

THE INTERNATIONAL  
REGULATION OF BIOTECHNOLOGY.  
THE CASE OF rDNA TECHNIQUES  
(1973-1982)

PHILIPPE GOUJON

ABSTRACT. The 1970s rapidly became a focus for public interest and excitement. All areas of biology were influenced by the revolution in technical developments and in particular by the rDNA technique. This technology has been used, and still is used, to create recombinant DNA from a variety of viral, animal and bacterial sources. There is serious concern that some of these artificial recombinant DNA molecules could prove biologically hazardous. This article is about the adventure of the regulation of the use of rDNA technique, research and work. In focusing on public policy and regulation, and in particular on the European public and science policies, the intention is to study how societies learn to digest new knowledge and to manage its consequences. Taking into account that this learning process is a multidimensional one and that the debates about biotechnology were from the start international, we will show that the process of regulating a new technology is very complex. We will also reveal how ethical and moral intentions can be confronted, in the debates and negotiating processes, with other interests, such as personal, sectorial, community, national, international, economic, legal and political interests.

KEY WORDS. Biotechnology, biotechnology regulation, biotechnology decision, rDNA techniques, Asilomar, biohazard, science policy, genetic engineering.

The word "ethics" corresponds, curiously, with a phonetic fragment of "genetics." Questions, doubts of an ethical nature, appear with each new advance in research and technology, more particularly when these advances seem likely to bestow on man the capacity of mastering the living being and his evolution. Ethics and genetics; these two terms are often associated, frequently without our really knowing how to define the first, nor if our questions should even really turn around research activities or their application.

Ethics is a global conception of existence, it results from “a philosophical reflection enabling man to find his place in relation to himself and enabling him to apprehend the society of which he is part<sup>1</sup>.” Reflection on the ethical problems raised by the advances in what is commonly called genetic engineering is therefore indissociable from an investigation of the way in which this progress has been received, assimilated and controlled by the societies.

In focusing on public policy and regulation, in particular at European level, on the new techniques in genetic engineering during the 1970s, we will study how societies learn to regulate the arrival of new technological knowledge and possibilities, and to manage their consequences. Taking into account that this learning process is a multidimensional one and that the debates about biotechnology were from the start international and multi-sectorial, we will show at what point the processes designed to regulate a new technology become complex. We will show that the moral and ethical intentions are often confronted with, and must make allowance in the debates and negotiations for, other factors such as personal, sectorial, national, international, economic, legal and political interests.

#### I. RECOGNITION OF THE PROBLEM

The marriage between genetic engineering techniques and industrial microbiology has been so efficient in defining a new age that an important significant perception—though technically incorrect—was conveyed by this affirmation: biotechnology has come to be seen as a result of genetic manipulation techniques, as issuing from genetic engineering. It cannot be denied that biotechnology today has become inseparable from the technological revolution of the 1970s and 1980s, when scientists learned how to change precisely the genetic composition of living organisms, an art very quickly attached to the hope of “transmuting DNA into gold<sup>2</sup>.”

Biotechnology has been praised to the skies, high hopes placed in a better knowledge of DNA<sup>3</sup>, magic acronym, key—so it would seem—to a better world, it also created, however, anxieties about the use of these often esoteric techniques in the general public. These surge from the eugenic “theories” of the nazis and racists, their dreadful consequences, the cynicism of the days of the Vietnam War, the fear of the entente between the military and industry and, needless to say, the terrifying precedent of atomic fission. The biologists themselves talk of the promises of this new revolution, the apparently limitless potentialities opened up by the better knowledge of DNA now acquired by, and the endless new capacities gained through, its manipulation. In so doing, they remind us in their desire to see a happier outcome, of the experience of the physicists who built the first atomic bomb without having, before dropping it, any

real opportunity to consider its long-term consequences. The parallels that could be made between nuclear technology and biotechnology were ever present in the numerous debates on the latter.

Concerning this coincidence between the growing hopes for the commercial-scientific applications and the new biotechnology associated with genetic engineering and a deep anxiety regarding the potential risks, it should be pointed out that the field has acquired such notoriety as to make plausible the most extravagant claims about its power. However, an even stronger link has been suggested: the most important and most sensational promises of the new couple "biotechnology-genetic engineering," were made, largely announced and kept, to the great comfort of its image, on occasion of a technological evaluation process triggered by the question of deciding which controls to impose on this new technology, now so powerful that the scientists themselves, in 1974, called for a control of experiments and alerted politicians and society.

Following the discovery of the double helix by Watson and Crick, the genetic code was explained. After the work of Avery, and thanks to the work of Lederberg and many other scientists, the field of bacterial genetics gradually expanded. It will take several more decades of work and progress before Stanley Cohen and Herbert Boyer at Stanfield published <sup>4</sup> (and patented) their use of restriction enzymes with bacterial plasmids for the basic "cut and stick" operation that soon became known by the name of "genetic engineering," which marked the dawn of the age of genetic recombination and the "mastery of heredity". What Stanley Cohen and Herbert Boyer had done was simple enough in principle, even if the actual technique was extraordinarily complex. They took two organisms incapable of joining in nature, isolated a segment of the DNA of each of them using chemical scalpels called restriction enzymes, and combined the two fragments of material in a plasmid that was then introduced in a host cell. This cell incorporate the plasmid and began to replicate it indefinitely, thus generating identical copies of the new chimera. We hasten to add that Boyer was contacted by a financier named Robert Swanson, a former biochemist, after the invention of the technique. He asked Boyer whether their technique could enable the creation of an organism expressed in proteins foreign to its constitution. Boyer replied to this in the affirmative and did so deploying all the forces of modern biotechnology. Boyer borrowed five hundred dollars, joined Swanson to set up a company to exploit the potentialities of the new techno-science, and named the company "Genentech". In August 15, 1977, the scientists at Genentech succeeded in inserting the gene of somatostatin in the genome of live bacteria which subsequently produced it. In August 24, 1978, insulin was produced by the *E. coli* bacteria; many others followed since, including EPO (erythropoietin). Dozens of biotechnology companies were founded since

this success. Due to the talents of molecular biologists, genetic recombinations became common practice and the number of human genes to be inserted in bacteria and other simple organisms grew rapidly. These technical achievements were so impressive that Boyer made the cover of *Time* magazine in March 9, 1981, a very rare distinction for a scientist.

The implications regarding the public policy of this new technology, its potentialities and the biological revolution it initiated do not affect all the departments of government at the same time nor the same way. The reactions were, on the whole, heterogeneous and their harmonization a hard-won accomplishment.

## II. THE ASILOMAR CONGRESS AND ITS AMERICAN CONSEQUENCES

Certain scientists at the start of this revolution, aware of the potential risks, organized a conference in February of 1974 on the biological hazards. This hardly drew the attention of the scientific community or the media, but it did stimulate thought.

