COMMISSION OF THE EUROPEAN COMMUNITIES

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REVISED VERSION

Proposal for a

COUNCIL REGULATION (EEC)

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

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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

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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

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(presented by the Commission)

AMENDMENT OF THE VETERINARY MEDICINAL PRODUCTS DIRECTIVES

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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