Current and Future Trends in Harmonization in Europe and Internationally

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Abstract

In the European Community (EC), harmonization of approaches to safety was achieved by two legally binding directives, adopted in 1990. Since their adoption, the experience gained with both the contained use of genetically modified microorganisms and the deliberate release of genetically modified organisms has led to considerable advances in the regulatory framework, including a recent proposal for amendment of the contained use directive, the adoption of reduced information requirements and a first simplified procedure in the EC for plant R & D releases, and the development of consensus documents in the OECD. The ability to identify low risk applications will enhance the trend towards increasing differentiation of regulatory requirements.

The need for harmonized approaches to safety at the international level is urgent as GMO products are starting to be traded internationally. The adoption of the UNEP International Technical Guidelines for Safety in Biotechnology represents a major step forward in establishing an international biosafety framework. Together with UNEP's capacity-building program, the decision by the second Conference of the Parties to the Convention on Biological Diversity to develop a biosafety protocol, and other international and regional activities, this framework will play a key role in the development and uptake of biotechnology applications.

Modern biotechnology is an enabling technology across a very wide spectrum of sectors, from the production of pharmaceuticals and foods, to the use of organisms in the environment for clean-up. For this reason it is a key technology of the present and of the future. The trade in products developed using modern biotechnology, an increasing number of which contain living organisms such as seeds, will be on a world scale. Against that backdrop, it is clear that any controls should as far as possible be based on a harmonized approach in order to avoid the creation of trade barriers. But the first question to be asked is why controls are needed at all.

There has been wide recognition that the use of genetic modification techniques does not necessarily produce organisms that will pose risks to humans or the environment. Indeed, in most cases when only a small number of known and specific traits are inserted, the resulting organism will behave predominantly in the same way as the organism from which it is derived. Nonetheless, some degree of caution is appropriate because the introduced trait or genetic material could produce a significant change in behavior and because organisms introduced into different environments sometimes behave differently. The approach taken in most countries which have put controls

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into place has been to assess the risk of damage to human health or the environment and to decide on the measures that are necessary to reduce the risks to a low or negligible level.

There has been a clear trend in the type and scale of applications of modern biotechnology. The 1970s and 1980s saw the development from small scale contained uses to large and commercial scale uses. From the mid-1980s, we have had small scale releases of GMOs into the environment and now commercialization of GMO products which are intended to be used in the environment.

The regulatory controls adopted by the European Community in 1990 reflected this trend and the consequent difference in experience about the way various GMOs behave in different circumstances. Two legally binding directives apply to biotechnology activities: the Contained Use of Genetically Modified Microorganisms, and the Deliberate Release into the Environment of Genetically Modified Organisms.

The Contained Use Directive requires that only a risk assessment be carried out for small-scale operations involving GMOs that do not pose any risk to humans or the environment. For larger scale and commercial operations of such GMOs, and small-scale uses of more hazardous organisms, prior notification to the competent authority is required. Large-scale commercial operations involving hazardous organisms require prior consent from the authority. This hierarchy of controls reflects the clear aim of the directive to provide maximum oversight for those operations considered to be most risky. We have seen two main consequences of this approach: firstly, safety is fully provided for, and secondly, industry and research have been encouraged to work with low risk applications. This is borne out by the numbers for the UK, and for the EC as a whole: there have been no accidents which have threatened to affect human health or the environment up till now, and of the estimated 20,000 projects undertaken at any one time in the UK, the percentage of low risk activities to the total is about 95%. In particular, in a large industrial scale there are no activities notified in the UK involving more hazardous organisms; all such activities involve low risk organisms.

As regards contained uses, the Community policy operates essentially at national level. There is little exchange of information between the competent authorities about individual activities, except when activities could be reasonably foreseen to affect another Member State as a result of an accident. Regular meetings of the authorities facilitate harmonized implementation of the directive throughout the Community.

Since the Contained Use Directive came into force, there has been a steep increase in the number of individual activities: As an indication, in the UK there has been a 170% increase in the numbers of notifications in the first half of this year as compared with a similar period in 1993. Experience in other EC countries has been similar. On this basis, in the White Paper on Growth, Competitiveness and Employment published in 1993, the European Commission proposed that it might be appropriate in the near future to consider amending the directive to take account of the experience gained, both in the EC and elsewhere. Accordingly, discussions are now taking place between the Member States of the Community and the Commission about a proposal to amend the

Contained Use Directive. The proposal incorporates the internationally adopted approach of 4 containment levels, it is more strictly risk-based and it adjusts the triggers for the different regulatory requirements to reflect the experience gained.

The directive on the deliberate release of GMOs into the environment reflects the limited experience that had been gained by 1990 because it establishes only a consent regime which applies to all releases and marketing of GMOs. Despite initial misgivings about the directive when it was adopted because research and industry considered it too onerous and prejudicial to biotechnology applications, the experience with implementation in the UK has been positive, particularly as regards R & D releases. There have now been over 500 R & D releases in the Community, and over 20% of these were conducted in the UK. The overwhelming majority of the releases has involved crop plants, mainly oilseed rape, potato, sugar beet and maize. The main modifications have included herbicide tolerance, improved quality and yield characteristics and male sterility for the production of hybrids.

This directive requires a detailed dossier to be submitted to the competent authority, which decides whether or not to issue a consent within 90 days. Every consent has conditions attached to it. The minimum condition, required by the directive, is that the notifier send a report of the release to the authorities. Other conditions, such as specific risk management measures, may also be attached to the consent. Like the contained use regime, decisions on research releases are taken entirely at national level, although early on in the 90 day period, a summary of the information about the release is sent to all other Member States. The summary is a means of information exchange between competent authorities. Further, it gives information about any potential spread of the GMO to the environment of other Member States ; these can comment to the competent authority reviewing the notification within 30 days. In the EC therefore, there is regional cooperation, but not regional decision-making, for research and development releases.

