Introduction to the biosafety consensus documents

About the OECD's Working Group for biosafety

The OECD's Working Group on Harmonisation of Regulatory Oversight in Biotechnology (the "Working Group") comprises delegates from the 34 member countries of the OECD and the European Commission. Typically, delegates are from those government ministries and agencies which have responsibility for the environmental risk/safety assessment of products of modern biotechnology. The Working Group also includes a number of observer delegations and invited experts who participate in its work, such as Argentina, the Russian Federation, the United Nations Environment Programme (UNEP), the Secretariat of the Convention on Biological Diversity (SCBD), the Food and Agriculture Organization of the United Nations (FAO), the United Nations Industrial Development Organisation (UNIDO) and the Business and Industry Advisory Committee to the OECD (BIAC).

In recent years, with the increasing use of biotech products in many regions of the world, together with the development of activities relating to tropical and subtropical species, participation was enlarged to other non-member economies including Brazil, Bangladesh, the People's Republic of China, Colombia, India, Indonesia, Kenya, Moldova, Paraguay, the Philippines and South Africa, as well as the African Biosafety Network of Expertise from the New Partnership for Africa's Development, a body from the African Union (AU-NEPAD-ABNE). From July 2011 to December 2014, a programme was jointly implemented by the World Bank, the ILSI Research Foundation – Center for Environmental Risk Assessment (ILSI-CERA) and the OECD in the framework of the "Partnership for Biosafety Risk Assessment and Regulation", which developed new links, enhanced collaboration and supported the participation of four non-member economies in the activities of the Working Group.

Regulatory harmonisation

The Working Group was established in 1995[1] at a time when the first commercial transgenic crops were being considered for regulatory approval in a number of OECD member countries. From the beginning, one of the group's primary goals was to promote international regulatory harmonisation in biotechnology among members. Regulatory harmonisation is the attempt to ensure that the information used in risk/safety assessments, as well as the methods used to collect such information, is 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 countries, which avoids duplication, saves on scarce resources and increases the efficiency of the risk/safety assessment process. This, in turn, improves safety while reducing unnecessary barriers to trade (OECD, 2000).

The need for harmonisation activities at the OECD

The establishment of the Working Group and its programme of work followed a detailed analysis by member countries of whether there was a need to continue work on harmonisation in biotechnology at the OECD, and if so, what it should entail. This analysis was undertaken by the Ad Hoc Group for Environmental Aspects of Biotechnology (established by the Joint Meeting),[2] in 1994 mainly.

The Ad Hoc Group for Environmental Aspects of Biotechnology took into consideration, and built upon, the earlier work at the OECD which began in the mid-1980s. Initially, these OECD activities focused on the environmental and agricultural implications of field trials of transgenic organisms, but this was soon followed by a consideration of their large-scale use and commercialisation. (A summary of this extensive body of work is found in the annex to this introduction.)

Key background concepts and principles

The Ad Hoc Group for Environmental Aspects of Biotechnology took into account previous work on risk analysis that is summarised in *Safety Considerations for Biotechnology: Scale-up of Crop Plants* (OECD, 1993a). The following quote gives the flavour: "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." This body of work has formed the basis for environmental risk/safety assessment that is now globally accepted. In considering the possibilities for harmonisation, the Ad Hoc Group paid attention to these characteristics and the information used by risk/safety assessors to address them.

This was reinforced by the concept of familiarity, also elaborated in the above-mentioned document (OECD, 1993a). This concept "is based on the fact that most genetically engineered organisms are developed from organisms such as crop plants whose biology is well understood... Familiarity allows the risk assessor to draw on previous knowledge and experience with the introduction of plants and micro-organisms into the environment." For plants, familiarity takes account of a wide-range of attributes including, for example, knowledge and experience with "the crop plant, including its flowering/reproductive characteristics, ecological requirements, and past breeding experiences" (OECD, 1993a – see also the annex for a more detailed description). This illustrates the role of information related to the biology of the host organism as a part of an environmental risk/safety assessment.

The Ad Hoc Group for Environmental Aspects of Biotechnology also considered the document *Traditional Crop Breeding Practices: An Historical Review to Serve as a Baseline for Assessing the Role of Modern Biotechnology* (OECD, 1993b), which focuses on host organisms. It presents information on an initial group of 17 different crop plants, which are used (or are likely to be used) in modern biotechnology. It includes sections on phytosanitary considerations in the movement of germplasm and on current uses of these crop plants. There is also a detailed section on current breeding practices.

