. Knowledge of whether the crop can hybridise with the wild relative is also important, as is knowledge of the species forming the surrounding plant communities prior to introduction of the genetically engineered organism. Preliminary data from studies which, for whatever reasons, may not fulfil all necessary criteria for scientific evidence may nevertheless be useful to indicate possible adverse effects.

(b) Choosing the number and location of sampling sites

117. Where to sample, and how many sites to sample, to give an accurate picture are important considerations. The greater the number of sampling sites, the more likely one is to obtain early indications of changes and its potential adverse effects in the environment due to a genetically engineered organism, but the higher the cost. For example, for most of the weediness concerns, observations on the number of weeds or wild relatives, where they are found, and their relationship to other plants in the community, need to be performed in a statistically valid manner. The selection of the site for monitoring can be critically important.

(c) Developing a timetable for sampling

118. When to sample is an important consideration. For example, in developing a monitoring system for the emergence of resistance in pest insect populations, one must consider that some insect pests can have several generations per season (summer). Others have only one or two.

(d) Developing a standard approach to collecting/handling specimens

119. A standardised approach is essential to obtaining specimens that will give statistically significant results. With most pest moth species, for example, young caterpillars (early instars) are more sensitive to toxins, and therefore are preferable for use in the bioassays on insect resistance. Individuals collecting specimens must be able to successfully identify and collect only young caterpillars.

(e) Developing, standardising and validating testing conditions

120. A standardised set of testing conditions is also a key element. Subsequent to collection, the caterpillars must be handled in standardised conditions, which will optimise their responses in the testing situation. Accurate detection methods must be used. Also, development of a discriminating dose assay is an important feature for some types of monitoring (e.g., early detection of the emergence of resistance in pest insect populations), it is not for others (e.g., weediness).

(f) Duration of monitoring

121. Decisions must be made on how long one should monitor, since it may take a number of years for a problem to become apparent. A case in point is the time (ca. 15-20 years) it took between the introduction of a weed, *Bromus techtorum*, in the US Pacific Northwest, and the time it was seen as a major weed in the US.

122. Monitoring, in addition to detecting problems, makes scientific data available for future risk assessments, especially regarding long-term effects. It also provides feedback on whether the risk assessment is appropriate to the real situation (SRU, 1998).

E.3. How to implement a monitoring system

123. Several options for the implementation of environmental monitoring of GM products are described, which are not mutually exclusive.

(a) Reporting adverse effects

124. This requires that individuals using or associated with a genetically engineered organism product (e.g. manufacturers, distributors, farmers, governmental technical services) to report adverse effects that they suspect are caused by a genetically engineered organism. The advantages of such provisions are that they are relatively cheap. The disadvantages are that the monitoring agency may receive reports of effects that are unrelated to the genetically engineered organism, and guidance on what to report may be difficult to draft, even counterproductive, if the intent is the ability to identify unforeseen events.

(b) Voluntary plans

125. This option entails funding and developing a voluntary monitoring system.

(c) Mandatory plans

126. For mandatory plans, governments must have the authority to require that users as a group or as individuals provide the Agency information to address identified issues.

(d) “Planned” research activities

127. Research activities such as “farm-scale” evaluations, funded by the government or other groups, of the impact of GM crop plants on farmland, wildlife and others may be useful in monitoring the environmental effects of the GM plants within an agricultural setting. Collaboration between researchers and developers can lend credibility to such activities.

(e) International co-ordination

128. To reduce costs and to integrate experience and efficiency, existing activities like environmental monitoring programmes, agricultural, human health and environment surveys could be used in developing monitoring programmes (SRU, 1998). Based on the existing activities, a network/programme for general monitoring could be developed. Electronic databases on product approvals and risk assessment information, such as OECD’s BioTrack Online already exist, and the newly agreed Biosafety Protocol makes provision for development of the Clearing House mechanism.

F. DEALING WITH UNCERTAINTY AND THE USE OF PRECAUTION

129. In dealing with complex biological systems, some scientific uncertainty will always occur. As noted above, uncertainty is taken into account by risk assessors and risk managers. If in a given situation, the degree of uncertainty as to the risk presented by a hazard proves difficult to determine scientifically, many countries believe it is appropriate to take *precaution*. The Commission of the EC, for example, has advanced its understanding of precaution as meaning that preventive action may be taken although an identified possible hazard cannot be strictly linked to the activity (Commission of the EC 2000). This issue is still under debate and there is, as yet, no international consensus on what *precaution* is and when and how it should be applied in the risk analysis of genetically engineered organisms. To resolve this, it is clear that there should be a continuing discussion on this topic.

