COMMISSION OF THE EUROPEAN COMMUNITIES

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Brussels, 1 June 1993

Re-examined proposal for a SYN 310

COUNCIL DIRECTIVE

modifying Directives 65/65/EEC, 75/318/EEC and 75/319/EEC

relating to medicinal products

Re-examined proposal for a SYN 311

COUNCIL DIRECTIVE

modifying Directives 81/851/EEC and 81/852/EEC

on the approximation of the laws of the Member States

relating to veterinary medicinal products

(presented by the Commission pursuant to Article 149(2)(d)

of the EEC Treaty)

On 21 April 1993 the European Parliament examined three Common Positions reached by the Council on 17 December 1992 relating to the following proposals of the Commission:

- proposal for a Council Directive modifying Directives 65/65/EEC, 75/318/EEC and 75/319/EEC relating to medicinal products (**SYN 310**);

- proposal for a Council Directive modifying Directives 81/851/EEC and 81/852/EEC on the approximation of laws of the Member States relating to veterinary medicinal products (**SYN 311**);

- proposal for a Council Directive repealing 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 (**SYN 312**).

The parliament has, during the second reading of the co-operation procedure, adopted 13 amendments to the first proposal, 4 amendments to the second proposal and no amendments to the third proposal.

In accordance with Article 149(2)(d) of the Treaty, the Commission has re-examined the first two proposals, having it in mind to take up some of the amendments of the parliament, as described hereafter.

The Commission wishes, meanwhile, to remind the Parliament and the Council that the decentralised procedure for the authorisation of medicinal products for human and veterinary use instituted by these Directives will not be able to function in the absence of the European Medicines Evaluation Agency.

Consequently, the Commission hopes that the Parliament will be prepared rapidly to give its opinion on the change envisaged by the Council in the legal base of the proposal for a Regulation laying down Community procedures for the authorisation and the supervision of medicines for human and veterinary use, and establishing an European Agency for the evaluation of medicinal products (**SYN 309**). As far as this is concerned, the Commission recalls it preference for article 100A as the legal base for the Regulation.

REVISED PROPOSAL FOR A COUNCIL DIRECTIVE (SYN 310)

MODIFYING DIRECTIVES 65/65/EEC, 75/318/EEC AND 75/319/EEC RELATING TO MEDICINAL PRODUCTS

In accordance with Article 149(2)(d) of the Treaty, the Commission has re-examined the above proposal, having it in mind to take up 5 of the 13 amendments of the Parliament, as detailed in annex 1. The amendments rejected by the Commission can be found in annex 2.

1. **Amendments accepted by the Commission**

The Commission is ready to accept the amendments which it had already accepted in the first reading, but which the Council has not retained in its Common Position.

The additional reference to the interests of the consumer (third recital) constitutes a useful clarification of the concept of public health which already features there.

[illegible] European Agency [illegible] second paragraph [illegible] having a European number [illegible] medicinal product [illegible] authorised in the Community in the future will [illegible] The present [illegible] of this amendment [illegible] risk of [illegible] Community authorisations.

[illegible] national procedure [illegible] and not high-technology medicinal products dealt with under the centralised procedure, the examination of which requires a longer time-limit of the order of 210 days.

Two amendments relating to pharmacovigilance (Directive 65/65/EEC article 10 (1) and 75/319/EEC article 29g) have the merit of introducing a greater coherence with the corresponding text of articles 46 and 47 of the Regulation.

2. **Amendments rejected by the Commission**

The Commission is not prepared to accept the other eight amendments for the following reasons:

Concerning the amendment of article 7 (2) of Directive 65/65/EEC, the text of the common position is preferable because it defines in a more detailed manner the mechanism of co-ordination between the Member States when they receive simultaneously the same file, and moreover clarifies which documents should be exchanged, and what should be the time limits.

Four amendments introduce concepts and terminology into the field of pharmacovigilance incompatible with those practised by the Community and recommended by the World Health Organisation. The amendments concerned are those to article 10(2) of Directive 65/65/EEC, as well as those to articles 29a, 29b and 29d of Directive 75/319/EEC.

The amendment of article 13(1) third sub-paragraph (a) new of Directive 75/319/EEC aims to establish a right to indemnity when national authorities initiate hastily the supplementary period of 90 days which is allowed for in order to examine conflicts in decisions between Member States. The Commission considers that it falls to the national courts to sanction possible abuses in line with national law, without having to create a new right of damages under Community law.

The amendment of article 14 (4) of directive 75/319/EEC calls into doubt again the unity of the market and of the Community examination criteria, since it permits a medicinal product, considered through a Community arbitration procedure not to be efficacious, to remain authorised in the country of origin. It should be remembered that a traditional medicinal product, of which the efficacy recognised only by a single Member State, is not affected by the Community arbitration procedure, unless the firm which markets it itself decides to have it recognised by other countries, thus taking the risk of seeing it rejected.