A common approach to risk/safety assessment

An important aspect for the Ad Hoc Group for Environmental Aspects of Biotechnology was to identify the extent to which member countries address the same questions and issues during risk/safety assessment. Big differences would mean

difficulties in working towards harmonisation, while a high level of similarity would suggest it is more feasible.

This point was resolved by two studies considered by the Ad Hoc Group: one covered crop plants (OECD, 1995a; 1995b) while the other concerned micro-organisms (OECD, 1995c; 1995d). Both studies involved a survey with national authorities responsible for risk/safety assessment. The aim was to identify the questions they address during the assessment process (as outlined in national laws/regulations/guidance texts) in order to establish the extent of similarity among national authorities. The studies used the information provided in the OECD's "Blue Book" on Recombinant DNA Safety Considerations (OECD, 1986) as a reference point, in particular, the sections covering: 1) general scientific considerations; 2) human health considerations; and 3) environmental and agricultural considerations (Appendices B, C and D). Both studies showed a remarkably high degree of similarity among countries in the questions/issues addressed in risk/safety assessment.

The emergence of the concept of consensus documents

The Working Group was therefore established in the knowledge that national authorities have much in common in terms of the questions/issues addressed when undertaking risk/safety assessment. It also took into account those characteristics identified as part of the assessment (i.e. the organism, the introduced trait and the environment) around which harmonisation activities could focus.

It was further recognised that much of the information used in risk/safety assessment relating to the biology of host organisms (crop plants, trees, animals or micro-organisms) would be similar or virtually the same in all assessments involving the same organism. In other words, the questions addressed during risk/safety assessment which relate to the biology of the organism, for example the potential for gene transfer within the crop plant species, and among related species, as well as the potential for weediness remain the same for each application involving the same host species. This also applies to some extent to information related to introduced traits.

Consequently, the Working Group evolved the idea of compiling information common to the risk/safety assessment of a number of transgenic products, and decided to focus on two specific categories: the biology of the host species and traits used in genetic modifications. The aim was to encourage information sharing and prevent duplication of effort among countries by avoiding the need to address the same common issues in applications involving the same organism or trait. It was recognised that biology and trait consensus documents could be agreed upon relatively quickly by member countries (within a few years). This compilation process was quickly formalised in the drafting of consensus documents.

The purpose of consensus documents

The consensus documents are not intended to be a substitute for a risk/safety assessment, because they address only a part of the necessary information. Nevertheless, they should make an important contribution to environmental risk/safety assessment.

Consensus documents are intended to be a "snapshot" of current information, for use during the regulatory assessment of products of biotechnology. They are not intended to be a comprehensive source of information covering the full knowledge about a specific

host organism or trait; but they address – on a consensual basis – the key or core set of issues that countries believe to be relevant to risk/safety assessment.

The aim of the documents is to share information on these key components of an environmental safety review in order to prevent duplication of effort among countries. The documents are envisaged to be used: 1) by applicants as information to be given in applications to regulatory authorities; 2) by regulators as a general guide and reference source in their reviews; and 3) by governments for information sharing, research reference and public information.

Originally, it was said that the information in the consensus documents is intended to be mutually recognised or mutually acceptable among OECD member countries, though the precise meaning of these terms is still open for discussion. During the period of the Ad Hoc Group for Environmental Aspects of Biotechnology and the early days of the Working Group (1993-95), the phrase "mutual acceptance of data" was discussed. This concept, borrowed from OECD's Chemicals Programme, involves OECD Council decisions that have legally binding implications for member countries. In the case of the consensus documents, there has never been a legally binding commitment to use the information they contain, though the Working Group is interested in enhancing the commitment of countries to make use of the documents. Participation in the development of documents, and the intention by countries to use the information, is done in "good faith." It is expected, therefore, that reference will be made to relevant consensus documents during risk/safety assessments. As these documents are publicly available tools, they can be of interest for any country wishing to use them in national assessments.

The process through which consensus documents are initiated and brought to publication

There are a number of steps in the drafting of a specific consensus document. The first step occurs when a delegation, in a formal meeting of the Working Group, makes a proposal to draft a document on a new topic, typically a crop species or a trait. If the Working Group agrees to the proposal, a provisional draft is prepared by either a single country or two or more countries working together ("lead country approach"). Typically, the lead country(ies) has had experience with the concerned crop or trait and is able to draw on experts to prepare a provisional draft.

