COMMISSION OF THE EUROPEAN COMMUNITIES

REVISED VERSION

COM(88) 779 final
Brussels, 9 February 1989

Proposal for a
COUNCIL REGULATION (EEC)

laying down a Community procedure for the establishment of tolerances for residues of veterinary medicinal products

---

Proposal for a
COUNCIL DIRECTIVE

amending Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products

---

Proposal for a
COUNCIL DIRECTIVE

extending the scope of Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products and laying down additional provisions for immunological veterinary medicinal products

---

(presented by the Commission)

AMENDMENT OF THE VETERINARY MEDICINAL PRODUCTS DIRECTIVES

AMENDMENT OF THE VETERINARY MEDICINAL PRODUCTS DIRECTIVES

EXPLANATORY MEMORANDUM AND REPORT TO THE COUNCIL

1. INTRODUCTION

In accordance with Article 23(1) of Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products (O.J. L 317, 6.11.1981, p. 1) and in accordance with its legislative programme on the completion of the internal market, the Commission is expected to present to the Council proposals containing all appropriate measures for the removal of any remaining barriers to the free movement of veterinary medicinal products. In addition, Article 5 of Directive 87/22/EEC on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology (O.J. no L 15, 17.1.1987, p. 38), requires the Commission to present proposals to harmonize the conditions for authorizing the manufacture and placing on the market of the veterinary medicinal products referred to in Article 2(2) of Directive 81/851/EEC, which are currently excluded from the scope of that Directive.

This package of three legislative proposals is intended to represent a first step towards the implementation of these mandates. Taken as a whole, the package has four major objectives :

a) The institution of a centralised Community system for determining binding tolerances (acceptable levels) for residues of veterinary medicinal products in foodstuffs of animal origin.

b) The improvement of the decentralised Community procedure which enables a person who has obtained authorization to market a veterinary medicinal product in one Member State to apply for its extension to the other Member States.

c) The updating of the detailed provisions of the veterinary medicines directives, in the light of developments since 1981.

d) The extension of the veterinary medicines directives to cover immunological veterinary medicinal products.

The mandate conferred upon the Commission by Directive 87/22/EEC also refers to homeopathic veterinary medicinal products and to radiopharmaceuticals.

At the present time the Commission has little information available about the basis for or the extent of the use of homeopathy in veterinary medicine, or the basis on which such products might be regulated in order to protect public health. Although it will keep the matter under review, the Commission does not intend to bring forward proposals on these products at this time.

Radiopharmaceuticals are medicinal products based upon radionuclides (radioactive isotopes) which are mainly used for diagnostic purposes. Although there has been very considerable growth recently in the use of

radiopharmaceuticals in human medicine, this development has not yet been paralleled in veterinary medicine. So far as the Commission is aware, hardly any radiopharmaceuticals are authorized for use in veterinary medicine by the Member States at the present time, and the limited uses which do occur are for experimental purposes only. In these circumstances, the Commission does not consider it appropriate to bring forward specific proposals at this time, although it will keep the situation under review.

2. THE EXPERIENCE WITH THE EXISTING DIRECTIVES

The two original directives relating to veterinary medicinal products (Directives 81/851/EEC and 81/852/EEC) were closely modelled on the rules existing at that time for proprietary medicinal products for human use (Directives 65/65/EEC, 75/318/EEC and 75/319/EEC). In particular the procedures laid down in order to facilitate the adoption of a common position by Member States in respect of marketing authorizations for veterinary medicinal products in Chapter IV of Directive 81/851/EEC were identical to the procedures then laid down in respect of proprietary medicinal products for human use by Directive 75/319/EEC.

In so far as veterinary medicinal products are concerned, these procedures have not been a success. Only one application has been forwarded to the Committee for Veterinary Medicinal Products in accordance with the provisions of Article 17 of Directive 81/851/EEC in respect of a well-known antibiotic for use in dogs and cats.

The biotechnology-high technology procedure established by Directive 87/22/EEC also applies to applications for veterinary medicinal products, and although it is still too soon to offer a definitive assessment of the procedure, which only came into effect on 1 July 1987, three applications are currently pending.

3. THE SCOPE OF THE PROPOSALS AND THEIR RELATIONSHIP WITH THE DIRECTIVES ON MEDICINAL PRODUCTS FOR HUMAN USE

Because of the very limited use which has been made, in particular of the procedures in Directive 81/851/EEC, the Commission has had to consider whether it would not be more appropriate to create an alternative system for the approval of veterinary medicines within the Community.

Many of the principles involved in the regulation of veterinary medicinal products are the same as for proprietary medicinal products. Indeed, in this package the Commission is proposing that a number of changes which have been made or proposed to the rules applicable to proprietary medicinal products should be extended to cover veterinary medicinal products. Nevertheless there are fundamental differences resulting from the widespread use of medication for prophylactic prurposes, concern for the safety of the persons handling veterinary medicinal products and administering them to animals, the need to consider the impact of veterinary medicines on the environment, and to take account of the practical farming conditions under which medicines are administered to animals.

In addition, account must be taken of the fact that the use of veterinary medicinal products in food producing animals will result in residues in foodstuffs of animal origin. Differing assessments of the safety of residues which may create problems not only for the free movement of veterinary medicinal products but also for the free movement of the foodstuffs concerned.

During the preparation of this package of proposals, the services of the Commission invited the Member States, the industry, consumer groups, and interested professional organizations to submit comments on the choice of an appropriate system for authorizing the marketing of veterinary medicinal products within the Community. As a result of these consultations, it is clear that there is substantial support for the establishment of a centralised Community procedure for the authorization of major new products. Nevertheless, many questions remain open on the manner in which such a system would operate, the resources which would be made available to it, and the interrelationships between national and Community responsibilities. There is also concern that the running in period for such a system would inevitably be a period of uncertainty and some confusion.

Moreover, a number of the Member States have requested that any decisions about the choice of a future system for the free movement of veterinary medicinal products should be made in parallel with the choice of a system to guarantee the free movement of proprietary medicinal products for human use. The Commission is currently engaged in detailed consultations on this matter, and in accordance with its obligations under the existing pharmaceutical directives and its White Paper programme,

the Commission intends to present proposals in the Autumn of 1989.

In these circumstances, the Commission considers that it would be premature at the present time to propose a definitive procedure for the authorization of veterinary medicinal products at the Community level. It intends to continue consultations, with a view to completing its proposals within one year.

Nevertheless, the Commission considers that there are other major changes to the veterinary medicir directives which should be proposed now and on which it should be possible to reach rapid agreement. These changes concern, in particular, residues of veterinary medicines and the operation of the decentralised "multi-state" procedure for authorization of veterinary medicinal products under directive 81/851/EEC.

4. RESIDUES OF VETERINARY MEDICINAL PRODUCTS

As noted above, the administration of veterinary medicinal products to food producing animals is likely to result in very small quantities of the veterinary medicinal product being present in foodstuffs of animal origin. Although the potential risk presented by residues has been recognised for some time, the analytical methods available were not sufficiently sensitive to detect residues at the very low levels at which there are encountered. It was therefore sufficient to provide that no detectable residues should be present in foodstuffs and to establish withdrawal periods accordingly.

However, in recent years there have been remarkable development in analytical techniques which mean that, in some cases, it is now possible to detect residues at levels as low as one part per billion, or even to detect whether a single molecule of a given compound is present in a carcass. As a result of these developments, it has been possible to conduct pharmacokinetic studies in animals treated with certain veterinary medicinal products which have shown that an initial rapid decrease of drug concentration in the animal is followed by a longer and much slower phase of depletion.

It is therefore clear that the notion of a zero residue is no longer adequate either as a regulatory tool, or as an instrument for consumer protection. In reality a zero tolerance is today no more than a function of the sensitivity of the analytical method used, on the basis that the more one looks for something, the more likely one is to find it.

In these circumstances, contemporary scientific opinion suggests that the concept of the zero tolerance has to be replaced by a careful scientific evaluation of the potential risks presented by residues of veterinary medicinal products in foods. This evaluation, which is conducted in accordance with broadly similar principles to those used for assessing food additives, entails the conduct of toxicological tests in laboratory animals. Using the results of these studies, the toxicological no effect level in the most sensitive species is determined and expressed in terms of milligrams per kilogram bodyweight. The no effect level is then divided by the appropriate safety factor, usually between 100 and 1000, to determine the acceptable daily intake in man. The

acceptable daily intake is then divided between the various foodstuffs concerned, on the basis of usual dietary intakes, to arrive at a tolerance for each of the food products of animal origin concerned (muscle tissue, liver, kidney, eggs, milk etc.)

In assessing the safety of residues, other potential risk factors must also be taken into consideration such as immunological effects (allergic reaction or immuno-suppression) and microbiological effects, such as the effects on microbial resistance.

In addition, the effects that residues may have on the industrial processing of foodstuffs must also be considered, for example in the manufacture of dairy products such as yoghurt and cheese.

Differences in the laws of countries about residues of veterinary medicines can have a profound impact not only on the free movement of veterinary medicinal products but also on the free movement of foodstuffs of animal origin, which are, of course, of far greater economic significance. For this reason, at the international level, increasing importance has been atached to this problem, culminating, in 1986, in the establishment of a Codex Alimentarius Committee for Residues of Veterinary Drugs in Foods.

At the Community level, the Committee for Veterinary Medicinal products has set up a working party on the safety of residues to provide the Commission with advice. Following the general approach outlined above, the group has prepared recommendations on chloramphenicol, the sulfonamide group, the nitrofuran group, trimethoprim and dapsone. These recommendations will be finalised

shortly, and the Commission will publish them once they are available. In addition, work on a number of other compounds is at an advanced stage, including the benzimidazole and the nitroimidazole groups.

At the present time, however, there is no mechanism by which thes recommendations can be given legislative effect throughout the Community, other than by a series of ad hoc directives to be adopted by the Council. In order to ensure the proper protection of public health, and in order to progress towards an internal market for this sector, the Commission considers it indispensible that an appropriate procedure shoud be established which will result in the progressive implementation of approved tolerances for all substances which are used in veterinary medicinal products within the Community. In view of the fact that some 150 compounds may need to be assessed, it seems appropriate to allow for a transitional period of about 8 years for the completion of this work. Moreover the establishment of tolerances at the Community level will enable the Community as a whole to play a full role in the work in this field currently being undertaken by international organizations.