In June of 1973, the annual meeting of the Gordon Conference on Nucleic Acids was held in New Hampton in the United States, and was mainly devoted to the question of the risks involved in recombinant DNA (rDNA) research and techniques. The joint chairmen of the conference, Maxime Singer and Dieter Soll, drafted a letter<sup>5</sup> to the National Academy of Sciences and the Institute of Health requesting the creation of an advisory committee to evaluate the biological risks of rDNA research and to recommend appropriate action. The letter was published in the prestigious journal *Science*. In reaction to this letter, and in February of 1974, the National Academy of Sciences announced that Paul Berg would head such advisory committee. The eleven members, all involved in rDNA research, were aware of the extremely rapid development of the research and techniques and shared misgivings about their potential risks. Their report was published in the journal *Science* on July 26, 1974<sup>6</sup> and, almost simultaneously (though slightly abridged), in the scientific journal *Nature*. In view of its historic importance, the text of Berg's letter is transcribed here:

### Potential Biohazards of Recombinant DNA Molecules

Recent advances in techniques for the isolation and rejoining of segments of DNA now permit construction of biologically active recombinant DNA molecules in vitro. For example, DNA restriction endonucleases, which generate DNA fragments containing cohesive ends especially suitable for rejoining have been used to create new types of biologically functional bacterial plasmids carrying antibiotic resistance markers and to link *Xenopus laevis* ribosomal DNA to DNA from a bacterial plasmid. This latter recombinant plasmid has been shown to replicate stably in *Escherichia coli*, where it synthesizes RNA that is complemen-

tary to *X. Laevis* ribosomal DNA. Similarly, fragments of *Drosophila* chromosomal DNA have been incorporated into both plasmid and bacteriophage DNAs to yield hybrid molecules that can infect and replicate in *E. coli*.

Several groups of scientists are now planning to use this technology to create recombinant DNAs from a variety of other viral, animal and bacterial sources. Although such experiments are likely to facilitate the solution of theoretical and practical biological problems, they would also result in the creation of novel types of infectious DNA elements whose biological properties cannot be completely predicted in advance.

There is serious concern that some of these artificial recombinant DNA molecules could prove biologically hazardous. One potential hazard in current experiments derives from the need to use a bacterium like *E. coli* to clone the recombinant DNA molecules and to amplify their number. Strains of *E. coli* commonly reside in the human intestinal tract, and they are capable of exchanging genetic information with other types of bacteria, some of which are pathogenic to man. Thus, new DNA elements introduced into *E. coli* might possibly become widely disseminated among human, bacterial, plant, or animal populations with unpredictable effects.

Concern for these emerging capabilities was raised by scientists attending the 1973 Gordon Research Conference on Nucleic Acids, who requested that the National Academy of Sciences give consideration to these matters. The endorsement of the Academy of Life Sciences of the National Research Council on this matter propose the following recommendations.

First, and most important, that until the potential hazards of such recombinant DNA molecules have been better evaluated or until adequate methods are developed for preventing their spread, scientists throughout the world join with the members of this committee in voluntarily deferring the following types of experiments.

- Type 1: Construction of new, autonomously replicating bacterial plasmids that might result in the introduction of growth determinants for antibiotic resistance or bacterial toxin formation into bacterial strains that do not at present carry such determinants; or construction of new bacterial plasmids containing combinations of resistance to clinically useful antibiotics unless plasmids containing such combinations of antibiotic resistance determinants already exist in nature.

- Type 2: Linkage of all or segments of the DNAs from oncogenic [cancer-inducing] or other animal viruses to automatically replicating DNA elements such as bacterial plasmids or other viral DNAs. Such recombinant DNA molecules might be more easily disseminated to bacterial populations in humans and other species, and thus possibly increase the incidence of cancer or other diseases.

Second, plans to link fragments of animal DNAs to bacterial plasmid DNA or bacteriophage DNA should be carefully weighed in light of the fact that many types of animal cell DNAs contain sequences common to RNA tumor viruses. Since joining of any foreign DNA to a DNA replication system creates new recombinant DNA molecules whose biological properties cannot be predicted with certainty, such experiments should not be undertaken lightly.

Third, the director of the National Institute of Health is requested to give immediate consideration to establishing an advisory committee charged with (i) overseeing an experimental program to evaluate the potential biological and ecological hazards of the above type of recombinant DNA molecules; (ii) developing procedures which will minimize the spread of such molecules within human and other populations; and (iii) devising guidelines to be followed by investigators working with potentially hazardous recombinant DNA molecules.

Fourth, an international meeting of involved scientists from all over the world should be convened early in the coming year to review scientific progress in this area and to further discuss appropriate ways to deal with the potential biohazards of recombinant DNA molecules.

The above recommendations are made with the realization (i) that our concern is based on judgments of potential rather than demonstrated risk since there are few available experimental data on the hazards of such DNA molecules and (ii) that adherence to our major recommendations will entail postponement or possibly abandonment of certain types of scientifically worthwhile experiments. Moreover, we are aware of many theoretical and practical difficulties involved in evaluating the human hazards of such recombinant DNA molecules. Nonetheless, our concern for the possible unfortunate consequences of indiscriminate application of these techniques motivates us to urge all scientists working in this area to join us in agreeing not to initiate experiments of types 1 and 2 above until attempts have been made to evaluate the hazards and some resolution of the outstanding questions has been achieved.

Paul Berg, Chairman; David Baltimore; Herbert W. Boyer; Stanley N. Cohen; Ronald W. Davis; David S. Hogness; Daniel Nathans; Richard Roblin; James D. Watson; Sherman Weissman; Norton D. Zinder.

Committee on Recombinant DNA, Molecules Assembly of Life Sciences, National Research Council, National Academy of Sciences, Washington DC 20418.

A congress was prepared and organized in response to this letter. It was held in Asilomar, California, in February of 1975: one hundred and forty biologists from seventeen countries took part to outline the risks for the environment and human health that might result from experiments with recombinant DNA. This congress received considerable coverage from the world press. The descriptions and interpretations published afterwards took account of numerous aspects of the conference and their upshot.

At its most factual, this congress represented a meeting of invited scientists in which eminent specialists discussed the risks that might be associated with work and techniques involving recombinant DNA and the ways of containing or reducing these conjectural hazards. The scientific press remarked that all—or nearly all—the participants, were impatient to return to their work, and opposed any regulation to their research. The

mood, according to an article in *Science News*, was "inflexible, self-satisfied and aggressive <sup>7</sup>." When the congress was well in its stride and seemed in all probability to be headed towards denying the moratorium requested by the eleven specialists in their letter of July 26, 1974, an invited lawyer read a statement on the legal responsibilities of researchers responsible for a biohazard. The last speaker, professor Harold Green from George Washington University Law School, captured the full attention of the congressists with a communication entitled "Some conventional aspects of the legislation and the way in which they are likely to affect you in the form of, say, a damages and interest suit for several million dollars <sup>8</sup>." The fear of being involved as the defendant with a very substantial financial risk would soon lead to where more "altruistic" considerations had failed. The following day, during the closing session, the researchers adopted a safety program. Such program emerged from numerous discussions on the different levels of risk in order to classify experiments and concerning the corresponding physical confinement to be required in laboratories to guarantee the confinement of potential hazards. Among the more constructive ideas put forward by the British contingent, such as Sydney Brenner, mention may be made here of biological confinement. This idea, an entirely new concept, resulted in an agreement to use inactivate *E. coli* as host organism for the chimeras obtained from recombinant DNA, in the hope that the use of a biologically weak host organism would prevent the chimeras from surviving in any natural environment. This line of argument was the starting contour for an entire area of evaluation research into the risks during the course of the years to come, on the whole reassuring, but still limited by the logical impossibility of proving the opposite.

