Activities of the OECD group of national experts on safety in biotechnology

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For the last fifteen years the development of biotechnology has been at the center of a confused controversy on its potential risks, characterised largely by a lack of a sufficient understanding of scientific advances and by the difficulty of apprehending its interdisciplinary aspects. Biotechnology was certainly one of the first technologies to be subjected at a very early stage of its development to guidelines or regulations, such as those issued by the US National Institute of Health in 1976 and similar ones set up in other countries to control work with recombinant DNA organisms.

With the emergence of commercial applications in the early 80s, safety continued to be an issue of concern and questions were raised as to whether large scale applications implied different and/or additional risks. It is that time that the Organisation for Economic Cooperation and Development, undertook to launch, through its Committee for Scientific and Technology Policy (CSTP), an activity on biotechnology.

The Committe's work started in 1981. The first activity reviewed the dominant scientific and technological trends and pointed to the main policy problems, leading to the publication:

— Biotechnology-International trends and Perspectives, 1982.

Based on this, the Committee decided to carry out follow-up activities, two on urgent and specific policy issues (safety and patent protection), and two on more general policy areas (government policies in R&D and long-term economic impacts). Of those four, the safety issue was recognised to be of overriding importance and has thus become a continuous activity, with three major publications (Tab. 1):

— R-DNA Safety Considerations, 1986;

— Safety Considerations for Biotechnology — 1992; and

— Safety Evaluation of Foods Derived by Modern Biotechnology: Concepts and Principles, 1993;

— with several more publications (on crop plant issues) in preparation for 1994.

The remaining three activities were carried out sequentially. Each lasted from 2 to 3 years, leading to the following publications:

— Biotechnology and Patent Protection — an International Review, 1985;

— Biotechnology and the Changing Role of Government, 1988;

— Biotechnology — Economic and Wider Impacts, 1989.

With the completion of the follow-up activities, the Committee decided to examine biotechnology in more specific sectors, first in agriculture and food production, which led to the report:

— Biotechnology, Agriculture and Food, 1992 and currently in the environment.

Work on safety started with the completion of the preceding activity on trends and perspectives. An initial meeting of secretariat experts in December 1982 defined a number of principles, the first of which was about scientific rationale: "Guidelines, rules and regulations have to be based on the best available scientific knowledge, and they have to be sufficiently flexible to adapt to new knowledge". This simple postulate, uncontroversial for the scientific community and basic to all rational discussion, has been much argued about, and has politically not always been accepted.

As safety assurance came to dominate government policies with regard to biotechnology, it was reasonable that it also became an ongoing OECD activity, the centre-piece of OECD's biotechnology work. The Organisation thus responded to the public and government concern about genetic modification, in a political atmosphere marked by environmental movements which mirrored or reinforced those concerns.

OECD's work on biotechnology safety has become indispensable to member countries, for reasons which are different from those underlying the organisation's long-term involvement in nuclear safety and in the control of chemicals. These two OECD activities responded to a history of serious risk problems and accidents some of which endangered the environment or human health. In contrast, the biotechnology safety activity accompanied the very first developments of the new technology and even preceded them.

Biotechnology in the narrow sense, of recombinant DNA techniques has not known a single confirmed accident in all the 17 years since genetic engineering has been in operation; this was largely due to the great precautions taken early on but also to the fact that the technology is inherently less unsafe than many observers had feared. Thus, OECD's biotechnology safety work is part of a new and more sensitive policy and public awareness context than may have existed for earlier technologies.

The first sign of strong government involvement in the safety activity came in 1983, at a time when the applications of biotechnology began to take place outside contained laboratory conditions and when the first products were beginning to be commercialised. In that year, the Committee created an "Ad Hoc Group of National Experts on Safety and Regulations in Biotechnology". The Group had the main task of establishing scientific criteria for the safe use of genetically engineered organisms in industry, agriculture and the environment.

Approximately eighty experts, including representatives of scientific research, industry, government and regulatory bodies, as well as members of national r-DNA Committees, worked for three years under the Chairmanship of Dr. Roger Nourish from the UK to draft the report ***R-DNA Safety Considerations*** published in 1986, subsequently known as the "Blue Book".

