II

(Acts whose publication is not obligatory)

COUNCIL

COUNCIL DIRECTIVE

of 28 September 1981

on the approximation of the laws of the Member States relating to veterinary medicinal products

(81/851/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 primary purpose of any rules for the production and distribution of veterinary medicinal products must be the safeguarding of public health;

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

Whereas, in so far as the Member States already have certain provisions laid down by law, regulation or administrative action governing veterinary medicinal products, such provisions differ in essential principles; whereas this results in the hindering of trade in medicinal products within the Community, thereby directly affecting the establishment and functioning of the common market;

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

Whereas the provisions of this Directive which concern veterinary medicinal products are, although appropriate, not adequate for veterinary medicinal products used to confer active immunity, to diagnose the state of immunity and to confer passive immunity or for medicinal products based on radioactive isotopes; whereas it is therefore advisable not to prescribe their application to such products for the present;

Whereas medicated feedingstuffs do not come within the scope of this Directive; whereas, however, it is necessary, for both public health and economic reasons, to prohibit the use of unauthorized medicinal products in the manufacture of medicated feedingstuffs;

Whereas marketing authorization shall be refused where a medicinal product lacks therapeutic effect or where there is insufficient proof of such effect; whereas the concept of therapeutic effect must be understood as being the effect promised by the manufacturers;

Whereas such authorization shall also be refused where the withdrawal period indicated is not long enough to eliminate health hazards arising from residues;

(1) OJ No C 152, 5. 7. 1976, p. 1.
(2) OJ No C 293, 13. 12. 1976, p. 64.
(3) OJ No C 299, 18. 12. 1976, p. 12.

Whereas, in order gradually to achieve freedom of movement of veterinary medicinal products, the granting of marketing authorizations in several Member States for the same medicinal product should be made easier;

Whereas, for this purpose, a Committee for Veterinary Medicinal Products, composed of representatives of the Member States and of the Commission, should be set up and should be responsible for giving an opinion on whether a particular veterinary medicinal product complies with the requirements set out in this Directive;

Whereas this Directive is only one stage in the achievement of the aim of freedom of movement of veterinary medicinal products; whereas, for this purpose, new measures will prove necessary, in the light of experience gained — especially within the said Committee — for the removal of the remaining barriers to freedom of movement;

Whereas, in order to facilitate the movement of veterinary medicinal products and to prevent the checks carried out in one Member State from being repeated in another, minimum requirements for manufacture and imports from third countries and the grant of authorization relating thereto, should be applied to veterinary medicinal products, as specified in 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 (1),

HAS ADOPTED THIS DIRECTIVE:

CHAPTER I

Definitions and scope

Article 1

1. The definitions laid down in Article 1 of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (2) shall apply to this Directive.

2. For the purposes of this Directive, the following definitions shall apply:

— 'veterinary medicinal product' shall mean any medicinal product intended for animals,

— 'ready-made veterinary medicinal product' shall mean any veterinary medicinal product prepared in advance which does not comply with the definition of proprietary medicinal products and which is marketed in a pharmaceutical form which may be used without further processing,

— 'pre-mix for medicated feedingstuffs' shall mean any veterinary medicinal product prepared in advance with a view to the subsequent manufacture of medicated feedingstuffs,

— 'medicated feedingstuffs' shall mean any mixture of a veterinary medicinal product or products and feed or feeds which is ready prepared for marketing and intended to be fed to animals without further processing, because of its curative or preventive properties or other properties as a medicinal product covered by Article 1 (2) of Directive 65/65/EEC.

3. Until Community rules are adopted for medicated feedingstuffs, Member States may lay down that this term shall include semi-finished products which are manufactured from a pre-mix for medicated feedingstuffs for which an authorization pursuant to Article 4 of this Directive has been issued and feedingstuffs, where such semi-finished products are intended to be processed by further mixing with feedingstuffs to become medicated feedingstuffs ready for use. Member States shall ensure that such semi-finished products are subject to the control of the competent authorities and that they are used exclusively for the manufacture of medicated feedingstuffs under the conditions which governed the marketing authorization for the pre-mix for medicated feedingstuffs.

