COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 19.11.1996
COM(96) 584 final

96/0279 (CNS)

Proposal for a

COUNCIL REGULATION (EC)

amending Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin

(presented by the Commission)

EXPLANATORY MEMORANDUM

I. COUNCIL REGULATION (EEC) NO 2377/90

On 26 June 1990, the Council adopted Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin (OJ No L 224, 18.8.1990, p. 1), hereinafter referred to as "the Regulation". The aim of this Regulation is to protect public health and to prevent the establishment of maximum residue limit at national level from hindering the free movement of veterinary medicinal products and foodstuffs within the European Union.

The effect of the combined provisions of the Regulation and of Article 4 of Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products (OJ No L 317, 6.11.1981, p. 1), as amended by Directive 90/676/EEC of 13 December 1990 (OJ No L 373, 31.12.1990, p. 15), has been as follows:

- since 1 January 1992, the date on which the Regulation entered into force, it has not been possible to authorize the placing of a veterinary medicinal product on the market unless a maximum residue limit has been established beforehand at Community level (new substance);

- substances whose use was authorized on that date have had to be progressively evaluated, so that from 1 January 1997 the use of substances for which maximum residue limits had not been established would be prohibited in the Community (old substances).

Pursuant to the Regulation, on the basis of the scientific opinion of the Committee for Veterinary Medicinal Products (hereinafter referred to as CVMP), it falls to the Commission to adopt, in accordance with the procedure of the Regulatory Committee, a legally binding decision classifying the substance in question in one of the four annexes to the Regulation:

- Annex I, restricted to substances for which a maximum residue level may be fixed after an evaluation of the toxicological risks that substance presents for human health;

- Annex II contains substances not subject to maximum residue levels;

- Annex III covers substances for which in the absence of adequate scientific data it is not possible to establish a definitive maximum residue limit but which without presenting a hazard for the health of the consumer may be the subject of a maximum residue limit for a specified period required for the completion of scientific studies;

- Annex IV is for substances for which no maximum residue limit can be established because the substances concerned constitute, at whatever limit, a hazard to the health of the consumer.

The Commission has then classified some 282 of the most widely used substances in veterinary medicine in one of the Annexes to the Regulation by adopting the following Regulations:

- Regulation (EEC) No 675/92, OJ L 73, 19.3.1992, p. 8
- Regulation (EEC) No 3093/92, OJ L 311, 28.10.1992, p. 18
- Regulation (EEC) No 895/93, OJ L 93, 17.4.1992, p. 10
- Regulation (EC) No 3425/93, OJ L 312, 15.12.1993, p. 12
- Regulation (EC) No 3426/93, OJ L 312, 15.12.1993, p. 15
- Regulation (EC) No 955/94, OJ L 108, 29.4.1994, p. 8
- Regulation (EC) No 1430/94, OJ L 156, 23.6.1994, p. 6
- Regulation (EC) No 2703/94, OJ L 287, 8.11.1994, p. 19
- Regulation (EC) No 3059/94, OJ L 323, 16.12.1994, p. 15
- Regulation (EC) No 1102/95, OJ L 110, 17.5.1995, p. 9
- Regulation (EC) No 1441/95, OJ L 143, 27.6.1995, p. 22
- Regulation (EC) No 1442/95, OJ L 143, 27.6.1995, p. 26
- Regulation (EC) No 1798/95, OJ L 174, 26.7.1995, p. 20
- Regulation (EC) No 2796/95, OJ L 290, 5.12.1995, p. 1
- Regulation (EC) No 2804/95, OJ L 291, 6.12.1995, p. 8
- Regulation (EC) No 281/96, OJ L 37, 15.5.1996, p. 9
- Regulation (EC) No 282/96, OJ L 37, 15.2.1996, p. 12
- Regulation (EC) No 1140/96, OJ L 151, 26.6.1996, p. 6
- Regulation (EC) No 1147/96, OJ L 151, 26.6.1996, p. 26

The harmonization thus achieved has enabled the Community to play a more active and coordinated role in the international harmonization work undertaken within the Codex Alimentarius Committee for residues of veterinary medicinal products in foodstuffs and the JECFA (Joint FAO/WHO Expert Committee on Food Additives).

