Regulatory aspects of biotechnology in Europe, with particular reference to veterinary science *

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Summary: Advances in the life sciences and their applications through biotechnology have posed growing challenges to public policy-makers and legislators in several areas, particularly research, agriculture, industry and environment. As a result, legislative and other policy responses in the European Community are evolving in a context of continuing rapid change, under the pressure of the political imperative to complete the internal common market, and also strongly influenced by the wider international commitments of the world's major trading bloc.

Scientific advances offer the possibility of achieving high standards of protection for human and animal health and the environment. However, the complex interactions of animal science, agriculture and internal market policy, and consumer reactions and perceptions vis-a-vis food and the social and economic consequences of innovation, demand sustained efforts to ensure open communication to maintain public confidence in the results of scientific progress, and in the rationale for public policy and legislation.

KEYWORDS: Biotechnology - Consumers - Environment - Feedstuffs - Genetic modification - Public information - Public policy - Regulation - Safety - Transgenic animals - Vaccines.

INTRODUCTION

This review is written some one and a half decades since the first use of restriction enzymes for artificial and deliberate recombination of lengths of DNA molecule, a third of a century since Crick and Watson postulated the double helix structure of DNA, and nearly half a century since Avery demonstrated that DNA is the vector of genetic information. The scientific story of modern biotechnology remains one of continuing, even accelerating, intellectual achievement and excitement.

Since the conference at Asilomar in 1975, the story has been one not of scientific achievement alone, but of implications and applications spreading ever wider, with economic, social, political and regulatory consequences. In this article, a view is presented from a European perspective of how the progress of biotechnology has been perceived and received by various groups; focusing particularly on its regulation, and on the regulation of its applications to animal health, nutrition and performance.

* This is not a statement of the policy of the European Economic Community; opinions expressed engage only the author.

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Abbreviations used in this paper

BAP : Biotechnology Action Programme (EEC)
BEP : Biomolecular Engineering Programme (EEC)
BRIC : Biotechnology Regulation Inter-service Committee (EEC)
BRIDGE : Biotechnology Research and Innovation for Development and Growth in Europe (EEC)
CAP : Common Agricultural Policy (EEC)
CUBE : Concertation Unit for Biotechnology in Europe (EEC)
CVMP : Committee for Veterinary Medicinal Products (EEC)
DG : Directorate-General (EEC)
DNA : deoxyribonucleic acid
EC : European Community
ECLAIR : European Collaborative Linkage of Agriculture and Industry through Research (EEC)
ECU : European Currency Unit (EEC)
EEC : European Economic Community
FAST : Forecasting and Assessment in Science and Technology (EEC)
GATT : General Agreement on Tariffs and Trade
GILSP : Good Industrial Large-Scale Practice (OECD)
GMM : genetically modified micro-organism
GMO : genetically modified organism
MECU : million ECU
NCA : National Competent Authority (EEC)
OECD : Organisation for Economic Co-operation and Development
OTA : Office of Technology Assessment (USA)
R & D : Research and Development
rDNA : recombinant DNA
RTD : Research and Technological Development (EEC)
BACKGROUND

The responses to biotechnology: from research to policy coordination

From the mid-1970's, Commission scientists conscious of the dramatic developments in the life sciences argued for a Community research programme in the field of genetic engineering and enzymology – collectively referred to as "biomolecular engineering". It was not until late 1981 that an initial, modest programme was launched: "BEP", the Biomolecular Engineering Programme, ran from 1982 to 1986, with a budget of 15 MECU (the European Currency Unit or ECU is roughly comparable to the US dollar; currently, it is worth rather more, in the early 1980's, rather less) (3). Long before then, and not long after Asilomar, the widespread debate on rDNA safety had led the Commission to prepare a proposal for a Community Directive requiring strict and statutory containment standards for rDNA experiments (4). This was debated from 1978 to 1982, with Member State experts and with the European Parliament. During these years, the scientific debate advanced. Experience accumulated with DNA recombination, without concomitant accidents or unforeseeable surprises. With some inevitable time-lag, the diminishing concerns filtered through to governmental and political circles. In consequence, the outcome of the long debate in the Community institutions was Council Recommendation 82/472 (14), recommending that Member States institute national registration of rDNA work. This was implemented, with varying speed and intensity of surveillance, in most (but not all) Member States in the years which followed.

The research programme "BEP" included two projects on risk (or "safety") assessment, and this element has been substantially amplified in subsequent programmes. The Biotechnology Action Programme (BAP) (75 MECU, 1985-1989) devoted over 5 MECU to research into methods of detecting leaks from containment of recombinant organisms, and into methods of detecting or monitoring the spread of deliberately-released recombinant organisms (or the horizontal movement of plasmids) in the open environment – air, soil, water. At the time of writing, over 50 laboratories, in all Member States, are involved. A further call for proposals relating to safety assessments associated with the release of genetically-engineered organisms in the environment was announced mid-1990, deadline 15 September, as part of the "BRIDGE" programme (Biotechnology Research and Innovation for Development and Growth in Europe; 1990-1993; 100 MECU) (17). BAP and BRIDGE have supported pre-competitive, cost-shared projects designed to strengthen the scientific base of European industry. They have included, amongst other areas, work on molecular virology and genetics relevant to the development of animal vaccines, using genes coding for viral coat proteins.

