

COUNCIL DIRECTIVE

of 22 December 1986

on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology

(87/22/EEC)

THE COUNCIL OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Economic Community, and in particular Article 100 thereof,

Having regard to the proposal from the Commission ⁽¹⁾,

Having regard to the opinion of the European Parliament ⁽²⁾,

Having regard to the opinion of the Economic and Social Committee ⁽³⁾,

Whereas the essential aim of any rules governing the production and distribution of medicinal products must be to safeguard public health ;

Whereas high-technology medicinal products requiring lengthy periods of costly research will continue to be developed in Europe only if they benefit from a favourable regulatory environment, particularly identical conditions governing their placing on the market throughout the Community ;

Whereas Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products ⁽⁴⁾, as last amended by Directive 83/570/EEC ⁽⁵⁾, makes provision for certain procedures for coordinating national decisions relating to the placing on the market of proprietary medicinal products for human use ; whereas pharmaceutical undertakings may, according to these provisions, request a Member State to take due account of an authorization already issued by another Member State ;

Whereas Council Directive 81/851/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to veterinary medicinal products ⁽⁶⁾ makes provision for a procedure for coordinating national decisions relating to veterinary medicinal products ;

Whereas, however, these procedures are not sufficient to open up to high-technology medicinal products the large Community-wide single market they require ;

Whereas, in this technically advanced sector, the scientific expertise available to each of the national authorities is not always sufficient to resolve problems posed by high-technology medicinal products ;

Whereas it is consequently important to provide for a Community mechanism for concertation, prior to any national decision relating to a high-technology medicinal product, with a view to arriving at uniform decisions throughout the Community ;

Whereas it is desirable to extend this Community concertation to immunological products and substitutes for blood constituents developed by means of new biotechnological processes, and to new products based on radioisotopes, the development of which in Europe can only take place if a sufficiently large and homogeneous market exists ;

Whereas the need for the adoption of new technical rules applying to high-technology medicinal products or for the amendment of existing rules must be examined during a preliminary concertation between the Member States and the Commission within the competent Committees so as not to endanger the advance of pharmaceutical research whilst at the same time ensuring optimum protection of public health within the Community,

HAS ADOPTED THIS DIRECTIVE :

Article 1

Before taking a decision on a marketing authorization or on the withdrawal or, subject to Article 4 (2), suspension of a marketing authorization in respect of the medicinal products listed in the Annex, Member States' authorities shall, in accordance with Articles 2, 3 and 4, refer the matter for an opinion to the Committees referred to in Article 8 of Directive 75/319/EEC and Article 16 of Directive 81/851/EEC.

Article 2

1. As soon as they receive an application for marketing authorization relating to a medicinal product referred to in the Annex (Lists A and B), the competent authorities shall, at the request of the person responsible for placing the product on the market, bring the matter before either

⁽¹⁾ OJ No C 293, 5. 11. 1984, p. 1.
⁽²⁾ OJ No C 36, 17. 2. 1986, p. 152.
⁽³⁾ OJ No C 160, 1. 7. 1985, p. 18.
⁽⁴⁾ OJ No L 147, 9. 6. 1975, p. 13.
⁽⁵⁾ OJ No L 332, 28. 11. 1983, p. 1.
⁽⁶⁾ OJ No L 317, 6. 11. 1981, p. 1.

the Committee for Proprietary Medicinal Products or the Committee for Veterinary Medicinal Products, in accordance with their competence, for an opinion. Any such request shall be submitted in writing to the competent authorities concerned at the same time as the application for marketing authorization and a copy shall be sent to the Committee concerned.

2. As soon as they receive an application for marketing authorization relating to a medicinal product developed by means of new biotechnological processes and referred to in List A in the Annex, the competent authorities shall be required to bring the matter before the Committee for Proprietary Medicinal Products or the Committee for Veterinary Medicinal Products, in accordance with their competence, for an opinion.

3. Paragraph 2 shall not apply if, when submitting the application for marketing authorization, the applicant certifies to the competent authorities of the Member State concerned that :

- (i) neither he nor any other natural or legal person with whom he is connected has, during the preceding five years, applied for authorization to place a product containing the same active principle(s) on the market of another Member State ; and
- (ii) neither he nor any other natural or legal person with whom he is connected intends, within the five years following the date of the application, to seek authorization to place a product containing the same active principle(s) on the market of another Member State.

In this case, the competent authorities shall notify the appropriate Committee of the application and forward to it a summary of product characteristics as described in Article 4a of Directive 65/65/EEC ⁽¹⁾, as last amended by Directive 87/21/EEC ⁽²⁾ or an equivalent document provided by the applicant if a proprietary medicinal product referred to in the second paragraph of Article 34 of Directive 75/319/EEC or a veterinary medicinal product is involved.

If, within five years of the first application, one or more subsequent applications for authorization to place a product containing the same active principle derived from the same route of synthesis on the market are made to the competent authorities of the other Member States by the person responsible for placing the original product on the market or with his consent, that person shall forthwith inform the competent authorities of the Member State to whom the first application was made and the matter shall be brought before the appropriate Committee for an opinion.

⁽¹⁾ OJ No 22, 9. 2. 1965, p. 369/65.

