

## SECOND COUNCIL DIRECTIVE

of 20 May 1975

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

(75/319/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;

Having regard to the Opinion of the European Parliament <sup>(1)</sup>;

Having regard to the Opinion of the Economic and Social Committee <sup>(2)</sup>;

Whereas the approximation begun by Council Directive 65/65/EEC <sup>(3)</sup> of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products should be continued and the implementation of the principles laid down in that Directive should be ensured;

Whereas in order to reduce the disparities which remain, rules should be laid down on the control of proprietary medicinal products and the duties incumbent upon the Member States' competent authorities should be specified with a view to ensuring compliance with legal requirements;

Whereas, in order to progress towards free movement of proprietary medicinal products, the issue of authorizations to place one and the same proprietary medicinal product on the market in two or more Member States should be facilitated;

Whereas, for this purpose, a Committee for Proprietary Medicinal Products should be set up, consisting of representatives of the Member States and of the Commission, responsible for giving an opinion as to whether a particular proprietary medicinal product complies with the requirements set out in Directive 65/65/EEC;

Whereas this Directive represents merely one step towards achievement of the objective of the free movement of proprietary medicinal products; whereas, therefore, further measures with a view to abolishing any remaining barriers to the free movement of proprietary medicinal products will be necessary in the light of experience gained, particularly in the abovementioned Committee;

Whereas in order to facilitate the movement of proprietary medicinal products and to prevent the controls carried out in one Member State from being repeated in another, minimum requirements should be laid down for manufacture and imports coming from third countries and for the grant of the authorization relating thereto;

Whereas it should be ensured that, in the Member States, the supervision and control of the manufacture of proprietary medicinal products is carried out by a person who fulfils minimum conditions of qualification;

Whereas, moreover, the provisions of this Directive and of that of Directive 65/65/EEC which relate to proprietary medicinal products, although appropriate, are inadequate for vaccines, toxins and serums, proprietary medicinal products based on human blood or blood constituents, proprietary medicinal products based on radio-active isotopes and homeopathic proprietary medicinal products; whereas the application thereof should consequently not be imposed at the present time in respect of such proprietary medicinal products;

Whereas certain rules in this Directive entail amendments to various provisions of Directive 65/65/EEC,

HAS ADOPTED THIS DIRECTIVE :

## CHAPTER I

**Application for authorization to place proprietary medicinal products on the market**

*Article 1*

Member States shall take all appropriate measures to ensure that the documents and particulars listed

<sup>(1)</sup> OJ No 96, 2. 6. 1965, p. 1677/65.

<sup>(2)</sup> OJ No 107, 19. 6. 1965, p. 1825/65.

<sup>(3)</sup> OJ No 22, 9. 2. 1965, p. 369/65.

in points 7 and 8 of Article 4, second paragraph, of Directive 65/65/EEC are drawn up by experts with the necessary technical or professional qualifications before they are submitted to the competent authorities. These documents and particulars shall be signed by the experts.

#### Article 2

The duties of the experts according to their respective qualifications shall be:

- (a) to perform tasks falling within their respective disciplines (analysis, pharmacology and similar experimental sciences, clinical trials) and to describe objectively the results obtained (qualitatively and quantitatively);
- (b) to describe their observations in accordance with Council Directive 75/318/EEC<sup>(1)</sup> of 20 May 1975, on the approximation of the laws of the Member States relating to analytical, pharmacotoxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products, and to state, in particular:
  - in the case of the analyst, whether the product is consistent with the declared composition, giving any substantiation of the control methods employed by the manufacturer;
  - in the case of the pharmacologist or the specialist with similar experimental competence, the toxicity of the product and the pharmacological properties observed;
  - in the case of the clinician, whether he has been able to ascertain effects on persons treated with the product which correspond to the particulars given by the applicant in accordance with Article 4 of Directive 65/65/EEC, whether the patient tolerates the product well, the posology the clinician advises and any contra-indications and side-effects;
- (c) where applicable, to state the grounds for using the published references mentioned in point 8 (a) and (b) of Article 4, second paragraph, of Directive 65/65/EEC under the conditions set out in Directive 75/318/EEC.

