Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use

TITLE IX

PHARMACOVIGILANCE

Article 101

The Member States shall take all appropriate measures to encourage doctors and other health care professionals to report suspected adverse reactions to the competent authorities.

[[F1]The Member States may impose specific requirements on doctors and other health-care professionals in respect of the reporting of suspected serious or unexpected adverse reactions.**]**

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

[[F1]*Article 102*

In order to ensure the adoption of appropriate and harmonised regulatory decisions concerning the medicinal products authorised within the Community, having regard to information obtained about adverse reactions to medicinal products under normal conditions of use, the Member States shall operate 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.

Member States shall ensure that suitable information collected within this system is communicated to the other Member States and the Agency. The information shall be recorded in the database referred to in point (l) of the second subparagraph of Article 57(1) of Regulation (EC) No 726/2004 and shall be permanently accessible to all Member States and without delay to the public.

This system shall also take into account any available information on misuse and abuse of medicinal products which may have an impact on the evaluation of their benefits and risks.**]**

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

[[F2]*Article 102a*

The management of funds intended for activities connected with pharmacovigilance, the operation of communication networks and market surveillance shall be under

the permanent control of the competent authorities in order to guarantee their independence.**]**

Textual Amendments

F2 Inserted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

Article 103

The marketing authorization holder shall have permanently and continuously at his disposal an appropriately qualified person responsible for pharmacovigilance.

[[F1]That qualified person shall reside in the Community and shall be responsible for the following:**]**

(a) the establishment and maintenance of a system which ensures that information about all suspected adverse reactions which are reported to the personnel of the company, and to medical representatives, is collected and collated in order to be accessible at least at one point within the Community;

(b) the preparation for the competent authorities of the reports referred to in Article 104, in such form as may be laid down by those authorities, in accordance with the guidance referred to in Article 106(1);

(c) ensuring that any request from the competent authorities for the provision of additional information necessary for the evaluation of the benefits and risks afforded by a medicinal product is answered fully and promptly, including the provision of information about the volume of sales or prescriptions of the medicinal product concerned;

(d) the provision to the competent authorities, of any other information relevant to the evaluation of the benefits and risks afforded by a medicinal product, including appropriate information on post-authorization safety studies.

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

[**[F1]Article 104

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.

Save in exceptional circumstances, these reactions shall be communicated electronically in the form of a report in accordance with the guidelines referred to in Article 106(1).

2 The marketing authorisation holder shall be required to record all suspected serious adverse reactions which are brought to his attention by a health-care professional and to report them promptly to the competent authority of the Member State on whose territory the incident occurred, and no later than 15 days following the receipt of the information.

3 The marketing authorisation holder shall be required to record and report all other suspected serious adverse reactions which meet the notification criteria in accordance with

the guidelines referred to in Article 106(1), of which he can reasonably be expected to have knowledge, promptly to the competent authority of the Member State in whose territory the incident occurred, and no later than 15 days following the receipt of the information.

4 The marketing authorisation holder shall ensure that all suspected serious unexpected adverse reactions and any suspected transmission via a medicinal product of any infectious agent occurring in the territory of a third country are reported promptly in accordance with the guidelines referred to in Article 106(1), so that the Agency and the competent authorities of the Member States in which the medicinal product is authorised are informed of them, and no later than 15 days following the receipt of the information.

5 By way of derogation from paragraphs 2, 3 and 4, in the case of medicinal products which are covered by Directive 87/22/EEC or which have qualified for the procedures laid down in Articles 28 and 29 of this Directive or which have been the subject of the procedures under Articles 32, 33 and 34 of this Directive, the marketing authorisation holder shall also ensure that all suspected serious adverse reactions occurring in the Community are reported in such a way as to be accessible to the reference Member State or to any competent authority acting as reference Member State. The reference Member State shall assume the responsibility of analysing and monitoring such adverse reactions.