In the case of new veterinary medicinal products intended for use in food producing animals, the establishment of a tolerance by the Community will be required before any Member State may authorize the product. In order to alleviate any burden which this requirement may impose on the industry, it is proposed that such products should also be automatically eligible for the Community coordination procedure estalished by Directive 87/22/EEC.

So far as the procedure is concerned, the Commission is proposing that the actual task of evaluating the risks presented by residues should continue to be undertaken within the Committee for Veterinary Medicinal Products. This Committee is made up of representatives of the Member States, usually of the officials responsible for the registration of veterinary medicinal products in their own countries. In order to assist the Committee in its work, a technical secretariat will be established. Following examination of a substance, it is envisaged that the conclusions of the Committee will be communicated to the person responsible for marketing the substance concerned and to the Member States for comment before a definitive decision is reached. The final decision on the establishment of a tolerance will be taken by the Commission in close cooperation with the Committee for Veterinary Medicinal Products, using the so called regulatory committee procedure which requires the approval of a qualified majority of Member States (Procedure III, variant a of Council Decisions 87/373/EEC of 13 July 1987 laying down the procedures for the exercise of implementing powers conferred on the Commission, O.J. No L 197 of 18.7.1987, p. 33).

Once a tolerance is agreed, the Commission will be required to publish a summary assessment of the safety of residues of the compound concerned.

There are a limited number of compounds for which it is not necessary to establish a tolerance either because their toxicity is very low or because they are substances which occur naturally in the treated animal. The Commission is propositng that these products should be included in a list in an additional annex to the regulation which would be adopted in accordance with the

procedure described above.

5. THE MULTI-STATE PROCEDURE FOR VETERINARY DRUG REGISTRATION

Various reasons have been advanced for the failure of the multi-state registration procedure created by Chapter IV of Directive 81/851/EEC. In particular, the procedure is said to be unattractive to the industry because of the high-threshold number of Member States to whom an application must be addressed and the fact that the industry has no right to a hearing before the Committee.

As an interim measure, the Commission is therefore proposing to transpose into Directive 81/851/EEC the multi-state procedure established for proprietary medicinal products for human use by Directive 83/570/EEC (O.J. No L 332 of 28.11.1983, p. 1). This directive requires Member States to take the authorization granted by the original Member State into due consideration when considering subsequent applications in respect of the same product. Only in exceptional cases should the other Member States not be able to accept the inital authorization, in which case the matter is referred to the Committee for Veterinary Medicinal Products for opinion. In addition, the threshold number of Member States to which an application must be made is reduced from five to two and the company is given a right of a hearing before the Committee.

The Commission is also proposing that the Council should increase the weight of opinions of the Committee for Veterinary Medicinal Products by requiring Member States to implement the opinions with 60 days. Thus where the opinion of the Committee is favourable, the Member States

concerned by the application will be expected to authorize the product within this timelimit, subject to the conditions laid down in the opinion. On the other hand, where the opinion is a negative one, the Member State which originally authorized the product will be expected to reconsider its position and withdraw the product from the market.

In addition to these legislative changes, the Commission intends to increase the resources available to the Committee so that work on the preparation of guidelines on the assessment of veterinary medicinal products can be intensified.

6. THE DETAILED PROPOSALS FOR AMENDMENT OF THE EXISTING DIRECTIVES

The proposal for a Directive amending Directives 81/851/EEC, 81/852/EEC and 87/22/EEC also contains a number of proposals for the amendment of the rules applicable to veterinary medicinal products in the Community. While certain of these proposals are for the extension to the veterinary medicinal products sector of changes which have previously been adopted or proposed in respect of proprietary medicinal products for human use, other are specific to veterinary medicinal products. The main changes can be summarized as follows.

6.1 The relationship between the veterinary medicines directives and the rules relating to additives for use in animal feed

As a result of technological developments, certain practical difficulties have arisen in distinguishing between products which should be regarded as veterinary medicinal products and products which should be regarded as additives for animal feedingstuffs which fall within the scope of Directive 70/524/EEC (O.J. No L 270, 14.12.1970, p. 1).

In order to clarify the situation, the Commission is proposing that the definition of a veterinary medicinal product should be amended to expressly exclude products which are administered to animals orally and are intended for long term-use in healthy animals for nutritional purposes. The Commission is currently preparing amendements to Directive 70/524/EEC to ensure that all such products are covered by that directive.

6.2 The distribution of veterinary medicinal products

Within the Member States, veterinary medicinal products are distributed through a variety of different channels. In some Member States, the veterinarian has a predominant role in distribution, in other, the pharmacist, while in certain Member States a considerable proportion of veterinary medicinal products are distributed through specialist animal health product distributors or agricultural cooperatives. This matter was considered in detail by the European Parliament in its resolution of 13 April 1984 on the basis of a report prepared by Mr Hord (O.J. No C 127, 4.5.1984, p. 193).

After careful consideration of the problem, the Commission has decided that it would not be appropriate, at the present time, to include in the directives relating to veterinary medicinal products detailed rules laying down which professions should be permitted to distribute veterinary medicinal products. Nevertheless, in the interests of public health and in order to avoid distortions of competition, the Commission considers it necessary to bring forward proposals to ensure that the distribution of veterinary medicinal products takes place only through officially authorized channels in each Member State. To this end, the Commission is proposing that a new Chapter on the distribution of veterinary medicinal products should be inserted into Directive 81/851/EEC which will require all distributors to maintain detailed records of all transactions and to hold these record open for inspection by the competent authorities for a period of at least three years. Similar obligations are also imposed on manufactures of veterinary medicinal products by Article 27(f) and on manufacturers and distributors of active substances which may be used in the manufacture of veterinary medicinal products by Article 1(5).

6.3 Administration of non-authorized veterinary medicinal products to animals

At the present time, Article 4(2) of Directive 81/851/EEC prohibits any administration to animals of veterinary medicinal products which have not been authorized by Member States except during the conduct of clinical trials, or in the case of veterinary medicinal products

which have not been prepared in advance and are intended for the treatment of a particular animal or a small number of animals. Experience suggests that some amendment to these provisions is required.

In the first instance, the Commission considers that as a matter of principle the exemption in favour of products prepared extemporaneously for a limited number of animals should be restricted to products which are prescribed by a veterinarian in respect of animals which are under his direct personal care.

Secondly, the Commission is aware that a number of farmers have been diversifying into new activities such as fish-farming or the rearing of goats or other exotic species. Inevitably the development of veterinary medicinal products intended for the treatment of such species takes some time, and in certain instances may not even be economically viable. Thus the veterinarian may not have an authorized remedy available for the treatment of sick animals under his care. In these special circumstances, Member States should be able to permit the veterinarian to administer veterinary medicinal products which have been authorized for use in other animal species or medicinal products authorized for use in human beings provided that detailed records are kept and, in the case of food-producing animals, a lengthy withdrawal period is applied to avoid any risk to the consumer.

Thirdly, the Commission has become aware that the strict application of Article 4(2) is causing practical difficulties for veterinarians who are providing services on a transfrontier basis in accordance with the

provisions of Directive 78/1026/EEC concerning the mutual recognition of diplomas, certificates and other evidence of formal qualifications in veterinary medicine, including measures to facilitate the effective exercise of the right of establishment and freedom to provide services. (O.J. No L 362, 23.12.1978, p. 1) Veterinarians usually carry a stock of medicines with them when providing veterinary services. In order to avoid a situation where the veterinarian is obliged to hold separate stocks of medicines in each Member State, the Commission is proposing a very limited exception to Article 4(2) which will enable the veterinarian to carry with him and administer to animals veterinary medicinal products which are authorized in the country where he is established, and although not authorized in the country in which he provides services are, nevertheless, therapeutically equivalent to other veterinary medicinal products which are authorized in that country.

6.4 Environmental risk

As noted above, the use of veterinary medicinal products may in certain instances result in potential risks for the environment. In an amendment to Article (7) of Directive 81/851/EEC, the Commission is therefore proposing that where necessary, manufacturers should be required to include in their application for marketing authorization a discussion of the potential risks presented by the product to the environment which can be considered by the competent Community or national authorities when deciding whether or not to grant authorization.

6.5 Protection of Innovation

Like other medicinal products, the developement of new veterinary medicinal products has become increasingly time consuming and risky. In order to complete all the tests and trials which are required, about eight years research is required for the development of a major new product together with an investment in the order of 50 million ECUs. Products derived from biotechnology are having an increasing impact, and according to one recent estimate, by 1995 they will account for approximately one third of the market.

Within the Community, the market for veterinary medicinal products is about 5 %-10 % of the size of the market for medicinal products for human use. It is, in many sectors a highly competitive market. The funds available for the developement of new products are therefore limited, and the number of major new products being introduced into the market is relatively low.

If the European industry is to remain competitive with third countries, it is important that it should be offered equivalent prospect for the developement of new products. The establishment of an efficient procedure of obtaining a marketing authorization valid throughout the Community will make an important contribution in this respect. However the problem of the so-called second applicant must also be considered.

When an application for a new veterinary medicinal product is submitted, the applicant must provide not only

the results of the anatytical tests but also he results of the pharmaco-toxicological and clinical studies which demonstrate the efficacy of the product and its safety in animals and human beings. By way of an exception another company way submit an application for marketing authorization in respect of a veterinary medicinal product which is similar to a medicine already authorized by submitting a summary dossier consisting of references to published literature about the safety and efficacy of the product together with a complete analytical dossier, and the results of any necessary biovailibility studies which show that the products have equivalent effects.

In fact, however, the published literature is often incomplete or inappropriate. Confronted by this problem, certain national authorities have tended to be not too demanding as regards the bibliographical evidence submitted by the second applicant. This practice seriously penalises the innovatory manufacturer who has had to meet the high costs of conducting the pharmaco-toxicological and clinical studies, while his product can be copied within a short period and at a very much lower costs. Moreover the protection of an innovatory veterinary medicinal product by patent is not always possible, either because of the limited scope of patent protection or because a substantial proportion of the effective patent life has been lost due to the time necessary to complete development work and obtain authorization.