4. Additives covered by Council Directive 70/524/EEC of 23 November 1970 concerning additives in feedingstuffs (3), as subsequently amended, where they are incorporated in animal feedingstuffs and supplementary animal feedingstuffs in accordance with that Directive, shall not be considered as veterinary medicinal products for the purposes of this Directive.

5. Member States shall take any necessary steps to ensure that antibiotics and hormone substances which may be used for the preparation of veterinary medicinal products are made available to only

(1) OJ No L 147, 9. 6. 1975, p. 13.
(2) OJ No 22, 9. 12. 1965, p. 369/65.
(3) OJ No L 270, 14. 12. 1970, p. 1.

natural or legal persons duly authorized to be in possession of them under national laws.

Article 2

1. The provisions of this Directive shall apply to veterinary medicinal products offered for sale *inter alia* in the form of proprietary medicinal products, ready-made veterinary medicinal products or pre-mixes for medicated feedingstuffs.

2. The provisions of this Directive shall not apply to:

— medicated feedingstuffs,

— veterinary medicinal products used in order to produce active immunity, diagnose the state of immunity and produce passive immunity,

— veterinary medicinal products based on radioactive isotopes,

— veterinary medicinal products not prepared in advance and intended for one particular animal or a small number of animals,

— homeopathic medicinal products.

3. However, medicated feedingstuffs may be prepared only from pre-mixes which have been authorized under this Directive. Within two years of the notification of this Directive, the Council shall, on the basis of a Commission report accompanied if necessary by appropriate proposals, deliberate on a list of pharmacological molecules which may be used for preparing pre-mixes and on the procedure for drawing up this list.

Article 3

Member States may permit exemptions from the provisions of Article 4 (1) on their territory in respect of veterinary medicinal products intended solely for aquarium fish, cage birds, homing pigeons, terrarium animals and small rodents, provided that such products do not contain substances the use of which requires veterinary control and that all possible measures have been taken to prevent unauthorized use of the products for other animals.

CHAPTER II

Application for marketing authorization for veterinary medicinal products

Article 4

1. No veterinary medicinal product may be marketed in a Member State unless authorization has previously been issued by the competent authority in that Member State.

2. No veterinary medicinal product may be administered to animals unless the authorization referred to above has been issued, except for tests of veterinary medicinal products referred to in point 10 of Article 5.

Article 5

For the purpose of obtaining the marketing authorization provided for in Article 4, the person responsible for marketing shall lodge an application with the competent authority of the Member State.

The following particulars and documents shall be appended to the application:

1. name or corporate name and permanent address or registered place of business of the person responsible for marketing and of the manufacturer, if different;

2. name of the veterinary medicinal product (brand name, non-proprietary name, with or without a trade-mark or name of the manufacturer; scientific name of formula, with or without a trade-mark or name of the manufacturer);

3. qualitative and quantitative particulars of all the constituents of the veterinary medicinal product, using the usual terminology but not empirical chemical formulae and giving the international non-proprietary name recommended by the World Health Organization, if such a name exists;

4. brief description of the method of preparation;

5. therapeutic indications, contra-indications and side-effects;

6. dosage for the various species of animal for which the veterinary medicinal product is

intended, its pharmaceutical form, method and route of administration and proposed shelf life if less than three years;

7. reasons for the precautionary and safety measures to be taken when using the veterinary medicinal product, if applicable;

8. indication of the withdrawal period necessary between the last administration of the veterinary medicinal product to animals under normal conditions of use and the production of foodstuffs from such animals in order to ensure that such foodstuffs do not contain any residues which might constitute a health hazard to the consumer;

9. description of the control testing methods employed by the manufacturer (qualitative and quantitative analysis of the constituents and the finished product, specific tests, e.g. sterility tests, tests for the presence of pyrogens, for the presence of heavy metals, stability tests, biological and toxicity tests, tests on intermediate products);

10. results of:

— physico-chemical, biological or microbiological tests,

— toxicological and pharmacological tests,

— clinical trials.

The results of the toxicological and pharmacological tests must relate more particularly to the metabolism of the active ingredients in the animal and as far as possible to the mode and duration of their elimination, if such data are important for the purpose of checking the indicated withdrawal period.