The report devises general guidelines for the evaluation of large-scale use of r-DNA organisms and represents a major step forward in the history of biotechnology since the Asilomar conference in California (1975), where small-scale research guidelines were defined. It also constitutes a first step in the harmonization process of safety principles and practices among the member countries of the Organisation.

The OECD Council adapted in 1986 the recommendations of the report, which, though not formally binding, expressed a high degree of commitment by member countries to adapt the common scientific framework set out in the report.

The government representatives in the Group of National Experts come from a number of different government ministries and agencies which all have a direct interest in biotechnology safety: science and technology, environment, public health, agriculture and others. Thus, the main task, but also the chief difficulty, of the group is to reconcile the varying perspectives of these agencies and to promote an interdepartmental and interdisciplinary approach. The discussions of the Group have often reflected these differences, particularly between agencies for science and technology and for the environment. To facilitate dialogue, the OECD Environment Directorate, and through it the Environment Committee, has actively participated in these discussions and looks to the Group for help with policy analysis and programme coordination.

The Safety book makes three fundamental points which convey the general approach of the experts:

Any risks raised by r-DNA organisms are expected to be of the same nature as those associated with conventional organisms. Such risks may, furthermore, be assessed in generally the same way as non-recombinant DNA organisms.

Although r-DNA techniques may result in organisms with a combination of traits not observed in nature, they will often have inherently greater predictability compared to conventional methods of modifying organisms.

There is no scientific basis to justify specific legislation for r-DNA organisms.

On the basis of these general assumptions, a new concept was defined for the safe handling of industrial applications of low-risk r-DNA organisms. This concept advocates a minimum level of control, **"Good Industrial Large Scale Practice"** (GILSP), based on existing good industrial practices. A number of criteria were also set out which r-DNA organisms should meet in order to be assigned GILSP status and to be handled in conditions of Good Industrial Large Scale Practice.

The importance of the GILSP concept can hardly be over-estimated given that the vast majority of industrial applications have used intrinsically low-risk organisms. A specific recommendation was made for industry to utilise, wherever possible, such low-risk organisms in industrial applications of r-DNA techniques.

The approach of **R-DNA Safety Considerations** to the safety of agricultural and environmental applications was, of necessity, different at the time. The OECD experts felt that the safety assessment of organisms for agricultural and environmental applications was less developed than for industrial applications. General safety guidelines or criteria were, therefore, premature and a provisional case-by-case approach was recommended. They acknowledged, however, that considerable data was available on the environmental and human health effects of living organisms and that this should be used to guide risk assessment.

Thus, a largely encouraging expert view had replaced the concerns of the 1970s: the risks long associated with biotechnology remained purely conjectural.

OECD Member countries, as well as India and Latin American countries, adapted in their national safety guidelines or legislations the general OECD safety principles. These principles have often become a guide to the ministries and government departments sharing responsibility for biotechnology and have thus contributed to building up a common national, as well as international, approach.

As the safety books' flexible approach called for the adaptation of safety assessments to new knowledge, a revision was undertaken in 1988 by a follow-up "Group of National Experts on Safety in Biotechnology" (GNE).

This revision aimed at the elaboration of GILSP criteria and the identification of general safety principles for agricultural and environmental applications of plants and microorganisms (Tab. 2, 3, 4).

OECD principles and recommendations (Tab. 3, 4) were adapted in the guidelines and/or legislations of countries within and outside the OECD area. They have thus contributed to the international harmonisation of safety policies; this is particulary important when considering the inherently international character of biotechnology.

As the GILSP concept was relatively new, the GILSP criteria were elaborated to assist countries in their correct interpretation. The revision provides, for each criterion, an illustration of the nature of the different requirements and of the way these should be met.

The second major area of revision concerned the safety of the introduction of genetically modified organisms into the environment for agricultural or environmental purposes. The number of field tests performed since 1986, and the increasing number of those planned, led the OECD experts to define a set of **"Good Developmental Principles"** (GDP). These principles were to guide researchers in the design of small-scale field experiments with genetically modified plants and microorganisms. To date, more than 800 experiments, at more than 1100 sites, have been carried out in the world. New

knowledge and this experience enabled the development of GDP, judged to be premature in 1986.