The extensive experience gained with the release of crop plants has resulted in reduced information requirements for notifications to release crop plants. It also enabled the UK and France to request, in 1994, to apply a simplified procedure to notify plant breeding programs in a single application. This procedure is now applied throughout the Community. In addition, the UK introduced a fast track procedure for releases considered to be of low risk to the UK environment by our statutory advisory committee, the Advisory Committee on Releases to the Environment. The key criteria for deciding whether a release is of low risk are susceptibility of the GMO to low temperatures, very low seed dispersal and the lack of hybridization with wild relatives. Notifications under the fast track are processed within 30 days, rather than the standard statutory 90-day period, but each proposed release is still thoroughly scrutinized and consent from the competent authority is still required. Here our experience has been similar to that with contained uses: the regulations assure safety and the fast track procedures encourage the industry to develop low risk GMOs and applications.

Whereas 15% of the R & D releases fell under fast track in 1994, the percentage had increased to 52% by mid-1996.

The competent authorities are now considering further simplified procedures, including notification only.

The Deliberate Release directive also establishes a single market for all products containing GMOs, except those that are appropriately covered by other Community product legislation, such as medicinal products for human and veterinary use. In other words, there is a gateway to the Community market via the competent authority in the Member State in which the product is first intended to be marketed. Recognizing that organisms can behave differently in different environments, the directive provides for all the Member States to review the dossier of the intended product and its safety. If any Member State objects to the proposed marketing, well defined committee and voting procedures come into play to decide on the notification. So far there have been 13 notifications to market in the Community. Seven of these have been reviewed favorably and the remainder have yet to be decided.

While the directive establishes a single regime for the marketing of GMO products which is harmonized throughout the Community, differences nonetheless exist between the Member States as regards their interpretation of the exact scope of the directive and the extent of the risk assessment required, and the labelling and monitoring that should be required in individual cases. These differences have led to considerable delays in the decision-making process which are causing concern both to potential producers in the EC and potential exporters to the Community. Considerable efforts are being made to overcome these difficulties, the goal being to achieve greater harmonization in the review of marketing dossiers and speedier approval procedures. The committee of competent authorities, and Member States and the Commission face an important challenge in the short term to improve the procedures, particularly to deal with the increasing number of product applications, and the approval of products in countries outside the European Community. Some products will be commodity crops and their downstream products, when once approved in a country, will be often mixed with non-modified crops and products. The policies adopted will need to take account of that fact. Further cooperation is needed to harmonize the level and type of information required for marketing dossiers and the approach to risk assessment. The mutual acceptability of data is of increasing importance, and is being developed by the competent authorities as well as by the OECD and in EC-US bilaterals.

Despite the differences within the Community, considerable harmonization was achieved with the coming into force of the directives. The controls, both for contained uses and for deliberate releases, are triggered when specified techniques have been used, usually to generate an organism which will produce large quantities of a particular product, such as the active ingredient of a pharmaceutical, or which will behave in a new way, such as to be tolerant to a specific herbicide. The EC approach is considered by some to be at odds with the approach taken in some other countries where

the triggers for the regulatory controls are different. One of the main reasons for the differences is that some countries have adopted existing product legislation, whereas others, such as the European Community, have put measures into place that apply to all organisms and products. However, while the triggers are seemingly different, the risk assessments and evaluations, and consequent risk management measures required, are in most cases very similar. Therefore, in countries with controls, the controls usually apply in some form or another to organisms with new traits which would be unlikely to occur in nature. This is not to say that looked at from a global perspective, there is full harmonization but that there is a high degree of concordance between countries and regions.

These basically similar approaches to the control of GMOs are reflected by two key events which took place at the end of 1995. Firstly, the second Conference of the Parties on the Convention on Biological Diversity decided to develop a biosafety protocol Secondly, the UNEP International Technical Guidelines for Safety in Biotechnology were adopted in Cairo.

The UNEP guidelines, which were first developed by the Netherlands and the UK, focus on organisms with novel traits. They set out relatively detailed approaches to risk assessment and risk management for contained uses and deliberate releases in addition to outlining mechanisms for control at the national, regional and international levels. The guidelines are already being used. Last year the UK and Argentina signed a bilateral arrangement to apply the guidelines. Taking up the capacity building aspects in the guidelines, UNEP has initiated a pilot scheme to put the guidelines into place in countries which as yet have limited experience.

The development of a biosafety protocol to the Convention on Biological Diversity is starting at the end of July in Denmark, the aim being to have completed a draft protocol by 1998. The protocol is to address the transboundary movement of living modified organisms resulting from modern biotechnology. The guidelines, which include technical issues, will provide a valuable interim measure until the protocol is in place and will also facilitate its implementation. Together, the protocol and the guidelines represent the key complementary components of the international framework for safety which will promote global harmonization.

Global harmonization is urgently needed as more and more countries come to use modern biotechnology and to trade in its products.

The reasons for seeking rapid harmonization at the regional and global level are clear. Nonetheless, the pace of scientific development and experience implies that international instruments must be sufficiently flexible to avoid burdens that are not necessary from the point of view of safety, and that would hinder the transfer of technology and extensive trading in biotechnology products. Most importantly, the international framework must build on experience and cooperation at the national and regional as well as the international level. International harmonization has already been achieved to a certain extent; now it is necessary to develop it further and to put it into practice. The challenge facing the international community is to put the frame

work and its implementation into place in a time frame that is compatible with the rate of developments in biotechnology.