In regard to the regulatory strand of Community responses to biotechnology, see paragraph 3) below. In addition to regulation and to research, a third important and continuing strand has been technology assessment. The US Congressional Office of Technology Assessment ("OTA"), founded in 1972, has attracted world-wide interest in its role at the interface between science and public policy. In particular, it has produced a series of excellent reports on biotechnology and related topics since 1981 (26). Partly drawing on this model, partly inspired by the role of US "think-tanks" such as the Rand Corporation and the Hudson Institute, the European Community agreed in 1978 to create a programme known as "FAST" (Forecasting and Assessment in Science and Technology), implemented by a unit of the same title within the Commission's Directorate-General for Science, Research and Development (DG XII).
One of the three priority topics of FAST was a wide-ranging assessment of biotechnology, under the heading "Bio-Society". This was published along with the other recommendations in a December 1982 report, and, in conjunction with inputs from other Commission services, inspired two official communications the following year (5, 6).

The Commission communication recognised the multi-faceted character of biotechnology. Its multi-disciplinary roots and multi-sectoral fields of application demanded the involvement of several services, and the October 1983 communication (6) outlined six "action priorities", effectively amounting to a Community strategy for biotechnology.

1) **Research and training** programmes (see above, BAP and BRIDGE; a further 164 MECU biotechnology programme, "BIOTECH", 1990-1994, is currently under debate) (12);

2) **Pricing of raw materials of agricultural origin** for industrial use (new regimes introduced in 1986 brought prices for industrial use of sugar and starch closer to world market prices, and were essential elements for encouraging the development of new, non-food outlets for European agriculture);

3) **Regulatory developments** (see below);

4) **Intellectual property rights** (a proposal for the protection of biotechnological inventions was put forward by the Commission in October 1988 (9) and is still under intense debate in European Parliament, Council and Member States, often closely in conjunction with debate on a proposed regulation for a Community-wide system of plant breeders' rights) (10);

5) **Demonstration projects**, at the interfaces between agriculture and industry (the ECLAIR programme, 80 MECU, 1989-1993 (18) stands for "European Collaborative Linkage of Agriculture and Industry through Research", and typically involves pre-competitive R & D work on new and improved inputs to agriculture, new and improved cultivars and downstream transformation; such work will be amplified, with genuine demonstration projects, in a new programme now before Council and Parliament) (11).

6) **Concertation** (an inter-service coordination function, administratively located in DG XII and funded under the research budget from the BAP and BRIDGE programmes).

This six-point strategy has in fact been implemented over the subsequent years, in the sense that action on the lines envisaged has followed on all six points. These involve research, agricultural and regulatory policy matters, and their coordination. Given the continuing nature of policy requirements in each of these areas, and the continuing challenges to policy (not least from scientific and technical progress), all of the issues remain current in the 1990's, in spite of the specific actions taken: "Plus ça change, plus c'est la même chose" (the more things change, the more they remain the same).

Amongst the actions taken by the Commission to enhance coordination was the establishment in February 1984 of a high-level, inter-service "Biotechnology Steering Committee", supported by a secretariat ("CUBE": the Concertation Unit for Biotechnology in Europe). CUBE was charged with monitoring and inter-service coordination, in conjunction with the other interested services; responsibilities
amplified by extension to Community-Member State coordination in the context of BAP and subsequent biotechnology programmes. Meeting infrequently, the Biotechnology Steering Committee established in July 1985 a Biotechnology Regulation Inter-service Committee ("BRIC"), which has met almost forty times in the past five years, to exchange information and seek to develop consensus on regulatory initiatives in biotechnology – particularly in line with the 1986 communication of the Commission (8), and in concertation with work elsewhere, particularly at the OECD (25).

The multi-faceted character of biotechnology poses growing problems of inter-agency, inter-Ministerial and (within the Commission) inter-service coordination. These have been described elsewhere (2); illustrative is the fact that when the European Parliament debated biotechnology, from a public hearing in November 1985 to the adoption of resolutions in February 1987 (22, 23), six different committees were involved. Similarly in the regulatory area, each individual initiative may be conceived and developed within one area – worker safety, animal welfare, environmental protection, food safety, pharmaceutical or veterinary medicinal products, pesticides, animal feedstuffs, etc. The proposed initiative is thereafter led by the service concerned within the Commission, in dialogue with the corresponding sectoral interest groups, with Member State Ministries, and corresponding Ministers and their advisers, in the Council of Ministers, and with the corresponding lead committee on the European Parliament.