II. ADAPTATION OF COUNCIL REGULATION (EEC) No 2377/90 TO THE NEW COMMUNITY SYSTEM OF MARKETING AUTHORIZATIONS

Since the Regulation was adopted, the regulatory environment for veterinary medicinal products has been radically altered following the entry into force of the Community system of marketing authorizations resulting from Council Regulation (EEC) No 2309/93 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products[1] and Council Directives 93/40/EEC[2] and 93/41/EEC.[3]

The CVMP is henceforth responsible to the European Agency for the Evaluation of Medicinal Products (hereafter referred to as "the Agency") which deals with requests for authorization to place human and veterinary medicinal products on the market in accordance with the so-called centralized procedure and to which it falls, under Regulation (EEC) No 2309/93, to issue an opinion on the maximum residue limits of veterinary medicinal products which are acceptable in foodstuffs of animal origin. With a view to legal consistency, the Regulation should therefore be adapted by conferring on the Agency the task of dealing with applications for the establishment, amendment and extension of maximum residue limits and by aligning the decision making process with that of the centralized procedure (role of Agency Secretariat, time limits, appeals). Account should also be taken of Council Regulation (EC) No 297/95 on fees payable to the European Agency for the evaluation of medicinal products[4] which lays down *inter alia* that fees are charged by the Agency for examining applications for the establishment, amendment and extension of maximum residue limits.

Moreover, it is necessary to adapt the period for submitting draft measures to the regulatory committee to allow the Community to meet its obligations under the Agreements on the application of sanitary and phytosanitary measures which emerged from the multilateral negotiations of the Uruguay Round, approved on behalf of the European Community by Council Decision 94/800/EC of 22 December 1994.[5] This agreement creates a transparency obligation as regards health measures which necessitates the introduction of reasonable periods for consulting members of the World Trade Organization.

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1 OJ L 214, 24.8.93, p. 1.
2 OJ L 214, 24.8.93, p. 31.
3 OJ L 214, 24.8.93, p. 40.
4 OJ L 35, 15.2.9.95, p. 1.
5 OJ L 336, 23.12.94, p. 1.

III. EXTENSION OF THE DEADLINE OF 1 JANUARY 1997 FOR THE REVISION OF OLD SUBSTANCES

Article 7(2) of the Regulation provides for the gradual evaluation of old substances and Article 14 lays down that, with effect from 1 January 1997, "the administration to food producing animals of veterinary medicinal products containing pharmacologically active substances which are not mentioned in Annexes I, II or III shall be prohibited within the Community".

To this end, the Commission published as an annex to Volume VI of the Regulations on medicinal products in the European Community a timetable for the evaluation of old substances. The number of substances to be evaluated between 1992 and 1997 was then estimated at 400. In view of the difficulties encountered by the industry in collecting the data necessary to establish dossiers and by the national authorities in evaluating them, this timetable was changed and published in the form of a Commission communication in the Official Journal of the European Communities on 29 September 1993.[6]

The Member States bearing most of the burden of the evaluation work through the CVMP were unable, however, to allocate sufficient resources for the revision work to be completed by the deadline originally laid down by the Council. For its part, the industry became involved in a major process of reevaluation and updating of dossiers.

There is no doubt that as a result of this exercise, the market in veterinary medicinal products will have become more transparent, thus improving consumer protection. It is, however, clear that the scale of the task far exceeded available resources and that, in spite of the considerable efforts of the Agency since commencing its activities on 1 January 1995, the evaluation currently underway will not be completed by 1 January 1997.

Therefore, in order to allow this Community procedure to continue on a sound scientific basis and not to deprive veterinary surgeons and other users of substances needed to protect animal health, the time limit originally laid down should be extended by two years. However, for obvious reasons of consumer protection and transparency, this extension should be restricted to those substances for which dossiers were presented to the Agency before 1 January 1996.

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6 OJ C 263, 29.9.93, p. 5.