6 Unless other requirements have been laid down as a condition for the granting of the marketing authorisation, or subsequently as indicated in the guidelines referred to in Article 106(1), reports of all adverse reactions shall be submitted to the competent authorities in the form of a periodic safety update report, immediately upon request or at least every six months after authorisation and until the placing on the market. Periodic safety update reports shall also be submitted immediately upon request or at least every six months during the first two years following the initial placing on the market and once a year for the following two years. Thereafter, the reports shall be submitted at three-yearly intervals, or immediately upon request.

The periodic safety update reports shall include a scientific evaluation of the risk-benefit balance of the medicinal product.

[[F3]7 The Commission may amend paragraph 6 in view of experience gained through its operation. That measure, designed to amend non-essential elements of this Directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 121(2a).**]**

8 Following the granting of a marketing authorisation, the marketing authorisation holder may request the amendment of the periods referred to in paragraph 6 in accordance with the procedure laid down by Commission Regulation (EC) No 1084/2003[(1)].

9 The holder of a marketing authorisation may not communicate information relating to pharmacovigilance concerns to the general public in relation to its authorised medicinal product without giving prior or simultaneous notification to the competent authority.

In any case, the marketing authorisation holder shall ensure that such information is presented objectively and is not misleading.

Member States shall take the necessary measures to ensure that a marketing authorisation holder who fails to discharge these obligations is subject to effective, proportionate and dissuasive penalties.

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

F3 Substituted by Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the implementing powers conferred on the Commission.

Article 105

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 marketed in the Community in order to allow all competent authorities to share the information at the same time.

2 Making use of the network referred to in paragraph 1, Member States shall ensure that reports of suspected serious adverse reactions that have taken place on their territory are promptly made available to the Agency and the other Member States, and in any case within 15 days after their notification at the latest.

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

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

Article 106

1 In order to facilitate the exchange of information on pharmacovigilance within the Community, the Commission, after consulting the Agency, the Member States and interested parties, shall draw up guidelines on the collection, verification and presentation of adverse reaction reports, including technical requirements for electronic exchange of pharmacovigilance information in accordance with internationally agreed formats, and shall publish a reference to an internationally agreed medical terminology.

Acting in accordance with the guidelines, marketing authorisation holders shall use internationally agreed medical terminology for the reporting of adverse reactions.

These guidelines shall be published in Volume 9 of The Rules governing Medicinal Products in the European Community and shall take account of international harmonisation work carried out in the field of pharmacovigilance.

2 For the interpretation of the definitions referred to in points (11) to (16) of Article 1 and of the principles outlined in this Title, the marketing authorisation holder and the competent authorities shall follow the guidelines referred to in paragraph 1.

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

Article 107

1 Where, as a result of the evaluation of pharmacovigilance data, a Member State considers that a marketing authorisation should be suspended, revoked or varied in accordance

with the guidelines referred to in Article 106(1), it shall forthwith inform the Agency, the other Member States and the marketing authorisation holder.

2 Where urgent action to protect public health is necessary, the Member State concerned may suspend the marketing authorisation of a medicinal product, provided that the Agency, the Commission and the other Member States are informed no later than the following working day.

When the Agency is informed in accordance with paragraph 1 in relation to suspensions and revocation, or the first subparagraph of this paragraph, the Committee shall prepare an opinion within a time-frame to be determined depending on the urgency of the matter. In relation to variations, the Committee may upon request from a Member State prepare an opinion.

Acting on the basis of this opinion, the Commission may request all Member States in which the product is being marketed to take temporary measures immediately.

[F3The decision on the final measures concerning the product shall be adopted in accordance with the management procedure referred to in Article 121(3).**]]**

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

F3 Substituted by Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the implementing powers conferred on the Commission.

[*F3Article 108*

The Commission shall adopt any amendments which may be necessary to update provisions of Articles 101 to 107 to take account of scientific and technical progress. Those measures, designed to amend non-essential elements of this Directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 121(2a).**]**

Textual Amendments

F3 Substituted by Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the implementing powers conferred on the Commission.

(1) **[**[F1]OJ L 159, 27.6.2003, p. 1.**]**

Textual Amendments

F1 Substituted by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.