The provisional draft is first reviewed by the Bureau of the Working Group[3] to ensure that it addresses the range of issues normally covered by consensus documents and is of sufficiently high quality to merit consideration by the Working Group as a whole.

Based on the comments of the Bureau, a first draft is prepared for consideration by the full Working Group. This is the opportunity for each delegation to review the text and provide comments based on their national experiences. Inputs are incorporated in a second draft, which is again circulated to the Working Group. At this point, the Working Group may be asked to recommend that the document be declassified. Such a recommendation is only forthcoming when all delegations have come to a consensus that the document is complete and ready for publication. Sometimes, however, the text may need a third or even more discussions in the Working Group before a declassification can be contemplated.

When the Working Group has agreed to recommend a document for declassification, it is forwarded to the supervisory committee – the Joint Meeting – which is invited to declassify the document. Following the agreement of the Joint Meeting, the document is then published.

It is important to note that the review of consensus documents is not limited to formal meetings of the Working Group. Much discussion also occurs through electronic means, especially via the protected website dedicated to the Working Group. This enables a range of experts to have input into drafts.

For a number of documents, it has also been necessary to include information from non-member countries. This wider share of expertise has become increasingly important in recent years with the development of activities relating to tropical and subtropical species. This has been particularly true in the case of crop plants where the centre of origin and diversity occurs in a non-member country(ies). In these cases, UNEP, UNIDO and the FAO have assisted in the preparation of documents by identifying experts from concerned countries. For example, this occurred with the consensus document on the biology of *Oryza sativa* (rice) published in 1999.

The full series of consensus documents developed by the Working Group is also published in compendium documents, as it is the case for these volumes 5 and 6 issued in 2016. Previous volumes 3 and 4 were published in 2010 (covering 2007-10), while volumes 1 and 2 were issued in 2006 (covering1996-2006) (OECD, 2010b; 2010c; 2006a; 2006b).

Current and future trends in the Working Group

The Working Group continues its work on the preparation of specific consensus documents, and on the efficiency of the process by which they are developed. An increasingly large number of crops and other host species (trees, animals, micro-organisms) are being modified, for an increasing number of traits, and the Working Group aims to fulfil the current needs and be prepared for emerging topics.

At the OECD Workshop on Consensus Documents and Future Work in Harmonisation, held in Washington, DC in October 2003, the Working Group considered how to set priorities for drafting future consensus documents among the large number of possibilities. The workshop also recognised that published consensus documents may be in need of review and updating from time to time, to ensure that they include the most recent information. The Working Group considers these aspects on a regular basis when planning future work. For the preparation of future documents, the workshop identified the usefulness of developing a standardised structure of consensus documents. The Working Group contemplated to develop, firstly, a guidance document on "Points to consider" for consensus documents on the biology of cultivated plants that was published in 2006, and then that of the trait documents. The "Points to consider' document, included in Volumes 3 and 4 of the compendia series, is currently under review by the Working Group to update it with the latest developments.

Within the important ongoing activities of the Working Group, a new document is being developed on the "Environmental considerations for the risk/safety assessment for the release of transgenic plants". Focused on the core of the biosafety work that is applied to crops and trees, and taking into account the most recent views from countries of all regions of the world, this document will constitute a key guidance tool for developers, assessors and regulatory authorities. It is expected to be published around 2017.

Other projects are implemented to prepare consensus documents on the biology of animals, to date on the Atlantic salmon (*Salmo salar*), and on the mosquito *Aedes aegypti*, for which some genetically engineered strains are used since 2014 in limited areas to control the virus-vector insect population and participate in the fight against the tropical

diseases such as dengue fever and chikungunia that have been dramatically extending in many regions of the world over the last decade.

The Working Group is also considering projects on micro-organisms, therefore opening to new areas, for instance, bioenergy, with the preparation of a document on eukaryotic micro-algae having started recently. The photosynthetic cyanobacteria are potential providers of renewable energy and are of special interest as they can be cultivated year round on non-arable land, alleviating the pressure on farmland and freshwater resources that would be exerted by crops grown for biofuel purposes, as stated in the proceedings of the OECD Conference on Biosafety and the Environmental Uses of Micro-Organisms set up by the Working Group in 2012 (OECD, 2015a). Other biotechnology developments applied to micro-organisms might be considered to prepare future documents: updated review of biofertilizer organisms living in symbiosis in crop roots and optimising the nitrogen fixation, or biocontrol agents acting as plant protection products to control disease and attack by insects and other herbivores. Other exploratory fields may comprise bioremediation by using living organisms for removing contaminants from the environment such as polluted land, or the development of detergents containing micro-organisms.