The figures below give an overview of the situation on 1 March 1996:

	Annex I	Annex II	Total
Substances undergoing evaluation in the Agency	32	69	101
Substances undergoing evaluation for which further data has been requested from the firms concerned	22	10	32
Substances whose evaluation has not yet begun	35	78	113
Total	89	157	246

The evaluation of prospective Annex I substances is estimated to involve 250 hours of work and prospective Annex II substances around 30 hours of work. Therefore, 11090 hours of work are still needed to complete the evaluation of old substances.

Given an 8-hour working day, 1 386 working days are then still needed for this activity. However, the Member States do not allocate the same resources to this work. The table below shows the time that the national experts spend on this activity, based on a 240 working-day year:

France (two experts)	100%	480 days
Netherlands (two experts)	50%	240 days
United Kingdom	70%	168 days
Germany	25%	120 days
Italy	25%	60 days
Sweden	25%	60 days
Denmark	25%	60 days
Ireland	25%	60 days
Austria	10%	24 days
Finland	10%	24 days
Portugal	10%	24 days
Spain	10%	24 days
Belgium	10%	24 days
Total		**1 368 days**

However, this calculation does not take account of the time needed for industry to respond to requests for additional information (around 6 months), meetings and the delays inherent in the decision making process. It is therefore reasonable that, to complete the evaluation of old substances under conditions which are satisfactory from both the scientific and public health protection point of view, the time limit laid down by the Regulation should be extended to 1 January 1999.

IV. ESTABLISHMENT OF MAXIMUM RESIDUE LIMITS FOR SUBSTANCES UNDERGOING CLINICAL TRIALS

Article 4(2) of Directive 81/851/EEC lays down that "from 1 January 1977 the Member States shall not permit foodstuffs for human consumption to be taken from test animals unless maximum residue limits have been established by the Community in accordance with the provisions of Regulation (EEC) No 2377/90 and an appropriate withdrawal period has been established to ensure that this maximum limit will not be exceeded in the foodstuffs".

This means that, from 1 January 1997, unless a maximum residue limit is established before a clinical trial is carried out, foodstuffs from animals used in the clinical trial and possibly the animals themselves (regardless of the time that has elapsed since the trial) would have to be destroyed.

Moreover, whereas for old substances, Article 4 of the Regulation lays down that provisional maximum residue limits may be established 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, it stipulates that as regards new substances, this possibility may be used only in "exceptional circumstances".

Clinical trials are carried out in order to assess the effectiveness of the substance, relatively early in the development process and certainly well before all the information and data which has to be given in an application to establish a maximum residue limit for a pharmacologically active substance used in veterinary medicinal products in accordance with Annex V of Regulation (EEC) No 2377/90 is available.

The primary objective of Regulation (EEC) No 2377/90 is to protect the health of consumers and it is normal that such protection should apply where animals have been the subject of clinical trials. However, notwithstanding this objective, it is also necessary to ensure that no undue damage is done to the research and development capacity of the pharmaceutical industry in Europe and to avoid a situation where European pharmaceutical companies are obliged to carry out their tests outside Europe.

In the same way as with old substances, it is possible to establish provisional maximum residue limits for substances undergoing clinical trials. Annex V should be amended so that initially only certain data is provided, which nonetheless constitutes a sound scientific basis for the evaluations. To this end, a specific annex for substances undergoing clinical trials which are the subject of a provisional maximum residue limit and an appropriate withdrawal period guaranteeing protection of consumer health would have to be added to Regulation (EEC) 2377/90. As regards the fees to be paid to the Agency, a suitable solution should be applied under Regulation (EC) No 297/95,[7] which could envisage the fee thus paid being deducible from that ultimately due in connection with an application made under Article 6 of the Regulation.

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7 OJ No L 35, 15.2.95, p. 1.

