

COMMISSION DIRECTIVE 2000/37/EC**of 5 June 2000****amending Chapter VIa 'Pharmacovigilance' of Council Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products****(Text with EEA relevance)**

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Community,

Having regard to Council Directive 81/851/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to veterinary medicinal products ⁽¹⁾, as last amended by Directive 93/40/EEC ⁽²⁾, and in particular Article 42i thereof;

Whereas:

- (1) In order to ensure the continued safety of veterinary medicinal products in use, it is necessary to ensure that pharmacovigilance systems in the Community are continually adapted to take account of scientific and technical progress.
- (2) For public health protection, relevant data on adverse effects in humans related to the use of veterinary medicines should be collected and evaluated.
- (3) The pharmacovigilance systems should consider the available data on lack of efficacy.
- (4) In addition, collection of information on adverse reactions due to off-label use, investigations of the validity of the withdrawal period and on potential environmental problems may contribute to improve regular monitoring of good usage of veterinary medicines.
- (5) It is necessary to take account of changes arising as a result of international harmonisation of definitions, terminology and technological developments in the field of pharmacovigilance.
- (6) The increasing use of the mutual recognition procedure established by Directive 81/851/EEC requires that current procedures for reporting and dissemination of suspected adverse reactions be amended to ensure better co-ordination between Member States.
- (7) The increasing use of electronic means of communication of information on adverse reactions to veterinary medicinal products marketed in the Community is intended to allow a single reporting point for adverse reactions, at the same time ensuring that this information is shared with the competent authorities in all Member States.

- (8) It is necessary to further define terms currently used within the veterinary pharmacovigilance systems.
- (9) It is the interest of the Community to ensure that the veterinary pharmacovigilance systems for centrally authorised medicinal products and those authorised by other procedures are consistent.
- (10) Holders of marketing authorisations should additionally be proactively responsible for ongoing pharmacovigilance of the veterinary medicinal products they place on the market.
- (11) The measures provided for in this Directive are in conformity with the opinion of the Standing Committee on veterinary medicinal products,

HAS ADOPTED THIS DIRECTIVE:

Article 1

Chapter VIa 'Pharmacovigilance' of Directive 81/851/EEC is hereby amended as follows:

1. Article 42a, is hereby replaced by the following text:

'Article 42a

In order to ensure the adoption of appropriate regulatory decisions concerning the veterinary medicinal products authorised within the Community, having regard to information obtained about suspected adverse reactions to veterinary medicinal products under normal conditions of use, the Member States shall establish a veterinary pharmacovigilance system. This system shall be used to collect information useful in the surveillance of veterinary medicinal products, with particular reference to adverse reactions in animals and in human beings related to the use of veterinary medicinal products, and to evaluate such information scientifically.

Such information shall be collated with available data on the sale and prescription of veterinary medicinal products.

This system also takes into account any available information related to the lack of expected efficacy, off-label use, investigations of the validity of the withdrawal period and on potential environmental problems, arising from the use of the product, interpreted in accordance with the Commission guidelines referred to in Article 42g, which may have an impact on the evaluation of their benefits and risks.'

⁽¹⁾ OJ L 317, 6.11.1981, p. 1.

⁽²⁾ OJ L 214, 24.8.1993, p. 31.

2. Article 42b, is hereby replaced by the following:

'Article 42b

For the purpose of this Directive, the following definitions shall apply:

- (a) "adverse reaction" means a reaction which is harmful and unintended and which occurs at doses normally used in animals for the prophylaxis, diagnosis or treatment of disease or the modification of physiological function,
- (b) "human adverse reaction" means a reaction which is noxious and unintended and which occurs in a human being following exposure to a veterinary medicine,
- (c) "serious adverse reaction" means an adverse reaction which results in death, is life-threatening, results in significant disability or incapacity, is a congenital anomaly/birth defect, or which results in permanent or prolonged signs in the animals treated;
- (d) "unexpected adverse reaction" means an adverse reaction, the nature, severity or outcome of which is not consistent with the summary of the product characteristics,
- (e) "periodic safety update reports" means the periodical reports containing the records referred to in Article 42d;
- (f) "post-marketing surveillance studies" means pharmacoepidemiological study or a clinical trial carried out in accordance with the terms of the marketing authorisation, conducted with the aim of identifying and investigating a safety hazard relating to an authorised veterinary medicinal product,
- (g) "off-label use" means the use of a veterinary medicinal product that is not in accordance with the summary of the product characteristics, including the misuse and serious abuse of the product.

For the interpretation of the definitions and principles outlined in this chapter, the marketing authorisation holder and the competent authorities shall refer to the detailed guidance referred to in Article 42g.'

3. Article 42c is hereby amended as follows:

- (a) in the first paragraph, the words 'person responsible for placing the veterinary medicinal product on the market' are changed to 'marketing authorisation holder';
- (b) in point (a) of the second paragraph, the words 'at a single point' are changed to 'in order to be accessible at least at one point within the Community';
- (c) in point (b) of the second paragraph the words 'relevant national or Community guidance' are changed to 'guidance referred to in Article 42g';
- (d) to the second paragraph the following point (d) is added:
'd) the provision to the competent authorities, of any other information relevant to the evaluation of the benefits and risks afforded by a veterinary medicinal product, including appropriate information on post-marketing surveillance studies.'