The proposed amendment to point 10 of Article 5 of Directive 81/851/EEC is intended to rationalise the present situation along the lines that have already been

accepted for proprietary medicinal products in Directive 87/21/EEC (O.J. No L 15, 17.1.1987, p. 36).

The second applicant will only be permitted to present an abridged application, omiting the results of the pharmaco-toxicological tests and clinical trials if he can :

- obtain the consent of the original manufacturer, or
- provide a complete bibliography which covers all the points necessary for the assessment of the safety and efficacy of the product (in practice such a complete bibliography is rarely available).

Otherwise he will be obliged to wait until ten years have elapsed since the authorization of the original product.

This ten year period will enable the partial recovery of the research investment, hich might not be protected otherwise, for example by a patent.

Although in the case proprietary medicinal products for human use, the Council decided that this ten year period should in certain cases be reduced to six years, the Commission is of the opinion that different considerations apply in the case of veterinary medicinal products, which are not usually the subject of price controls and whose costs are not covered by public funding.

6.6 Information about veterinary medicinal products

A series of amendments to Directive 81/851/EEC are designed to improve the information available about

veterinary medicinal products. The competent authorities of the Member States or the Community will be required to establish a summary of the essential characteristics of each authorized product. This summary will serve as the basis for verifying the accuracy of the information included on the labelling of veterinary medicinal products and on package leaflets, the use of which will be made compulsory unless all the relevant information can be provided on the labels.

In addition a series of amendments to Article 14 will require the person responsible for marketing to keep the competent authorities of the Member States or the Community properly informed of any changes in the status of the veterinary medicinal product, or of any additional information which might lead to the reassessment of the product.

6.7 Exports of veterinary medicinal products

In May 1988 the World Health Assembly approved a proposal to extend the scope of the WHO Certification Scheme on the quality of pharmaceutical products moving in international trade to cover veterinary medicinal products. In the light of this development, the Commission is proposing that the amendments previously proposed in respect of exports of medicinal products for

human use (COM(87)697 final) should also apply to veterinary medicinal products.

At the present time, Article 24 of Directive 81/851/EEC requires that all manufacturers of veterinary medicinal products must be in possession of an authorization. To avoid any abiguity, the Commission is proposing that the Directive should expressly provide that authorization is required, even though all the products manufactured are intended for export. Thus the existing provisions of Community legislation, and the new requirements discussed in section 6.6 below will apply. At the request of either the manufacturer or the authorities of the recipient country, the Member State concerned will issue a certificate in accordance with the arrangements agreed by the World Health Organisation that the manufacturer is authorized to manufacture veterinary medicinal products. In addition, the Member States will annexe to the certificate the approved summary of product characteristics mentioned in the previous section. This summary will enable the competent authorities in the recipient country to verify rapidly the authorized conditions for use of a product in the exporting country. Conversely, the absence of a summary will immediately alert the autorities to the fact that the veterinary medicinal products concerned are not authorized for use in the exporting Member State and they will be able to draw the appropriate conclusions in the light of the explanations given by the company and the prevailing conditions in the recipient country.

6.8 Obligations on manufacturers

At the present time, authorization to manufacture veterinary medicinal products is granted by the competent authorities of the Member State in which a manufacturer is established, who are responsible for ensuring that the manufacturer satisfies the legal requirements laid down. The Commission is proposing to supplement these provisions by introducing into Directive 81/851/EEC a specific requirement for manufacturers to comply with the principles of good manufacturing practice for veterinary medicinal products. The detailed requirements of good manufacturing practice would be adopted in a specific Directive to be adopted by the so-called regulatory committee procedure, which requires the agreement of a qualified majority of Member States, in accordance with the provisions of Directive 81/852/EEC. In fact, work on the preparation of a code of good manufacturing practices for medicinal products is at an advanced stage of preparation, and this could, after suitable adjustments, also provide the basis for a future code of good manufacturing practices for veterinary medicinal products.

7. THE PROPOSAL TO EXTEND THE DIRECTIVES TO COVER IMMUNOLOGICAL PRODUCTS

The proposal to extend the scope of the Directives to cover immunological veterinary medicinal products establishes the principle that these products may be placed on the market only after an authorization has been granted by the competent authorities. In addition, the

proposal lays down certain fundamental requirements for the category of products concerned. However, it is envisaged that the Council will delegate to the Commission the power to adopt the detailed changes which are necessary to Directive 81/852/EEC relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products to take account of the special characteristics of these products. In order to implement these changes, the Commission will act in cooperation with the Committee on the Adaptation to Technical Progress of the Directives on the removal of Technical Barriers to Trade in the Veterinary Medicinal Products Sector created by Directive 87/20/EEC, using the so-called regulatory committee procedure, which requires the approval of a qualified majority of the Member States for the adoption of the measures by the Commission (Procedure III, variant a of Council Decision 87/373/EEC of 13 July 1987 (O.J. No L 197, 18.7.1987, p. 33) laying down the procedures fo the exercise of implementing powers conferred on the Commission.) It is envisaged that work on the preparation of these detailed changes will be undertaken during 1989, in parallel with the discussion of these proposals, so that the changes can be formally adopted immediately after the Council approves the framework Directive and come into effect at the same time. If for any reason, this work is delayed, it is envisaged that the entry into force of the framework Directive will be postponed until it is complete.

In addition to certain detailed changes which are made to the rules governing the declaration of the composition of veterinary medicinal products to take account of the

biological origin of these products, there are two major areas where the regulation of immunological veterinary medicinal products requires a somewhat different approach from the regulation of other categories of veterinary medicinal products :

i) It is important to ensure that manufacturers of immunological veterinary medicinal products are able to attain high levels of batch-to-batch consistency in their manufacturing operations, and the proposal contains specific provisions to this effect ;

ii) the immunization of animals agains disease is closely linked with the overall pattern of disease existing within a given territory. Thus in addition to the criteria of quality, safety and efficacy, Member States should be empowered to prohibit the use of immunological veterinary medicinal products for other objectively justified reasons.

The other changes which are necessary to take account of the particular nature of immunological veterinary medicinal products, for example the wide variety of pharmaceutical forms used and the risk of the "shedding" of vaccines into the environment will be considered during discussions on the amendment of the testing requirements in the annexe to Directive 81/852/EEC.

8. CONCLUSIONS

In accordance with the provisions of Articles 8A and 8C of the Treaty establishing the European Economic Community, the Commission requests the Member States to take the measures necessary to comply with this package of proposals by 1 January 1992.

The Commission has taken into account the requirements of Article 8C of the Treaty and has concluded that no special provision seems to be justified at this stage.

The Commission has also studied the question of the high levels of health, safety, environmental and consumer protection required by the terms of Article 100 A, paragraph 3. It has done so following consultation of the industrial and social partners concerned, and in the light of an analysis of the risks inherent in this area and of the current technical capabilities of the European industry. The proposals take full account of these considerations in the light of the overall objectives of this provision of the Treaty.

Proposal for a
COUNCIL REGULATION (EEC)

laying down a Community prccedure for the establishment of tolerances for residues of veterinary medicinal products

THE COUNCIL OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Economic Community, and in particular Article 43 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 use of veterinary medicinal products in food-producing animals may result in the presence of residues in foodstuffs obtained from treated animals,

Whereas in accordance with the principles laid down by Council Directive 81/851/EEC(4) it is necessary to ensure that the withdrawal period between the last administration of a veterinary medicinal product to food-producing animals and the production of foodstuffs from such animals is long enough to ensure that such foodstuffs do not contain any residues which might constitue a health hazard to the consumer ;

---

(1)

(2)

(3)

(4) O.J. No L 317, 6.11.1981, p. 1

Whereas, as a result of scientific and technical progress it is possible to detect the presence of residues of veterinary medicines in foodstuffs at ever lower levels ;

Whereas it is therefore necessary to establish tolerances for the maximum levels of residues which may be accepted in foodstuffs of animal origin in accordance with generally recognised principles of safety assessment ;

Whereas the establishment of different tolerances by Member States may hinder the free movement of veterinary medicinal products and of foodstuffs of animal origin ;

Whereas therefore it is necessary to lay down a procedure for the establishment of tolerances for residues of veterinary medicinal products by the Community, following a single scientific assessment of the highest possible quality ;

Whereas the need for the establishment of tolerances by the Community is recognised in the Community rules relating to trade in foodstuffs of animal origin ;

Whereas therefore no new veterinary medicinal product containing a new active substance not previously used in food-producing animals should be authorized for use in the Community unless a tolerance for residues of that substance has been established by the Community ; whereas the person responsible for marketing a new veterinary medicinal product of this nature should be permitted to avail himself of the procedures established by Council Directive 87/22/EEC 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[5] ;

---

(5) OJ No L 15, 17.1.1987, p.38.

Whereas arrangements must also be made for the establishment of tolerances for substances which are currently used in veterinary medicines administered to food-producing animals ; whereas however in view of the complexity of this matter and the large number of substances involved, long transitional arrangements are required ;

Whereas the tolerances should be adopted by a rapid procedure which ensures close cooperation between the Commission and the Member States through the Committee for Veterinary Medicinal Products established by Directive 81/851/EEC ; whereas an urgent procedure is also required to ensure the swift review of any tolerance which may not be sufficient to protect public health ;

Whereas the information necessary to assess the safety of residues should be presented in accordance with the principles laid down by Council Directive 81/852/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products(6), as amended by Directive 87/20/EEC(7) ;

HAS ADOPTED THIS REGULATION :

---

(6) O.J. No L 317, 6.11.1981, p. 16.

(7) O.J. No L 15, 17.1.1987, p. 34.

Article 1

For the purposes of this Regulation, the following definitions shall apply :

1. "residues of veterinary medicinal products", all active ingredients of veterinary medicinal products or metabolites thereof which remain in meat or other foodstuffs originating from the animal to which the medicinal product in question has been administered.