GDP identifies three key safety factors: (Tab. 5, 6, 7, 8,) the characteristics of the organisms, the characteristics of the research site, and the use of apropriate experimental conditions. It also defines the different ways in which GDP can be met. Whilst existing national or international codes of good practice for the safe conduct of research address primarily human health and worker safety, GDP also takes into account environmental safety.

The revision has been published with the title ***Safety Considerations for Biotechnology — 1992***.

From 1991 on, the GNE has been continuing and broadening its activity to cover a number of areas, some of these new. Safety work in the Secretariat has been carried out in close co-operation by the Directorate for Science, Technology and Industry (DSTI) and the Environment Directorate, which are sharing the tasks. These areas are:

— Guiding principles for large scale releases of genetically modified organisms, extending to plants (completed), microorganisms (ongoing), and animals (planned).

This work has included the completion of general statements of safety principles for all modified organisms (the **"Preamble"** document), as well as specific work on crop plants, leading in particular to the production of the reports: ***Scientific Considerations Pertaining to the Environmental Safety of the Scale-up of Crop Plants Developed by Biotechnology, Historical Review of Traditional Crop Breeding Practices*** *and* ***Analysis of Field Release Experiments***. It also includes programmes biofertilisers, live vaccine, bioremediation/biomining, biopesticides, biofeeds.

— Safety assessment of food produced by biotechnology, from terrestrial and aquatic organisms (by the Environment Directorate in co-operation with DSTI).

Work focusing on terrestrial organisms has led to the publication ***Safety Evaluation of Foods Derived by Modern Biotechnology — Concepts Principles, 1993.***

This book has been timely. It came at critical moment, responding to the public concerns and discussions in some Member countries about new foods based on biotechnology. The book elaborates scientific principles to be considered in making evaluations of new foods or food components based on a comparison with foods that have a safe history of use. The most practical approach to determine the safety of foods derived by modern biotechnology is to consider whether they are "substantially equivalent" to analogous traditional food products. The case studies in this report illustrate the application of the concept of substantial equivalence. For new foods to which this concept is not applicable, further work is continuing.

— Reviews of monitoring methods for genetically modified organisms in the environment as well as a computerised pointer system for releases, leading to the annual publication on diskettes of the "BIOTRACK" pointer system (Environment Directorate).

Safety considerations of various kinds will remain crucial to the development of biotechnology for years to come. The OECD is likely to continue to play a role — perhaps a dominant one — in the discussion of such considerations and in the future elaboration and updating of safety principles.

OECD Member governments are discussing (summer 1993) the conditions and organisational details of the role the OECD may be asked to play, and particulary the future role of various OECD Committees. These now include not only the Committee for Scientific and Technological Policy, but also others which have more recently shown interest and activities in biotechnology, not least the Environmental Policy Committees (EPOC). The mandate of the Group of National Experts on Safety in Biotechnology is coming to an end in March 1994. A new mandate may reflect the broadening of public policy challenges of biotechnology, and related broadening of departmental interests.

There is today a general consensus that extreme safety concerns of the 70s were not justified and indeed, after many years of research and even production using recombinant organisms, the foreseen risks of biotechnology remain purely conjectural. However, as safety is an issue that will ultimately determine the acceptance and progress of biotechnology, it is important to continue to review this field as it develops and to ensure that due account is taken of the experience accumulated through the years and of the best scientific knowledge available. This approach should allow us to realize the many benefits of biotechnology while ensuring the protection of health and of the environment.

References

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Działania grup eksperckich OECD w zakresie bezpieczeństwa w biotechnologii

Streszczenie

Organizacja Ekonomicznej Współpracy i Rozwoju (OECD) podjęła działania w zakresie biotechnologii w 1981 r. Dotyczą one w szczególności analizy trendów rozwojowych, bezpieczeństwa pracy, ochrony własności intelektualnej oraz środowiska.

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biotechnology, OECD, safety.