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amending Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin

THE COUNCIL OF THE EUROPEAN COMMUNITIES

Having regard to the Treaty establishing the European Community, and in particular Article 43 thereof,

Having regard to the proposal from the Commission,

Having regard to the opinion of the European Parliament,

Having regard to the opinion of the Economic and Social Committee,

Whereas, since Council Regulation (EEC) No 2377/90 was adopted, the regulatory environment of veterinary medicinal products has been radically altered, in particular as a result of the entry into force of Council Regulation (EEC) No 2309/93 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products[1] and of Council Directive 93/40/EEC amending Directives 81/851/EEC and 81/852/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products;[2]

Whereas the Committee for Veterinary Medicinal Products is henceforth responsible to the European Agency for the Evaluation of Medicinal Products and whereas it falls to this Agency, through this Committee, to issue an opinion on the maximum residue limits of veterinary medicinal products which are acceptable in foodstuffs of animal origin in accordance with Regulation (EEC) No 2377/90;

Whereas Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the European Agency for the Evaluation of Medicinal Products[3] establishes the fees payable to the Agency for examining applications for the establishment, amendment and extension of maximum residue limits;

Whereas it is necessary, consequently, to adapt Regulation (EEC) 2377/90 by conferring on the Agency the task of dealing with applications for the establishment, amendment and extension of maximum residue limits and by aligning the decision-making process with respect to the authorization and supervision of medicinal products for veterinary use with that introduced by Regulation (EEC) No 2309/93;

Whereas the Agreement on the application of sanitary and phytosanitary measures which emerged from the multilateral negotiations of the Uruguay Round, approved on behalf of the European Community by Council Decision 94/800/EC of 22 December 1994 concerning the conclusion on behalf of the European Community, as regards matters within its competence, of the agreements reached in the Uruguay Round multilateral

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[1] OJ No L 214, 24.8.1993, p. 1.
[2] OJ No L 214, 24.8.1993, p. 31.
[3] OJ No L 35, 15.2.1995, p. 1.

negotiations (1986-1994)[4], creates transparency obligations as regards health measures; whereas Regulation (EEC) No 2377/90 must therefore be adapted in order to enable the Community to fulfil its obligations under this Agreement;

Whereas Council Directive 81/851/EEC as amended by Directive 93/40/EEC prohibits from 1st January 1997 foodstuffs for human consumption being taken from animals used for clinical trials unless maximum residue limits have been established by the Community; Whereas, Regulation (EEC) No 2377/90 has to be amended in order to allow the use of this procedure for substances undergoing clinical trials; for this purpose, the level of development of the substance concerned should be taken into account; the information and particulars to be included in an application for the establishment of a MRL within the meaning of Annex V of this Regulation should be reviewed;

Whereas it is necessary to maintain on the market substances the use of which was authorized on the date when Regulation (EEC) No 2377/90 entered into force and for which applications were submitted to the Commission or to the Agency before 1 January 1996, in order to make it possible to continue their scientific evaluation in the best possible conditions, given the resources available,

HAS ADOPTED THIS REGULATION

Article 1

Regulation (EC) 2377/90 is amended as follows:

1. The following Article is inserted:

"*Article 4(a)*

A provisional maximum residue limit may be established for a pharmacologically active substance undergoing clinical trials, provided that there are no grounds for supposing that residues of the substance concerned at the level proposed present a health hazard to consumers. A suitable waiting period shall be fixed to guarantee that this provisional maximum residue limit is respected. This provisional maximum residue limit shall apply for a defined period of time, which shall not exceed two years.

The list of pharmacologically active substances used in the context of clinical trials for which provisional maximum residue limits have been established, together with their appropriate time periods, shall be contained in Annex III(a), which shall be adopted in accordance with the procedure laid down in Article 8. Except as provided for in Article 9, any amendments to Annex III(a) shall be adopted in accordance with the same procedure."

[4] O.J. N° L 336 of 23.12.94, p. 1

2. Article 6 is replaced by the following text:

"*Article 6*

1. In order to obtain the inclusion in Annex I, II or III of a pharmacologically active substance which is intended for use in veterinary medicinal products for administration to food- producing animals, an application to establish a maximum residue limit shall be submitted to the European Agency for the Evaluation of Medicinal Products set up by Council Regulation (EEC) No 2309/93, hereinafter referred to as the "Agency".

   This application shall contain the information and particulars referred to in Annex V and shall conform with the principles laid down in Directive 81/852/EEC. When a provisional maximum residue limit as referred to in Article 4(a) of this Regulation has been established, only the data needed to complete Annex V have to be supplied.