2. "tolerance", the maximum level of residues of veterinary medicinal products which may be accepted by the Community and which do not present a hazard for the health of the consumer of foodstuffs of animal origin.

Article 2

A tolerance shall be established in accordance with the provisions of this Regulation, having regard to all the information available, and in accordance with generally recognised principles of safety assessment. A tolerance may be reduced to take account of the level of residues which is expected to result from the correct administration of the veterinary medicinal product to the animal species concerned. It may also be reduced where it appears that residues may cause difficulties for the industrial processing of foodstuffs. A tolerance shall be expressed in terms of micrograms per kilogram (parts per billion) on a fresh weight basis. Where necessary, a separate tolerance shall be established for each foodstuff of animal origin (muscle tissue, liver, kidney, fat, skin, milk, eggs, honey etc.).

The list of substances used as active ingredients in veterinary medicinal products in respect of which tolerances have been established shall be contained in Annex I to this Regulation, which shall be adopted in accordance with the procedure laid down in Article 9. Except as provided for in Article 10, any amendments to Annex I shall be adopted in accordance with the same procedure.

Article 3

Where, having regard to the nature and pattern of use of a substance used as an active ingredient in veterinary medicinal products, it is not necessary to establish a tolerance for residues of that constituent or its metabolites, that substance shall be included in a list in Annex II to this Regulation. Annex I. shall be adopted in accordance with the procedure laid down in Article 9. Except as provided for in Article 10, any amendments to Annex II shall be adopted in accordance with the same procedure.

Article 4

A provisional tolerance may be adopted for a substance used as an active ingredient in veterinary medicinal products provided that there are no grounds for supposing that residues of the substance concerned at the level proposed present a hazard for the health of the consumer. A provisional tolerance shall apply for a defined period of time, which shall not exceed three years, and shall not be renewed more than once.

The list of substances used as active ingredients in veterinary medicinal products in respect of which provisional tolerances have been established shall be contained in

Annex III to this Regulation, which shall be adopted in accordance with the procedure laid down in Article 9. Except as provided for in Article 10, any amendments to Annex III shall be adopted in accordance with the same procedure.

Article 5

Where it appears that a tolerance cannot be established in respect of a substance used as active ingredient in veterinary medicinal products because residues of the substances concerned, at whatever level, in foodstuffs of animal origin constitute a hazard to the health of the consumer, that substance shall be included in a list in Annex IV to this Regulation. Annex IV shall be adopted in accordance with the procedure laid down in Article 9. Except as provided for in Article 10, any amendements to Annex IV shall be adopted in accordance with the same procedure.

The administration of the substances listed in Annex IV to food-producing animals shall be prohibited throughout the Community.

Article 6

A Member State shall not authorize the marketing of a veterinary medicinal product intended for administration to food-producing animals containing an active substance which was not authorized for use in veterinary medicinal products intended for administration to food-producing animals in the Member State concerned on the date of entry into force of this Regulation unless the substance concerned has been included in Annex I, II or III.

Unless it is developed by one of the biotechnological processes listed in Part A of the Annex to Directive 87/22/EEC, a veterinary medicinal product covered by the provisions of the preceding paragraph shall be regarded as a high-technology medicinal product to which Part B of the Annex to Directive 87/22/EEC applies.

Article 7

1. In order to obtain the inclusion of an active substance referred to in Article 6 in Annex I, II or III to this Regulation, the person responsible for marketing shall submit an application to the Commission. The application shall contain the information and particulars referred to in Annex V and shall conform to the principles laid down in Directive 81/852/EEC.

2. After verifying that the application is submitted in correct form, the Commission shall forthwith submit the application for examination by the Committee for Veterinary Medicinal Products established by Article 16 of Directive 81/851/EEC (hereinafter referred to as "the Committee"). The Committee may request one of its Members to act as rapporteur and to undertake an initial evaluation of the application.

3. Within 120 days of referral of the application to the Committee, and having regard to the observations formulated by the members of the Committee, the Commission shall prepare a draft of the measures to be taken. However if, after consulting the Committee, the Commission considers that the information submitted by the person responsible for marketing is insufficient to

enable such a draft to be prepared, the Commission may request that person to provide additional information. If the person responsible for marketing agrees to provide such information, the Commission will prepare a draft of the measures to be taken within 90 days of its receipt.

4. The draft of the measures to be taken shall be communicated forthwith by the Commission to the Member States and to the person responsible for marketing. Within a further 60 days the person responsible for marketing may, at his request, explain himself orally or in writing before the Committee. The Commission may, at the request of the applicant, extend this time limit.

5. Within a further 60 days the Commission shall submit the draft measures to the Committee for adoption in accordance with the procedure laid down in Article 9.

Article 8

The following provisions shall apply in respect of substances which are authorized for use as active ingredients in veterinary medicinal products on the date of entry into force of this Regulation :

1 After consulting the Committee, the Commission shall publish a timetable for the consideration of these substances, including time limits for submission of the information referred to in Annex V. The Member States and persons responsible for marketing the veterinary medicinal products concerned shall ensure that all relevant information is submitted

to the Commission in accordance with the requirements of Annex V and in conformity with the principles laid down in Directive 81/852/EEC before the relevant time limits.

2. After verifying that the information is submitted in correct form, the Commission shall forthwith submit the information to the Committee for examination. The Committee may request one of its members to act as rapporteur and to undertake an initial evaluation of information.

3. Having regard to the observations formulated by the members of the Committee, the Commission shall prepare a draft of the measures to be taken. However if, after consulting the Committee, the Commission considers that the information submitted by the person responsible for marketing is insufficient to enable such a draft to be prepared, the Commission may request that person to provide additional information, within a specified period.

4. The draft of the measures to be taken shall be communicated forthwith by the Commission to the Member States and those persons responsible for marketing who have submitted information to the Commission. These persons may, at their request, explain themselves orally or in writing before the Committee.

5. The Commission shall forthwith submit the draft measures to the Committee for adoption in accordance with the procedure laid down in Article 9.

Article 9

1. Where the procedure laid down in this Article is to be followed, matters shall be referred to the Committee by the chairman either on his own initiative or at the request of a Member State.

2. The representative of the Commission shall submit to the Committee a draft of the measures to be adopted. The Committee shall deliver its opinion on the draft within a time-limit set by the chairman, having regard to the urgency of the matter. It shall act by a qualified majority, the votes of the Member States being weighted as provided for in Article 148(2) of the Treaty. The chairman shall not vote.

3. (a) The Commission shall adopt the measures envisaged where they are in accordance with the opinion of the Committee.

(b) Where the measures envisaged are not in accordance with the opinion of the Committee, or if no opinion is adopted, the Commission shall without delay propose to the Council the measures to be adopted. The Council shall act by a qualified majority.

(c) If within three months of the proposal being submitted to it, the Council has not acted, the proposed measures shall be adopted by the Commission.

Article 10

1. Where a Member State, as a result of new information or a reassessment of existing information, considers that the urgent amendment of a provision contained in Annexes I to IV is necessary in order to protect human or animal health, and therefore requires swift action to be taken, that Member State may temporarily suspend the operation of the provision concerned in its own territory. In that case, it shall immediately notify the other Member States and the Commission of the measures, attaching a statement of the reasons therefor.

2. The Commission shall as soon as possible examine the grounds given by the Member State concerned and shall consult the Member States within the Committee and shall then deliver its opinion forthwith and take appropriate measures. The Commission shall immediately notify the Council and the Member States of any measures taken. Any Member State may refer the Commission's measures to the Council within 15 days of such notification. The Council, acting by a qualified majority may take a different decision within 15 days of the date on which the matter was referred to it.

3. If the Commission considers that it is necessary to amend the provision of Annexes I to IV concerned in order to resolve the difficulties referred to in paragraph 1 and to ensure the protection of human health, it shall initiate the procedure laid down in Article 11 with a view to adopting those amendments ; the Member State

which has taken measures under paragraph 1 may maintain them until the Council or the Commission has taken a decision in accordance with the abovementioned procedure.

Article 11

1. Where the procedure laid down in this Article is to be followed, matters shall be referred to the Committee by the chairman either on his own initiative or at the request of a Member State.

2. The representative of the Commission shall submit to the Committee a draft of the measures to be adopted. The Committee shall deliver its opinion on the draft within a time-limit set by the chairman, having regard to the urgency of the matter. It shall act by a qualified majority, the votes of the Member States being weighted as provided for in Article 148(2) of the Treaty. The chairman shall not vote.

3. (a) The Commission shall adopt the measures envisaged, where they are in accordance with the opinion of the Committee.

(b) Where the measures envisaged are not in accordance with the opinion of the Committee, or if no opinion is adopted, the Commission shall without delay propose to the Council the measures to be adopted. The Council shall act by a qualified majority.

(c) If within 15 days of the proposals being submitted to it, the Council has not acted, the proposed measures shall be adopted by the Commission.

Article 12

Any changes which are necessary to adapt Annex V to take account of scientific and technical progress shall be adopted in accordance with the procedure laid down in Article 2c of Directive 81/852/EEC.

Article 13

As soon as possible after the amendment of Annexes I, II, III or IV, the Commission shall publish a summary assessment of the safety of the substances concerned. The confidential nature of any proprietary data shall be respected.

Article 14

Member States shall ensure that the withdrawal periods between the last administration of a veterinary medicinal product to animals and the production of foodstuffs from such animals are established in such a manner as to ensure that the tolerances provided for in accordance with this Regulation are not exceeded.

Article 15

Member States may not prohibit or impede the putting into circulation within their territories of foodstuffs of animal origin on the ground that they contain residues of veterinary medicinal products if the quantity of residue does not exceed the tolerance provided for in Annex I or III, or if the substance concerned is listed in Annex II.

Article 16

With effect from 1 January 1997, the administration to food producing animals of veterinary medicinal products containing active substances which are not mentioned in Annexes I, II or III shall be prohibited within the Community, except in the case of clinical trials which have been notified to or approved by the competent authorities.

Article 17

This Regulation shall in no way prejudice the application of Community legislation prohibiting the use in livestock farming of certain substances having a hormonal action.