It is interesting to note that the Asilomar Congress was met with diverse receptions from its commentators. For some, the organizers were to be congratulated for their goodwill in having invited the representatives of the press, for the integrity and transparency of their attempt to communicate their concerns to a broader public. Other commentators, however, took the Asilomar Congress in the context of an elitist tradition characterized by the arrogant assumption that only those with a real understanding of complex subjects could take part in the making of decisions. Such elitism may be opposed by the fact that democratic processes imply representation from a wider background than the scientific community alone.

The genetic engineering developments on which the Congress focused started a fundamental debate on the control of science and technology or, if that debate already existed, intensified and extended it to all fields of life sciences and technology, their applications and implications. The debate sparked off by Asilomar was heated, and became the burning

issue. Journalists, cartoonists and politicians could not resist the temptation to exaggerate and simplify. Scientists were often shocked by the popular misconceptions of the issues and by the violent attacks to which they were subjected, in particular, of those coming from the major ecological movements. However, certain leading scientists agreed with the critics and continued to demand safety measures, or even a total moratorium, on all research with recombinant DNA. The upshot of all these factors was an animated public debate involving scientists facing the wrath of public interest groups or local politicians—often, for that matter, ill-informed.

Public concern in the United States reached a climax in 1976-1977, a period corresponding to the introduction in Congress of proposals (bills) to regulate rDNA research. During the same period, after the Asilomar Congress, the National Institute of Health (NIH), under its director, Donald Frederickson, set about developing a regulatory framework for conducting such research under the NIH Recombinant DNA Advisory Committee (NIHRAC). The first version of this regulatory framework was enacted by the NIH in June 23, 1976 and published by the *Federal Register* in July 7, 1976.

One main characteristic of the debates in the United States was the gradual development of a structured, balanced response from the scientific community. The American Society of Microbiology (ASM) played an important part in this process, but many professional associations connected with biological and medical sciences and techniques joined up with the ASM in a grand alliance, thanks to the semi-formal contacts among their executives and to the big networks capable of delivering fast responses. The ASM enacted a recommendation approved and widely distributed in May of 1977. This emphasized the required scientific and technical skills, and placed all responsibility for regulatory measures within the Department of Health, Education and Welfare (DHEW). An advisory committee was to be set up, consisting, in addition to lawyers, of representatives with an appropriate technical expertise. The recommendation likewise stressed delegation of responsibility at the level of the institutions involved in this kind of research to local committees formed by experts at the institutions and representatives of the public. This recommendation proposed exempting low-risk experiments (lowest confinement level: P1) from regulation, more particularly stating the need to preserve a certain flexibility in order to adapt to and re-evaluate regulation in light of the experience acquired. All these points will hold good not only in the discussions over the years ahead, but also in other countries and their legislations.

During 1977, the scientists' concerns were, in actual fact, communicated to the public and to interested members of the Congress. Some amendments were made to the first bills, integrating advice from scientists

communicated by the senators or representatives, relays between the Congress and scientists. Information indicating non-dissemination or unwanted effects had considerable influence on the course of events.

In September of 1977, Senator Adlai Stevenson wrote that most of the legislations under review were ill equipped for reaching their objective, that is, the protection of the public without managing to curb research. He declared his intention to explore the use of existing laws in order to regulate studies on recombinant DNA.

In November of 1977, the ASM expressed its concern regarding the apparently unreasoned haste of attempts to establish a legislation to regulate research on recombinant DNA without first consulting the qualified scientists and medical experts, and the need to make allowance for the fact that the first allegations concerning rDNA investigation were characterized by an uncontrolled imagination and, very often, by overstated assertions made by persons not having a knowledge of infectious diseases. The ASM stressed the urgent need for a minimum provisional legislation to extend the regulatory frame to include all rDNA activities, regardless their sources of funding.

Throughout late 1977 and 1978, the ASM continued to work closely alongside the Congress committee, and the prospect of any federal legislation faded. However, this success was not self-evident. A national conference on "Recombinant DNA and the Federal Government" was held in October of 1980, with presentations by federal officials from the agencies concerned with the matter (seventeen federal agencies attended), by congressmen and their advisors in charge of legislative activities in the field, and by lawyers from Washington specialized in such problems.

The American experience, after Asilomar, was of great importance and constituted an example of an open dialogue between the scientific and political circles. The first lesson that might be learnt is that Congress, as an authority, was able to react promptly once public health was raised as an issue. The second lesson is that the legislative process is adequate in the sense that it is sufficiently slow to prevent an ill-adapted, hurriedly-passed legislation. Our third lesson is the attention on part of Congress to the scientific community and its capacity to modify its opinion when presented with new, well founded arguments. This does not, of course, mean that the legislation is dead and buried. There are still several Congress committees that continue to hold hearings about NIH activities and research involving rDNA. There is also a specialized medical press that continues to follow the problem. Finally, if nothing else, the simple excitement surrounding the problem will sustain the topicality of the question of knowing whether or not there should be any government involvement in rDNA research and technology. These three factors might explain why Congress have show interest in the problem.

The adopted regulation may be connected with the absence, during this period, of shortcomings on genetic research and engineering, with the initial economic successes that resulted therefrom, with the prospect of a considerable potential market, and also with the position of leadership in the scientific and economic fields of biotechnology that the United States seek to defend. More generally, and more fundamentally, the American experience offers, for scientists in all fields and for legislations elsewhere in the world, a lesson on the way to manage the interface between science, technology and society, while keeping to transparency, democracy and method; a lesson which will, consequently, be generally accepted and considered effective.

### III. THE BRITISH REACTION

When “the Berg letter” appeared in 1974, British scientists were the most affected in Europe, due to their number of programs and research centers involved. This work was financed by the universities or by the research councils, so it was a simple matter for the Department of Education and Science to call a halt to all investigations involving recombinant DNA techniques until such time as the government should set a regulatory frame in place.

