CHIMIA 48 (1994) Nr. 10 (Oktober)

Chimia 48 (1994) 469–470

ISSN 0009–4293

Biotechnology – Ethical and Political Pressure

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Only rarely a scientific matter is debated in such an emotional and lively way as in the case of biotechnology. This seems to be mainly due to the fact that despite of a clear differentiation between the terms biotechnology and genetic engineering confusion exists in the mind of the public and even among scientists.

A consumer's journal recently published an article under the title 'Is genetic engineering taking over our shops?' [1]. Worried consumers questions: Are they selling genetically engineered vegetables? Or do cheese, bread or beer contain substances manufactured by genetic engineering? Consumers suspect that everyone who does not expressly distance themselves from this new technology is secretly supplying genetically engineered foods and products. Shop-keepers label their areas as 'Genetic engineering-free zones'.

In a survey, admittedly not representative, 75% of mostly young persons questioned in Basel during the winter of 1993 supported the idea of drugs and vaccines manufactured by genetic engineering, but *ca.* 70% rejected genetically engineered tomatoes and rennet for cheese-making.

Biotechnology covers all methods for producing specific substances with the aid of living organisms like social consumables such as beer and wine, or medicines, agricultural chemicals, fertilizers, supplements for human and animal foods, and other substances. Although the fermentation of beer and wine is a bio-technological process known for centuries, and although the laws of genetics have been utilized since the stone-age for breeding animals and plants, the public only began to take an interest in biotechnology *ca.* 20 years ago when the American scientists *Cohen* and *Boyer* reported on the production of recombinant bacteria in 1973. Incidentally, this was the 'Date of birth' of genetic engineering also called gentechnology. Later the public became more and more interested in statements and questions concerning biotechnology in general and gentechnology in particular. Not only authorities and scientific organisations, but also the media were involved. The public war startled when genetic material was created that could be recombined across species. Controversial discussions, even among authorities have considered very strict regulations or even bans.

We all are specialists in this new branch of science and know the anxiety of the man in the street. The restrictions and controls which one has applied to himself show that the responsibilities of the scientists involved have been and are being taken seriously. However, also it never must be forgotten that the public expects and demands the topmost care and responsibility from everyone at all stages of research and production.

Unfortunately, totally unrealistic horror stories have slowed down technological developments in Europe. Various laws, regulations and even bans promulgated in many countries under the pressure of a disturbed populace have not been limited to the necessary control and licensing regulations to ensure quality, safety and efficacy of the products and their manufacture, but have very greatly delayed or even completely prevented research and development work. Overreactive, bureaucratic regulations have prevented the building of research centres or have led to their moving away. This hampering of technology in Europe not only has meant loss of jobs but also that valuable drugs already available in the USA and in Japan still cannot be introduced here.

However, this should not make us resigned. We have to uncover the various possibilities and opportunities of biotechnology and to inform the public of potential problems. Only by the most possible transparency can the widespread anxiety about the future be calmed and the foundations laid of evaluating the potential benefits.

Both biotechnology in general and genetic engineering in particular involve many different specialist fields. That is why very varied legal regulations also have to be obeyed (*Table 1*). The particular legal situations in the different coun-

Table 1. *Influences of Biotechnology, Laws and Regulations*

Influence of biotechnology on	Laws and regulations
– Environment	Different laws and regulations (*e.g.* GCP)
– Man/animal/plant	
– Production	*e.g.* GMP, GLP
– Product	

Table 2. *Levels of Stringency and Levels of Safety*

Safety level	OECD	USA NIH Production	Germany	EC
No risk	GILSP	Exempt	Safety level 1	Group I
Low risk	C1	BL-1-LS	Safety level 2	
Medium risk	C2	BL-2-LS	Safety level 3	Group II
High risk	C3	BL-3-LS	Safety level 4	

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tries shall not be mentioned explicitely, details can be found in the two remarkable brochures by *Ryser* and *Weber* [2].

With regard to 'GMP and validation in biotechnology': The GMP introduced for chemical manufacture in 1962, and the validation of the manufacturing processes and the analytical methods additionally required since the 1980s, are categorically required by licensing authorities in the case of biotechnological production processes. They cover criteria to protect workers, the environment and the products. Different levels of stringency are required depending on the level of safety (*Table 2*). The microoganisms most used for working with rDNA (*E. coli, B. subtilis, Sach. cerevisiae, etc.*) can be considered as harmless, even in large-scale production plants (GILSP: Good Industrial Large Scale Practice). However, unknown microorganisms are never classed as free of risk. Even with a low risk (safety level 2), care has to be taken to prevent escape of the organisms. At the levels 3 and 4 the demands made are at least those applicable to sterile drugs, such as air-locks for personnel, equipment and materials, showers, regular control of apparatus and sterilizers, special staff training, *etc.* In addition the escape of organisms in the effluent air, into water or wastes must completely be prevented.

Laboratories and production centres are regularly inspected by the authorities. As a basis for their inspections, the authorities require detailed descriptions of the plant, the work undertaken, the organization and the responsible staff, *e.g.* in a so-called *Drug Master File* (DMF), which takes the safety steps required in the factory into consideration. In addition, as with conventional medicines, efficacy, safety and pharmaceutical quality have to be demonstrated for the licensing (registration) of drugs manufactured by biotechnological methods. In principle, the different national authorities still examine the documentation independently according to their own rules. However, a centralized procedure is planned for the EC and can already be used voluntarily (*Fig.*).