Article 18

This Regulation shall enter into force on 1 January 1992.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels For the Council

ANNEX V

Information and particulars to be included in an application for the establishment of a tolerance for residues of a veterinary medicinal product.

1. Administrative particulars

1.1. Name or corporate name and permanant address of the person responsible for placing the veterinary medicinal product on the market

1.2. Name of the veterinary medicinal product

1.3. Qualitative and quantitative composition in terms of active principles, with mention of the international non-proprietary name recommended by the World Health Organization where such name exists

1.4. Manufacturing authorization

1.5. Marketing authorizations

1.6. Summary of the characteristics of the veterinary medicinal product prepared in accordance with Article 5a of Directive 81/854/EEC

2. Identity

2.1. International non-proprietary name

2.2. IUPAC name

2.3. CAS name

2.4. Classification
- therapeutic
- pharmacological

2.5. Synonyms and abbreviations

2.6. Structural formula

2.7. Molecular formula

2.8. Molecular weight

2.9. Degree of impurity

2.10 Qualitative and quantitative composition of impurities

2.11 Description of physical properties
- fusion point
- boiling point
- vapour pressure
- solubility in water and organic solvents expressed in g/l with indication of temperature
- density
- spectra of refraction, rotation, etc.

3. Toxicological studies

3.1. Short term toxicological studies

3.2. Long term studies

3.3. Studies on reproduction

3.4. Studies on teratogenicity

3.5. Studies on mutagenicity

3.6. Studies for carcinogenicity

3.7. Studies of immunological effects

3.8. Studies of microbiological effets

3.9. Observations in humans

3.10. Other biological effects.

4. Metabolic and residue studies

4.1. Absorption, distribution, excretion and biotransformations.

4.2. Determination of residues

4.3. Methods of residue analysis

4.4. National maximum residue limits

6. Recommendations

6.1. Level causing no toxicological effect

6.2. Estimate of temporary acceptable daily intake for man

6.3. Estimate of maximum residue levels in food with the specification of the residue of concern

6.4. Methods of residue analysis

6.5. Further work or information
- required
- desirable

8. References.

Proposal for a

COUNCIL DIRECTIVE

amending Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products.

THE COUNCIL OF THE EUROPEAN COMMUNITIES,

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

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

In cooperation with the European Parliament(2),

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

Whereas Article 23(2) of Council Directive 81/851/EEC(4) provides that the Commission should submit to the Council a proposal containing appropriate measures leading towards the elimination of any remaining barriers to trade or to the free movement of veterinary medicinal products not later than four years after the implementation of the abovementioned Directive;

---

(1)

(2)

(3)

(4) O.J. No L 317, 6.11.1981, p. 1

Whereas the Directives on the approximation of laws relating to veterinary medicinal products must be adapted to scientific progress and improved to take account of the experience acquired since their adoption ;

Whereas it is necessary from the point of view of public health and the free movement of veterinary medicinal products for the competent authorities to have at their disposal all useful information on authorized veterinary medicinal products in the form of approved summaries of the characteristics of products ;

Whereas the approximation of laws brought about in this connection must enable a veterinary medicinal product, manufactured and marketed in one Member State on the basis of harmonized provisions, to be allowed into another Member State, taking due consideration of the initial authorization, save in exceptional cases submitted for a binding opinion to the Committee for Veterinary Medicinal Products set up by Directive 81/851/EEC ;

Whereas the system for leaflets accompanying veterinary medicinal products should be improved ;

Whereas it is advisable to stipulate more precisely the cases in which the results of pharmacological and toxicological tests or clinical trials do not have to be provided with a view to obtaining authorization for a veterinary medicinal product which is essentially similar to an innovative product, while ensuring that innovative firms are not placed at a disadvantage ; whereas, however, there are reasons of public policy for not repeating tests carried out on animals without over-riding cause ;

Whereas the guarantees of the quality of veterinary medicinal products manufactured within the Community should be maintained by requiring compliance with the principles of good manufacturing practice for medicinal products irrespective of the final destination of the products ;

Whereas the Commission should be empowered to define in detail the principles of good manufacturing practice for veterinary medicinal products in close coo tion with the Committee for Adaptation to Technical Progr of the Directive on the Removal of Technical Barriers to Trade in the Veterinary Medicinal Products Sector established by Article 2c of Council . . . Directive 81/852/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in in respect of the testing of veterinary medicinal products (5), as amended by Directive 87/20/EEC(6);

Whereas measures should be taken to improve the provision of information for third countries about the conditions of use of veterinary medicinal products within the Member States and the Community;

Whereas measures should be taken to ensure that distributors of veterinary medicinal products are authorised by Member States and maintain adequate records,

HAS ADOPTED THIS DIRECTIVE:

. . .

(5) O.J. No L 317, 6.11.1981, p.16

(6) O.J. No L 15, 17.1.1987, p. 34

ARTICLE 1

Directive 81/851/EEC is hereby amended as follows :

1. In Article 1(2), the first indent is replaced by the following :

"-'veterinary medicinal product' shall mean any medicinal product intended for animals.

However products or substances which are intended for long term use by oral administration to healthy animals for nutritional purposes shall not be considered as veterinary medicinal products."

2. Article 1(5) is replaced by the following :

"5. Member States shall take all necessary measures to ensure that no person shall have on his premises or under his control any substance which may be used as a veterinary medicinal product unless expressly authorised under the legislation of the Member State concerned.

For the purposes of implementing this provision, Member States shall maintain a register of producers and dealers and other persons who are permitted to be in possession of active substances which may be used in the manufacture of veterinary medicinal products which are available only on veterinary prescription. Such persons shall be required to maintain detailed records of all dealings in active substances

which may be used in the manufacture of veterinary medicinal products and to make these records available for inspection by the competent authorities for a period of at least three years.

Before the date of implementation of this Directive, Member States shall communicate to the Commission a list of the veterinary medicinal products which are available without veterinary prescription."

3. In Article 2, the fourth indent of paragraph 2 is deleted.

4. Article 4 is replaced by the following:

"Article 4

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

2. No veterinary medicinal product may be administered to animals unless the authorization referred to above has been issued, except for the tests of veterinary medicinal products referred to in point 10 of Article 5 which have been notified to or approved by the competent national authorities in accordance with the national rules in force.

3. However Member States may permit veterinary medicinal products prepared extemporaneously by a veterinarian

or in a pharmacy in accordance with the terms of a veterinary prescription or an official formula to be administered to a particular animal or a small number of animals by a veterinarian or under his direct personal responsibility.

Moreover, Member States may permit the administration to animals of

- veterinary medicinal products authorized for use in the Member State concerned in accordance with the provisions of this Directive for use in another animal species ;

- medicinal products which have been authorized for use in the Member State concerned in human beings in accordance with the provisions 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( );

which have been prescribed by a veterinarian, provided that the animals to be treated have been examined by the veterinarian personally and the veterinarian concludes that there is no authorized therapy which will be effective for the treatment of the animals concerned. The veterinarian shall be required to maintain adequate records of the date of examination of the animals, the clinical diagnosis, the medicinal products prescribed, the dosages administered, the duration of treatment and the withdrawal periods recommended, and to make these records available for

( ) OJ No L

Inspection by the competent authorities for a period of at least three years.

Where the administration of such medicinal products to food producing animals is permitted, the veterinarian shall be responsible for ensuring that the withdrawal period applied is sufficient to ensure that foodstuffs derived from treated animals do not contain any residues which might constitute a health hazard for the consumer.

4. Notwithstanding paragraph 2, Member States shall ensure that veterinarians providing services in another Member State can take with them and administer to animals under their direct care small quantities of veterinary medicinal products other than immunological veterinary medicinal products which are not authorized for use in the Member State in which the services are provided (host Member State), providing that the following conditions are satisfied :

(a) the marketing authorization provided for in paragraph 1 has been granted by the competent authorities of the Member State in which the veterinarian is established ;

(b) the veterinary medicinal products are transported by the veterinarian in the original manufacturer's packaging ;

(c) in the case of veterinary medicinal products intended for administration to food-producing animals, the products carried have the same qualitative and quantitative composition in terms of active principles as products authorized in accordance with paragraph 1 for use in the host Member State ;

(d) prior to the administration of the products to animals, the veterinarian shall be required to ascertain the conditions for use of the corresponding veterinary medicinal products in the host Member State, including the withdrawal period, and the veterinarian shall be required to take all measures incumbent upon him to ensure that the rules applying in the host Member State are complied with ;

(e) the veterinarian shall not furnish any veterinary medicinal product to the owner or keeper of the animals treated in the host Member State unless this is permissible on the basis of Community law or the law of the Member State concerned ;

(f) the veterinarian shall be required to keep detailed records of the animals treated, the clinical diagnosis, the veterinary medicinal products administered, the dosage administered, the duration of treatment and the withdrawal period applied. These records shall be available for inspection by the competent authorities for a period of at least three years;

(g) the overall range and quantity of veterinary medicinal products carried by the veterinarian shall not exceed that generally required by good veterinary practice."

5. Article 5 is replaced by the following:

"Article 5

For the purpose of obtaining the 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 provided by the applicant :

1. name or corporate name and permanent address or registered place of business of the person responsible for marketing and, if different, of the manufacturer or manufacturers involved and of the sites where manufacturing operations are carried out ;

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 or 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

formula and giving the international non-proprietary name recommended by the World Health Organisation, if such a name exists ;

4. 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 products intended, its pharmaceutical form, method and route of administration and proposed shelf life. ;

7. If applicable, reasons for any precautionary and safety measures to be taken for the storage of the product, during its administration to animals, and for the disposal of waste products, together with an indication of any potential risks presented by the product to the environment and the health of humans, animals or plants ;

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. Where necessary, and in particular in the case of veterinary medicinal products containing an active substance not previously used in veterinary medicine, which are the subject of a request for marketing authorization in the Member States concerned

for the first time, the applicant shall propose and justify a tolerance level for residues which may be accepted in foodstuffs without risk for the consumer, together with appropriate validated analytical detection methods.

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, test 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.