In July of 1974, a committee —the Ashby Working Party— was set up to decide whether research should be continued. Its report was published in December of 1974<sup>9</sup>. It recommended the pursuit of research provided appropriate precautions were taken, in particular biological confinement. The swiftness of this response allowed the British scientists to make use of the concepts developed by the Ashby Working Party in Asilomar in February of 1975. The government replied by setting up, under the direction of Sir Robin Williams, another working party in August of 1975 to prepare a code of practice to regulate all activities involving genetic manipulation. This committee gave its answer in twelve months<sup>10</sup>. However, the British scientific community was frustrated by two years of lost time in its work. The committee further recommended the creation of a supervisory authority for genetic manipulation and a regulatory framework. Consequently, the Genetic Manipulation Advisory Group (GMAG) was set up by the Department of Education and Science. It held its first meeting in January of 1977. Its members included eight scientists and medical experts, four public representatives, four commercial representatives (from the trade unions), four employees involved and two representatives of management, one appointed by the Confederation of British Industry, the other by the Committee of University Vice-Chancellors and Principals.

The concept of "representation of the general interest" was an innovation and allowed a more efficient communication with the public, despite the fact that GMAG meetings remaining private.

The GMAG followed the advice of the Williams Report as to a regulatory framework to analyze studies on rDNA, concerning in particular four levels of physical confinement from the lowest level up to the strictest confinement level. This scheme was abandoned in 1979 and replaced by a risk evaluation scheme. The largest confinement level was above the restriction levels for the bottom confinement level laid down by the NIH.

The publication of the Williams Report and the creation of the GMAG allowed scientific work to resume in the United Kingdom, where 16 level-III confinement installations were constructed. At the request of the GMAG, the Medical Research Council (MRC) also financed training courses for biological safety officers at Porton Down, the government microbiological research center, now the Center for Applied Microbiology and Research. Following the introduction of the evaluation scheme in 1979, most experiments have since been recategorized in confinement I in which no more is required than "good microbiological practice."

The 1970s saw an increasing demand in many countries for the improvement of health and safety at work, and so growing awareness of the risks influenced the debate around rDNA. In 1974, the United Kingdom adopted an intelligent law: the Health and Safety at Work Act, giving more extensive powers to the government's Health and Safety Commission, such law being implemented by to the Health and Safety Executive (HSE) and the Factory Inspectorate.

Further specific legal regulations followed under this act, requiring that all establishments (including the ministry and research institutes) set up local safety committees. Regulations concerning genetic and operational manipulations were likewise introduced (SI 1978 No. 752) since August first of 1978. These latter demanded that "persons should not carry on genetic manipulation unless they have previously notified the Health and Safety Executive and the Genetic Manipulation Advisory Group." The GMAG did not give its opinion until the proposals had been discussed at the level of the local biological safety committees.

The regulations concerning genetic manipulations in the United Kingdom introduced a definition to the expression "genetic manipulation" that was used in all European legal proposals, as well as in numerous draft national laws.

Genetic manipulation means the formation of new combinations of heritable material by the insertion of nucleic acid molecules, produced by whatever means outside the cell, into any virus, bacterial plasmid or other vector system so as to allow their incorporation into a host organism in which they do not naturally occur, but in which they are capable of continued propagation.

The GMAG's development of a risk evaluation scheme in 1979, implemented since the 1980s, subdued scientific nerves as to the possibility of overzealous safety committees, useless delays and an excess of transparency that may damage economic and commercial interests, and distort national and international industrial and economic competition.

Seeing that the United Kingdom did not have a hard and fast description of "good microbiological practice," a policy memo was put together for "Guidelines for Microbiological Safety" by the scientists themselves in a "Joint Coordinating Committee for the Implementation of Safe Practices in Microbiology." The GMAG accepted this in July of 1980. The action of the Joint Coordinating Committee was outstanding in the debate in the United Kingdom, as well as the contributions by certain scientific names, in particular Sydney Brenner, who formulated for the first time—in July of 1978—the initial concept of the risk evaluation scheme that had proven to be such a great success. It was introduced in March of 1979 and revised in January of 1980. The local biological safety committees could operate with ease handling a risk evaluation that was supple enough to allow due consideration of medical or scientific information during the decision-making process. The scheme led to the majority of the research to be reclassified in level I. The development of a new strain of *E. coli* by S. Brenner allowed the GMAG to incorporate the concept of biological confinement in its risk evaluation scheme with more confidence. Thus, the categorization of the rDNA studies was carried out by the local biological safety committees.

The Williams Report and the GMAG code of practice came out before publication of the NIH guidelines (June of 1976), with the result that those European countries involved in rDNA research decided initially to adopt the regulatory frameworks of the GMAG. In general, the lack of a generalized legislative working structure such as the Health and Safety at Work Act made the introduction of legislation to cover genetic engineering all the more complex. This absence also explains the fact that, since the regulatory framework of the NIH was introduced with the lowest confinement requirements and with a codified system of categorization, almost all the main European countries decided to adopt it. However, the implementation methods and standards vary greatly.

Such was the background of the first European legislative initiative by the European Commission, an initiative that we shall describe later.

#### IV. THE EUROPEAN REACTION: FROM A DIRECTIVE TO A RECOMMENDATION

If the regulation, development and use of a new technology are complex at a State level, they reach an even greater order of complexity when a community of several states is concerned, as is the case in the European

Community. The complex sectorial make-up (the General Divisions) of the European Commission, the problem of the coordination and harmonization of its actions and the heterogeneity of national and corporate interests compound this complexity. If we bear in mind that biotechnology is essentially multidisciplinary, multi-sectorial, both scientifically and as regards its multinational and multi-international applications and implications, we begin to see the difficulties of putting in place a European regulation that is sufficiently homogeneous and binding or influential for the Member States to respect.

The need for an integrated approach (which, incidentally, gives its name to the title of a European Parliament resolution adopted on February of 1987) has been recognized since 1983. Six priority actions (research and education, price of agricultural raw materials for industrial use, regulation of biotechnologies, industrial ownership, pilot projects, conciliation) were decided, their start-up implying at least five Directorate-Generals<sup>11</sup>. To support the action to regulate the biotechnologies, the Commission established internal structures under the authority of the "Biotechnology Steering Committee," the secretariat of which was provided by the Consultation Unit (CUBE). The creation of the European Biotechnology Coordination Group (EBCG)<sup>12</sup> in 1985, by the main European sectorial federations, not through an industrial initiative but at the request of Etienne Davignon (then Vice-President of the EEC) to count with an intersectorial conciliation structure for the initiatives of the Commission of the European Communities in biotechnology, met the need for a representation of the bio-industries capable of expression via a trans-sectorial organ of communication<sup>13</sup>. This body was also useful for a dialogue with the European or international authorities (e.g., the OECD), or with foreign bio-industrials (from America, Japan, etc.).

Let us attempt to take stock of the 1980s.

The expert opinion of the state of play in connection with genetic engineering, as seen by Commission services is to be found in Directorate-General XII (DGXII), the base of a team of scientists recruited to carry out research in biological safety under the Euratom treaty who could identify (and interact with) competent external scientists.