Special guidelines have been issued in the EC and in USA for biotech products. They cover production and quality control as well as the preclinical biological safety testing of drugs manufactured by genetic engineering and of monoclonal antibodies. In the case of new genetically engineered products it is necessary to submit analytical methods to determine the purity of the bacterial proteins or the DNA and to detect unnatural modifications of the recombinant product. Possible degradation products and biological impurities derived from the host organism as well as biological modifications of the product must be examined or excluded.

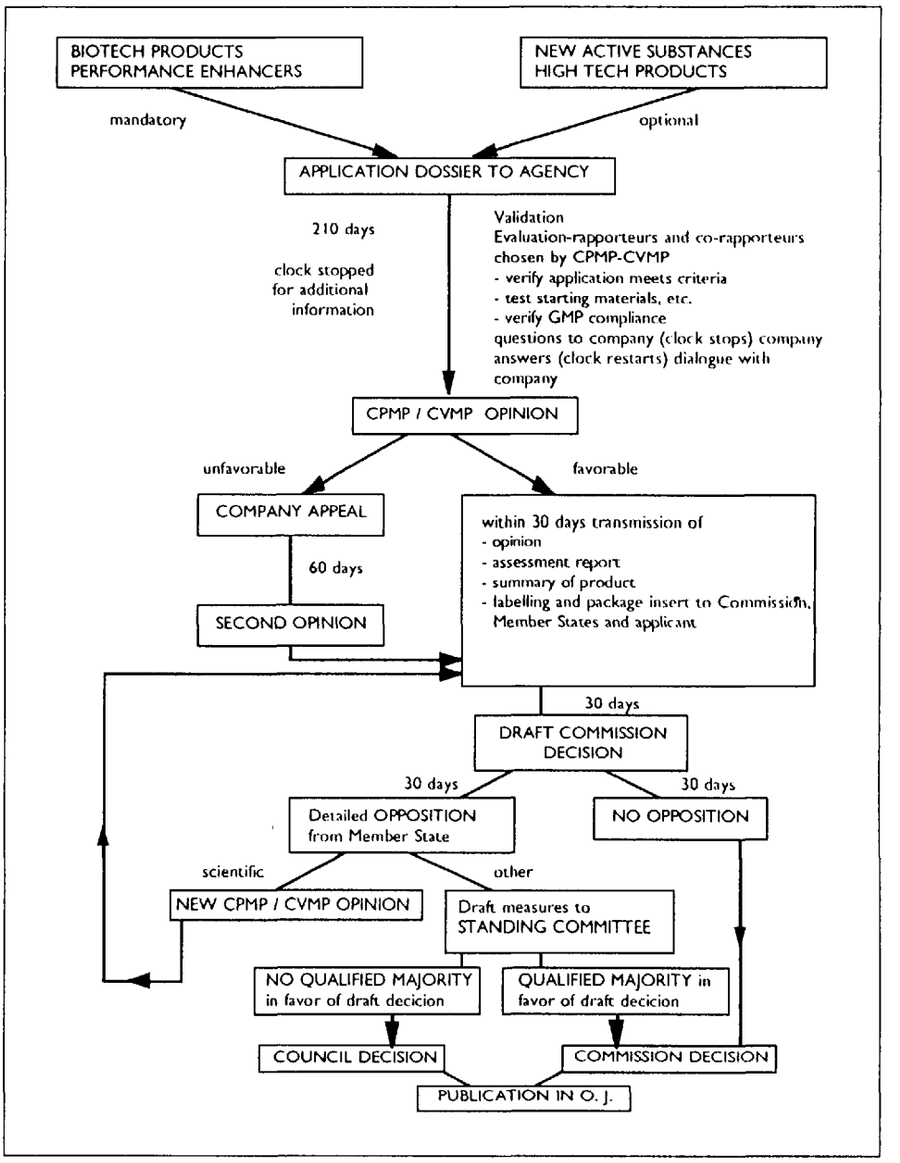

Figure. *Centralized procedure* (compulsory: biotechnological products; optional: NCE, high-tech products)

In general, apart from validating the analytical methods, validation of the manufacturing processes for the active ingredient and the finished product is required since even minor changes can affect the properties of a product.

It is to be hoped that the obstacles to technology will soon be a thing of the past, and that the opportunities offered by biotechnology and genetic engineering in medicine and industry will be fully grasped very soon in Europe also.

Conclusion

Biotechnology is debated in an emotional and lively way under the pressure of a disturbed populace misleaded by authorities into promulgating overreactive and bureaucratic regulations. Specialists in this new branch have seriously taken the responsibilities and applied restrictions and self-controls. Nevertheless, it has to be accepted that the public expects and demands the highest care at all levels of research and production. For the manufacture by biotechnological methods, different criteria to protect workers, the environment, and the products are required.

Received: September 6, 1994

[1] *Coopzeitung*, Nr. 32, 11.08.94.

[2] S. Ryser, M. Weber, 'Gentechnologie – eine Chronologie und Gentechnik – Was läuft bei Roche', Editiones <Roche>, Basel, 1990/1991.