Detailed reports by the experts shall form part of the particulars accompanying the application which the applicant submits to the competent authorities.

<sup>(1)</sup> See page 1 of this Official Journal.

#### Article 3

In the event of Article 2 of this Directive not being complied with, Article 5, second paragraph, of Directive 65/65/EEC shall apply.

### CHAPTER II

#### Examination of the application for authorization to place proprietary medical products on the market

#### Article 4

In order to examine the application submitted in accordance with Article 4 of Directive 65/65/EEC, the competent authorities of the Member States:

- (a) must verify whether the particulars submitted in support of the application comply with the said Article 4 and examine whether the conditions for issuing an authorization to place proprietary medicinal products on the market (marketing authorization) are complied with;
- (b) may submit the proprietary medicinal product for testing by a State laboratory or by a laboratory designated for that purpose in order to ensure that the control methods employed by the manufacturer and described in the particulars accompanying the application in accordance with point 7 of Article 4, second paragraph, of Directive 65/65/EEC are satisfactory;
- (c) may, where appropriate, require the applicant to supplement the particulars accompanying the application in respect of the items listed in the second paragraph of Article 4 of Directive 65/65/EEC. Where the competent authorities avail themselves of this option, the time limits laid down in Article 7 of the said Directive shall be suspended until such time as the supplementary information required has been provided. Likewise, these time limits shall be suspended for the time allowed the applicant, where appropriate, for giving oral or written explanation.

#### Article 5

Member States shall take all appropriate measures to ensure that:

- (a) the competent authorities verify that manufacturers and importers of products coming from third countries are able to carry out manufacture in compliance with the particulars supplied pursuant to point 4 of Article 4, second paragraph, of Directive 65/65/EEC and/or to carry out controls according to the methods described in the particulars accompanying the application in accordance with point 7 of Article 4, second paragraph, of that Directive;

(b) the competent authorities may allow manufacturers and importers of products coming from third countries, in exceptional and justifiable cases, to have certain stages of manufacture and/or certain of the controls referred to in (a) carried out by third parties; in such cases, the verifications by the competent authorities shall also be made in the establishment designated.

#### Article 6

Where a leaflet is enclosed with the packaging of a proprietary medicinal product Member States shall take all appropriate measures to ensure that it applies to the product in question only.

All the information given in the leaflet must be in accordance with the particulars and documents supplied pursuant to Article 4 of Directive 65/65/EEC and must be approved by the competent authorities.

The leaflet must include at least the following information:

- (a) name and domicile or corporate name and domicile or registered place of business of the person responsible for marketing the product and, where applicable, of the manufacturer;
- (b) name and qualitative and quantitative particulars of the product in terms of its active ingredients.

The international non-proprietary names recommended by the World Health Organization should be used where such names exist;

- (c) in the absence of a decision to the contrary by the competent authorities:
  - therapeutic indications,
  - contra-indications, side effects and special precautions for use.

Information and decisions under the first and second indents shall take into account the results of the clinical trials and pharmacological tests provided for in point 8 of Article 4, second paragraph, of Directive 65/65/EEC and in the case of the information referred to under the second indent, of experience acquired in use after marketing;

- (d) directions for use of the product (method of administration, duration of treatment if this should be limited, normal dosage);

(e) special storage precautions, where applicable.

Other information shall be clearly separate from that referred to above.

Member State may require that a leaflet be included with the packaging.

#### Article 7

Notwithstanding the provisions of Chapter IV and of Article 21 of Directive 65/65/EEC, Member States may require that the proprietary medicinal product shall be labelled so as to indicate on the container and/or outer packaging and/or on the package leaflet other requirements essential to safety or for the protection of public health, including any particular precautions to be taken in using the product and any other warnings based on the results of the clinical trials and pharmacological tests mentioned in point 8 of Article 4, second paragraph, of Directive 65/65/EEC, or resulting from experience in the course of use of the proprietary medicinal product after marketing.