The amendment to article 29f first paragraph (a) new of Directive 75/319/EEC risks creating a system of press censorship. The Commission does not think it appropriate that national or community authorities should institute a system of prior authorisation for any information, which concerns medicinal products, even if it is alarmist.

ANNEX 1 AMENDMENTS ACCEPTED BY THE COMMISSION

Common position of the Council	Amendments
Third recital	
Whereas in the interests of public health it is necessary that decisions on the authorization to place medicinal products on the market be exclusively based on the criteria of quality, safety and efficacy; whereas these criteria have been extensively harmonized by Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products, by Council Directive 75/319/EEC, and by Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of the Member States relating to analytical, pharmacotoxicological and clinical standards and protocols in respect of the testing of medicinal products; whereas, however, Member States should exceptionally be able to prohibit the use on their territory of medicinal products which infringe objectively defined concepts of public order or public morality;	Whereas in the interests of public health and consumers of medicinal products it is necessary that decisions on the authorization to place medicinal products on the market be exclusively based on the criteria of quality, safety and efficacy; whereas these criteria have been extensively harmonized by Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products, by Directive 75/319/EEC, and by Council Directive 75/318/EEC of 20 May 1975 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 medicinal products; whereas, however, Member States should exceptionally be able to prohibit the use on their territory of medicinal products which infringe objectively defined concepts of public order or public morality;

Common position of the Council	Amendments
ARTICLE 1(4) Article 4b, second paragraph a (new) (Directive 65/65/EEC)	
	Before a medicinal product is placed on the market the competent authorities shall forward to the European Agency for the Evaluation of Medicinal Products a copy of the decision together with the summary of the product characteristics referred to in this Article. The Agency shall give the authorized medicinal product a European Register number which shall be marked on the packaging; the register number shall be preceded by the initials of the Member States in which the product has been authorized.
ARTICLE 1(6) Article 7(1) (Directive 65/65/EEC)	
1. Member States shall take all appropriate measures to ensure that the procedure for granting an authorization to place a medicinal product on the market is completed within 210 days of the submission of a valid application.	1. Member States shall take all appropriate measures to ensure that the procedure for granting an authorization to place a medicinal product on the market is completed within 140 days of the date the application is submitted.
ARTICLE 1(9) Article 10(1) (Directive 65/65/EEC)	
1. Authorization shall be valid for five years and shall be renewable for five-year periods, on application by the holder at least three months before the expiry date and after consideration of a dossier updating the information previously submitted.	1. Authorization shall be valid for five years and shall be renewable for five-year periods, on application by the holder at least three months before the expiry date and after the competent authority has considered a dossier containing up-to-date pharmacovigilance data and the other information relevant to the supervision of the medicinal product.

Common position of the Council	Amendments
ARTICLE 3(3) Article 29g (Directive 75/319/EEC)	
In order to facilitate the exchange of information about pharmacovigilance within the Community, the Commission, in consultation with the Agency, Member States and interested parties, shall draw up guidance on the collection, verification and presentation of adverse reaction reports.	In order to facilitate the exchange of information about pharmacovigilance within the Community, the Commission, in consultation with the Agency, Member States and interested circles, shall draw up guidance on the collection, verification and presentation of adverse reaction reports. Such guidance shall take into account the work carried out by the WHO on the harmonization of terminology and classification in the field of pharmacovigilance. It shall also establish the arrangements for use of the data-processing network between the competent authorities in the event of an alert concerning a manufacturing fault or serious undesirable reactions, and other pharmacovigilance information on medicinal products marketed in the Community.

ANNEX 2 AMENDMENTS REJECTED BY THE COMMISSION

Common position of the Council	Amendments
ARTICLE 1(6) **Article 7(2) (Directive 65/65/EEC)**	
2. Where a Member State notes that an application for authorization submitted after 1 January 1995 is already under active examination in another Member State in respect of that medicinal product, the Member State concerned may decide to suspend the detailed examination of the application in order to await the assessment report prepared by the other Member State in accordance with Article 4b.	2. In assessing applications for authorization, the competent marketing authorities shall assist each other and may entrust one another with assessments of all or part of the dossier.
The Member State concerned shall inform the other Member State and the applicant of its decision to suspend detailed examination of the application in question. As soon as it has completed the examination of the application and reached a decision, the other Member State shall forward a copy of its assessment report to the Member State concerned.	The competent authorities of the Member States shall notify the Agency and the other Member States of any applications for marketing authorization they receive.
Within 90 days of the receipt of the assessment report, the Member State concerned shall either recognize the decision of the other Member State and the summary of the product characteristics as approved by it, or, if it considers that there are grounds for supposing that the authorization of the medicinal product concerned may present a risk to public health, it shall apply the procedures set out in Articles 10 to 14 of Directive 75/319/EEC.	A Member State that receives notification shall, if the same application for authorization has been submitted in another Member State, contact the latter with a view to coordinating their action and issuing the assessment report jointly. If the Member States with an interest in the application do not reach agreement, they may, once all other possibilities have been exhausted, have recourse to the procedure laid down in Chapter III of Directive 75/319/EEC.