However, and without prejudice to the law relating to the protection of industrial and commercial property :

a) The applicant shall not be required to provide the results of toxicological and pharmacological tests and clinical trials if he can demonstrate :

i) either that the veterinary medicinal product is essentially similar to a product authorized in the country concerned by the application and that the person responsible for the marketing of the original veterinary

medicinal product has consented to the toxicological, pharmacological or clinical references contained in the file on the original veterinary medicinal product being used for the purpose of examining the application in question ;

ii) or by detailed references to the scientific literature presented in accordance with the second paragraph of Article 1 of Directive 81/852/EEC that the constituent or constituents of the veterinary medicinal product have a well established medicinal use, with recognized efficacy and an acceptable level of safety ;

iii) or that the veterinary medicinal product is essentially similar to a product which has been authorized within the Community, in accordance with the Community provisions in force, for not less than ten years and is marketed in the Member State for which the application is made.

b) In the case of new veterinary medicinal products containing known constituents not hitherto used in combination for therapeutic purposes, the results of toxicological and of pharmacological tests and of clinical trials relating to that combination must be provided, but it shall not be necessary to provide references relating to each individual constituent.

11. a summary in accordance with Article 5a of the product characteristics, one or more specimens or mock-ups of the sales presentation of the veterinary medicinal product together with a package insert where one is to be enclosed.

12. a document showing the that 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 together with a list of those countries to which an application for marketing authorization has been made and an explanation of the reasons for which any Member State or third country has refused to grant authorization for the veterinary medicinal product concerned."

6. The following Article 5a is inserted :

"Article 5a

The summary of the product characteristics referred to in point 11 of the second paragraph of Article 5 shall contain the following information :

1. Name of the veterinary medicinal product,

2. Qualitative and quantitative composition in terms of the active ingredients and constituents of the

excipient, knowledge of which is essential for proper administration of the medicinal product ; the International non-proprietary names recommended by the World Health Organization shall be used, where such names exist, or failing this, the usual common name or chemical description.

3. Pharmaceutical form.

4. Pharmacological properties and, in so far as this information is useful for therapeutic purposes, pharmacokinetic particulars.

5. Clinical Particulars

5.0 target species,
5.1 therapeutic indications, specifying the target species,
5.2 contra-indications,
5.3 undesireable effets (frequency and seriousness),
5.4 special precautions for use,
5.5 use during pregnancy and lactation,
5.6 interaction with other medicaments and other forms of interaction,
5.7 posology and method of administration,
5.8 overdose (symptoms, emergency procedures, antidotes)(if necessary),
5.9 special warnings for each target species,
5.10 withdrawal periods,
5.11 special safety precautions to be taken by the person administering the product to animals.

6. Pharmaceutical Particulars :

6.1 incompatibilities (major),

6.2 shelf life, when necessary after reconstitution of the product or when the container is opened for the first time,

6.3 special precautions for storage,

6.4 nature and contents of container,

6.5 name or style and permanent address or registered place of business of the holder of the marketing authorization,

6.6 special precautions for the disposal of unused product or waste materials, if any."

7. The following Article 5b is inserted :

"Article 5b

When the marketing authorization referred to in Article 4(1) is issued, the person responsible for placing that product on the market shall be informed, by the competent authorities of the Member State concerned, of the summary of the product characteristics as approved by them. The competent authorities shall take all necessary measures to ensure that the information given in the summary is in conformity with that accepted when the marketing authorization is issued or subsequently."

8. The last paragraph of Article 7 is amended as follows :

"The experts' detailed reports shall form a part of the documentation which the applicant shall lodge with the

competent authorities. A brief curriculum vitae of the expert shall be appended to each expert report."

9. Article 9(2) is replaced by the following:

"2. may submit the medicinal product, its active principles and it necessary intermediate products or other constituent materials for testing by a State laboratory or by a laboratory designated for that 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."

10. Article 14 is replaced by the following :

"Article 14

1. After an authorization has been issued, the person responsible for placing the product on the market must, in respect of the control methods provided for in point 9 of the second paragraph of Article 5, take account of technical and scientific progress and introduce any changes that may be required to enable the veterinary medicinal product to be checked by means of generally accepted scientific methods. These changes must be accepted by the competent authorities of the Member States concerned.

2. The person responsible for marketing shall forthwith inform the competent authorities of any new

information which might entail the amendment or further examination of the particulars and documents referred to in Article 5 or the approved summary of the product characteristics referred to in Article 5b. In particular the person responsible for marketing shall forthwith inform the competent authorities of any prohibition or restriction imposed by the competent authorities of any country in which the veterinary medicinal product is marketed and of any serious unexpected reaction occuring in animals or human beings.

3. The person responsible for marketing shall be required to maintain records of all reported suspected adverse reactions arising in animals and human beings. For the purpose of this provision, a failure of the veterinary medicinal product to achieve the expected therapeutic effect shall be considered an adverse reaction. These records shall be kept for at least five years and shall be made available to the competent authorities upon request.

4. The person responsible for marketing shall immediately inform the competent authorities, with a view to authorization, of any alteration he proposes to make to the particulars and documents referred to in Article 5."

11. Chapter IV is replaced by the following :

"CHAPTER IV

Committee for Veterinary Medicinal Products

Article 16

1. In order to facilitate the adoption of a common position by the Member States with regard to decisions on the issue of marketing authorizations and to promote thereby the free movement of veterinary medicinal products, a Committee for Veterinary 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 Committee's task shall be to examine, at the request of a Member State or the Commission and in accordance with Articles 17 to 22, questions concerning the application of Articles 11, 36 and 49.

3. The Committee shall draw up its own rules of procedure.

Article 17

1. In order to make it easier to obtain a marketing authorization in at least two other Member States taking into due consideration an authorization issued in one Member State in accordance with Article 4, the

holder of the latter authorization may submit an application to the competent authorities of the Member States concerned together with the information and documents referred to in Articles 5, 5a and 5b. He shall testify to its identity with the dossier accepted by the first Member State, specifying any additions it may contain, and shall certify that all the dossiers filed as part of this procedure are identical.

2. The holder of the marketing authorization shall notify the Committee of this application, inform it of the Member States concerned and send it a copy of this authorization. He shall also inform the Member State which granted him the initial authorization and notify it of any additions to the original dossier ; that State may require the applicant to provide it with all the particulars and documents necessary to enable it to check the identity of the dossiers filed with the dossier on which took its decision.

3. The holder of the marketing authorization shall notify the dates on which the dossiers were sent to the Member States concerned. As soon as the Committee has noted that all the Member States concerned are in possession of the dossier, it shall forthwith inform all the Member States and the applicant of the date on which the last Member State concerned received the dossier. The Member State(s) concerned shall either grant the authorization valid for their markets within a period of 120 days of the aforementioned date, taking into due consideration the authorization issued within the meaning of paragraph 1, or put forward a reasoned objection.

Article 18

1. Where a Member State considers that it is unable to grant a marketing authorization, it shall forward to the Committee and to the person responsible for placing the veterinary medicinal product on the market its reasoned objection in accordance with Article 11, within the time limits stipulated in Article 17 (3).

2. Upon the expiry of this period, the matter shall be referred to the Committee and the procedure referred to in Article 21 shall be applied.

3. On receipt of the reasoned objection referred to in paragraph 1, the person responsible for placing the product on the market shall immediately send the Committee a copy of the particulars and documents enumerated in Article 17(1).

Article 19

If several applications submitted in accordance with Articles 5 and 5a have been made for a marketing authorization for a particular veterinary medicinal product, and one or more Member States have granted and authorization while one or more of the other Member States have refused it, one of the Member States concerned or the Commission may refer the matter to the Committee for application of the procedure referred to in Article 21.

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

In both cases, the person responsible for placing the veterinary medicinal product on the market shall be informed of any decision of the Committee to apply the procedure laid down in Article 14.

Article 20

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 a request for a marketing authorization or on the suspension or revocation of an authorization.

Article 21

1. The competent authorities shall draw up an assessment report and comments on the dossier as regards the results of the analytical and toxico-pharmacological tests on, and clinical trials of, any veterinary medicinal products containing a new active substance which are the subject of a request for a marketing authorization in the Member States concerned for the first time.

2. As soon as the notification referred to in Article 17 is received, the competent authorities shall immediately communicate to the Member States concerned

any assessment report accompanied by a summary of the dossier relating to a particular veterinary medicinal product. This report shall also be communicated to the Committee where a matter is referred to the Committee pursuant to Article 18.

The assessment report shall also be forwarded to the other Member States concerned and to the Committee as soon as a matter is referred to the Committee under the procedure laid down in Article 19. Any assessment report so forwarded shall remain confidential.

The competent authorities shall bring the assessment report up to date as soon as it is in possession of information which is of importance for the evaluation of the balance between effectiveness and risk.

Article 22

1. Where reference is made to the procedure described in this Article, the Committee shall consider the matter concerned and issue a reasoned opinion within 60 days of the date on which the matter was referred to it.

In the case referred to in Article 18 the person reponsible for placing the product on the market may, at his request, explain himself orally or in writing and provide additional information before the Committee issues its opinion. The Committee may extend the time limit referred to in the preceding paragraph to give the applicant time to explain himself orally or in writing.

In the case referred to in Article 19, the person responsible for placing the product on the market may be asked to explain himself orally or in writing.

2. The Committee's opinion shall concern the grounds for the objection provided for in Article 18(1) and the grounds on which the marketing authorization has been refused, suspended or withdrawn in the cases described in Article 19.

The Committee shall immediately inform the competent authorities and the person responsible for placing the product on the market of its opinion.

3. The competent authorities shall implement the opinion of the Committee with 60 days of its receipt.

4. Where an application for marketing authorization is submitted in respect of a product which is the subject of an opinion of the Committee and the competent authorities have reasons for not applying the opinion of the Committee, they shall forthwith request the Committee to reconsider its opinion, in accordance with the procedure laid down in this Chapter.

Article 23

The Commission shall report to the Council and the European Parliament every two years on the operation of the procedure laid down in this Chapter."