### CHAPTER III

#### Committee for Proprietary Medicinal Products

#### Article 8

1. In order to facilitate the adoption of a common position by the Member States regarding marketing authorizations, a Committee for Proprietary Medicinal Products, hereinafter referred to as 'the Committee', is hereby set up. The Committee shall consist of representatives of the Member States and of the Commission.

2. The responsibility of the Committee shall be to examine, in accordance with Articles 9 to 14, the questions referred to it by a Member State concerning the application of Articles 5, 11 or 20 of Directive 65/65/EEC.

3. The Committee shall draw up its own Rules of Procedure.

#### Article 9

1. The Member State which has issued a marketing authorization for a proprietary medicinal product shall forward to the Committee a dossier containing a copy of the authorization together with the particulars and documents specified in Article 4,

second paragraph, of Directive 65/65/EEC, if the person responsible for marketing has requested the forwarding to at least five other Member States.

2. The Committee shall forthwith forward the dossier to the competent authorities of the Member States so specified.

3. Such forwarding shall be deemed to be equivalent to submitting an application for marketing authorization, within the meaning of Article 4 of Directive 65/65/EEC, to the said authorities.

#### *Article 10*

1. If, within a period of 120 days after the date of the forwarding referred to in Article 9 (2), no objection is notified to the Committee by the competent authorities of the Member States specified, the Committee shall formally record the fact and forthwith inform the Member States concerned.

2. Where a Member State considers that it is unable to authorize the marketing of the proprietary medicinal product, it shall forward its reasoned objection, within the said period of 120 days, on the basis of Article 5 of Directive 65/65/EEC.

#### *Article 11*

1. In the cases referred to in Article 10 (2), the Committee shall consider the matter and give a reasoned opinion within not more than 60 days from the expiry of the time limit laid down in Article 10.

2. The opinion of the Committee shall deal with the compliance of the proprietary medicinal product with the conditions set out in Article 5 of Directive 65/65/EEC.

The Committee shall forthwith inform the Member States concerned of its opinion or, in the event of a divergence, of the opinions of its members.

3. The Member States concerned shall reach a decision on the application for marketing authorization not more than 30 days after the date on which the information provided for in Article 10 (1) or paragraph 2 of this Article is given. They shall forthwith inform the Committee of their decision.

#### *Article 12*

1. If several applications submitted in accordance with Article 4 of Directive 65/65/EEC have been made for marketing authorization for a particular proprietary medicinal product, and one or more

Member States have granted an authorization while one or more of the other Member States have refused it, one of the Member States concerned may bring the matter before the Committee.

The same shall apply where one or more Member States have suspended or revoked the marketing authorization while one or more other Member States have not done so.

2. The Committee shall consider the matter and give a reasoned opinion within 120 days at the most.

3. The opinion of the Committee shall only deal with the grounds on which authorization was refused, suspended or revoked.

The Committee shall forthwith inform the Member States concerned of its opinion or, in the event of a divergence, of the opinions of its members.

4. The Member States concerned shall give notice within 30 days of the action they intend to take following the Committee's opinion.

#### *Article 13*

The Committee may set a time limit for a fresh examination on the basis of particulars relating to the conditions laid down in Articles 5, 11 or 20 of Directive 65/65/EEC obtained in the meantime by the Member States, in particular by those which have authorized the proprietary medicinal product.

#### *Article 14*

The competent authorities of Member States may, in specific cases where the interests of the Community are involved, refer the matter to the Committee before reaching a decision on an application for a marketing authorization, its suspension or revocation.

#### *Article 15*

1. The Commission shall report to the Council annually on the operation of the procedure laid down in this Chapter and its effects on the development of intra-Community trade. It shall report for the first time two years after the entry into force of this Directive.