As its main hopes rested on a proposal for a Community-wide research program, the DGXII "biological team" followed closely the international debate on the safety of rDNA research. In January 20, 1977, they organized a meeting of all the chairmen of the national committees in charge of the control of rDNA research. The purpose of the meeting was to study the way in which the Commission might contribute towards a compulsory strand of the guidelines concerning this type of research, such as it existed among the Member States, as well as to how the Commission might be placed to promote its harmonization. The first objective was particularly

important for industrials. The resulting opinion was that the Commission should pass a directive demanding the setting up of a national control committee, define their terms of reference, and promote agreement of the guidelines.

DGXII, in consultation with the Scientific and Technical Research Committee (CREST), the European Science Foundation (ESF) and other sources of scientific advice, proceeded, throughout the following year, to formulate a "Proposal for a Council Directive establishing safety measures against the conjectural risks associated with recombinant DNA work <sup>14</sup>." The legal base of this proposal was article 235 <sup>15</sup>. The Commission put this before the Council on December 5, 1978. The preamble stressed, in positive terms, the value of pure and applied science, and the need to combine protection of the person, the conservation of food reserves and the environment, and rDNA research. It was clear on the international character and the conjectural epidemiology, and about the fact that a delay in the development of research among the Member States could affect their scientific and technical competitiveness. The rapid evolution of science, the need to consider local circumstances and the requirement to maintain scientific industrial secrecy and intellectual property were also acknowledged. Since this proposal, both aspects—the ethical and industrial/economic interests—are now in evidence. The definition of work on recombinant DNA was identical to that for genetic manipulation in the implemented regulation in the United Kingdom.

In substance, the proposed Directive required a preliminary notification to, and authorization from, the national authorities before starting any activity involving recombinant DNAs. The national authorities would develop a categorization system and inform the Commission accordingly, while the latter would publish them. The Member States were supposed to submit to the Commission the list of authorization granted at the end of each year, with a covering general report on their experiments and problems. Article V of the Directive provides for revision where necessary, at regular intervals not to exceed a period of two years, thus introducing a measure of flexibility. As this proposed Directive became the subject of debate in the European Parliament, the Commission team, scientists and authorities at DGXII level, were alerted by the American opinion swing in 1978 towards non-legislation. The American NIHRAC and British GMAC continued to gain experience. The scientific debate pressed on, and consensus took shape around the recognition that certain of the initial fears had been exaggerated. The Director of the NIH, Don Frederickson, visited Gunther Schuster, Director-General of DGXII in 1978, to discuss the lessons of the American experience. He pointed out it that was advisable to avoid an overly strict and determined legal control.

The Parliament had begun its analyses and added amendments setting out the confinement requirements more rigidly. Inspired, however, by experiences in the United States and the United Kingdom, the Commission—on Schuster's advice—decided in 1980 to "scupper" the Directive and replace it with a proposal for a Council Recommendation<sup>16</sup>. In substance, this non-mandatory proposal recommended the Member States to adopt laws, regulations and administrative measures subject to notification, and not to authorization, for all works carried out in rDNA.

#### CONSULTATIONS AND REACTIONS

##### SCIENTIFIC AND TECHNICAL RESEARCH COMMITTEE (CREST)

During a meeting with the Scientific and Technical Research Committee (CREST) in September of 1978, the Commission recognized the importance of rDNA technology for the understanding of the structures of genetic functions which, in the long term, might well revolutionize certain methods of agricultural and industrial production. The risk associated with rDNA work was particularly "conjectural and controllable." Reference was made to experiments and other considerations encouraging the idea that man and his environment, having survived the continual flux of information between species, could be considered to be relatively tolerant to any new form of recombinant DNA.

The examples of regulation in the United States and the United Kingdom were cited. American rules were mentioned as to being more supple in the future and, for the United Kingdom, that the current code of good practice was applied on a voluntary basis, but with the understanding that the health and safety inspectors had wide powers to enforce implementation of the recommended precautions. The other Member States were presented as being similarly preparing a regulatory system. The national committees in France, in the Netherlands, in Denmark and in Belgium had been assigned the task of indexing the work in progress and to analyze the proposals for research. Besides the United Kingdom, only one Member State, the Netherlands, clearly declared its intention to introduce a legislation to regulate rDNA research. The Commission was also careful to stress the importance of the reports and analyses from the ESF's ad hoc committee on rDNA research and from the Standing Committee on Recombinant DNA of the European Molecular Biology Organization (EMBO) in the elaboration, and for the adoption, of regulatory systems at Member-State level.

Despite the declining evaluation and the real importance of the conjectural risks, the Commission put forward six reasons for a national legislation:

- 1) the seriousness of the risks;

- 2) the expansion of rDNA work;
- 3) the transnational nature of the risks;
- 4) research in the laboratories of private companies (with the risk that, in the absence of relevant legal provisions, private laboratories and industry would not follow the same rules as those in the public sector);
- 5) the need to establish harmony between the Member States (so as to avoid disparities and a concentration of activities at the most permissive sites);
- 6) the great value of the legislation on rDNA technology (rDNA was presented as an ideal way of arriving at a compatibility between the legislation and the development of modern technology, and to prepare a first base for the provisions that, inevitably, must be taken to protect man against his own inventions).

#### THE ECONOMIC AND SOCIAL COMMITTEE (ESC)

The draft Community Directive was presented to the Council in December of 1978, but the first official response came from the ESC, a committee representing management and labor. Their report delivered in July of 1979, dwelt on the declining evaluation of risks and on the absence of any specific problems. It stressed that the introduction of safety measures was not in itself proof of danger. Industry and agriculture, on the other hand, would benefit from the application of the new technology and, in general, had doubts as to the usefulness of the Directive. However, this evaluation supposed a continuous self-discipline on the part of the scientific community that could not be guaranteed. Certain countries (the Netherlands) considered that legislation might help to reduce the latent suspicion among the population, stressing that if a legislation were adopted, it would need to be adaptable to rapid change. The ESC report nonetheless backed the Commission draft directive, and proposed the ESC to hold a public hearing with the Commission to consider the scientific opinion as well as the opinions of the unions, industries, agriculture and the general public interests. The Commission responded to the shift of opinion by replacing its draft Directive with a proposal for a Council recommendation in June of 1980<sup>17</sup>.

#### THE EUROPEAN SCIENCE FOUNDATION (ESF) (FORUM OF EUROPEAN RESEARCH COUNCILS)

The ESF set up an "Ad hoc Committee on Recombinant DNA Research" in 1976. The evolution of their appraisals, between 1976 and 1981, illustrates the rapid change of scientific opinion concerning the risks, a characteristic trend of these years in the United States, in the Commission and among the Member States. The ESF, in its meeting in September 10 of 1976, in Amsterdam, discussed the first version of the guidelines published by the

NIH, together with the report of the United Kingdom Working Party on the Practice of Genetic Manipulation. The ESF analyzed the two systems, but finally recommended the English one, in part because that system account all laboratories (public and private) and also because it brought out the importance of the legal support made possible by the Health and Safety at Work Act. The necessity of a certain flexibility was also emphasized.