⁽²⁾ See page 36 of this Official Journal.

4. Where the Committee has, in accordance with this Directive, issued a favourable opinion on the placing on the market of a high-technology medicinal product, the competent authorities shall refer the matter to the Committee for a new opinion before deciding on the withdrawal or, subject to Article 4 (2), suspension of the marketing authorization for the medicinal product in question.

5. The competent authorities or the Commission may also consult the Committee for Proprietary Medicinal Products on any technical question concerning the proprietary medicinal products referred to in the second paragraph of Article 34 of Directive 75/319/EEC.

6. The competent authorities or the Commission may also consult the Committee for Veterinary Medicinal Products on any technical question concerning the veterinary medicinal products referred to in the second and third indents of Article 2 (2) of Directive 81/851/EEC.

Article 3

1. The representative of the Member State which initiated the procedure referred to in Article 2 shall act as rapporteur and shall provide all information relevant to the evaluation of the medicinal product. Information thus disclosed shall strictly confidential.

2. The person responsible for placing the medicinal product in question on the market shall immediately be informed of the referral to the Committee. He may, at his own request, provide the Committee with oral or written explanations.

3. When placing the matter before the Committee, the Member State concerned shall ensure that the person responsible for placing the medicinal product on the market transmits to all the members of the Committee an identical summary of the dossier consisting of the summary of the product characteristics together with the reports of the analytical, pharmaco-toxicological and clinical experts.

In addition, a complete and updated copy of the dossier for the application for marketing authorization lodged with the Member State or Member States concerned shall be transmitted to the Committee by the person responsible for placing the product on the market, who shall certify that all the dossiers submitted to the competent authorities and to the Committee in respect of the medicinal product in question are identical.

4. All available evaluation reports and drug-monitoring reports relating to the same medicinal product shall be forwarded to the Committee by the authorities of the Member States and by the person responsible for placing the product in question on the market.

Article 4

1. When the questions referred to it relate to an application for marketing authorization, the Committee shall issue its opinion thirty days before the expiry of the time limits provided for in Article 7 of Directive 65/65/EEC and Article 4 (c) of Directive 75/319/EEC, or in Articles 8 and 9 (3) of Directive 81/851/EEC, as appropriate. To this end, the Member State which referred the matter shall inform the Committee without delay of any extension and of the beginning and end of any suspension of the time limits concerned.

2. When a proposal to suspend or withdraw a marketing authorization is referred to it, the Committee shall fix an appropriate time limit for issuing its reasoned opinion, having regard to the requirements for the protection of public health. However, in cases of urgency, the Member States may suspend the marketing authorization in question without waiting for the opinion of the Committee provided that they forthwith inform the Committee thereof, indicating the reasons for the suspension and justifying the urgency of this measure.

3. The Committee shall forthwith notify its opinion and, where relevant, any dissenting opinions expressed therein, to the Member State concerned and the person responsible for placing the product on the market.

4. The Member State concerned shall reach a decision on the action it intends to take following the Committee's opinion not later than 30 days after receipt of the information provided for in paragraph 3. It shall forthwith inform the Committee of its decision.

Article 5

Subject to the application of other Community provisions, Member States shall communicate to the Commission in accordance with Articles 8 and 9 of Council Directive

83/189/EEC of 28 March 1983 laying down a procedure for the provision of information in the field of technical standards regulations⁽¹⁾, draft technical regulations relating to the production and marketing or proprietary medicinal products as defined in Article 1 of Directive 65/65/EEC.

Within one year of adoption of this Directive, the Commission will submit to the Council proposals for Regulations to harmonize, along the lines of Directive 75/319/EEC, the conditions for authorizing the manufacture and placing on the market of the proprietary medicinal products excluded by Article 34 of Directive 75/319/EEC and of the veterinary medicinal products referred to in Article 2 (2) of Directive 81/851/EEC, in view of in particular of the safety problems arising in production and use.

Article 6

Member States shall take the measures necessary to comply with this Directive not later than 1 July 1987. They shall forthwith inform the Commission thereof.

Article 7

This Directive is addressed to the Member States.

Done at Brussels, 22 December 1986.

For the Council

The President

G. SHAW

⁽¹⁾ OJ No L 109, 26. 4. 1983, p. 8.

*ANNEX***LIST OF HIGH-TECHNOLOGY MEDICINAL PRODUCTS****A. Medicinal products developed by means of the following biotechnological processes :**

- recombinant DNA technology,
- controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes, including transformed mammalian cells,
- hybridoma and monoclonal antibody methods.

B. Other high-technology medicinal products

- other biotechnological processes which, in the opinion of the competent authority concerned constitute a significant innovation,
 - medicinal products administered by means of new delivery systems which, in the opinion of the competent authority concerned, constitute a significant innovation,
 - medicinal products containing a new substance or an entirely new indication which, in the opinion of the competent authority concerned, is of significant therapeutic interest,
 - new medicinal products based on radio-isotopes which, in the opinion of the competent authority concerned, are of significant therapeutic interest,
 - medicinal products the manufacture of which employs processes which, in the opinion of the competent authority concerned, demonstrate a significant technical advance such as two-dimensional electrophoresis under micro-gravity.
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