Thus the multi-faceted, cross-cutting or "horizontal" character of biotechnology has to be sliced into the "vertical" requirements of the institutions responsible for policy-making, legislation, and executive action. It is the intention of the Commission in the latter half of 1990 to publish a new general communication on biotechnology, led by the Industry service (DG III), and emphasising the promotion in Europe of the "competitiveness of the economic activities based on biotechnology" – a phrase presumably embracing agriculture. As already indicated, the 1990 communication must inevitably treat the same topics as that of 1983 – amongst them research, agriculture, regulation; so what will be new?

Evidently seven years have seen great progress in the life sciences, but the resulting novelty in the policy arenas derives from the progressive application and commercialisation of biotechnology in health, agriculture, environment and other areas. It becomes more visible. It raises regulatory issues, not only of speculative risks to health or environment, but extending even into ethical domains. Questions of "socio-economic impact" are raised, in the context of specific molecules or more generally, and these concerns impinge increasingly on policy-making and regulation, not least in the area of veterinary products.

Having explained at length the evolving complexity of the policy context for biotechnology, similar issues are now traced in the specific contexts of agricultural and internal market policy.

**Agricultural policy**

The original objectives of the common agricultural policy ("CAP") of the European Community are detailed in Article 39 of the founding treaty, reproduced below:
"Article 39

1. The common agricultural policy shall have as its objectives:

(a) to increase agricultural productivity by developing technical progress and by ensuring the rational development of agricultural production and the optimum utilisation of the factors of production, particularly labour;

(b) to ensure thereby a fair standard of living for the agricultural population, particularly by the increasing of the individual earnings of persons engaged in agriculture;

(c) to stabilise markets;

(d) to guarantee regular supplies; and

(e) to ensure reasonable prices in supplies to consumers.

2. In working out the common agricultural policy and the special methods which it may involve, due account shall be taken of:

(a) the particular character of agricultural activities, arising from the social structure of agriculture and from structural and natural disparities between the various agricultural regions;

(b) the need to make the appropriate adjustments gradually; and

(c) the fact that in Member States agriculture constitutes a sector which is closely linked with the economy as a whole.”.

The generality and breadth of these objectives provide a legal base for the many specific directives and regulations through which the CAP is implemented. In general, the legal base for agricultural policy measures is Article 43, which provides for the issuing of regulations and directives and the making of decisions. These legislative acts depend upon a qualified majority decision by the Council of Ministers — for agricultural matters, in practice, the Ministers of Agriculture.

Scientific and technical progress, at every level from basic biology to near-term, application-orientated agricultural research, has contributed greatly to the transformation of policy problems and priorities in European agriculture. In particular, the growth of productivity and the price support policies have combined to bring the Community into surplus in a growing number of product areas, and the cost of the policy has increasingly become a central issue in the debate on the growth and control of the Community budget.

This shift of emphasis has several inevitable consequences, and changes the relative political priorities of the various objectives named in Article 39 of the Treaty.

An agreement in February 1988 between the three major Community Institutions — Commission, Council and Parliament — set limits for the following five years on the growth of Community resources, and on the percentage which agricultural support would form of the total budget. Within agriculture, this led to specific control measures, such as quotas on milk production, and the “stabiliser” system whereby cereal production in excess of a defined total (currently 160 million tonnes) gives rise to a corresponding reduction in the price paid to producers.
The apparently inexorable and world-wide growth of agricultural productivity (at least in the temperate zones of Western Europe and North America), combined with saturated markets, have led to increasing economic and political conflicts between the major producing areas. Resolution of shortage problems within agriculture, and recognition of the beneficial effect of increasing world trade on national economic growth, have in recent years led towards political consensus on moving towards agricultural systems less sheltered than in the early post-war decades from the pressures and challenges of global competition; cf. the declaration at the Toronto Summit (of the seven major economies and the European Community) in June 1988: "In agriculture... our negotiations in Geneva must develop a framework approach... concerning the reduction of all direct and indirect subsidies and other measures affecting... agricultural trade. The objective of the framework approach would be to make the agricultural sector more responsive to market signals". A similar sentiment was reiterated at the close of the Houston Summit in July 1990.

These changes in the global context have led to a number of changes in the role which research is expected to play in support of the agricultural policy of the Community:

* a) the use of research to promote quality and cost competitiveness, and hence a greater attention to market demand (by final consumers or by industry);
* b) a lesser emphasis on increasing productivity, since if markets and production are limited, the effects of increasing productivity demand various uncomfortable changes;
* c) the use of research to discover and/or develop new outlets for agriculture, a diversification of agricultural production – hence programmes such as ECLAIR;
* d) demonstration projects, with the same object as c) but using known technology; some Member States seeking to link such projects with the "set aside" programmes for surplus agricultural land.