THE EUROPEAN MOLECULAR BIOLOGY ORGANIZATION (EMBO)

The ESF sought other opinions and invited the Standing Advisory Committee on Recombinant DNA to compare the regulatory provisions in the United States and those in the United Kingdom. The EMBO report was completed in October of 1976 and distributed in the ESF meeting of the 26th of the same month. The result, based on the ad hoc committee report but including the amendments adopted at the ESF meeting, essentially recommended:

- authorization, subject to the necessary precautions to ensure the protection of the public and its members and that of the flora and fauna and the environment, of the pursuit of work involving recombinant DNA,
- that sufficiently precise guidelines be observed by all researchers and laboratories.

It approved the recommendations and the codes of practice adopted by the United Kingdom as guidelines for European rDNA research, provided a European committee that included representatives of the national authorities responsible for the interpretation of the recommendations and codes of practice for rDNA research, from the Standing Advising Committee on Recombinant DNA Research, and from the European Medical Research Councils; it also included representatives from agricultural research, and was set up under the care of the ESF. It stressed that this committee would convene fairly quickly with regular frequency so as to enable the follow-up and good mutual flow of information, meaningful consultation, and discussion of the decisions about specific experiments. Authorities with the task to interpret the recommendations and codes of practice, monitor their implementation for rDNA, and advise researchers, must be established at national level, as should register laboratories conducting rDNA research.

STATEMENT FROM THE ESF LIAISON COMMITTEE  
ON RECOMBINANT DNA RESEARCH<sup>18</sup>

Charged with the promotion of the necessary harmonization of rDNA guidelines, the committee found, in its meeting of January 14 to 15, 1989, that its mission was sufficiently accomplished to warrant its dissolution. Given the volume of information stating that rDNA, per se, did not represent significant new biological risks (an opinion already accepted by

certain national committees), and taking into account the economic and industrial potentialities of the new technology, the liaison committee reaffirmed its opinion that there was no justification for a specific new legislation for rDNA research and techniques, and that there did not seem to be any good reason for establishing supplementary risk evaluation programs. The report was approved during the ESF meeting of November 12, 1981. Their opinion that the debate had virtually ended was largely shared. Many scientists gave a similar opinion at the hearing held by the ESC which, generally speaking, focused more on the social risks, such as the concentration of knowledge in the hands of industry, leading to commercial (or even military) applications that were not necessarily beneficial. Nevertheless, certain members of the ESC later confirmed that, despite these statements, they inclined towards tightening up of the legal regulations even if they had to be frequently revised to allow changes in risks evaluation.

#### REPORT OF THE NORTH ATLANTIC ASSEMBLY (NAA)

In parallel with the proceedings of the ESF and the ESC, two parliamentary bodies also looked into the problem of rDNA safety: the North Atlantic Assembly—an interparliamentary assembly of the North Atlantic Alliance, forming a link between the NATO authorities and the members of Parliament—and the assembly of the Council of Europe, united with the democracies of Eastern Europe (whose numbers increased in the 1990s with the democratization of that region).

In 1978, the North Atlantic Assembly set up a subcommittee for genetic manipulation which, in eight months, drafted a report entitled “The potential benefits of recombinant DNA research and the postulated risks on whether there was a need for regulations or legislation and on the aspects of commercialization”. The group was chaired by Robert McCrindle (United Kingdom), and included members from France, Germany and the United States.

The NAA group contacted numerous scientists, including the ESF group. Its attention was drawn to the consensus of factors emerging around good safety practice and the similarity of national guidelines. The NAA group noted the rapid adaptation of guidelines under NIHRAC and recommended, in January of 1979, its expansion from 11 to 25 members to increase its scientific representation. It also contacted the World Health Organization (WHO) in February of 1980, asking if a universal set of guidelines regulating rDNA was necessary and whether the WHO was prepared to act as a regulatory authority. The answer to both questions was affirmative. However, the WHO stressed that any activity would have to spring from national initiatives. Taking into account the increasingly marked absence of real risks, it was considered that, even if the WHO were to pass

a resolution, it was difficult to envisage the Member States treating it as mandatory.

The conclusion of the NAA subcommittee, which was published in March of 1981<sup>19</sup>, was that

the benefits of recombinant DNA research outweigh the risks and that maximum encouragement should be given to develop this research for the benefit of mankind. Nevertheless, we feel that controls are still envisable on certain aspects of research such as experiments using highly dangerous pathogens or on the germ cells in human beings. We argue however for a flexible set of control guidelines which both protect from any possible dangers that may arise but at the same time do not hamper research, so that the public may benefit as soon as possible from all the possibilities offered by the implementation of this new technology.

#### REPORT OF THE COUNCIL OF EUROPE

A similar consensus developed in the Council of Europe, in particular in a report drafted by Mr. Elmquist and presented by their Legal Affairs Committee. A public parliamentary hearing had been held in May of 1981 under the title "Genetic engineering: risks and chances for human rights." Their report was based on this hearing and took account of the work carried out by the NAA, the European Commission, the Economic and Social Committee of the EC and by the ESF. The final recommendation was adopted by the Parliamentary Assembly in January 26, 1982. It made a distinction between "concerns arising from uncertainty as to the health safety and environmental implications of experimental research" and "those arising from the longer term legal, social and ethical issues raised by the prospect of knowing and interfering with a person's heritable genetic pattern"<sup>20</sup>.

On account to the first concern, the resolution insisted on the potential value of the new techniques and the considerable progress in knowledge. It referred to the freedom of scientific research as a fundamental value, but stressed the obligations and responsibilities regarding health, public safety and the non-contamination of the environment. It took note of the initial uncertainties, but considered that these had been largely settled to such a point as to allow an easing off on the controls and confinement measures initially envisaged. It supported strict levels of comparable protection being set in all countries for the public, as well as for laboratory staff against the risks implied by the manipulation of pathogenic microorganisms in general, whatever techniques may be used.

Turning to the legal, social and ethical problems, the resolution made reference to articles 2 and 3 of the European Convention on Human Rights implying "the right to inherit a genetic pattern which has not been artificially changed," but went on to add that "the explicit recognition of

this right must not impede development of the therapeutic applications of genetic engineering (gene therapy), which hold great promise for the treatment and eradication of certain diseases which are genetically transmitted.”

DIVIDED OPINION ON ADOPTING  
THE RECOMMENDATION

During the debate on the Commission proposal for a Council recommendation, rather than a directive, for the control of rDNA work, opinion in the European Parliament was largely split. Subsequent to its hearing in May of 1981, the Economic and Social Committee continued to support a directive, thereby clashing with the Commission. At the European Parliament, the Rapporteur was Domenico Ceravolo, an Italian Communist. His report found that, even if the risks were due only to a set of hypothetical events, this did not constitute a justification for thinking that they were any less significant nor any less valid. The conjectural risks could not be disregarded, for no appropriate criterion was available for their evaluation<sup>21</sup>. However, the liberals and conservatives, in this period representing a majority in the Parliament, supported the Commission's proposals mindful that an excessively mandatory legislation could stunt the growth of the European biotechnological industry<sup>22</sup>. The proposal for a recommendation was approved by the Parliament in early 1982<sup>23</sup> and adopted by the Council in June of the same year.