2. In the light of experience the Commission shall, not later than four years after the entry into force of this Directive, submit to the Council a proposal containing appropriate measures leading towards the abolition of any remaining barriers to the free movement of proprietary medicinal products. The Council shall take a decision on the Commission proposal no later than one year after its submission.

## CHAPTER IV

**Manufacture and imports coming from third countries***Article 16*

1. Member States shall take all appropriate measures to ensure that the manufacture of the proprietary medicinal products is subject to the holding of an authorization.

2. The authorization referred to in paragraph 1 shall be required for both total and partial manufacture, and for the various processes of dividing up, packaging or presentation.

However, such authorization shall not be required for preparation, dividing up, changes in packaging or presentation where these processes are carried out, solely for retail supply, by pharmacists in dispensing pharmacies or by persons legally authorized in the Member States to carry out such processes.

3. Authorization referred to in paragraph 1 shall also be required for imports coming from third countries into a Member State; this Chapter and Article 29 shall have corresponding application to such imports as they have to manufacture.

*Article 17*

In order to obtain the authorization referred to in Article 16, the applicant must meet at least the following requirements:

- (a) specify the proprietary medicinal products and pharmaceutical forms which are to be manufactured or imported and also the place where they are to be manufactured and/or controlled;
- (b) have at his disposal, for the manufacture or import of the above, suitable and sufficient premises, technical equipment and control facilities complying with the legal requirements which the Member State concerned lays down as regards both manufacture and control and the storage of products, in accordance with Article 5 (a).
- (c) have at his disposal the services of at least one qualified person within the meaning of Article 21.

The applicant must provide particulars in support of the above in his application.

*Article 18*

1. The competent authority of the Member State shall issue the authorization referred to in Article 16 only after having made sure of the accuracy of the particulars supplied pursuant to Article 17, by means of an inquiry carried out by its agents.

2. In order to ensure that the requirements referred to in Article 17 are complied with, authorization may be made conditional on the carrying out of certain obligations imposed either when authorization is granted or at a later date.

3. The authorization shall apply only to the premises specified in the application and to the proprietary medicinal products and pharmaceutical forms specified in that same application.

*Article 19*

The holder of an authorization referred to in Article 16 shall at least be obliged:

- (a) to have at his disposal the services of staff who comply with the legal requirements existing in the Member State concerned both as regards manufacture and controls;
- (b) to dispose of the authorized proprietary medicinal products only in accordance with the legislation of the Member States concerned;
- (c) to give prior notice to the competent authority of any changes he may wish to make to any of the particulars supplied pursuant to Article 17; the competent authority shall in any event be immediately informed if the qualified person referred to in Article 21 is replaced unexpectedly;
- (d) to allow the agents of the competent authority of the Member State concerned access to his premises at any time;
- (e) to enable the qualified person referred to in Article 21 to carry out his duties, for example by placing at his disposal all the necessary facilities.

*Article 20*

1. The Member States shall take all appropriate measures to ensure that the time taken for the procedure for granting the authorization referred to in Article 16 does not exceed 90 days from the day on which the competent authority receives the application.

2. If the holder of the authorization requests a change in any of the particulars referred to in Article 17 (a) and (b), the time taken for the procedure relating to this request shall not exceed 30 days. In exceptional cases this period of time may be extended to 90 days.

3. Member States may require from the applicant further information concerning the particulars supplied pursuant to Article 17 and concerning the qualified person referred to in Article 21; where the competent authority concerned exercises this right, application of the time limits referred to in paragraphs 1 and 2 shall be suspended until the additional data required have been supplied.

*Article 21*

1. Member States shall take all appropriate measures to ensure that the holder of the authorization referred to in Article 16 has permanently and continuously at his disposal the services of at least one qualified person, in accordance with the conditions laid down in Article 23, responsible in particular for carrying out the duties specified in Article 22.

2. If he personally fulfils the conditions laid down in Article 23, the holder of the authorization may himself assume the responsibility referred to in paragraph 1.