130. A number of other Intergovernmental Organisations have also been involved in efforts to describe how to deal with scientific uncertainty. In recent years, a number of international instruments have addressed the issue of *precaution*. To date, there are a variety of approaches. The relationship between the precautionary approach and sound science is also a matter of current debate. A listing of

examples in which some aspect of a precautionary approach is addressed is found in a number of conventions and international documents in which “measures”, “approaches”, “principles”, and “actions” are cited in relation to precaution (see References to Precaution).

131. The term, *precautionary approach*, described in Principle 15 of the 1992 Rio Declaration on Environment and Development, represents an approach to dealing with scientific uncertainty and the weight of evidence when addressing threats to the environment. Principle 15 states that “In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.” The precautionary approach is reaffirmed in the Preamble and Article 1 of the Cartagena Protocol on Biosafety (adopted on 29 January 2000 in Montreal) to the 1992 UN Convention on Biological Diversity, which refers to the “precautionary approach contained in Principle 15 of the Rio Declaration.”

132. The Protocol states that “lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate, with regard to the import of the living modified organism in question” (Article 10.6). It recognises that “trade and environment agreements should be mutually supportive with a view to achieving sustainable development” (Preamble) and emphasises that the Protocol shall not be interpreted as implying a change in the rights and obligations of a Party under any existing international agreements” (Preamble). The Protocol includes also articles on risk assessment (Article 15 and Annex III) and risk management (Article 16). The Working Group acknowledges the general principles and the points to consider in risk assessments as outlined in Annex III of the Protocol.

133. Article 5.7 of the Agreement on Sanitary and Phytosanitary Measures under the World Trade Organization also addresses uncertainty. That article states that “in cases where relevant scientific evidence is insufficient, a Member may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent information, including that from the relevant international organisations as well as from sanitary or phytosanitary measures applied by other Members. In such circumstances, Members shall seek to obtain the additional information necessary for a more objective assessment of risk and review the sanitary and phytosanitary measure accordingly within a reasonable period of time.”

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ANNEX 1:

NATIONAL AND REGIONAL EXPERIENCES

THE RELATIONSHIP BETWEEN FOOD SAFETY AND ENVIRONMENTAL SAFETY IN THE EUROPEAN UNION

134. Regarding food safety and environmental safety, there are two main regulations in the EU covering safety assessment of genetically modified organisms. The Regulation (EC) No 258/97 [1)] (Novel Foods Regulation) applies to the placing on the market within the European Union foods and food ingredients that have not been previously used for human consumption. The Directive 90/220/EEC [2)] relates to the protection of humans and the environment should genetically modified organisms be released into the environment either for experimental purposes or as commercial products.

135. One goal of the Novel Foods Regulation was to allow the implementation of the "one door, one key" principle in safety assessment [3)]. Category (a) of Article 1 (2) of the Regulation covers food and food ingredients containing or consisting of genetically modified organisms as described by Directive 90/220/EEC. Article 9 (2) lays down that in this case the decision of authorisation shall respect the environmental safety requirements of Directive 90/220/EEC to ensure that all appropriate measures are taken to prevent the adverse effects on human health and the environment. The information submitted under the Regulation (EC) No 258/97 should include information on experimental releases carried out under part B of Directive 90/220 or, where appropriate, the consent authorising the placing on the market provided in part C of Directive 90/220.

136. Following the implementation of the Novel Foods Regulation, all foods and food ingredients which contain or consist of genetically modified organisms and which on the date of its coming into force have not been used for human consumption, require an authorisation granted under the Novel Foods Regulation before marketing. This implies that, even if a product containing or consisting of a GMO that has been submitted under part C of Directive 90/220/EEC and has been granted consent, it may not be placed on the market as a food or food ingredient until it is authorised under the Novel Foods Regulation.

137. The Novel Foods Regulation does not cover feed uses. Therefore, the environmental and human health assessment linked to the marketing of products containing or consisting of GMOs and intended for feed uses falls under Directive 90/220/EEC. This implies that a product containing or

consisting of GMOs which is to be placed on the market for both food and feed uses, will have to be assessed under both the Regulation (EC) No 258/97 and Directive 90/220/EEC.

138. The Novel Foods Regulation does not cover the placing on the market of seeds destined for cultivation. Therefore, the environmental and human health assessment linked to the placing on the market of genetically modified seeds for cultivation purposes falls under Directive 90/220/EEC, even in those cases where the products of the cultivation of the crops are going to be used exclusively for food. However, the assessment linked to the placing on the market of foods and food ingredients containing or consisting of GMOs resulting from the cultivation of those seeds, will be carried out under the Novel Foods Regulation.

139. One aspect discussed in relation to food safety is the possible content of GMOs in conventional food and the relation to labelling requirements. In the EU, products which contain more than 1% GMO have to be labelled. The aspect of unintended contamination with GMO is of special interest regarding organic food production. In most of the member states, environmental aspects are also addressed as issues of public concern.