In October 1984, the Committee of Ministers of the Council of Europe adopted almost the same text as the recommendation for their (at the time) twenty one Member States with a rather greater degree of flexibility for Member States, who could decide freely as to the risk categories necessitating a notification (because, it was argued, the biological risk had been overestimated). It was also stressed that studies would continue on the ethical questions.

With the adoption of Recommendation 82/472, suggesting national notification systems in respect to work on recombinant DNA, the debate on regulation in Europe died down for some years. Such recommendation came as a rational response to uncertainties; it authorized those Member States engaged in large-scale research activities, having the corresponding monitoring systems in place, to develop and adapt them to the perceived requirements. Aware of public feelings, the scientists involved cooperated spontaneously with the national authorities; international harmonization developed via the usual scientific networks and the authorities such as those already mentioned.

The discussions that led to the recommendation of 1982 were followed by a period of some years of relative calm, at least as to the initiatives to regulate biotechnology. As pointed out in the previous description of

communications from the Commission in 1983, 1984 and 1985, the general feeling in the departments responsible for various sectorial products was that the applications of the new biotechnology, linked to the sectors, did not pose an insurmountable problem and could be dealt with by the sectorial legislations.

The situation evolved however as the large-scale production biotechnological installations and the demand for the dissemination of genetically modified organisms multiplied. Public interest and attention was stimulated, again and again, by a considerable journalistic coverage centering on:

- 1) the scientific discoveries and their impact on knowledge;
- 2) the economic implications and potential;
- 3) the ecological and industrial risks stressed by the ecological groups;
- 4) the ethical aspects (screening the population, *in vitro* fertilization, the problem of interfering with nature, the danger represented by scientists playing the sorcerer's apprentice). The World Council of Churches (WCC) drafted and published a rather hostile report containing glaring inaccuracies<sup>24</sup>.

The entry of ecological interests into the political debate on biotechnology was one of the more notable developments of the 1980s; at the same time, the public authorities at national and Community level reinterpreted their general responsibility for the protection of the environment in relation to the challenges of the new processes and products resulting from biotechnology.

The Biotechnology Regulation Interservice Committee was instituted at Community level in July of 1985 under DGXI and DGIII. Its task was to facilitate consultation between the services responsible for the preparation of draft directives; currently, these concern the confined use of genetically modified micro-organisms (Directive 90/220 of April 23, 1990 and Regulation No. 258/97 of January 27, 1997) and information for the consumers (Regulation of January 27, 1997, No. 258/97 and No. 1139/98). These directives, which followed the Council recommendation for the regulation of rDNA, tell a different story.

It should be remembered that this was, and still is, more complex with the problem of harmonization due to the conflict of interests in the Commission, in particular between the Directorate-Generals. It should further be pointed out that pressure from ecologists increased as more of the genetic engineering techniques left the laboratory and gave rise to industrial applications. Although the new techniques could legitimately claim the description of technology proper, the interaction in Europe with the ecological movements was more a collision than an accommodation; this, at Parliament level, made itself felt by a marked attention towards the Greens. The Greens, because of their political gains in the late 1980s,

spurred other political parties to a new strategic will (to win back lost votes) to show their own “green orientation and inclinations.” A restrictive approach towards the new technology struck them as a popular and easy course of their action.

With such coincidence of popular fears, political interests and opportunist or conservative bureaucracies, the scientific protestations were few and frequently ignored, even when they came from Nobel Prize winners. The OECD report, stressing that there was no scientific basis in favor of a specific legislation for rDNA, was noted for its prestige and authority in support of just such a legislation. DGXII lost, for a while, its fight for influence in the Commission; its proposal to offer scientific advice was vigorously rejected and counter-attacked. The opinion of safety specialists from the EFB was aggressively rejected by the Director General of DGXI.

A similar reaction of rejection greeted the suggestion (at BRIC level) that the details of a rapidly evolving field should be worked out by technical experts in the Standards Committees. DGXI represented the head of the line concerning biotechnological legislation, but not to its standards. Consequently, the technical details of scope, a central problem in the American debates, were defined in annex to each of the biotechnological directives—90/219 (confined use) and 90/220 (dissemination)—in terms specific to the comprehension of the science legislators during the 1980s, as modified by the experts chosen by the ministers for the environment, who removed these annexes from the field of the procedures of the “committees for the adaptation of the technical program”. The consequences in terms of cost, delay and dispute dominated the debates on regulation during the 1980s.

European industry had sought to establish a communications network for the expression of bio-industrial interests. However, this failed to take on the task of expressing energetically these interests. This setback became evident on the disappearance of the EBCG. This was, on the one hand, largely brought about by the fact that each sector was jealous of its independence, making it unbearable that one of them should try to gain supremacy. On the other hand, certain federations had the feeling that their freedom of action in their own section had been reduced (a clear sign of insufficient consultation). Finally, these situations resulted in divergent views among the federations, some wishing to strengthen the structure, others to weaken it, which led to the rift. Nonetheless, following this check, the Spring of 1989 saw the emergence of the Senior Advising Group on Biotechnology (SAGB) in the European Council of Chemical Industry Federations (CEFIC). The SAGB<sup>25</sup> provided an industrial forum allowing debate on aspects of Community policy in the matter of biotechnology, with the aim of promoting a climate of support for biotechnology. The SAGB gradually led to the development and structuring of the dialogue

between the bio-industry and the EEC, enabling an account to be taken at Community level to the urgent need to redirect the Community policy on biotechnology with a view to competitiveness. Continuing to defend stubbornly their main sector interests, the federations displayed a conservatism similar to that encountered within the Commission. In the early 1990s, the general situation evolved with the realization, even at Commission level, of the consequences of the failure with inter-services coordinations. At the request of President Delors in 1990, the Secretary-General began to appoint the Biotechnology Coordination Committee (BBC) and upheld and developed the central role of the BBC within the Commission services. The Commission acted as a brake on the autonomous behavior of the individual DGs and developed de facto a greater degree of horizontal transparency in the Commission. A greater degree of transparency developed vis-à-vis the outside. Round table discussions with industry and a more general spread of non-governmental representatives of interests became a new characteristic of the activities of the BBC. The communication of 1991 announced that the European Standards Committee was to be charged with the development of standards for biotechnology.

The fact remains, however, that the hostility towards this new technology was far from spent. If a DG had been thwarted at the BBC, a telephone call or a fax could soon mean a letter from a member of the European Parliament to the Secretary-General; nor was there any lack of activist organizations to bring forward the arguments to the public sphere.

The balance between the pro and anti-biotechnology camps still remains delicate. In spite of the advances made during recent years, regulations on biotechnology and, in particular, the legislation concerning genetically modified organisms, still remain problematic. The adopted directives are still far from coming to a broad consensus, and require further improvement. Considering the stakes (economic, political and ethical), the complexity and the multiplicity of the forces involved, the constant evolution of the field and the antagonistic pressures, one thing is certain: the debate is far from finished, and the perfect regulation is yet to be invented.