Common position of the Council	Amendments
ARTICLE 1(9) Article 10(2), first subparagraph (Directive 65/65/EEC)	
2. In exceptional circumstances, and following consultation with the applicant, an authorization may be granted subject to certain specific obligations, <u>including</u>:	2. In exceptional <u>and duly substantiated</u> circumstances, and following consultation with the applicant, an authorization may be granted subject to certain specific obligations, <u>defined and reviewed annually by the Agency, to</u>:
- <u>the carrying out of</u> further studies following the granting of authorization;	- <u>conduct</u> further studies following the granting of authorization;
- <u>the notification of adverse reactions to</u> the medicinal product.	- <u>report side-effects of</u> the medicinal product.

Common position of the Council	Amendments
ARTICLE 3(1) **Article 13(1), third subparagraph a (new)** **(Directive 75/319/EEC)**	
	Any delays arising in the marketing of a medicinal product because this procedure has been initiated hastily or with the sole intention of causing a delay may entitle the applicant to demand compensation in accordance with the legislation applicable in the Member State in question.
Article 3(1) **Article 14(4) (Directive 75/319/EEC)**	
A decision adopted in accordance with this Article shall be addressed to the Member States concerned by the matter and to the person responsible for marketing. The Member States shall either grant or withdraw marketing authorization, or make any adjustment to the terms of a marketing authorization which may be necessary to comply with the decision within 30 days of its notification. They shall inform the Commission and the Committee thereof.	A decision adopted in accordance with this Article shall be addressed to the Member States concerned by the matter and to the person responsible for marketing. The Member States shall either grant or withdraw marketing authorization, or make any adjustment to the terms of a marketing authorization which may be necessary to comply with the decision within 30 days of its notification. In adopting its decision, the Member State in which the authorization was originally granted shall take into account experience with the medicinal product in question. An existing national authorization may be upheld, even in the event of a prior negative Decision in accordance with this Article, if the medicinal product is harmless and of high quality. They shall inform the Commission and the Committee thereof.

Common position of the Council	Amendments
ARTICLE 3(3) Article 29a (Directive 75/319/EEC)	
In order to ensure the adoption of appropriate regulatory decisions concerning the medicinal products authorized within the Community, having regard to information obtained about adverse reactions to medicinal products under normal conditions of use, the Member States shall establish a pharmacovigilance system. This system shall be used to collect information useful in the surveillance of medicinal products, with particular reference to adverse reactions in human beings, and to evaluate such information scientifically.	In order to ensure the adoption of appropriate regulatory decisions concerning the continued authorization of medicinal products within the Community, having regard to information obtained about the side-effects of medicinal products under normal conditions of use, Member States shall establish a pharmacovigilance system for collecting information about the side-effects of medicinal products in human beings and for the scientific evaluation of such information, such that the information about side-effects is systematically related to the information on the consumption of medicinal products.
ARTICLE 3(3) Article 29b, indents (Directive 75/319/EEC)	
- "adverse reaction" means a reaction which is harmful and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or treatment of disease or the modification of physiological function;	- "side-effects" means a reaction which is harmful and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or treatment of disease or the modification of physiological function;
- "serious adverse reaction" means an adverse reaction which is fatal, life-threatening, disabling, incapacitating, or which results in or prolongs hospitalization;	- "serious side-effects" means an unfavourable reaction which is fatal, life-threatening, disabling, incapacitating, or which results in hospitalization or prolonged hospitalization;
- "unexpected adverse reaction" means an adverse reaction which is not mentioned in the summary of product characteristics;	- "unexpected side-effects" means an unfavourable reaction which is not mentioned in the summary of product characteristics;
- "serious unexpected adverse reaction" means an adverse reaction which is both serious and unexpected.	- "serious unexpected side-effects" means an unfavourable reaction which is both serious and unexpected.

Common position of the Council	Amendments
ARTICLE 3(3) Article 29d(1)(Directive 75/319/EEC)	
1. The person responsible for placing the medicinal product on the market shall be required to record and to report all suspected serious adverse reactions which are brought to his attention by a health care professional to the competent authorities immediately, and in any case within 15 days of their receipt at the latest.	1. The person responsible for placing the medicinal product on the market shall be required to record and to report all suspected serious unexpected side-effects which are brought to his attention by a qualified health care professional to the competent authorities immediately, and in any case within 15 days of their receipt.
ARTICLE 3(3) Article 29f, first paragraph a (new) (Directive 75/319/EEC)	
	The Member States shall take steps to ensure that pharmacovigilance data which is not officially confirmed and which may give rise to unnecessary alarm is not disseminated. The dissemination of data which has not been officially confirmed, if it proves to be inaccurate, may be the subject of compensation in accordance with the legislation of each Member State.