140. Based on experiences gained on the risk assessment of the release of genetically modified organisms into the environment carried out according to the requirements of the Directive 90/220/EEC [1)] and the first [2)] and second [3)] adaptation of this Directive, the Environment Council, on 25 June 1999, reached a ‘political agreement’ to adopt a common position on the Commission Proposal to amend Directive 90/220/EEC. The Common Position was adopted on 9 December 1999 and the second reading was completed in Parliament on 12 April 2000. The new regulatory system will not, however, be fully implemented for eighteen months after final adoption.

141. The Directive deals with the experimental releases of GMOs in Part B and the placing on the Community market in Part C. Part B refers to deliberate releases for any other purpose than for placing on the market which are limited to individual member states. Before any of the procedures leading to first consent, an environmental risk assessment has to be carried out in accordance with the precautionary principle. This requirement is specified in Annex II (Principles for the environmental risk assessment) and Annex VI (Guidelines for the assessment report). Whilst only one national competent authority is responsible for granting a consent for the standard procedure according Part B, all competent authorities are involved in the standard procedure regarding the placing on the market according Part C. All decisions follow a standardised regulatory procedure. For placing on the market consent is given only when possible objections have been clarified either on national or on European level. Consent is given for a maximum of 10 years. Monitoring is obligatory. Labelling is required. It must be stated clearly that “this product contains genetically modified organisms”. According to Annex IV A.7 the notifier should provide information on the genetic modification for the purposes of placing on one or several registers modifications in organisms, which can be used for the detection and identification of particular GMO products to facilitate post-marketing control and inspection. A safeguard clause is included, where a member state has the possibility to restrict or prohibit provisionally the use and/or sale of a GMO or the product on its territory. This decision can be made as a result of additional information made available since the date of the consent and affecting the environmental risk assessment in the way that this GMO as or in a product constitutes a risk to human health or the environment.

142. Further harmonisation, standardisation, transparency and flow of information have been key issues for the amendment of the Directive 90/220/EEC.

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THE EXPERIENCE OF NORWAY

143. Norway is a special case. The Norwegian Act relating to the production and use of genetically modified organisms (Gene Technology Act) covers all uses of GMOs, whether they are going to be used as food or not. The purpose of the Act is to ensure that production and use of genetically modified organisms take place in an ethically and socially justifiable way, in accordance with the principle of sustainable development and without detrimental effects on health and the environment. According to one of the sections of the Act concerning approval it is required that:

- Deliberate release of genetically modified organisms may only be approved when there is no risk of detrimental effects on health or the environment. In deciding whether or not to grant approval to the applicant, significant emphasis shall also be placed on whether the deliberate release represents a benefit to the community and a contribution to sustainable development.

FARM-SCALE EVALUATIONS IN THE UNITED KINGDOM

144. The UK has taken a proactive approach to improving the assessment of longer-term risks from releases of GM crops into the environment. The farm-scale evaluation programme is designed to see what effects, if any, the management of herbicide tolerant GM crops will have on farmland wildlife. The results will help inform the Government's decision on whether to allow unrestricted commercial cultivation of GM crops in the UK.

145. The concern has been raised that commercial planting of genetically modified herbicide tolerant crops will lead to changes in agricultural practice which could be harmful to farmland wildlife. The UK Government and the plant breeding industry, through the industry body SCIMAC (Supply Chain Initiative on Modified Agricultural Crops), agreed that the first farm-scale plantings of the GM crops closest to approval for general cultivation in the UK – herbicide tolerant oil seed rape, beet (sugar and fodder) and fodder maize – would be the subject of a scientific investigation into their impact on farmland wildlife. These 'farm-scale evaluations' are to test the environmental safety of the GM crops.

146. The research is being funded by the UK Government and carried out by independent contractors. The progress of the research is overseen by a steering committee of scientific experts from our statutory nature conservation organisation English Nature, environmental non-Governmental organisations (including the Royal Society for the Protection of Birds), and academia. The Scientific Steering Committee is independent from Government, the biotechnology industry and the contractors. The purpose of the committee is to ensure that the research carried out by the contractors is of the highest scientific standards.

147. During 1999, GM oil seed rape and GM fodder maize were planted in the spring and GM winter oil seed rape was planted in the autumn. The basic design adopted is to have farms on which a GM crop and a non-GM equivalent (the same crop species, of an equivalent variety, but not genetically modified) are grown. The abundance and diversity of wildlife in the two crops is then compared. Methods of assessing biodiversity were developed during the 1999 season, and focus on species groups indicative of longer-term change, and of change higher up the food chain. Monitoring is carried out on vegetation in and around the field, the soil seed bank, slugs and snails, and insects (e.g. butterflies, beetles and bees) and other invertebrates. The results will be extrapolated to assess the effects on mammals and birds.