#### CONCLUSION

If we limit ourselves to the story here under review, that of the regulation of recombinant DNA techniques, what lessons can we learn? Begun by the scientists, the debate on the regulation of rDNA research and technology may be considered as a genuine prototype for all attempts to find a balance between the need to control and legislate, and the development of a new technology. This debate laid the foundations to the provisions that have been made to protect man against his own technical successes. During the debate, the reasoned communication and thoughtfulness among the vari-

ous partners and the cooperation, from the outset, between the scientists involved with the authorities—this with salutary initiatives—were decisive in the success booked in the United States and in the United Kingdom or throughout Europe.

These factors allow the regulation to be characterized by flexibility enabling it to adapt to an extremely rapid evolution, and the regulatory process to avoid, by its complexity, unduly hasty decisions that might be detrimental both to scientific and industrial research, and to economic competitiveness.

This example also shows, now that a post-modern current is carrying an increasingly widespread suspicion to the advances of techno-science, that a regulation adapted to the feats of reason and their implications is still possible, if measures are abreast of technical development and not a posteriori. It remains beyond doubt, however, that the pluridimensionality, plurisectoriality and plurinationality of the scientific and technological fields, and of their applications and implications cause difficulties in all attempts to regulate, taking any meaningful account of the social, political, economic and ethical risks and problems, in particular, as is shown with brilliant clarity by the turn this story takes, once industrial and economic interests swing into action.

## NOTES

- 1 F. Séruselet, "Vers une approche des définitions du concept de l'éthique", *La lettre éthique*, Vol. 5, 1990.
- 2 Title of the first chapter of the work by Sharon McAuliffe and Kathleen McAuliffe, *Life for Sale*, ed. Coward, McLann and Georghegan, New York, 1981.
- 3 Deoxyribonucleic acid: a molecule having the structure of a double helix and representing the chemical basis of heredity. Present in chromosomes and in mitochondria and chloroplasts.
- 4 S.N. Cohen, A.C.Y. Chang, H.W. Boyer and R.B. Helling, "Construction of biologically functional bacterial plasmids in vitro", *Proc. Natl. Acad. Sci., USA*, Vol. 70, 1973, pgs. 3240-3244.
- 5 M.F. Singer and D. Soll, "DNA hybrid molecules", *Science*, Vol. 181, 1973, pg. 1114.
- 6 Paul Berg, et al., "Potential Biohazards of Recombinant DNA Molecules", *Science*, Vol. 185, 1974, pg. 303.
- 7 Janet H. Weinberg, "Decision at Asilomar", *Science News*, 22 March 1975, pg. 196.
- 8 Michaël Rogers, "The Pandora's Box Congress", *Rolling Stone*, 19 June 1975, pg. 77.
- 9 HMSO, *Report of the Working Party on the Practice of Genetic Manipulation*, Williams Working Party, Comnd. 6600, Her Majesty's Stationery Office, London, 1974.
- 10 HMSO, *Report of the Working Party on the Practice of Genetic Manipulation* (Williams Working Party) Comnd. 6600, Her Majesty's Stationery Office, London, 1976.
- 11 The main Directorate-Generals concerned by biotechnology that we may cite in this article are: DGIII: internal market and industrial affairs, IV: competition, V: employment, social affairs and education, VI: agriculture and rural development, XI: environment, nuclear safety and civil protection, XII: science, research and development, XIII: telecommunications, the information industry and innovation (in 1989, education and consumer protection became separate services, split off from DGV and XI respectively).
- 12 Member European sectorial federations of the EBCG in 1991: Association of Microbial Food Enzyme Producers (AMFEP), Conseil Européen des Fédérations de l'Industrie Chimique (CEFIC), Confédération des Industries Agro-Alimentaires, Comité Européen des Obteneurs des Variétés Végétales (COMASSO), European Federation of Pharmaceutical Industries' Association (EFPIA), Fédération Européenne de la Santé Animale (FEDESA), Green Industry Biotechnology Platform (GIBIP), International Group of National Associations of Agrochemical Manufacturers (GIFAP). Member national bio-Industrial associations of the EBCG since April 1989: Associazione Nazionale per lo Sviluppo delle Biotechnologie (Italy) (ASSOBIOTEC), Bioindustry Association (United Kingdom) (BIA), Bioresearch Ireland (Ireland) (BRI), Foreningen af Biotechnologiske Industrier i Danmark (Denmark) (FBID), Groupe Belge de la Coordination de la Bio-industrie (Belgium) (GBCB), Nederlandse Industriële en Agrarische Biotechnologie Associatie (Netherlands) (NIABA), Organisation Nationale Interprofessionnelle des Bio-Industries (France) (ORGANIBIO).

- 13 Interesting to note that the European Council of Chemical Industry Federations (CEFIC) gave the EBCG a chairman and a secretary and defrayed the costs of the secretariat.
- 14 European Commission, Proposal ... *Official Journal of the European Communities*, 301, pgs. 5-7.
- 15 "If any action by the Community appears necessary to achieve, in the functioning of the Common Market, one of the aims of the Community in cases where this Treaty has not provided for the requisite powers of action, the Council, acting by means of a unanimous vote on a proposal of the Commission and after the Assembly has been consulted, shall enact the appropriate provisions."
- 16 European Commission, *Draft Council Recommendation concerning the registration of recombinant DNA work*, Com (80), Vol. 467, 8 July 1980.
- 17 European Commission, *Draft Council Recommendation, concerning the Registration of recombinant DNA work*, COM (80), Vol. 467, 8 July 1980.
- 18 This committee brought together the representatives of the national rDNA committees.
- 19 North Atlantic Assembly, *Genetic Manipulation (Recombinant DNA Research, Application and Regulation)*, 1981.
- 20 Council of Europe, *"Thirty-Third Ordinary Session of the Parliamentary Assembly, Recommendation 934 (1982) on genetic engineering"*. Text adopted by the Assembly on 26 January 1982 (22nd sitting).
- 21 This remains a problem for all attempts at "risk assessment" and underlines the basic limits inherent in this approach: to evaluate the risks implied by new technologies, reference is possible only to the risks implied by an existing technique similar, even if only remotely, to the new technique.
- 22 J. Becker, "Recombination DNA Research: EEC dispute", *Nature*, 24/31 December 1981.
- 23 Council Recommendation (472 EEC). Concerning the registration of work involving recombinant DNA, 1982.
- 24 World Council of Churches, *Biotechnology: its challenges to the church and to the world, Report by WCC Subunit on Church and Society*, WCC Geneva, 1989.
- 25 Members of the SAGB in 1991: Ferruzzi, Hoechst, Hoffmann-La Roche, ICI plc, Monsanto Europe SA, Rhône-Poulenc, Sandoz Pharma Ltd., Unilever plc.