12. Article 24(1) is replaced by the following :

"1. Member States shall take all appropriate measures to ensure that the manufacture of veterinary medicinal products is subject to the holding of an authorization. This manufacturing authorization shall be required notwithstanding that the veterinary medicinal products manufactured are intended for export."

13. The following Article 24a is inserted :

"Article 24 a

At the request of the manufacturer, the exporter or the authorities of an importing third country, Member States shall certify that a manufacturer of veterinary medicinal products is in possession of the authorization referred to in Article 24. When issuing such certificates, Member States shall comply with the following conditions :

1. Member States shall have regard to the prevailing administrative arrangements of the World Health Organization.

2. For veterinary medicinal products intended for export which are already authorized on their territory, they shall supply the summary of the product characteristics as approved in accordance with Article 5b or, in the absence thereof, an equivalent document.

Where the manufacturer is not in possession of a marketing authorization, he shall provice the authorities responsible for establishing the certificate referred to in the first paragraph with a declaration explaining why no marketing authorization is available."

14. In Article 27, the following is added :

"f) comply with the principles and the guidelines of good manufacturing practice for medicinal products laid down by Community law."

15. In Article 27, the following is added:

g) maintain detailed records of all veterinary medicinal products supplied by him to wholesalers or, where this is permitted by the laws of the Member State concerned, to retailers, veterinarians or farmers. The following information shall be recorded in respect of each transaction, whether or not it is made for payment :

- date ;
- name of the veterinary medicinal product ;
- quantity supplied ;
- name and address of the recipient.

These records shall be available for inspection by the competent authorities for a period of 3 years.

16. The following Article 27a is inserted :

"Article 27 a

The principles and guidelines of good manufacturing practices for medicinal products referred to in Article 27(f) should be adopted in the form of a Directive addressed to Member States in accordance with the procedure laid down in Article 2c of Council Directive 81/852/EEC, after taking into consideration the specific nature of veterinary medicinal products ; detailed guidelines shall be published by the Commission and revised as appropriate to take into consideration scientific and technical progress."

17. In Article 34

- The first paragraph is replaced by the following:

  "The competent authority of the Member State concerned shall ensure by means of repeated inspection that the legal requirements relating to veterinary medicinal products are complied with."

- The following third paragraph is added:

  "The officials representing the competent authority shall report after each of the inspections mentioned in the first paragraph on whether the manufacturer complies with the principles and guidelines of good

manufacturing practice laid down by Community law. The manufacturer shall be informed of the content of such reports and shall be entitled to request a second inspection."

18. In Article 39, the following second paragraph is added :

"Upon reasoned request, Member States shall forthwith communicate the reports referred to in the third paragraph of Article 34 to the competent authorities of another Member State. If, after considering the reports, the Member State receiving the reports considers that it cannot accept the conclusions reached by the competent authority of the Member State in which the report was established, it shall inform the competent authority concerned of its reasons and may request further information. In the case of prolonged disagreement between Member States, the Member State(s) shall inform the Commission."

19. Article 42 becomes Article 42(1) and the following paragraphs are added :

"2. The person responsible for the marketing of a veterinary medicinal product shall be obliged to notify the Member States forthwith of any action taken by him to suspend the marketing of a product or to withdraw a product from the market, together with the reasons for such action. Member States shall ensure that this information is brought to the attention of the Committee forthwith.

3. Member States shall ensure that appropriate information about actions taken pursuant to paragraphs 1 and 2 which may effect the protection of health in third countries is forthwith brought to the attention of the relevant international organisations, with a copy to the Committee."

20. In the first paragraph of Article 43, points 2, 7 and 8 are replaced by the following, and the following point 9a is inserted :

"2. A statement of the active ingredients expressed qualitatively and quantitatively per dosage unit or according to the form of administration for a particular volume or weight, using the international non-proprietary names recommended by the World Health Organization, where such names exist, or where no such names exist, the usual common names.

7. The withdrawal period, even if this is nil, in the case of veterinary medicinal products administered to food-producing animals.

8. Expiry date, in plain language.

9a. Special precautions for disposal of unused product or waste material, if any."

21. In Article 48, the first paragraph is replaced by the following :

"The inclusion of a package insert in the packaging of veterinary medicinal products shall be obligatory unless all the information required by this Article can be conveyed on the packaging itself. Member States shall take all appropriate measures to ensure that the information included on a package insert of a veterinary medicinal product relates solely to the veterinary medicinal product concerned."

22. In the second paragraph of Article 48, point (e) is replaced by the following and the following point (h) is added:

"e) the withdrawal period, even if this is nil, in the case of veterinary medicinal products administered to food-producing animals ;

h) special precautions for the disposal of unused product or waste materials, if any."

23. The final paragraph of Article 48 is deleted.

24. The following Chapter VIII is inserted :

"CHAPTER VIII

Distribution of veterinary medicinal products

Article 51

1. Member States shall take all appropriate measures to ensure that wholesale dealing in veterinary medicinal products is subject to the holding of an authorization and to ensure that the time taken for the procedure for granting this authorization does not exceed 90 days from the date on which the competent authority receives the application.

2. In order to obtain the authorization referred to in paragraph 1, the applicant shall have at his disposal suitable and sufficient premises complying with the legal requirements laid down in the Member State concerned as regards the storage and handling of products.

3. The holder of the authorization referred to in paragraph 1 shall be required to maintain detailed records. The following information shall be recorded in respect of each incoming or outgoing transaction :

(a) date ;
(b) name of the veterinary medicinal product ;
(c) name of the manufacturer ;
(d) manufacturers batch number, expiry date ;
(e) quantity received or supplied ;
(f) name and address of the supplier or recipient.

At least once a year, a detailed audit shall be carried out, and incoming and outgoing supplies shall be reconciled with supplies currently held in stock and any discrepancies recorded.

These records shall be available for inspection by the competent authorities for a period of three years.

4. Member States shall take all appropriate measures to ensure that wholesalers supply veterinary medicinal products only to persons permitted to carry out retail activities in accordance with the provisions of Article 52, or to other persons who are lawfully permitted to receive veterinary medicinal products from wholesalers.

Article 52

1. Member States shall take all appropriate measures to ensure that the retail supply of veterinary medicinal products is conducted only by persons who are expressly permitted to carry out such operations by the legislation of the Member State concerned.

2. Any retailer of veterinary medicinal products shall be required to maintain detailed records. The following information shall be recorded in respect of each incoming or outgoing transaction :

(a) date ;
(b) name of the veterinary medicinal product ;
(c) name of the manufacturer ;

(d) manufacturers batch number, expiry date ;

(e) quantity received or supplied ;

(f) name and address of the supplier or recipient ;

(g) name and address of the prescribing veterinarian if any, date of prescription ;

At least one a year, a detailed audit shall be carried out, and incoming and outgoing supplies shall be reconciled with supplies currently held in stock and any discrepancies recorded.

These records shall be available for inspection by the competent authorities for a period of three years.

However, Member States may dispense retailers of veterinary medicinal products from the obligation to maintain detailed records in respect of products supplied by them in small transactions for the treatment of companion animals such cats, dogs, 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 all possible measures have been taken to prevent the unauthorized use of the products for other animals.

Article 53

Where, in accordance with the legislation of a Member State a person responsible for marketing a veterinary medicinal product is permitted to supply samples of the product directly to a veterinarian or other authorized person, the veterinarian or other authorized person shall

be required to maintain the records referred to in Article 52(2) in respect of medicines received and subsequently supplied by him, whether or not such supply is made for payment."

25. Chapter VIII becomes Chapter IX and Articles 51, 52 and 53 become Articles 54, 55 and 56 respectively.

Article 2

1. Member States shall take the necessary measures to comply with this Directive not later than 1 January 1992. They shall forthwith inform the Commission thereof.

2. Requests for marketing authorization lodged from the date set out in paragraph 1 must comply with the provisions of this Directive.

3. Within four years of the date set out in paragraph 1, Article 1 where relevant, shall be progressively extended to existing veterinary medicinal products.

Article 3

This Directive is addressed to the Member States.

Done at Brussels,

For the Council,

The President

Proposal for a

COUNCIL DIRECTIVE

extending the scope of Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products and laying down additional provisions for immunological veterinary medicinal products.

THE COUNCIL OF THE EUROPEAN COMMUNITIES,

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

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

In cooperation with the European Parliament(2),

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

Whereas disparities in the provisions laid down by law, regulation or administrative action by Member States may hinder trade in immunological veterinary medicinal products within the Community ;

Whereas the essential aim of any rules governing the production, distribution or use of veterinary medicinal products must be to ensure a high level of protection of public health ;

---

(1)

(2)

(3)

Whereas the provisions of Council Directive 81/851/EEC (4), although appropriate, are not adequate for veterinary medicinal products used in order to produce active immunity, to diagnose the state of immunity and to produce passive immunity (immunological veterinary medicinal products) ;

Whereas in accordance with Article 5 of Council Directive 87/22/EEC of 22 December 1986 on the approximation of national provisions relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology(5), the Commission is required to submit proposals to harmonize the conditions for authorizing the manufacture and placing on the market of immunological veterinary medicinal products ;

Whereas, before an authorization to market an immunological veterinary medicinal product can be granted, the manufacturer must demonstrate his ability to attain batch-to-batch consistency ;

Whereas the competent authorities should also be empowered to prohibit the use of an immunological veterinary medicinal product when the immunological responses of the treated animals will interfere with the operation of a national or Community programme for the eradication or control of animal disease ;

Whereas changes will be required to the requirements for the testing of veterinary medicinal products laid down in Annex I to Council Directive 81/852/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to

---

(4) O.J. No L 317, 6.11.1981, p. 1

(5) O.J. No L 15, 17.1 1987, p. 38

analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products(6), as amended by Directive 87/20/EEC(7), to take account of the special nature of immunological veterinary medicinal products ; whereas the Commission should be empowered to adopt the necessary changes in close cooperation with the Committee for the Adaptation to Technical Progress of the Directives on the Removal of Technical Barriers to Trade in the Veterinary Medicinal Products Sector, thus ensuring greater quality, safety and effectiveness,

HAS ADOPTED THIS DIRECTIVE :

(6) O.J. No L 317, 6.11.1981, p. 16.