The Community, like most of its trading partners, is committed to GATT and to the success of the current "Uruguay Round" of negotiations; but it is clear (at the time of writing in mid-1990) that the liberalisation of world trade in agriculture is one of the more contentious issues on the agenda. It is feared and resisted in many quarters, including some Agriculture Ministries, because it is felt that it would accelerate pressures for structural adjustment and the trends towards "rationalisation" with consequent "rural desertification". At the same time, advocates of liberalisation have not been slow to present weighty economic and political arguments. A paper (24) in July 1990 from an Australian advocate reckons the global benefit of trade liberalisation at $400 billion per year, of which over half would accrue to the European Community. The Economist (21), veteran of a century and a half's battle for free trade, comments: "European politicians tempted to duck such awkward decisions should ask themselves whether the freedom to subsidise a sector that contributes less than 3% of Europe's GDP is worth saving if it puts the world's entire multilateral trading system in jeopardy."

To complete this review of the agricultural policy context, looking especially at those aspects having a bearing on biotechnology and veterinary regulation, three further strategically significant and partly interconnected factors should be mentioned.
Firstly, attention to consumer requirements has become much more than an issue of cost and quality of products. A range of widely-publicised issues — pesticide residues, food poisoning, the welfare of farm animals in intensive units, the environmental consequences of intensive animal units or loss of biological diversity attributed to large-scale monoculture — have led to some generalised loss of trust by consumers in their food supply; and to specific demands by some consumers relating to the methods of production used (cf. demands for "organic farming", rejection of additives and growth-promoters).

Secondly, regardless of impact on food quality, there is growing political concern about environmental degradation, local and global, with a recognition that agriculture has contributed to the problems, and must be profoundly implicated in the solutions.

Thirdly, on a more long-term and global scale, there is growing concern about the food supply/demand balance, and the ability of the world’s agricultural systems to sustain, indefinitely and without further environmental degradation, a human population rising to 10 billion or more within a few decades. For a recent sombre view, reference could be made to the successive "State of the World" reports from the Worldwatch Institute (1). Their successive annual reports have been devoting increasing attention to biotechnology. While they are critical of the role of profit-orientated private sector capital, they recognise the essential role of science and technology, and recognise that although biotechnology may be advancing too slowly in improving plant characteristics, it has contributed important advances to animal productivity.

Consumer demands, environmental constraints, global needs — all of these, together with the progress and potentials of research, are influencing the evolution of the agricultural policy of the European Community, and the consequent regulatory initiatives including those related to biotechnology.

Internal market policy and the Single European Act

The completion of the internal common market by the end of 1992 has been one of the major policy priorities of the Community institutions since 1985. In a "White Paper" that year (7) the Commission listed 300 proposals designed to remove all remaining barriers to the free movement of goods, services, capital and people. The adoption of legislation to promote the harmonisation or "approximation" of national law has progressed too slowly during previous years, in part because of the requirement for unanimous decisions at Council of Ministers for matters based on Article 100.

The "Single European Act" adopted in July 1987 was a modification of the original EC Treaty, with several aims. Article 8A enshrined the "1992" objective; Article 100A effectively replaced the old Article 100 on internal market legislation, and like several other elements of the new Act, legislation based on it would be adopted by qualified majority at Council, following a new "cooperation procedure" allowing greater powers of amendment to the European Parliament. This procedure would be the basis for most of the 300 legislative proposals.

The Single Act also brought significant institutional reinforcement to Community efforts in "Research and Technological Development", by adding a Title VI, with
this heading ("RTD") to the EC Treaty. This defined the aim of the Community’s RTD efforts as being to strengthen the scientific basis for Europe’s industrial competitiveness, with particular reference to international trade (Article 130F, paragraph 1). In paragraph 3 of the same Article, emphasis is laid on the connection between the RTD effort and the completion of the internal market, along with the implementation of other common policies. Thus a firm legal base underpins the linkage of Community research programmes to development of the scientific basis for harmonised Community regulations.

Of the 300 proposals in the 1985 White Paper, some have been dropped, others combined, new proposals added, giving by the beginning of 1990 a net target of some 279 measures to be adopted by Council by the end of 1992. Veterinary and phytosanitary control measures account for 77 of these — over a quarter — and of these 77, at least 50 have now been put forward by the Commission. The topic of specifically veterinary legislation is discussed below, after a review of the general progress on regulation relating to biotechnology.

REGULATION RELATING TO BIOTECHNOLOGY

In general, the regulation of biotechnology is dealt with under:

**Sectoral provisions:**
- foodstuffs and related (> 300 directives)
- human and veterinary medicinal products (major new proposals imminent, for a "European Medicines Agency" and a new "centralised" procedure)
- animal feedstuffs, additives, test and inspection procedures
- pesticides
- other agricultural policy initiatives, including veterinary provision relating to disease control and protection of public health;

but there are also:

**"Horizontal" provisions:**
- animal welfare
- general product safety
- worker safety (e.g. vis-a-vis biological agents);

and, amongst the "horizontal", some rDNA-specific:

- registration of laboratory rDNA work (14)
- contained use of genetically-modified micro-organisms (GMMs) (19)
  - non or pre-commercial
  - commercial
- field release of genetically-modified organisms (GMOs) (20)
  - experimental
  - market authorisation.
Other regulatory initiatives concern **intellectual property**:

- patents (proposed directive for the protection of biotechnological inventions under discussion) (9)
- plant breeders’ rights (proposed Community Regulation under discussion) (10).