In recent years, the Working Group started to exchange knowledge and promote discussion on the new plant-breeding techniques and their potential impact of risk/safety assessment. An OECD workshop was organised on these matters by the Working Group in 2014, and the report will be published soon.

The OECD Task Force for the Safety of Novel Foods and Feeds

The OECD Task Force for the Safety of Novel Foods and Feeds ("Task Force"), established in 1999, addresses aspects of the assessment of human food and animal feed derived from genetically engineered crops. As with the Working Group, the main focus of the Task Force work is to ensure that the types of information used in risk/safety assessment, as well as the methods to collect such information, are as similar as possible amongst countries. The approach is to compare transgenic crops and derived products with similar conventional ones that are already known and considered safe because of recognised experience in their use. Harmonised methods and the sharing of information are facilitated through the Task Force's activities.

Similarly to the biosafety programme, the main outcome of the foods and feeds programme is the set of consensus documents on compositional considerations of new varieties of specific crops. The Task Force documents compile a common base of scientific information on the major components of crop plants, such as key nutrients, toxicants, anti-nutrients and allergens. These documents constitute practical tools for regulators and risk/safety assessors dealing with these new varieties, with respect to foods and feeds. To date, 26 consensus documents have been published on major crops and on general considerations for facilitating harmonisation. They constitute the Series on the Safety of Novel Foods and Feeds which is also available on the OECD's website (*www.oecd.org/env/ehs/biotrack*).

The full series of consensus documents developed by the Task Force was published in 2015 in two compendium documents, Volume 1 covering 2002-08 and Volume 2 covering 2009-14 (OECD, 2015b; 2015c).

The Working Group and the Task Force are implementing closely related and complementary programmes, focused on environmental aspects for the first and on food and feed aspects for the second. Their co-operation on issues of common interest resulted

in the first document developed jointly by the two bodies, the "Consensus document on molecular characterisation of plants derived from modern biotechnology", published in 2010 (included in Volume 3 of the current series).

Notes

1. The original title of the Working Group was the "Expert Group for the Harmonisation of Regulatory Oversight in Biotechnology". It became an OECD working group in 1998.
2. The Joint Meeting was the supervisory body of the Ad Hoc Group for Environmental Aspects of Biotechnology and, as a result of its findings, established the Working Group as a subsidiary body. Today, its full title is the Joint Meeting of the Chemicals Committee and the Working Party on Chemical, Pesticides and Biotechnology.
3. The Bureau comprises the Chair and Vice-Chairs of the Working Group. The Bureau is elected by the Working Group once per year. At the time of preparing this publication – Volumes 5 and 6 – the Chair is from the United States, and the Vice-Chairs from Australia, Belgium, Finland, Japan and Mexico.

Annex: OECD biosafety principles and concepts developed prior to the Working Group on Harmonisation of Regulatory Oversight in Biotechnology (1986-94)

Since the mid-1980s the OECD has been developing harmonised approaches to the risk/safety assessment of products of modern biotechnology. Prior to the establishment of the Working Group on Harmonisation of Regulatory Oversight in Biotechnology, the OECD published a number of 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. This annex notes some of the highlights of these achievements that were background considerations in the establishment of the Working Group and its development of consensus documents.

Underlying scientific principles

In 1986, the OECD published its first safety considerations for genetically engineered organisms (OECD, 1986). These included the issues relevant to human health, the environment and agriculture that 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. And,
- Encourage further research to improve the prediction, evaluation, and monitoring of the outcome of applications of recombinant DNA organisms."

The role of confinement in small-scale testing

In 1992, OECD published its *Good Developmental Principles* (OECD, 1992) for the design of small-scale field research involving transgenic plants and micro-organisms. This document 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).

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

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 transgenic plants. The OECD published general principles for scale-up (OECD, 1993a), which reaffirmed 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, 1993a).

The role of familiarity in risk/safety assessment

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.

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 (US-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 (US-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, 1993a). 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.

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 following (OECD, 1993a):

- "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."

Risk/safety assessment and risk management

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 effect 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, 1993a). 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 (OECD, 2000).

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