(7) O.J. No L 15, 17.1.1987, p. 34.

Article 1

1. Subject to the provisions of this Directive, Directive 81/851/EEC shall apply to immunological veterinary medicinal products.

2. For the purposes of this Directive "immunological veterinary medicinal product" shall mean a veterinary medicinal product used in order to produce active immunity, diagnose the state of immunity or produce passive immunity.

3. This Directive and Directive 81/851/EEC shall not apply to autogenous vaccines which are manufactured from the organisms found in discharges from the body of an animal and used for the treatment of the individual animal from which the organisms are derived.

Article 2

1. The quantitative particulars of an immunological veterinary medicinal product shall be expressed by mass or by international units or by units of biological activity or by specific protein content where possible as appropriate to the product concerned.

2. In respect of immunological veterinary medicinal products, in Directive 81/851/EEC the expressions "qualitative and quantitative particulars of the constituents" shall include particulars relating to biological activity or to protein content and "qualitative and quantitative composition" shall include the composition of the product expressed in terms of the

biological activity or of protein content.

3. In any document established in accordance with Directive 81/851/EEC in which the name of an immunological veterinary medicinal product is expressed, the common or scientific name of the active constituents shall also be included at least once ; it may be abbreviated in the remaining references.

Article 3

1. The competent authorities shall ensure that the manufacturing processes used in the manufacture of immunological veterinary medicinal products are properly validated and attain batch-to-batch consistency.

2. For the purpose of implementing Article 35 of Directive 81/851/EEC, the competent authorities may require persons responsible for marketing immunological veterinary medicinal products to submit to a competent authority copies of all the control reports signed by the qualified person in accordance with Article 30 of Directive 81/851/EEC.

The person responsible for marketing may be required to provide the competent authorities with a sample of each batch of immunological veterinary medicinal products manufactured, or to hold such samples in stock up to the expiry date for provision upon request to the competent authorities.

3. Where in the interests of human or animal health, the legislation of a Member State so provides, the competent

authorities may require persons responsible for marketing the immunological veterinary medicinal products to submit to a competent authority samples from each batch of the bulk and/or finished product for examination by a State laboratory or a laboratory designated for this purpose before release onto the market, unless another competent authority within the Community has previously examined the batch in question and declared it to be in conformity with the approved specification. Any such examination shall be completed within 60 days of the receipt of the samples.

Article 4

In the absence of specific Community legislation and in accordance with national legislation, the use of an immunological veterinary medicinal product may be prohibited in the whole or part of the territory of the Community or a Member State if it is established that :

a) the administration of the product to animals will interfere with the operation of a national or Community programme for the control or eradication of animal disease, or,

b) the disease against which the product is intended to confer immunity is substantially absent from the territory in question, or,

c) the administration of the product will cause difficulties in certifying the absence of contamination of foodstuffs obtained from treated animals.

The competent authorities of the Member States shall inform the Commission of all instances in which the provisions of this Article are applied.

Article 5

The amendments which are necessary in the testing requirements for veterinary medicinal products set out in the Annex to Directive 81/852/EEC to take account of the extension of the scope of Directive 81/851/EEC to cover immunological veterinary medicinal products shall be adopted in accordance with the procedure laid down in Article 2c of Directive 81/852/EEC.

Article 6

1. Member States shall take the necessary measures to comply with this Directive not later than 1 January 1992. They shall forthwith inform the Commission thereof.

   In the event of the amendments referred to in Article 5 not being adopted by 1 January 1991, the date set out in the first subparagraph shall be postponed to a date one year later than the date of adoption of those amendments.

2. Requests for marketing authorization for products covered by this Directive lodged after the date set out in the first subparagraph of paragraph 1 must comply with the provisions of this Directive.

3. Within three years of the date set out in the first subparagraph of paragraph 1 this Directive shall be progressively extended to existing immunological veterinary products.

Article 7

This Directive is addressed to the Member States.

Done at Brussels

For the Council

FINANCIAL STATEMENT

relating to the Commission proposals for the amendment of the veterinary medicinal products directives

1. Budget headings

N° A 1100 salaries of official and temporary agents

N° A 2510 travelling expenses of members of institutionalized committees

N° B 7750 action for the internal market

2. Legal basis

Article 100 A of the EEC Treaty

3. Description of the project

3.1 General objective

- the realisation of the internal market in the veterinary medicinal products sector

3.2 Specific objectives

a) the establishment of a centralized Community procedure for determining safe levels for residues of veterinary medicines in foodstuffs of animal origin

b) improvement of the Community authorization procedure for veterinary medicinal products, based on the extension of authorization from one Member State to the other Member States of the Community

c) the updating of the detailed provisions of the veterinary medicinal products directives in the light of developements since 1981

d) the extension of the veterinary medicines directives to cover veterinary vaccines (mandate from the Council, Article 5 paragraph 2 of Directive 87/22/EEC, O.J. No L 15 of 17.01.1987).

4. Justification of the Project

4.1 Justification of the Type of Project Proposed

The limited experience acquired from the existing Community procedures for the coordination of national decisions on the authorization of veterinary medicinal products suggests that real progress towards and intern l market in this sector can only be made by the establishment of centralised Community procedures for the assessmen' of the quality, safety and efficacy of veterinary medicinal products and for the assessment of the potential risks to the consumer of residues of veterinary medicines in foodstuffs of animal origin.

The present proposals constitute an interim step intended to resolve the problem of residues and improve the operation of existing procedures. Further proposals for the establishment of new procedures will be presented as soon as possible.

4.2 Interest of the project at Community level

The realisation of the internal market implies that all categories of industrially prepared veterinary medicinal products should be able to circulate throughout the Community. Moreover, differences between the rules of the Member States regarding the acceptance of veterinary medicinal products must also be reconciled in order to prevent repercussions on intra-Community trade in foodstuffs of animal origin, which is of far greater economic significance.

5. Financial Implications

5.1 General Considerations

The major financial implications result from an intensification of cooperation with Member States through :

- ıe examination together of applications for authorization to market veterinary medicinal products

- establishment of tolerances for residues of approximately 150 active substances used in veterinary medicine over an eight year transitional period from 1992 onwards

- drug-monitoring activites.

5.2 Particular Financial Consideration

a) Progressive establishment of a technical and scientific secretariat for the Scientific Committee for Veterinary Medicinal Products through the recruitment of the following additional personnel,to be found by internal redeployment or throug normal budgetary process

1991 2 administrators (A7)
1 assistant (B5)
1 secretary (C5)

1992 1 administrator (A7)
1 secretary (C5)

b) Appropriations for additional meetings estimated at (the provisions of funding will be considered in the context of the overall budget which will be granted by the budgetary authority under the heading "2510").

- 6 additional meetings of the Committee for Veterinary Medicinal Products each year (2 representatives per Member State) (currently ± 3 meetings a year at 10,500 ECU per meeting).

- 9 additional meetings of scientific working parties a year (1 representative per Member State) (currently ± 5 meetings a year at 540 ECU per meeting).

- 2 meetings a year of the Committee referred to in Article 2b of Directive 81/852/EEC ; travel expenses of two representatives per Member State (this committee has not yet been convened).

c) Appropriations for contracts with expert outside consultants ; approximately 50,000 ECU in 1992, to be granted by the budgetary authority, under the heading "B7750".

d) Appropriations for missions, participation in scientific symposia etc.

COMPETITIVENESS AND EMPLOYEMENT IMPACT STATEMENT

I. What is the main reason for introducing the measure ?

Realisation of the internal market ; improvement of the protection of public health ; updating of existing Community legislation relating to veterinary medicinal products.

II. Features of the businesses in question

Because of the relatively small size of the market, and the high costs of developing new products, only a limited number of large-sized companies are capable of producing innovatory veterinary medicinal products. However, a number of smaller and medium sized companies manufacture copies of well-established products which are off-patent.

The number of small and medium sized companies involved in the distribution of veterinary medicinal products is much greater as in the role of self-employed professional persons, such as veterinarians and pharmacists.

So far as the Commission is aware, there is no particular concentration of the businesses concerned in the regions.

III. What direct obligations does this measure impose on businesses ?

Manufacturers of veterinary medicinal products :

- obligation to submit data on the safety of residues of veterinary medicines in foodstuffs of animal origin to

the Commission to permit the establishment of harmonised residue tolerances by the Community. The submission of such data is already required by Member States.

- various additional obligations designed to improve the protection of public health in the veterinary medicines sector, in particular through somewhat increased obligations to submit data in support of applications for authorization and compliance with principles of good manufacturing practice. These provisions are already applied by certain Member States, and in many instances are analagous to measures applied to the manufacturers of medicinal products for human use.

Distributors of veterinary medicinal products, wholesalers and retailers :

- for wholesalers, the obligation to obtain authorisation to distribute veterinary medicinal products, to have appropriate premises and to maintain distribution records for a period of three years ;

- for retailers, to maintain distribution records for a period of three years.

These requirements are intended to prevent the diversion of veterinary medicinal products from the legitimate distribution circuit into the grey and black market zones of illicit non-authorized used and to facilitate the detection of abuses. Certain of these controls are already applied by Member States.

IV. What indirect obligations are local authorities likely to impose on businesses ?

None foressen.

V. Are there any special measures in respect of SMEs ?

No.

VI. What is the likely effect on :

a) the competitiveness of business

The greater degree of harmonisation of the requirements for authorization of veterinary medicinal products should help improve the competitiveness of both innovatory and generic manufacturers of veterinary medicinal products.

The provisions relating to distribution, which apply equally to all types of distributor, should not have any significant effect on competitiveness.

b) Employment

No significant effets are anticipated.

VII. Have both sides of industry been consulted on this proposal ?

In addition to the European federations representing the manufacturers of pharmaceuticals, veterinary medicinal products and animal feedingstuffs, associations representing pharmacists and veterinarians have been consulted on these proposals. There is general support for the principles underlying the proposals. However, the pharmacists and veterinarians would prefer stricter controls on distribution, each emphasising the role of its profession.