148. The Scientific Steering Committee reported at the end of the first year that the methodology of the farm scale evaluations was scientifically robust, and gave a firm base from which to proceed to full-scale trials in 2000. They advised that to give a satisfactory statistical base for the evaluations, there should be 25 fields (paired comparisons) of each GM crop each year for three years, with results expected after harvest of the crops planted in 2002.

149. In November 1999, a renewed agreement between Government and the industry body SCIMAC on the conduct of the farm scale evaluations was reached, to cover the three years through to harvest of crops planted in 2002. Key points of the agreement include:

- No general unrestricted cultivation of GM crops in the UK until the farm-scale evaluations are complete; no direct commercial benefits will be sought from these plantings by the consent holders.

- Plantings for the farm-scale evaluations are limited to 20-25 fields per crop per year subject to the advice and requirements on the independent Scientific Steering Committee.
- Proposals for any other field scale plantings of these crops will be decided by the Scientific Steering Committee taking into account the relevance of the proposals to biodiversity.
- None of the produce from GM crop plantings in the UK will be used in a way which is of direct commercial benefit to the consent-holders during farm-scale evaluation period.

The spirit of these conditions is to protect the farm-scale evaluations as being concerned with biodiversity research and not creeping commercialisation.

150. Maximum use is being made of the farm-scale evaluations by using them for further research purposes over and above the ecological research. Additional research on gene flow has been included because the split-field design (half GMO crop, half non-GMO equivalent) allows the depth of cross-pollination into the non-GMO half to be readily assessed. This will be used to test the assumptions made in the original risk assessment regarding the likelihood and extent of gene flow from the GM crops.

151. The locations of the trials are made public before sowing, and all results of the farm-scale evaluations will be made publicly available, including interim and progress reports – the first was published in November 1999. The expectation is that following harvest of the crops planted in 2002, the Scientific Steering Committee will have enough data to judge the impact of the cultivation of the GM crops on the environment: commercialisation of these crops in the UK is dependent on the outcome.

152. Further details may be obtained through the UK Department of the Environment, Transport and the Regions web site at: http://www.environment.detr.gov.uk/fse/index.htm.

ANNEX 2:

COMPARISON OF THE SCIENTIFIC ISSUES ADDRESSED IN NATIONAL RISK/SAFETY ASSESSMENT SYSTEMS

This annex shows the results of a study undertaken for this report. It identifies the key environment, human health and agricultural issues addressed by risk/safety assessors from a number of OECD Member countries. These key issues are addressed when undertaking environmental risk/safety assessments.

AUSTRALIA

A) KEY SCIENTIFIC ISSUES ADDRESSED

Environment Issues

- Establishment and competitiveness of the GMO in Australian ecosystems
- Transfer of the inserted genes to other organisms
- Effects on non-target organisms

Human Health Issues

- Pathogenicity of the GMO, compared with unmodified organism
- Nature of inserted genes, especially with regard to oncogenic potential or toxicity of expressed proteins
- Host-range of the GMO

Agriculture Issues

- Potential adverse effects resulting from the GMO itself or from gene transfer from the GMO to other species (e.g. increased weediness, reduced ability to control weeds)

- Development of resistance in non-target organisms
- Potential for adverse effects due to changes in agricultural practice

Other Issues

- Characterisation of the GMO in terms of the genetic modification and its phenotypic effects
- Biology and ecology of the parent organism
- Potential for gene transfer to other organisms

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

- Case-by-case assessment
- Stepwise procedure
- Requirement for high-quality data
- Partial containment of GMOs being used in field trials
- Open, transparent and accountable decisions.
- Monitoring for adverse effects

C) DESCRIPTION OF THE DECISION MAKING PROCEDURES

The Australian Government announced in May 1999 that it would establish an Office of the Gene Technology Regulator and associated legislative framework for genetically modified organisms. This Office will be fully operational by January 2001. In the interim period, applications for research, field trials and deliberate releases are overseen by the Genetic Manipulation Advisory Committee which is housed within the Interim Office of the Gene Technology Regulator within the Commonwealth Department of Health and Aged Care.

AUSTRIA

A) KEY SCIENTIFIC ISSUES ADDRESSED

Environment Issues

- dissemination of the GMO and the inserted genes, genetic stability
- establishment and competitiveness of the GMO in ecosystems, centres of genetic diversity of the recipient organism

- effects on non-target organisms and the food web

Human Health Issues

- molecular genetic characterisation of the GMO
- expression of gene products, toxicity, allergenicity, genetic stability
- antibiotic resistance genes

Agriculture Issues

- potential for adverse effects due to agricultural practice
- potential for multiple herbicide resistant crops/weeds
- development of resistance of target - organisms

Other issues

- feeding experiments
- potential for horizontal gene transfer to micro-organisms
- monitoring

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

Case-by-case approach, precautionary principle, futurity principle (restrictions must be proportionate), step-by-step principle (for deliberate releases), democratic principle (involving the public), ethical principle (responsibility for animals, plants and ecosystems). The state of science and technology is used as a reference for assessment and safety measures.