REVISED PROPOSAL FOR A COUNCIL DIRECTIVE SYN 311

MODIFYING DIRECTIVES 81/851/EEC AND 81/852/EEC ON THE APPROXIMATION OF LAWS OF THE MEMBER STATES RELATING TO VETERINARY MEDICINAL PRODUCTS

In accordance with Article 149(2)(d) of the Treaty, the Commission has re-examined the above proposal, in order to assimilate three of the four amendments from the parliament, as detailed in annex 1. The amendment rejected can be found in annex 2.

1. **Amendments accepted by the Commission**

The Commission is prepared to accept the amendments which it had already accepted during the first reading, but which the Council did not retain in its common position.

The role given to the European Agency (Directive 81/851/EEC, article 5b, third paragraph new) in attributing European number to each medicinal product which is authorised in the Community in the future will contribute to a greater transparency of the market. The present wording of this amendment envisages that the countries which have authorised the medicine should be mentioned, which will avoid any risk of confusion with the numbers attributed to community authorisations.

The reduction of the duration of the national examination procedure from 210 days to 140 (Directive 81/851/EEC, article 8(1)) takes account of the fact that, as a general rule, the national procedure concerns conventional medicines, and not high-technology medicines dealt with under the centralised procedure, the examination of which requires a longer time-limit, of the order of 210 days.

The amendment relating to pharmacovigilance (Directive 81/851/EEC article 42g) has the merit of introducing a greater coherence with the corresponding text of articles 46 and 47 of the Regulation.

2. **Amendments rejected by the Commission**

The Commission is not prepared to accept the amendment of article 15(1) of Directive 81/851/EEC, because it introduces into the five yearly re-examination of the authorization of a veterinary medicinal product concepts which are not clear and which appear to move away from the customary criteria of authorization (quality, security and efficacy).

ANNEX 1 AMENDMENTS ACCEPTED BY THE COMMISSION

Common position of the Council	Amendments
ARTICLE 1(5) Article 5b, third paragraph (new) (Directive 81/851/EEC)	
	Before a medicinal product is placed on the market the competent authorities shall forward to the European Agency for the Evaluation of Medicinal Products a copy of the decision together with the summary of the product characteristics referred to in this Article. The Agency shall give the authorized veterinary medicinal product a European Register number which shall be marked on the packaging; the registration number shall be preceded by the initials of the Member State in which the product's use has been authorized.
ARTICLE 1(6) Article 8(1) (Directive 81/851/EEC)	
1. Member States shall take all appropriate measures to ensure that the procedure for granting an authorization to place a veterinary medicinal product on the market is completed within 210 days of the submission of a valid application.	1. Member States shall take all appropriate measures to ensure that the procedure for granting an authorization to place a medicinal product on the market is completed within 140 days of the date the application is submitted.
ARTICLE 1(12) Article 42g (Directive 81/851/EEC)	
In order to facilitate the exchange of information about pharmacovigilance within the Community, the Commission, in consultation with the Agency, Member States and interested parties, shall draw up guidance on the collection, verification and presentation of adverse reaction reports.	In order to facilitate the exchange of information about pharmacovigilance within the Community, the Commission, in consultation with the Agency, Member States and interested circles, shall draw up detailed guidance on the collection, verification and presentation of adverse reaction reports. Such guidance shall take into account the work carried out by the WHO on the harmonization of terminology and classification in the field of pharmacovigilance, where this can be used in connection with veterinary medicinal products. The guidance shall also establish the arrangements for the use of the information network among the competent authorities in the event of an alert concerning a manufacturing fault or serious adverse reactions, as well as other pharmacovigilance information on veterinary medicinal products marketed in the Community.

ANNEX 2 AMENDMENTS REJECTED BY THE COMMISSION

Common position of the Council	Amendments
ARTICLE 1(9) Article 15(1) (Directive 81/851/EEC)	
1. Authorization shall be valid for five years and shall be renewable for five-year periods, on application by the holder at least three months before the expiry date and after consideration of a dossier updating the information previously submitted.	1. Authorization shall be valid for five years and shall be renewable for five-year periods, on application by the holder at least three months before the expiry date and after the competent body has considered a dossier containing updated pharmacovigilance data and the other information relevant to the monitoring of the product. When delivering its opinion the responsible body shall take account of any new information available on side-effects of the medicinal product, its efficacy and its place in its therapeutic class.

16

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