*Article 22*

1. Member States shall take all appropriate measures to ensure that the qualified person referred to in Article 21, without prejudice to his relationship with the holder of the authorization referred to in Article 16, is responsible, in the context of the procedures referred to in Article 25, for securing:

- (a) in the case of proprietary medicinal products manufactured within the Member States concerned that each batch of proprietary medicinal products has been manufactured and checked in compliance with the laws in force in that Member State and in accordance with the requirements of the marketing authorization;
- (b) in the case of proprietary medicinal products coming from third countries, that each production batch has undergone in the importing country a full qualitative analysis, a quantitative analysis of at least all the active constituents and all the other tests or checks necessary to ensure the quality of proprietary medicinal products in accordance with the requirements of the marketing authorization.

The batches of products which have undergone such controls in a Member State shall be exempt from the above controls if they are imported into another Member State, accompanied by the control reports signed by the qualified person.

A Member State may relieve the qualified person of responsibility for the controls prescribed under (b) for imported proprietary medicinal products which are to remain in that Member State, if appropriate arrangements have been made with the exporting country to ensure that those controls have been carried out in the exporting country. Where these products are imported in the packaging in which they are to be sold by retail, Member States may allow exceptions to the requirements laid down in Article 17.

2. In all cases and particularly where the proprietary medicinal products are released for sale the qualified

person must certify in a register or equivalent document provided for that purpose that each production batch satisfies the provisions of this Article; the said register or equivalent document must be kept up to date as operations are carried out and must remain at the disposal of the agents of the competent authority for the period specified in the provisions of the Member State concerned and in any event for at least five years.

*Article 23*

Member States shall ensure that the qualified person referred to in Article 21 fulfils the following minimum conditions of qualification:

- (a) Possession of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course of study, or a course recognized as equivalent by the Member State concerned, extending over a period of at least four years of theoretical and practical study in one of the following scientific disciplines: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology. However:
  - the minimum duration of the university course may be three and a half years where the course is followed by a period of theoretical and practical training of a minimum duration of one year and including a training period of at least six months in a pharmacy open to the public, corroborated by an examination at university level;
  - where two university courses or two courses recognized by the State as equivalent co-exist in a Member State and where one of these extends over four years and the other over three years, the three-year course leading to a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course or its recognized equivalent shall be considered to fulfil the condition of duration referred to in (a) in so far as the diplomas, certificates or other evidence of formal qualifications awarded on completion of both courses are recognized as equivalent by the State in question.

The course shall include theoretical and practical study bearing upon at least the following basic subjects:

- Applied physics
- General and inorganic chemistry
- Organic chemistry
- Analytical chemistry
- Pharmaceutical chemistry, including analysis of medicinal products
- General and applied biochemistry (medical)
- Physiology

Microbiology

Pharmacology

Pharmaceutical technology

Toxicology

Pharmacognosy (medical aspects) (study of the composition and effects of the active principles of natural substances of plant and animal origin).

Studies in these subjects should be so balanced as to enable the person concerned to fulfil the obligations specified in Article 22.

In so far as certain diplomas, certificates or other evidence of formal qualifications mentioned in (a) do not fulfil the criteria laid down above, the competent authority of the Member State shall ensure that the person concerned provides evidence of adequate knowledge of the subjects involved.

- (b) Practical experience for at least two years, in one or more undertakings which are authorized to manufacture proprietary medicinal products, in the activities of qualitative analysis of medicinal products, of quantitative analysis of active substances and of the testing and checking necessary to ensure the quality of proprietary medicinal products.

The duration of practical experience may be reduced by one year where a university course lasts for at least five years and by a year and a half where the course lasts for at least six years.

#### Article 24

1. A person engaging in the activities of the person referred to in Article 21 in a Member State at the time when this Directive is brought into force in that State but without complying with the provisions of Article 23 shall be eligible to continue to engage in those activities in the State concerned.