However,

(a) a copy of the published references relating to the toxicological and pharmacological tests and clinical trials and the data concerning the withdrawal period may be substituted for the relevant test results in the case of:

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

(ii) a new veterinary medicinal product, in which the active ingredients are identical to those of a known medicinal product with an established use;

(iii) a new veterinary medicinal product containing only known constituents that have already been used together in comparable proportions in adequately tested medicinal products with an established use;

(b) in the case of a new veterinary medicinal product containing known constituents not hitherto used together for therapeutic purposes, references to published data may be substituted for the tests on such constituents;

11. one or more specimens or mock-ups of the sales presentation of the veterinary medicinal product together with a package insert where a package insert is required;

12. a document showing that the manufacturer is authorized in his own country to produce veterinary medicinal products;

13. any marketing authorization for the relevant veterinary medicinal product which may have been obtained in another Member State or in a third country.

Article 6

Member States shall make all necessary arrangements to ensure that the documents and particulars listed in points 8, 9 and 10 of the second paragraph of Article 5 are drafted by experts with the requisite technical or professional qualifications before being submitted to the competent authorities.

These documents and particulars shall be signed by the experts in question.

Article 7

According to their particular qualifications, the role of the experts shall be:

1. to carry out such work as falls within their particular discipline (analysis, pharmacology and similar experimental sciences, clinical trials) and to describe objectively the results obtained in both quantitative and qualitative terms;

2. to describe their findings in accordance with Council Directive 81/852/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicologial and clinical standards and protocols in respect of the testing of veterinary medicinal products (1), and in particular to state:

   (a) in the case of analysts, whether the product conforms with the stated composition, providing any reasons for the control testing methods which the manufacturer is to use;

   (b) in the case of pharmacologists and appropriately qualified specialists:

   — the toxicity of the product and the pharmacological properties observed,

   — whether, after administration of the veterinary medicinal product under normal conditions of use and observance of the recommended withdrawal period, foodstuffs obtained from the treated animals contain residues which might constitute a health hazard to the consumer;

   (c) in the case of clinicians, whether they have found in animals treated with the product effects corresponding to the information furnished by the manufacturer pursuant to Article 5, whether the product is well tolerated, what dosage they recommend and what are the contra-indications and side-effects, if any;

3. to give reasons for the use of the references to published data referred to in point 10 (a) and (b) of the second paragraph of Article 5, according to the conditions laid down by Council Directive 81/852/EEC.

The experts' detailed reports shall form part of the documentation which the applicant shall lodge with the competent authorities.

CHAPTER III

Examination of applications for authorization — Authorization — Renewal of authorization

Article 8

Member States shall take all appropriate measures to ensure that the procedure for granting marketing authorization is completed within 120 days after the date of submission of the application.

In exceptional cases this time limit may be extended for a further 90 days. The applicant shall be notified of such extension before the expiry of the initial time limit.

Article 9

In order to examine the application submitted pursuant to Article 4, the competent authorities of the Member States:

1. shall check that the documentation submitted in support of the application complies with Article 5 and, on the basis of the reports drawn up by the experts pursuant to Article 7, ascertain whether the conditions for the issue of the marketing authorization have been fulfilled;

2. may submit the medicinal product for testing by a State laboratory or a laboratory designated for this purpose, in order to ensure that the control testing methods employed by the manufacturer and described in the application documents, in accordance with point 9 of the second paragraph of Article 5, are satisfactory;

3. may, where appropriate, require the applicant to provide further information as regards the items listed in Article 5. Where the competent authorities take this course of action, the time limits specified in Article 8 shall be suspended until the further data required have been provided. Similarly, these time limits shall be suspended for any period which the applicant may be given to provide oral or written explanations.

Article 10

Member States shall take all appropriate measures to ensure that:

1. the competent authorities ascertain that the manufacturers and importers of veterinary medicinal products from third countries are able to manufacture them in compliance with the details supplied pursuant to point 4 of the second paragraph of Article 5 and/or to carry out control tests in accordance with the methods described in the application documents under point 9 of the second paragraph of Article 5;

2. the competent authorities may authorize manufacturers and importers of veterinary medicinal products from third countries, where circum-

(1) See page 16 of this Official Journal.