Of particularly topical interest are the two rDNA-related directives adopted on 23 April 1990 for the contained use of GMMs (90/219/EEC) and the deliberate release of GMOs (90/220/EEC). Implementing legislation has to be introduced in Member States by 23 October 1991. The former distinguishes between “Group 1” GMMs, low-risk micro-organisms as defined by the “GILSP” (Good Industrial Large-Scale Practice) criteria of the OECD (25): and “Group II”, all others. Research operations (“Type A”) and commercial production (“Type B”) are separately treated. Notification requirements and authorisation (where required) are dealt with via designated national competent authorities.

The legal basis, Article 130S, is in Title VII of the EEC Treaty (Environment), and constitutes “floor” legislation, on top of which Member States may add national requirements (subject to compatibility with the Treaty).

The “deliberate release” directive is based on Article 100A, part of the legislation aiming to facilitate completion of the internal market. The preamble emphasises preventive action; the self-reproducing character of organisms, hence possibility of irreversible effects; the need to ensure the safe development of industrial products using GMOs (i.e. the intent, however apparently restrictive in detail, is fundamentally positive); case-by-case evaluation (i.e. we are not yet ready to define exemption categories); and a “step-by-step” approach from research to commercialisation.

The directive is in 4 parts, plus corresponding annexes, and can be summarised as follows:

**Part A: General** (Articles 1-4), definitions, exclusions (Annex I), a general obligation laid on Member States to take “all appropriate measures to avoid adverse effects”; and the requirement to define a “national competent authority” (NCA).

**Part B: for R & D or other activities not involving placing on the market** (Articles 5-9), requires notification to NCA of details as specified in Annex II; NCA transfers to Commission within 30 days, who transmit to other Member States within a further 30 days; the original NCA has to respond to the notifier within 90 days.

Where sufficient experience is judged to have accumulated, an NCA may propose to the Commission a simplified procedure. NCAs may also require public consultation. The notifier has to submit a post-release report on health and environment risks. There will be developed a system for the exchange of summary information.

**Part C: for placing on the market of products comprising or containing GMOs** (Articles 10-18), consent to marketing of such products is to be given only if the products comply with an environmental risk assessment as specified in Annexes II and III. For products covered by EC legislation providing for a specific environmental risk assessment similar to the provisions laid down in this directive, the remainder of Part C (Articles 11-18) need not apply. The Commission has to establish by 23 April 1991 a list of such EC legislation, but the list is so far empty.
Article 11 requires notification to NCA, which has within 90 days to provide a reasoned rejection (Article 12), or forward the application to the Commission, who transmit immediately to the other Member States. Absence of objection within 60 days leads to automatic approval.

If there are unresolved objections, there is a decision at Commission level in accordance with the Article 21 procedure.

**Part D: Final Provisions** (Article 19-24), defines the Commission-level committee decision procedure, and includes provision for adaptation to technical progress of the requirements specified in Annexes II and III.

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**VETERINARY LEGISLATION**

**Structures of responsibility**

This article does not attempt to provide a comprehensive statement and review of the history and aims of veterinary legislation within the European Community; but in this section, an outline is given of its main features as the context for a more specific focus on legislation for biotechnology. The "structures" involved within the Commission of the EC are DG VI (Agriculture); DG III (Internal Market and Industrial Affairs); and DG XII (Science, Research and Development).

Veterinary legislation within the Community has naturally been closely associated with the common agricultural policy. A number of specific sources of complexity need to be noted. Firstly, there remain substantial responsibilities at national level, effectively with Member State Ministries of Agriculture, for matters of animal health and disease control. Article 36 of the EC Treaty, unmodified by the Single European Act, allows national imposition of restrictive measures and prohibitions "in respect of importation, exportation or transit which are justified on grounds of public morality, public order, public safety, the protection of human or animal life or health...", although it goes on to state that "Such prohibitions or restrictions shall not, however, constitute either a means of arbitrary discrimination or a disguised restriction on trade between Member States".

Secondly, the agricultural policy has to interact closely with regulatory or other policies for the industry sectors upstream and downstream of the farm, which provide the farmer with products and services such as feedstuffs and veterinary medicinal products; and which transform and place on the market the products of agriculture. For various historical and institutional reasons, animal feedstuffs and additives have been dealt with as "agricultural legislation", as has the placing on the market of primary agricultural products, including live animals and unprocessed meat or other animal products.