2. The holder of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course — or a course recognized as equivalent by the Member State concerned — in a scientific discipline allowing him to engage in the activities of the person referred to in Article 21 in accordance with the laws of that State may — if he began his course prior to the notification of this Directive — be considered as qualified to carry out in that State the duties of the person referred to in Article 21 provided that he has previously engaged in the following activities for at least two years before the end of the tenth year following notification of this Directive in one or more undertakings authorized pursuant to Article 16: production supervision and/or qualitative analysis, quantitative analysis of active substances, and the necessary testing and checking under the direct

authority of the person referred to in Article 21 to ensure the quality of the proprietary medicinal products.

If the person concerned has acquired the practical experience referred to in the first subparagraph more than 10 years prior to the notification of this Directive, a further one year's practical experience in accordance with the conditions referred to in the first subparagraph will be required to be completed immediately before he engages in such activities.

3. A person who, at the time when this Directive is brought into force, is engaged in direct collaboration with a person referred to in Article 21 in production supervision activities and/or in qualitative and quantitative analysis of active substances and the testing and checking necessary to ensure the quality of proprietary medicinal products may, for a period of five years after this Directive has been brought into force, be considered as qualified to take up in that State the duties of the person referred to in Article 21 provided that that Member State ensures that the person shows evidence of adequate theoretical and practical knowledge and has engaged in the activities mentioned for at least five years.

#### Article 25

Member States shall ensure that the duties of qualified persons referred to in Article 21 are fulfilled, either by means of appropriate administrative measures or by making such persons subject to a professional code of conduct.

Member States may provide for the temporary suspension of such a person upon the commencement of administrative or disciplinary procedures against him for failure to fulfil his obligations.

### CHAPTER V

#### Supervision and sanctions

#### Article 26

The competent authority of the Member State concerned shall ensure by means of inspections that the legal requirements relating to proprietary medicinal products are complied with.

Such inspections shall be carried out by officials representing the competent authority who must be empowered to:

- (a) inspect manufacturing or commercial establishments and any laboratories entrusted by the holder of the authorization referred to in Article

16 with the task of carrying out checks pursuant to Article 5 (b);

- (b) take samples;
- (c) examine any documents relating to the object of the inspection, subject to the provisions in force in the Member States at the time of notification of this Directive and which place restrictions on these powers with regard to the descriptions of the method of preparation.

#### *Article 27*

Member States shall take all appropriate measures to ensure that the person responsible for marketing a proprietary medicinal product and, where appropriate, the holder of the authorization referred to in Article 16, furnish proof of the controls carried out on the finished product and/or the ingredients and of the controls carried out at an intermediate stage of the manufacturing process, in accordance with the methods laid down for the purposes of the marketing authorization.

#### *Article 28*

1. Notwithstanding the measures provided for in Article 11 of Directive 65/65/EEC, Member States shall take all appropriate measures to ensure that the supply of the proprietary medicinal product shall be prohibited and the proprietary medicinal product withdrawn from the market if:

- (a) the proprietary medicinal product proves to be harmful under normal conditions of use;
- (b) it is lacking in therapeutic efficacy;
- (c) its qualitative and quantitative composition is not as declared;
- (d) the controls on the finished product and/or on the ingredients and the controls at an intermediate stage of the manufacturing process have not been carried out or if some other requirement or obligation relating to the grant of the authorization referred to in Article 16 has not been fulfilled.

2. The competent authority may limit the prohibition to supply the product, or its withdrawal from the market, to those batches which are the subject of dispute.

#### *Article 29*

1. The competent authority of a Member State shall suspend or revoke the authorization referred to in Article 16 for a category of preparations or all preparations where any one of the requirements laid down in Article 17 is no longer met.

2. In addition to the measures specified in Article 28, the competent authority of a Member State may suspend manufacture or imports of proprietary medicinal products coming from third countries, or suspend or revoke the authorization referred to in Article 16 for a category of preparations or all preparations where Articles 18, 19, 22 and 27 are not complied with.

