

COUNCIL DIRECTIVE

of 26 January 1965

on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products

(65/65/EEC)

THE COUNCIL OF THE EUROPEAN ECONOMIC COMMUNITY,

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

Having regard to the proposal from the Commission;

Having regard to the Opinion of the European Parliament¹;

Having regard to the Opinion of the Economic and Social Committee²;

Whereas the primary purpose of any rules concerning the production and distribution of proprietary medicinal products must be to safeguard public health;

Whereas, however, this objective must be attained by means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the Community;

Whereas trade in proprietary medicinal products within the Community is hindered by disparities between certain national provisions, in particular between provisions relating to medicinal products (excluding substances or combinations of substances which are foods, animal feeding-stuffs or toilet preparations); and whereas such disparities directly affect the establishment and functioning of the common market;

Whereas such hindrances must accordingly be removed; and whereas this entails approximation of the relevant provisions;

Whereas, however, such approximation can only be achieved progressively; and whereas priority must be given to eliminating the disparities liable to have the greatest effect on the functioning of the common market;

HAS ADOPTED THIS DIRECTIVE:

CHAPTER I

Definitions and scope

Article 1

For the purposes of this Directive, the following shall have the meanings hereby assigned to them;

1. *Proprietary medicinal product:*

Any ready-prepared medicinal product placed on the market under a special name and in a special pack.

2. *Medicinal product:*

Any substance or combination of substances presented for treating or preventing disease in human beings or animals.

Any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings or in animals is likewise considered a medicinal product.

¹ OJ No 84, 4.6.1963, p. 1571/63.

² OJ No 158, 16.10.1964, p. 2508/64.

3. *Substance:*

Any matter irrespective of origin which may be:

— human, e.g.

human blood and human blood products;

— animal, e.g.

micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products, etc;

— vegetable, e.g.

micro-organisms, plants, parts of plants, vegetable secretions, extracts, etc;

— chemical, e.g.

elements, naturally occurring chemical materials and chemical products obtained by chemical change or synthesis.

Article 2

The provisions of Chapters II to V shall apply only to proprietary medicinal products for human use intended to be placed on the market in Member States.

CHAPTER II

Authorisation to place proprietary medicinal products on the market*Article 3*

No proprietary medicinal product may be placed on the market in a Member State unless an authorisation has been issued by the competent authority of that Member State.

Article 4

In order to obtain an authorisation to place a proprietary medicinal product on the market as provided for in Article 3, the person responsible for placing that product on the market shall make application to the competent authority of the Member State concerned.

The application shall be accompanied by the following particulars and documents:

1. Name or corporate name and permanent address of the person responsible for placing the proprietary product on the market and, where applicable, of the manufacturer.

2. Name of the proprietary product (brand name, or common name together with a trade mark or name of the manufacturer, or scientific name together with a trade mark or name of the manufacturer).

3. Qualitative and quantitative particulars of all the constituents of the proprietary product in usual terminology, but excluding empirical chemical formulae, with mention of the international non-proprietary name recommended by the World Health Organisation where such name exists.

4. Brief description of the method of preparation.

5. Therapeutic indications, contra-indications and side-effects.

6. Posology, pharmaceutical form, method and route of administration and expected shelf life if less than three years.

7. Control methods employed by the manufacturer (analysis and assay of the constituents and of the finished product, special tests, e.g. sterility tests, tests for the presence of pyrogenic substances, the presence of heavy metals, stability tests, biological and toxicity tests).

8. Results of:

— physico-chemical, biological or microbiological tests;

— pharmacological and toxicological tests;

— clinical trials.

However:

(a) a List of published references relating to the pharmacological tests, toxicological tests and clinical trials may be substituted for the relevant test results in the case of:

(i) a proprietary product with an established use, which has been adequately tested on human beings so that its effects, including side-effects, are already known and are included in the published references;

(ii) a new proprietary product, in which the combination of active constituents is

identical with that of a known proprietary product with an established use;

- (iii) a new proprietary product consisting solely of known constituents that have been used in combination in comparable proportions in adequately tested medicinal products with an established use;

- (b) In the case of a new proprietary product containing known constituents not hitherto used in combination for therapeutic purposes, references to published data may be substituted for the tests of such constituents.

9. One or more specimens or mock-ups of the sales presentation of the proprietary product, together with a package leaflet where one is to be enclosed.

10. A document showing that the manufacturer is authorised in his own country to produce proprietary products.

11. Any authorisation obtained in another Member State or in a third country to place the relevant proprietary product on the market.

Article 5

The authorisation provided for in Article 3 shall be refused if, after verification of the particulars and documents listed in Article 4, it proves that the proprietary medicinal product is harmful in the normal conditions of use, or that its therapeutic efficacy is lacking or is insufficiently substantiated by the applicant, or that its qualitative and quantitative composition is not as declared.

Authorisation shall likewise be refused if the particulars and documents submitted in support of the application do not comply with Article 4.

Article 6

The competent authorities of Member States may refuse to authorise the placing on the market of a proprietary medicinal product for use as a contraceptive where the sale of proprietary products intended principally for such purposes is prohibited under their laws.