Veterinary medicinal products have followed a regulatory track close to that of human pharmaceuticals, and, like processed foods, have been treated within the Directorate-General for Internal Market and Industrial Affairs. Naturally, there has been long-standing and close cooperation between the Commission services involved; but the historical and political special position of the agricultural sector, reflected
also in Ministerial structures throughout the Member States and elsewhere in the world, obliges one to recognise that differences are not a reflection but a cause of the separate treatment within the Commission.

The sections below reflect these separations, and the topics treated illustrate that the effects of a third element, science and technology, whether commanded or unsolicited, insistently impinge upon agriculture, its inputs, products and markets.

**Animal health and feedstuffs**

Basic political commitments to the harmonisation of veterinary and feedstuffs legislation have been made by successive Council Resolutions in 1974, 1981 and again on 10 May 1984 (15). The latest of these adopted a work programme, emphasising the importance of continued harmonisation work in the sectors concerned, to consolidate the internal market and ensure smooth running of the CAP by eliminating trade barriers, and “to achieve a product-quality sufficiently high to ensure protection of consumers and the environment”.

In the area of *Animal health*, the 1984 resolution envisaged the adoption by Council over the following years of proposals on:

- amendments to existing Directives, or new rules, concerning *trade* in live animals, fresh meat and eggs (for hatching or consumption) with reference to foot and mouth disease, brucellosis, classical swine fever, African swine fever, Aujeszky’s disease, swine vesicular disease, leucosis and public health

- programmes, or amendments to existing measures, on *combatting diseases*; particularly classical swine fever (hog cholera), foot and mouth disease

- various rules on *testing producers, inspection and standards*

- rules and standards concerning breeding animals and semen

- rules on medicated feedstuffs.

In the area of *feedstuffs*, the proposals envisaged related to additives, undesirable substances and compound feedstuffs.

The above programme provides a general overview of the domains of veterinary legislation. In general, no specific reference is made to biotechnology; but evidently biotechnology has over the years become of growing relevance to the diagnostic, therapeutic and prophylactic products involved in disease detection, control and prevention. Improved understanding of animal nutrition has similarly created opportunities for improved products.

In the area of feedstuffs, and following controversy in some countries over the use of single-cell protein, a Council Decision (82/471/EEC) was adopted to establish a positive list (including yeasts) of proteinaceous “substitution products” used in animal nutrition. The subsequently adopted guidelines for the assessment of such products specify the details to be supplied in the dossier, under four headings:

- *a*) micro-organisms, culture medium and manufacturing process, characteristics of product, presentation and conditions of use, methods of determination (details have to be provided of any genetic manipulation);
b) studies on the nutritional properties of the product;

c) studies on the biological consequences of the use of the product in animal nutrition;

d) other relevant studies (e.g. allergic or other effects in handling the product, and their prevention).

The regulation of veterinary medicines derived from biotechnology

For historical reasons, the development within the European Community of legislation regulating the placing on the market of veterinary medicines has tended to follow the regulation of medicinal products for human use.

The basic rules governing the marketing of veterinary medicinal products are contained in two Directives which were adopted by the Council in 1981 and entered into force in October 1983 (Directive 81/851/EEC and 81/852/EEC, Official Journal No. L 317; 6 November 1981). These Directives were based largely on the Directives applicable to medicinal products for use in human beings and they resulted in similar consequences for the free movement of veterinary medicinal products within the Community. In particular:

- in principle, the main criteria which should be taken into consideration by the Member States during the examination of an application for authorisation are the quality, safety and efficacy of the product concerned. These criteria have been extensively harmonised, as have certain aspects of the procedures for granting marketing authorisation (time limits, giving of reasons, publication of decisions, etc.) and for granting manufacturing authorisations (quality control, inspections, etc.)

- analytical, pharmaco-toxicological tests and clinical trials which have been conducted in accordance with the Community rules need no longer be repeated within the Community

- the batch control reports of the manufacturer are accepted by the other Member States without repetition of the individual control test

- the general requirements regarding labelling and package inserts have been harmonised

- a common list of colouring matters approved for use throughout the Community has been adopted.

However, there are significant differences in the detailed rules applicable to veterinary medicinal products which result from the widespread use of medication for prophylactic purposes and from the need to ensure that foodstuffs obtained from treated animals do not contain residues which might present a risk to the health of the consumer.

At present, this legislation does not apply to immunological products. The Commission has presented a proposal to the Council, to extend the scope of the Directives to cover immunological veterinary medicinal products [COM(88)779]. There is general agreement, among Member States of the Community and in the European Parliament, on the objectives of this legislation and it is hoped it may be adopted before the end of 1990, and enter into force in January 1992. In addition, it will be necessary to establish detailed standards and protocols for the testing of immunological veterinary medicinal products. A special working party has been established for this
purpose, working in close collaboration with the European Pharmacopoeia, which has traditionally taken a strong interest in the development of standards for veterinary vaccines.