### CHAPTER VI

#### Miscellaneous provisions

#### *Article 30*

Member States shall take all appropriate measures to ensure that the competent authorities concerned communicate to each other such information as is appropriate to guarantee that the requirements for the authorizations referred to in Article 16 or marketing authorizations are fulfilled.

#### *Article 31*

All decisions taken pursuant to Articles 18, 28 and 29 and all negative decisions taken pursuant to Articles 5 (b) and 11 (3) shall state in detail the reasons on which they are based. Such decisions 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 applying for such remedies.

#### *Article 32*

No decision concerning suspension of manufacture or of importation of proprietary medicinal products coming from third countries, prohibition of supply or withdrawal from the market of a proprietary medicinal product may be taken except on the ground set out in Articles 28 and 29.

#### *Article 33*

Each Member State shall take all the appropriate measures to ensure that decisions authorizing marketing, refusing or revoking a marketing authorization, cancelling a decision refusing or revoking a marketing authorization, prohibiting supply, or withdrawing a product from the market, together with the reasons on which such decisions are based, are brought to the attention of the Committee forthwith.



*Article 34*

This Directive shall apply only to proprietary medicinal products for human use.

Chapters II to V of Directive 65/65/EEC and this Directive shall not apply to proprietary medicinal products consisting of vaccines, toxins or serums, to proprietary medicinal products based on human blood or blood constituents or radioactive isotopes, or to homeopathic proprietary medicinal products. A list, for information purposes, of these vaccines, toxins and serums is given in the Annex.

*Article 35*

The following shall be substituted for point 7 of Article 4, second paragraph, of Directive 65/65/EEC:

'Description of the control methods employed by the manufacturer (qualitative and quantitative analysis 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, controls carried out at an intermediate stage of the manufacturing process).'

*Article 36*

The following shall be substituted for Article 11, second paragraph, of Directive 65/65/EEC:

'An authorization 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 referred to in Article 8 of this Directive or in Article 27 of the Second Council Directive 75/319/EEC (1) of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products have not been carried out.'

The following footnote shall be added:

'(1) OJ No L 147, 9. 6. 75, p. 13.'

*Article 37*

The following shall be substituted for Article 24 of Directive 65/65/EEC:

'Within the time limits and under the conditions laid down in Article 39 (2) and (3) of second Directive 75/319/EEC, the rules laid down in this Directive shall be applied progressively to proprietary medicinal products covered by an

authorization to place on the market by virtue of previous provisions'.

## CHAPTER VII

## Implementing provisions and transitional measures

*Article 38*

Member States shall bring into force the laws, regulations and administrative provisions needed in order to comply with this Directive within 18 months of its notification and shall forthwith inform the Commission thereof.

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

*Article 39*

1. As regards the authorizations referred to in Article 16 issued before the expiry of the time limit laid down in Article 38, Member States may grant an additional period of one year to the undertakings concerned to enable them to comply with the provisions of Chapter IV.

2. Within 15 years of the notification referred to in Article 38, the other provisions of this Directive shall be applied progressively to proprietary medicinal products placed on the market by virtue of previous provisions.

3. Member States shall notify the Commission, within three years following the notification of this Directive, of the number of proprietary medicinal products covered by paragraph 2, and, each subsequent year, of the number of these products for which a marketing authorization referred to in Article 3 of Directive 65/65/EEC, has not yet been issued.

*Article 40*

This Directive is addressed to the Member States.

Done at Brussels, 20 May 1975.

*For the Council*

*The President*

R. RYAN

## ANNEX

The expression 'vaccines, toxins or serums' used in Article 34 shall cover in particular:

- *agents used to produce active immunity*  
(such as cholera vaccine, BCG, polio vaccine, smallpox vaccine);
  - *agents used to diagnose the state of immunity*  
including in particular tuberculin and tuberculin PPD, toxins for the Schick and Dick Tests, brucellin;
  - *agents used to produce passive immunity*  
(such as diphtheria antitoxin, anti-smallpox globulin, antilymphocytic globulin).
-