C) DESCRIPTION OF THE DECISION MAKING PROCEDURES

In case of applications for deliberate release, the competent authority is either the Federal Ministry of Education, Science and Culture (for applications from University Institutes) or the Federal Ministry of Social Security and Generations (for all other applications).

- A copy is sent to the Federal Ministry of Agriculture, Forestry, Environment and Water Management / Federal Environment Agency comments to the competent authority.

- The Scientific Subcommittee on deliberate release and placing on the market of the Austrian Advisory Committee on Genetic Engineering provides scientific advice to the competent authority, and

- A public hearing has to be held after informing the public of the application, allowing for public scrutiny and comments to be made to the competent authority.

On the basis of these inputs a decision has to be taken by the competent authority.

In case of applications for placing on the market, the competent authority is the Ministry of Social Security and Generations, which consults with several other ministries (Education, Science and Culture, Environment, Agriculture, Economy and Labour) before taking a position within the European Union procedure.

CANADA

CANADIAN FOOD INSPECTION AGENCY

A) KEY SCIENTIFIC ISSUES ADDRESSED:

The Canadian Food Inspection Agency (CFIA) is responsible for the regulation of plants, animal feeds and animal feed ingredients, fertilizers and veterinary biologics, including those derived through biotechnology. The CFIA assesses plants with novel traits for their potential risk of adverse environmental effects, authorizes and oversees import permits, confined trials, unconfined release and variety registration.

Environmental Issues

The (CFIA) regulates the confined field trial evaluation of all plants with novel traits. Conditions prescribed by the CFIA are designed to minimize the possibility of adverse environmental impact. Regulatory criteria include: measures to prevent the transfer of pollen to other plants, inspection by CFIA staff and post-harvest land use restrictions.

Environmental risk assessment of plants with novel traits for unconfined environmental release considers the biology of the plant, its impact on the environment and on biodiversity, the possibility of gene flow and impact on non-target organisms. Agricultural issues are also taken into account, such as any potential changes in agricultural practices and the effect on sustainable agriculture.

Human Health Issues

Health Canada is responsible for assessing the human health safety of products derived through biotechnology including foods, drugs, cosmetics, medical devices and pest control products. In the case of novel foods, each safety assessment considers the process used to develop the novel food, its characteristics compared to those of its traditional counterpart, its nutritional quality, the potential presence of any toxicants or anti-nutrients, and the potential allergenicity of any proteins introduced into the food.

Other Issues

The CFIA's assessment also addresses information on the method by which a novel plant is produced, a complete description of any introduced genes and regulatory elements, their source and function.

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT:

Assessments are made on a case by case basis. All decisions on the suitability of novel plants for release are science-based and dependant on the safety of the novel plant in the environment.

C) DESCRIPTION OF THE DECISION MAKING PROCESS:

The environmental release of plants with novel traits is regulated by the Seeds Act and the livestock feed use regulated by the Feeds Act. Some crops are also subject to variety registration, based on merit, before they can be approved for full commercialization.

Health Canada is responsible for an assessment of the human food use of novel crops under the authority of the Food and Drugs Act.

Only when products are deemed as safe as their traditional counterparts are they approved for commercialization. Decision documents describing the assessment and its results are published by the CFIA and Health Canada and are available to the public.

DENMARK

A) KEY SCIENTIFIC ISSUES ADDRESSED

Environment Issues

- Possible dispersal of the inserted gene(s) through pollen or seed to non-agricultural ecosystems.
- Possible establishment in non-agricultural ecosystems
- Possible adverse effects on non-target organisms

Human Health Issues

- Complete and documented information of the inserted gene construction and resulting new products.

- Comparative studies, including screening for key toxicants (key adverse compounds) and key nutrients (key preferable compounds) in the host plant.
- Assessment of the new products by a combination of acute toxicity study and the digestibility in simulated mammalian gastric conditions.

Agriculture Issues

- Possible adverse effects to the agricultural environment caused by the genetically modified plant itself.
- Possible adverse effects to the agricultural environment caused by dispersal of pollen from the genetically modified plant to other crops or to related weedy species.
- Feed aspects, i.e. the possibility that adverse effects occur as a result of the use of the genetically modified plant or parts thereof as feed for animals. Data requirements include analysis of chemical composition, acute toxicity studies and results of feeding trials with target animals.

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

A precautionary approach in evaluation of the completeness and the quality of all data presented. Application of a case-by-case principle and respecting a step-wise procedure. Use of the familiarity concept.

C) DESCRIPTION OF THE DECISION MAKING PROCEDURES

Experimental releases

The competent authority is the National Forest and Nature Agency.

Experts from the National Forest and Nature Agency (environment), the National Plant Directorate (agriculture) and the National Food Directorate (health) examine the notifications.