From a relatively early point of time, it was clear that one of the most important commercial applications of biotechnology would be in the field of medicinal products, both for human and veterinary use. The pharmaceutical sector was therefore closely integrated into the overall Community action programme for biotechnology described above. In addition, it was necessary to consider whether any special sectoral initiatives were required.

Following numerous consultations with Member States, the professions and the industry, it became apparent that the advent of biotechnology should not fundamentally change the basis of medicines regulation within the Community. After all, the clinician, the end user of the product, is ultimately concerned with the therapeutic effects of the product, not the process by which it is derived.

However, three areas were identified where action was required. First, it was considered that steps should be taken to try to provide medicines derived from biotechnology with rapid access to a continental-scale market, through a special Community procedure to coordinate the decisions of Member States on these products.

Second, specific changes to the detailed technical requirements laid down in the legislation might be required, in particular to guarantee the quality and safety of these products. This aspect is being taken into consideration during the development of the detailed requirements for the testing of immunological products.

Third, while awaiting the outcome of general initiatives to improve the patentability in Europe of biotechnological inventions, steps should be taken to improve the protection of biotechnology medicines. The Commission therefore proposed the introduction of a limited ten-year protection for innovatory manufacturers. This protection which does not replace and is not a substitute for patent rights, ensures that the manufacturer of a new biotechnology product has a guarantee that for ten years no generic product or copy of his product will be authorised without his consent unless the copier has also carried out all the various tests and trials necessary to demonstrate the quality of the product. It is intended as an interim provision, pending decisions on a more complex issue of the extension of patent protection for biotechnological inventions and the extension of the effective life of pharmaceutical patents.

However, the most important aspect of the changes made was the introduction of the special Community coordination procedure for applications for authorisation concerning medicinal products derived from biotechnology under Directive 87/22/EEC (Official Journal No. L 15 of 17 January 1987).

The use of the procedure is compulsory in the case of applications to market veterinary medicinal products derived from biotechnology, including immunological products. For other high technology veterinary medicinal products, which are defined in the annex to Directive 87/22/EEC, the use of the procedure is optional.

As soon as it receives an application for authorisation, the Member State concerned must refer the application to the Committee for Veterinary Medicinal Products (CVMP) for an opinion. The CVMP consists of representatives of the Member States,
usually the persons responsible for deciding whether or not to licence veterinary medicines in their home countries, and of the EEC Commission which also acts as Secretariat to the Committee.

In order to enable as many Member States as possible to participate actively in the procedure, companies are encouraged to apply simultaneously for authorisation in as many Member States as possible, and the other Member States receive at least a detailed summary of the application and preferably a full dossier. One Member State, usually the Member State which first referred the application to the Committee, acts as rapporteur and prepares an initial evaluation of the product which is then circulated to the other Member States who add their own comments on the application. A single list of questions and comments is sent to the company which is expected to prepare a single consolidated response to all the questions. In addition, the company has a right to a hearing before the Committee gives its opinion. The opinion is not binding, but the Member States must decide what action to take within 30 days of the receipt of the opinion. The whole procedure must be completed within defined time limits, which ensures that the normal time limits allowed for the examination of applications at the nation level are not exceeded.

To date, the CVMP has had to consider applications for two types of product derived from biotechnology; performance enhancers, such as bovine somatotropin (BST), and vaccines.

Since there is no provision for voting within the CVMP, the Committee always tries to reach its opinions by consensus, and hitherto this has been possible because the Committee strictly limits its role to the evaluation of scientific questions linked with the three criteria, to the exclusion of economic, social or political considerations.

However, as noted above, the opinions of the Committee are not binding, and so the procedure cannot guarantee the adoption of uniform decisions about products binding throughout the Community.

In January 1990, Commission President Jacques Delors announced that the Commission would be proposing the creation of a European Medicines Evaluation Agency, and of centralised Community evaluation procedures leading to binding decisions throughout the Community for this category of medicinal product derived from biotechnology. At the time of writing (July 1990), the detailed preparation of legislative proposals was in progress and it was anticipated that they would be presented by the Commission in October 1990.

A further question, which has been the subject of substantial debate within the Community, concerns the criteria for the authorisation of new veterinary medicines which are intended for use as performance enhancers, particularly in connection with BST. A number of influential voices have been raised in favour of the introduction of a fourth hurdle, based on the demonstration of an economic and social need for the product. Although the fact that BST is derived from biotechnology is sometimes raised in this connection, this does not appear to be fundamental to the debate, which is more concerned with a public malaise about the unnecessary use of artificial inputs in agricultural production, in particular in animals. This issue is further discussed below.

Animal welfare

All Community Member States participate in the 18-nation Council of Europe, in which the democracies of Western Europe participate in various activities of
common interest. These have included debates and working groups on various topics of an ethical character, for instance, on human embryo research and in vitro fertilisation.

In the area of animal welfare also, Conventions have been developed by the Council of Europe, relating to the welfare of animals, including one on animals used in agriculture and another on the use of animals in scientific experimentation. The latter has also been incorporated in a Community Directive (16), and a Council Decision (13) has indicated the support of the Community for the former.