4. Article 42d, is hereby replaced by the following text:

'Article 42d

1. The marketing authorisation holder shall be required to maintain detailed records of all suspected adverse reactions occurring either in the Community or in a third country.

2. The marketing authorisation holder shall be required to record and to report all suspected serious adverse reactions and human adverse reactions related to the use of veterinary medicinal products, of which he can reasonably be expected to have knowledge, or which are brought to his attention, immediately to the competent authority of the Member State in whose territory the incident occurred, and in no case later than 15 calendar days following the receipt of the information.

3. The marketing authorisation holder shall ensure that the suspected serious and unexpected adverse reactions and human adverse reactions, occurring in the territory of a third country, are reported immediately in accordance with the guidance referred to in Article 42g, so that they are available to the Agency and to the competent authorities in the Member State(s) where the veterinary medicinal product is authorised, and in no case later than 15 calendar days following the receipt of the information.

4. In the case of veterinary medicinal products which have been considered within the scope of Directive 87/22/EEC, or which have benefited from the procedures of mutual recognition under Articles 8, 8a and 17(4) and veterinary medicinal products for which there has been a referral to the procedures under Articles 21 and 22 of this Directive, the marketing authorisation holder shall additionally ensure that all suspected serious adverse reactions and human adverse reactions, occurring in the Community, are reported in the format and at intervals to be agreed with the reference Member State or a competent authority designated as reference Member State, in such a way so as to be accessible to the reference Member State.

5. Unless other requirements have been laid down as condition of the granting of authorisation, records of all adverse reactions shall be submitted to the competent authorities in the form of a periodic safety update report, either immediately upon request or periodically as follows: six monthly for the first two years after authorisation, annually for the subsequent two years, and at the time of the first renewal. Thereafter, the periodic safety update reports shall be submitted at five-yearly intervals together with the application for renewal of the authorisation. The periodic safety update report shall include a scientific evaluation of the benefit and risks afforded by the veterinary medicinal product.

6. Following the granting of a marketing authorisation, the marketing authorisation holder may request the amendment of the periods referred to in this Article according to the procedure laid down by the Commission Regulation (EC) No 541/95 (*), if applicable.

(*) OJ L 55, 11.3.1995, p. 7.'

5. A new second paragraph is added to Article 42e:

'The Member States may impose specific requirements on veterinary practitioners and other health care professionals in respect of the reporting of suspected serious or unexpected adverse reactions and human adverse reactions, in particular where such reporting is a condition of the marketing authorisation.'

6. Article 42f, is replaced by the following text:

'Article 42f

1. The Agency, in collaboration with the Member States and the Commission shall set up a data-processing network to facilitate the exchange of pharmacovigilance information regarding medicinal products marked in the Community.

2. Making use of the network foreseen in the first paragraph, Member States shall ensure that reports of suspected serious adverse reactions and human adverse reactions, in accordance with the Standing Committee on veterinary medicinal products guidance referred to in Article 42g, that have taken place on their territory are immediately made available to the Agency and the other Member States, and in any case within 15 calendar days of their notification, at the latest.

3. The Member States shall ensure that reports of suspected serious adverse reactions and human adverse reactions, that have taken place on their territory are immediately made available to the marketing authorisation holder, and in any case within 15 calendar days of their notification, at the latest.'

7. Article 42g is amended as follows:

'Article 42g

(a) In order to facilitate the exchange of information about pharmacovigilance within the Community, the Commission, in consultation with the Agency, Member States and the interested parties, shall draw up guidance on the collection, verification and presentation of adverse reaction reports, including technical requirements for electronic exchange of veterinary pharmacovigilance information in accordance with internationally agreed terminology.

(b) This guidance shall be published in Volume 9 of the Rules governing medicinal products in the European Union and shall take account of international harmonisation work carried out in the field of pharmacovigilance.'

8. Article 42h is replaced by the following text:

'Article 42h

Where, as a result of the evaluation of veterinary pharmacovigilance data, a Member State considers that a marketing authorisation should be suspended, withdrawn or varied to restrict the indications or availability, amend the posology, add a contraindication or add a new precautionary measure, it shall forthwith inform the Agency, the other Member States and the marketing authorisation holder.

In case of urgency, the Member State concerned may suspend the marketing authorisation of a veterinary medicinal product, provided the Agency, the Commission and the other Member States are informed at the latest on the following working day.'

Article 2

Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive no later than 5 December 2001.

When the Member States adopt the provisions set out in paragraph 1, they shall contain a reference to this Directive or shall be accompanied by such reference at the time of their official publication. The procedure for such references shall be adopted by the Member States. The Member States shall communicate to the Commission the provisions of national law which they adopt in the field covered by this Directive.

Article 3

This Directive shall enter into force on the 20th day following its publication in the *Official Journal of the European Communities*.

Article 4

This Directive is addressed to the Member States.

Done at Brussels, 5 June 2000.

For the Commission

Erkki LIKANEN

Member of the Commission