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TABLE 1
OECD PUBLICATIONS ON BIOTECHNOLOGY

R-DNA SAFETY CONSIDERATIONS, 1986 SAFETY CONSIDERATIONS FOR BIOTECHNOLOGY, 1992 SAFETY EVALUATION OF FOODS DERIVED BY MODERN BIOTECHNOLOGY: Concepts and Principles, 1993
BIOTECHNOLOGY AND PATENT PROTECTION: An International Review, 1985 BIOTECHNOLOGY AND CHANGING ROLE OF GOVERNMENT, 1989 BIOTECHNOLOGY: Economic and Wider Impacts, 1989
BIOTECHNOLOGY: Agriculture and Food, 1992 BIOTECHNOLOGY FOR A CLEAN ENVIRONMENT, (completion planned in 1993)

TABLE 2
SUGGESTED CRITERIA FOR rDNA GILSP (GOOD INDUSTRIAL LARGE SCALE PRACTICE) MICROORGANISMS

Host Organism	rDNA Engineered Organism	Vector/Insert
Non-pathogenic	— Non-pathogenic	— Well characterised and free from known harmful sequences
No adventitious agents	— As safe in industrial setting as host organism, but with limited survival without adverse consequences in environment	— Limited in size as much as possible to the DNA required to perform the intended function; should not increase the stability of the construct in the environment (unless that is a requirement of the intended function)
Extended history of safe industrial use; OR		— Should be poorly mobilisable
Built-in environmental limitations permitting optimal growth in industrial setting but limited survival without adverse consequences in environment		— Should not transfer any resistance markers to microorganisms not known to acquire them naturally (if such acquisition could compromise use of drug to control disease agents)

TABLE 3

RECOMMENDATIONS SPECIFIC FOR INDUSTRY

EXCERPT FROM "RECOMBINANT DNA SAFETY CONSIDERATIONS", OECD, 1986

1. The large scale industrial application of recombinant DNA techniques should wherever possible utilise microorganisms that are intrinsically of low risk. Such microorganisms can be handled under conditions of good industrial large scale practice (GILSP).
2. If, following assessment using the criteria outlined in the report, a recombinant DNA microorganism cannot be handled merely by GILSP, measures of containment corresponding to the risk assessment should be used in addition to GILSP.
3. Further research to improve techniques for monitoring and controlling non-intentional release of recombinant DNA organisms should be encouraged in large-scale industrial applications requiring physical containment.

TABLE 4

RECOMMENDATIONS SPECIFIC FOR ENVIRONMENTAL AND AGRICULTURAL APPLICATIONS

EXCERPT FROM "RECOMBINANT DNA SAFETY CONSIDERATIONS", OECD, 1986

1. Considerable data on the environmental and human health effects of living organisms exist and should be used to guide risk assessments.
2. It is important to evaluate recombinant DNA organisms for potential risk, prior to applications in agriculture and the environment. However, the development of general international guidelines governing such applications is premature at this time. An independent review of potential risks should be conducted on a case-by-case* basis prior to the application.
3. Development of organisms for agricultural and environmental applications should be conducted 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.
4. Further research to improve prediction, evaluation, and monitoring of the outcome of applications of recombinant DNA organisms should be encouraged.

* Case-by-case means an individual review of a proposal against assessment criteria which are relevant to the particular proposal; this is not intended to imply that every case will require review by a national or other authority since various classes of proposals may be excluded.

TABLE 5

KEY SAFETY FACTORS

— the characteristics of the organism(s) used, including the introduced gene/genetic material
— the characteristics of the research site and surrounding environment
— the use of appropriate experimental conditions

TABLE 6
CHARACTERISTICS OF THE ORGANISMS

Characteristics of **plants** to be considered include:
— the biology of the reproductive potential of the plant, such as its flowers, pollination requirements and seed characteristics, and an extended history of controllable reproduction with lack of dissemination and establishment in an environment comparable to the research site
— the mode of action, persistence, and degradation of any newly acquired toxic compound
— the nature of biological vectors used in transfering DNA to plants
— interactions with other species and/or biological systems

TABLE 7
CHARACTERISTICS OF THE ORGANISMS

Characteristics of **microorganisms** to be considered include:
— dispersal, survival and multiplication
— interactions with other species and/or biological systems
— potential for gene transfer
— the mode of action, persistence and degradation of any newly acquired

TABLE 8
CHARACTERISTICS OF THE RESEARCH SITE

— important ecological and/or environmental considerations relative to safety in the specific geographical location (e.g. highwater table, heavy field run-off, etc.)
— climatic conditions
— size, e.g. physical area
— an appropriate geographical location in relation to proximity to specific biota that could be affected