Debate is in progress within the Commission services as to whether it is necessary or desirable to introduce legislation relating specifically to transgenic animals, or to the placing on the market of such animals and their products.

**THE FUTURE**

On both sides of the Atlantic, concern has been expressed about the gap between the general level of the public understanding of science, and the inevitably increasing dependence of society upon advanced science and technology, in agriculture as elsewhere. Public interest and responsive media have highlighted various problems of recent years, ranging from suspicions about residues in animal products (of pesticides, medicines, growth promoters, feed additives, etc.) to concerns about animal welfare in intensive units, food poisoning outbreaks, and the possible transfer of disease (specifically bovine spongiform encephalopathy) to man. Such reports and concerns have all damaged the climate of consumer confidence. The lack of understanding, or the sometimes poor quality of public debate have not inhibited, or have even amplified, such suspicions.

At the height of the controversy over steroid hormones, the Commission had to restate a democratic principle: "Scientific advice is important, but not decisive: this is a political matter, that has to be resolved by political means". The loss of trust by the consumer was not necessarily in the science; it could equally well be in any or all of the farmers, the industry or the public control and inspection procedures.

In the climate of distrust, various less valid arguments, of sectoral protectionism, or simplistic anti-technology movements, could cloak themselves in the respectability of concerns about various rather vaguely-phrased arguments of social, economic or ethical implications, or even of consumer need. The socio-economic assessments which need to accompany any major public policy measures, including the choices of research priorities for publicly-funded research or the institution of technology-related legislation, have been interpreted as a rationale for the imposition of arbitrary restrictions upon specific innovations.

In these circumstances, both the industry and the Commission have initiated activities to address the issues of public information, and the building or maintenance of public confidence. Of particular importance in the development of dialogue between public authorities, industry and public, are the consumer research organisations. Understandably suspicious of the industry, such groups have a commitment to scientific method and objective criteria in the interest of the consumer and the general public. From such commitments, dialogue can be built, given the maximum of integrity and transparency from the industry and from the scientific community. Public interest representatives such as the consumer representatives, or their appointed experts, may seek involvement, for example, in the definition of public interest research priorities, and could be welcomed.
The gradual development of a climate of greater trust has become a major object of public policy in biotechnology; for only in such a climate can it be expected that a science-based and objective regulatory framework will be politically acceptable, enjoying the confidence and contributing to the benefit of the general public.

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SCIENCES VÉTÉRINAIRES ET ASPECTS RÉGLEMENTAIRES DE LA BIOTECHNOLOGIE EN EUROPE. – M.F. Cantley.

Résumé: Si les biotechnologies ont fait progresser les sciences de la vie et leurs applications, elles génèrent par contre, pour les autorités responsables et le législateur, des défis de plus en plus nombreux dans différents domaines, dont la recherche, l’agriculture, l’industrie et l’environnement. Les dispositions réglementaires adoptées dans la Communauté européenne évoluent dans un contexte de changement rapide et constant, qu’expliquent l’impératif politique du marché unique et l’influence non négligeable des engagements internationaux plus larges du principal bloc commercial mondial.

Les progrès scientifiques permettent d’assurer un haut niveau de protection de la santé humaine et animale et de l’environnement. Cependant, les interactions complexes entre sciences vétérinaires, agriculture et politique commerciale, réactions et perceptions des consommateurs à l’égard des denrées alimentaires ainsi que les conséquences économiques et sociales des innovations exigent un effort de communication soutenu pour que la population reste confiante dans les résultats des progrès scientifiques et le bien-fondé des décisions officielles et de la législation.


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CIENCIAS VETERINARIAS Y ASPECTOS REGLAMENTARIOS DE LA BIOTECNOLOGÍA EN EUROPA. – M.F. Cantley.

Resumen: Los adelantos logrados en las ciencias de la vida y sus aplicaciones gracias a las biotecnologías plantean crecientes retos a las autoridades responsables y a los legisladores en diferentes campos, especialmente en investigación, agricultura, industria y medio ambiente. Las medidas reglamentarias aprobadas por la Comunidad europea, conocen una evolución
rápida y constante debida a los imperativos políticos del Mercado Unico y a la fuerte influencia de los compromisos internacionales más amplios del mayor bloque comercial del mundo.

Los progresos científicos permiten lograr altos niveles de protección de la salud humana y animal, así como del medio ambiente. Sin embargo, las complejas interacciones entre las ciencias veterinarias, la agricultura y la política comercial, las reacciones y las percepciones de los consumidores respecto a los productos alimenticios, tanto como las consecuencias económicas y sociales de las innovaciones, requieren grandes esfuerzos continuos de comunicación con el fin de mantener la confianza del público en los resultados de los progresos científicos y el fundamento de la política gubernamental y la legislación.


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REFERENCES