A summary of the notifications is sent to app. 50 organisations, research institutes etc.

Based on information from experts and the hearing procedure, the National Forest and Nature Agency writes a recommendation which is sent to the Minister of Environment and Energy. The Minister forwards the recommendation to the Environmental and Region Planning Committee in the Danish Parliament before he sends the final approval to the notifier.

Approval for placing on the market in EU

The competent authority and expert procedures are the same as for experimental releases.

The recommendation is sent to the Special Committee on Environmental Questions. After governmental confirmation, the Minister for Environment and Energy forwards the recommendation to the Environmental and Regional Planning Committee and European Affairs of the Danish

Parliament. Finally, the National Forest and Nature Agency sends the Danish position to the Commission.

GERMANY

A) KEY SCIENTIFIC ISSUES ADDRESSED

General Issues

– complete characterisation of the genetic modification (e.g. inserted gene construct (including marker genes), resulting products, gene transfer and identification methods.

Environment Issues

– possibility and consequences of survival and dissemination of the transgenic organism, gene transfer, effects on non-target organisms on biodiversity, soil, geophysical processes, etc.

Health Issues

– compositional analysis and comparison to a conventional counterpart (e.g. micro- and macronutrients, toxicants, anti-nutritional substances)

– toxicological requirements based on a case-by-case decision depending on the comparability to the conventional counterpart (especially studies regarding toxicity, digestibility, allergenicity)

Agriculture Issues

– possibilities and consequences of outcrossing to compatible wild species or to neighbouring fields, e.g. concerning herbicide resistance genes, change of host/pathogen relationships, weediness, (competitiveness, persistence of seeds, persistence of volunteers), tolerance to abiotic factors

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

– Precautionary principal, case-by-case approach, appropriate confinement measures to minimise spread of the organisms and genes, monitoring.

KOREA

A) KEY SCIENTIFIC ISSUES ADDRESSED

Environment Issues

- Precautionary principle
- Adverse effect on biological diversity
- Ecological toxicity including hazardous identification for non target organisms

Human Health Issues

- Identification (detection) methods to distinguish GM food from non-GM food
- Safety assessment methodology
- Approved level of protection

Agriculture Issues

- Identification of a GM organism
- Effects on other agricultural ecosystems

Other Issues

- pathogenesis of GMO itself

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

Implementation of Biosafety Protocol.

C) DESCRIPTION OF THE DECISION MAKING PROCEDURES

There is no regulatory framework for decision making so far

NORWAY

A) KEY SCIENTIFIC ISSUES ADDRESSED

Environment Issues

- Possible adverse effects on the environment, including non-target organisms
- Possible dispersal of genes from the GMO to the environment
- Possible change in farming practices, especially concerning use of pesticides

Agriculture Issues

- Possible adverse effects on the environment caused by changed use of pesticides as a consequence of use of GMO, included development of "super weeds"
- Possible adverse effects for animals caused by use of GMO or parts thereof as feed
- Possible adverse effects to the agricultural environment caused by dispersal of pollen from the GMO to other crops or to related weedy species.

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

- Precautionary approach
- Case-by-case principle
- To make sure that the production and use of genetically modified organisms takes place in an ethically and socially justifiable way, in accordance with the principle of sustainable development

C) DESCRIPTION OF THE DECISION MAKING PROCEDURE

The experimental releases

The competent authority is the Ministry of Environment.

The Ministry of Environment sends a copy of the notification to other relevant ministries, such as the Ministry of Agriculture, the Ministry of Health and Social Affairs, the Ministry of Fisheries and the Norwegian Biotechnology Advisory Board.

Experts from the Directorate for Nature Management examine the notification.

If necessary, the Directorate for Nature Management consults with the Norwegian Agricultural Inspection Service and the Norwegian Food Control Authority to examine the notification as well.

If necessary, the Directorate for Nature Management sends a summery of the notifications to different organisations, research institutes etc.

Based on information from experts and the hearing procedure, the Directorate for Nature Management writes a recommendation to the Ministry of Environment. On the basis of these inputs, a decision has to be taken by the Food Control Authority.

Approval for placing on the market in the EU.

The competent authority and experts procedures are as described for experimental releases.

The Ministry of Environment consults with other relevant authorities, for instance the Ministry of Agriculture and the Ministry of Health and Social Affairs. Finally, the Ministry of Environment sends the Norwegian position to the Commission.

UNITED STATES

UNITED STATES - ENVIRONMENTAL PROTECTION AGENCY

The US Environmental Protection Agency uses three laws to regulate GM products: two laws addressing pesticides, and a third addressing GM products in uses other than foods, drugs, cosmetics and pesticides. Currently, most GM products being submitted to the EPA for review are pesticides including novel microbial pesticide. Because pesticides are intended to be disruptive for some organism (i.e., the pest), an important component in evaluating the potential for adverse effects associated with a pesticide is the way in which the pesticide acts on the target pest. A pesticide that acts directly on the target pest through a toxic mechanism of action might also exert a similar effect on other organisms. Before EPA permits a pesticide to be used in the US, it must be shown that use of the pesticide will not cause an unreasonable adverse effect to the environment. To determine whether a GM product could cause such an effect, EPA reviews information on product characterisation, toxicology, non-target effects, exposure and environmental fate and small scale releases.