2. In order to obtain the inclusion in Annex III(a) of a pharmacologically active substance administered to food-producing animals and used in the context of clinical trials, an application to establish a provisional maximum residue limit shall be submitted to the Agency. This application shall contain the information and particulars referred to in Annex V, which shall be amended to that end.

3. The application shall also be accompanied by the fee due to the Agency for examining the application fixed by Regulation (EC) No 297/95.

3. Article 7 is replaced by the following text:

"*Article 7*

1. The Committee for Veterinary Medicinal Products referred to in Article 27 of Regulation (EEC) No 2309/93, hereinafter referred to as the "Committee", shall be responsible for formulating the Agency's opinion on the classification of substances in Annexes I, II, III, III(a) or IV of this Regulation.

2. Articles 52 and 53 of Regulation (EEC) No 2309/93 are applicable *mutatis mutandis* for the purposes of this Regulation.

3. The Agency shall ensure that the Committee's opinion is delivered within a period of 120 days following the reception of a valid application. If the information submitted by the applicant is not sufficient to enable such an opinion to be prepared, the Committee may ask the applicant to supply additional information within a specific time limit. The deadline for the opinion shall then be deferred until the additional information has been received.

4. The Agency shall forward the opinion to the applicant. Within 15 days of receipt of the opinion, the applicant may provide written notice to the Agency that he wishes to appeal. In that case he shall forward the detailed grounds for his appeal to the Agency within 60 days of receipt of the opinion. Within 60 days of the receipt of the grounds for appeal, the Committee shall consider whether its opinion should be revised and the reasons for the conclusion reached on the appeal shall be annexed to the report referred to in paragraph 7.

5. The Agency shall forward the definitive opinion of the Committee within 30 days of its adoption both to the Commission and to the applicant. The opinion shall be accompanied by a report describing the safety evaluation of the substance by the Committee and which shall give the grounds for its conclusions.

6. The Commission shall prepare draft measures taking account of Community legislation and shall start the procedure provided for in Article 8. The Committee referred to in Article 8 shall adapt its rules of procedure in order to take account of the tasks conferred upon it by this Regulation.

4. In Article 8, paragraph 1 is replaced by the following text:

"1. Where the procedure laid down in this Article is to be followed, the Commission shall be assisted by the Standing Committee for Veterinary Medicinal Products."

5. In Article 10, paragraph 1 is replaced by the following text:

"1. Where the procedure laid down in this Article is to be followed, the Commission shall be assisted by the Standing Committee for Veterinary Medicinal Products."

6. Article 12 is replaced by the following text:

"*Article 12*

As soon as possible after the amendment of Annexes I, II, III, IIIa or IV, the Agency shall publish a summary of the assessment of the safety of the substances concerned that have been examined by the Committee. The Agency shall provide the competent authorities with appropriate methods of analysis for tracing residues. The confidential nature of any proprietary data shall be respected."

7. In Article 13, the terms "in Annex I or III" **are replaced by** "in Annex I, III or IIIa".

8. Article 14 is replaced by the following text:

"*Article 14*

With effect from 1 January 1997, the administration to food-producing animals of veterinary medicinal products containing pharmacologically active substances which are not mentioned in Annexes I, II or III shall be prohibited within the Community.

With regard to substances whose use was authorized in veterinary medicinal products before the date on which this Regulation entered into force and for which applications to establish maximum residue limits were submitted either to the Commission or to the Agency before 1 January 1996, the prohibition date indicated in the previous subparagraph shall be deferred to 1 January 1999. Within three months of the adoption of this Regulation, the Agency will publish a list of these substances.

As from 1 January 1997, the Member States shall not allow foodstuffs destined for human consumption to originate from animals that have been subjected to clinical trails unless the substance in question is mentioned in Annex IIIa."

Article 2

This Regulation shall enter into force on 1 January 1997.

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

Done at .....

For the Council

The President

ISSN 0254-1475

COM(96) 584 final

DOCUMENTS

EN 03 15 05 10

Catalogue number : CB-CO-96-581-EN-C

ISBN 92-78-11557-6

Office for Official Publications of the European Communities

L-2985 Luxembourg