Article 7

Member States shall take all appropriate measures to ensure that the procedure for granting an

authorisation to place a proprietary medicinal product on the market is completed within 120 days of the date of submitting the application.

In exceptional cases this time limit may be extended for a further ninety days. The applicant shall be notified of such extension before the expiry of the initial time limit.

Article 8

Member States shall take all appropriate measures to ensure that the holder of an authorisation furnishes proof that the controls have been carried out on the finished product in accordance with the methods described by the applicant pursuant to item 7 of the second paragraph of Article 4.

Article 9

Authorisation shall not affect the civil and criminal liability of the manufacturer and, where applicable, of the person responsible for placing the proprietary medicinal product on the market.

Article 10

Authorisations shall be valid for five years and shall be renewed for five-year periods, on application by the holder within the three months preceding expiry.

CHAPTER III

Suspension and revocation of authorisation to market proprietary medicinal products

Article 11

The competent authorities of the Member States shall suspend or revoke an authorisation to place a proprietary medicinal product on the market where that product proves to be harmful in the normal conditions of use, or where its therapeutic efficacy is lacking, or where its qualitative and quantitative composition is not as declared. Therapeutic efficacy is lacking when it is established that therapeutic results cannot be obtained with the proprietary product.

An authorisation shall also be suspended or revoked where the particulars supporting the application as provided for in Article 4 are found to be incorrect, or when the controls on the finished product referred to in Article 8 have not been carried out.

Article 12

All decisions taken pursuant to Articles 5, 6 or 11 shall state in detail the reasons on which they are based. A decision shall be notified to the party concerned, who shall at the same time be informed of the remedies available to him under the laws in force and of the time limit allowed for the exercise of such remedies.

Authorisations to place a proprietary product on the market and decisions to revoke authorisations shall be published by each Member State in the appropriate official publication.

CHAPTER IV

Labelling of proprietary medicinal products

Article 13

The following particulars shall appear on containers and outer packages of proprietary medicinal products:

1. Name of the proprietary product which may be a brand name, or a common name together with a trade mark or name of the manufacturer, or a scientific name together with a trade mark or name of the manufacturer.
2. Next to the name of the proprietary product, a statement of the active constituents expressed qualitatively and quantitatively per dose-unit or as a percentage, according to the pharmaceutical form. The international non-proprietary names recommended by the World Health Organisation shall be used wherever they exist.
3. Reference number for production identification (manufacturer's batch number).
4. Number of the authorisation to place the proprietary product on the market.
5. Name or corporate name and permanent address of the person responsible for placing the proprietary product on the market and, where applicable, of the manufacturer.
6. Method of administration.
7. Expiry date for proprietary products with a shelf life of less than three years.

8. Special storage precautions, if any.

The pharmaceutical form and the contents by weight, by volume or by number of dose-units need only be shown on the outer packages.

Article 14

In the case of ampoules, the particulars required under the first paragraph of Article 13 shall be given on the outer packages. However, on the actual containers only the following particulars are required:

- name of the proprietary medicinal product;
- quantity of active constituents;
- route of administration;
- expiry date.

Article 15

As regards small single-dose containers, other than ampoules, on which it is impossible to give the particulars mentioned in Article 14, the requirements of Article 13 shall apply only to the outer package.

Article 16

In the case of narcotics, in addition to the particulars mentioned in Article 13, a special sign consisting of a double red line shall appear on both the outer package and the container.

Article 17

Where there is no outer package, the particulars which should feature on such a package pursuant to the preceding Articles shall be shown on the container.

Article 18

The particulars mentioned in items, 6, 7 and 8 of the first paragraph of Article 13 shall appear on the outer package and on the container of proprietary medicinal products in the language or languages of the country where they are being placed on the market.

Article 19

The provisions of this Chapter shall not prevent the particulars required by rules other than those to which this Directive relates from being given on outer packages or on containers.

Article 20

Where the provisions of this Chapter are not observed and an order addressed to the person concerned has remained without effect, the competent authorities of the Member States may suspend or revoke the authorisation to place the proprietary medicinal product on the market.

All decisions taken in pursuance of the preceding paragraph shall state in detail the reasons on which they are based. A decision shall be notified to the party concerned, who shall at the same time be informed of the remedies available to him under the laws in force and of the time limit allowed for the exercise of such remedies.

CHAPTER V

General and final provisions

Article 21

An authorisation to market a proprietary medicinal product shall not be refused, suspended or revoked except on the grounds set out in this Directive.

Article 22

Member States shall put into force the measures needed in order to comply with this Directive within

eighteen months of its notification and shall inform the Commission forthwith.

Article 23

Member States shall ensure that they communicate to the Commission the text of the main provisions of national law which they adopt in the field covered by this Directive.

Article 24

In the five years following the notification mentioned in Article 22, the rules for which provision is made in this Directive shall be applied progressively to proprietary medicinal products covered by an authorisation to place on the market by virtue of previous provisions.

Article 25

This Directive is addressed to the Member States.

Done at Brussels, 26 January 1965.

For the Council

The President

M. COUVE DE MURVILLE