A) KEY SCIENTIFIC ISSUES ADDRESSED

Environment Issues

- Effect of pesticidal substance on non-targets expected to be exposed in terms of toxicity
- Any history of prior environmental exposure or potential for altered exposure

- Whether gene transfer from crop plant to a wild relative is possible in the US, particularly if a trait has known non-target toxicity

Human Health Issues

- Demonstrated lack of toxicity/allergenicity to humans and animals, especially considering any history of prior human or animal exposure
- For pesticides that are proteins, acute oral toxicity, in vitro digestibility, amino acid homology to known toxins/allergens and biochemical characterisation
- Tests must be done with the pure pesticidal substance, not a whole food

Agriculture Issues

- For GM products based on the Bt delta-endotoxin, these products must be effective at controlling pests but the possibility of insects developing resistance to the Bt must be controlled
- Potential of a GM crop or a wild relative acquiring the introduced trait through outcrossing to become a noxious weed
- Potential for cross-pollination between GM crops and other crops and GM crops and wild or weedy relatives

Other Issues

- Source and nature of the newly introduced trait (one of the most important pieces of information)
- Biology of the plant with the new trait, including whether the plant has wild relatives growing near enough to the plant with the new trait for hybridisation to occur (one of the most important pieces of information)
- Potential for new exposures to other organisms in the environment of the introduced trait, through movement of the gene or movement of the pesticidal substance in the environment from the plant

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

- Ensuring that a GM product does not enter the food/feed chain prior to EPA review and approval
- Potential for pesticidal substance to persist and move in all environmental media (e.g. soil, water, air)

C) DESCRIPTION OF THE DECISION MAKING PROCEDURES

In general in the US the regulatory process for a pesticide involves three steps: (a) a preconsultation between EPA staff and a prospective applicant in which data necessary to obtain a testing permit (termed an "Experimental Use Permit" or EUP) and data that should be generated during EUP testing for submission to the Agency for review for product registration, is identified and discussed; (b) review of data for the EUP; and (c) review of data for product registration. Field tests during an EUP, like those done under an APHIS permit, are usually required to be done with strict containment measures to reduce environmental and human health concerns.

Data requirements are tiered, with the first tier of tests being done at a maximum hazard dose. Data on pesticidal substance expression levels and fate in the environment are also done. If adverse effects are seen in these first tier tests, the next tests are done to address possible effects due to the real exposure in the field.

For an EUP, issues such as containment and potential human dietary exposure and whether the crop or part of the crop tested is used as food or feed, are important considerations. In general, data gathered in the field during EUP testing provide the information needed for the next step, review to determine whether a product can be registered for use in the US. The law allows the EPA 120 days to make a determination on issuance of an EUP.

For registration, it typically takes a year for the EPA to review a package and reach a decision once the Agency receives a “complete” information package for the product. A complete data package (a dossier) typically includes information describing the GM crop (nature and source of the introduced trait, biology and ecology of the crop receiving the new trait), data/information on the human and environmental toxicology of the pesticidal substance, data on tissue expression of the pesticidal substance and environmental fate of the pesticidal substance and the trait itself (if wild or weedy species are present in the US). Also, evaluations include insect resistance management and exposure issues such as non-target effects and food consumption.

UNITED STATES - DEPARTMENT OF AGRICULTURE APHIS

The US Department of Agriculture has the responsibility to protect American agriculture from plant and animal health risks. As such, it has promulgated a set of codified rules governing the safe introduction of certain genetically modified organisms under the authority of the Federal Plant Pest Act and the Plant Quarantine Act. These regulations, codified in Title 7 of the Code of Federal Regulations (CFR), Part 340, provide procedures for obtaining a permit or for providing notification prior to "introducing" a regulated article. Regulated articles are considered to be organisms and products altered or produced through genetic engineering that are plant pests or for which there is reason to believe are plant pests. Introduction refers to any importation into or interstate movement through the United States, or release into the US environment outside an area of physical confinement. This system allows for field testing to be safely conducted while information is gathered about the characteristics of the regulated article and its safety to plants and the human environment relative to traditional organisms. Once this information is obtained, the regulations provide that an applicant can petition APHIS for a determination of non-regulated status for a product. APHIS reviews documentation provided by the applicant and other scientific information to assess the likelihood of whether the regulated article poses a greater plant pest risk or significant impact on the human environment than its traditional counterpart. Nonregulated status can be granted when an organism does not directly or indirectly cause disease or damage to plant, plant parts, or processed products of plants. Once this determination has been made, the product (and its offspring) no longer requires APHIS approval under these regulations for such introductions.

A) KEY SCIENTIFIC ISSUES ADDRESSED

Environment Issues

- Is the transgenic organism itself, or gene introgression from the transgenic organism into sexually compatible relatives, likely to have a more significant impact on non-target organisms compared to its traditional counterpart? In particular, will it be more harmful to beneficial organisms (such as pollinators, or parasites or predators of plant pests, biological control organisms, symbiotic soil micro-organisms, or nutrient recyclers) or threatened or endangered species?
- Will the transgenic organism be invasive outside of agriculture or have an adverse impact on plant resources?
- Will the transgenic organism likely lead to significant changes in agricultural practices? For example, consider changes in pest control, tillage practices, fertilisation, irrigation, or use of marginal lands or different habitats.

Human Health Issues

- Compared to the non-transgenic organism, has genetic engineering intentionally or indirectly lead to the expression, accumulation, or secretion of a toxin, allergen, or other product that is known to affect health of animals or humans? Consider the nature of the gene product and affected metabolic pathways, homology to known toxins or allergens, potential routes of exposure, and history and impacts of any prior exposure to animals and humans.
- Does the transformed plant or its product have unacceptably higher levels of naturally expressed toxicants that are routinely evaluated during development of similar varieties to ensure safety to humans or animals (e.g. gossypol in cotton)?
- Will use of the transgenic organism result in changes in agricultural practices or management of the environment in ways that pose more risks to human health than practices used with the non-transgenic counterpart?

Agriculture Issues

- Do the introduced genetic material (genes and regulatory sequences), or their products or vectors used for the transformation, pose a plant pest risk? Do they directly or indirectly cause disease, damage or injury to plants or parts thereof, or any processed, manufactured, or other products of plants. Similarly, will the transgenic plant or organism cause disease, damage, harm or injury to raw or processed agricultural commodities? Consider the disease or insect susceptibility of the transgenic plant; the plant pathogenic nature of the transgenic material, vectors, and donor organisms; and familiarity with similar traits.
- Is the transgenic plant more likely than the non-transgenic counterpart to become a weed or increase the weediness potential of sexually compatible relatives?

- Is the use of the transgenic plant or organism in agriculture likely to lead to a significant impact in the ability to control plant pests (weeds, insects, diseases)?

Other Issues

- What are the molecular genetic and phenotypic differences between the transgenic organism and its non-transgenic counterpart?
- Biology and taxonomy of the transgenic plant and the potential for genes from the transgenic plant to introgress into wild relatives.
- The distribution of wild relatives and their proximity to areas of production for the transgenic plant.

B) OTHER ISSUES IMPORTANT TO THE ASSESSMENT

Ensuring that appropriate containment or mitigation measures are in place during field testing and transport of the regulated article to prevent the transgenic material or its offspring from persisting in the environment and posing a plant pest risk or significant impact to the environment.

C) DESCRIPTION OF THE DECISION MAKING PROCEDURES

For permits or notifications, APHIS considers the type of modification, plant pest components used, the experimental design and the release environment, methods for biological containment, harvest and the final destruction of the plant material to ensure that there would be no significant plant pest risk or impact to the human environment from the controlled release. The States in which the introductions occur are notified and provided with an opportunity to concur with the APHIS decision, and place any additional restrictions on the introduction. Field data reports are required and are used to support petitions for non-regulated status.

The regulations at 7 CFR Part 340.6 and the APHIS Guide to Preparing and Submitting a Petition describe the process and the type of information that should be submitted to support a petition for non-regulated status. Petitions are reviewed for technical completeness, usually within 30 days. If there are deficiencies, a letter is sent to the petitioner requesting additional information or clarification. The petitioner then usually submits an amendment to address the concerns. Once satisfied, APHIS publishes a public notice seeking comment on the petition and makes copies available to the public. During this time, APHIS prepares an Environmental Assessment (EA) in accordance with the National Environmental Policy Act to address the potential for significant impact to the human environment from a determination of non-regulated status and the alternatives. Comments are reviewed and addressed in an APHIS Determination Document (the response drafted to the company regarding the plant pest status). The EA and Determination Document are made available to the public. To reach a determination of non-regulated status, it must be determined that the new variety:

- Does not exhibit any plant pathogenic properties;
- Is no more likely to become a weed than the non-engineered parent plant;
- Is not likely to increase the weediness of any sexually compatible plants;
- Will not cause damage to raw or processed agricultural commodities;

– Is unlikely to harm other organisms that are beneficial to agriculture.

ANNEX 3: LIST OF PARTICIPANTS IN THE WORKING GROUP ON HARMONIZATION OF REGULATORY OVERSIGHT IN BIOTECHNOLOGY

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