COMMISSION DECISION

of 18 July 2001

on the national provisions notified by Germany in the field of pharmacovigilance

(notified under document number C(2001) 1974)

(Only the German text is authentic)

(Text with EEA relevance)

(2001/571/EC)

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Community, and in particular Article 95(6) thereof,

Whereas:

I. THE FACTS

1. Relevant Community legislation

(1) The current Community provisions on pharmacovigilance, i.e. the supervision of medicinal products once they have been authorised, are contained in Chapter Va (Article 29a to 29i) of Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products [1], as last amended by Directive 2000/38/EC [2]. Chapter Va was added to Directive 75/319/EEC by Directive 93/39/EEC [3].

(2) The provisions on reporting adverse reactions which are relevant for this notification are contained primarily in Article 29d. Pursuant to Article 29d(1) the person responsible for placing the medicinal product on the market shall be required to recall and to report all suspected serious adverse reactions which are brought to his attention by a health-care professional immediately to the competent authority, and in any case within 15 days at the latest. Pursuant to Article 29d(2) records shall be maintained of all other suspected adverse reactions and shall be sumitted to the authorities at regular intervals. In Article 29i the Commission is authorised to update the provisions of Chapter Va, in accordance with the procedures laid down in Article 37a of Directive 75/319/EEC, to take account of scientific and technical progress.

(3) In the light of new knowledge in the field of pharmacovigilance, continued efforts to achieve international harmonisation of pharmacovigilance data and technological developments in electronic data collection and transmission, the Commission has made use of the authorisation contained in Article 29i and has amended several points of the abovementioned provisions by Directive 2000/38/EC. In so doing the Commission took as a base a high level of protection pursuant to Article 95(3) of the EC Treaty and in particular it has taken account of all new scientifically based developments. For the sake of legal clarity and irrespective of the scope of each amendment, the individual provisions have been entirely redrafted.

(4) The main objective of Directive 2000/38/EC is to remodel the pharmacovigilance systems, which to date have primarily been paper-based and organised at national level, into a Community-wide electronic data system. All pharmacovigilance information will be entered in this and then automatically stored in a data bank, to be set up by the European Agency for the Evaluation of Medicinal Products (hereafter referred to as the EMEA) established by Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products [4]. From there the data can be retrieved at any time by the member States, the Commission and the EMEA itself. This electronic network will be based on new knowledge and advances in the field of information technology, thereby making the collection and exchange of data more efficient, relieving the marketing authorisation holders of unnecessary reporting obligations and generally improving the surveillance of medicinal products in the Community.

(5) The central provisions on reporting adverse reactions are contained in the revised version of Article 29d(2) and (4) from the year 2000. Pursuant to the new version of Article 29d(2), the marketing authorisation holder is required to record and to report all suspected serious adverse reactions which are brought to his attention by a health-care professional immediately to the competent authority of the Member State, in whose territory the incident occurred, and in no case later than 15 days after

[1] OJ L 147, 9.6.1975, p. 13.
[2] OJ L 139, 10.6.2000, p. 28; corrected in OJ L 249, 4.10.2000, p. 26 and in OJ L 262, 17.10.2000, p. 46.
[3] OJ L 214, 24.8.1993, p. 22.
[4] OJ L 214, 24.8.1993, p. 1.

the receipt of the information. Pursuant to the new version of Article 29d(4) [1], the marketing authorisation holder shall also ensure that all suspected serious unexpected adverse reactions occurring in the territory of a non-member country and brought to his attention by a health-care professional are reported immediately to the EMEA and to the competent authorities of the Member State where the medicinal product is authorised, and in no case later than 15 days after the receipt of the information.

(6) Under the new version of Article 29f(1), the EMEA is required, in collaboration with the Member States and the Commission, to 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. Pursuant to paragraph 2 of this Article, making use of the above-mentioned network Member States shall ensure that reports of suspected serious adverse reactions 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 days of their notification.

2. **National provisions**

(7) The provisions notified by the Federal Republic of Germany relate to the provisions of sentences 2 to 8 of Section 29(1) of the Law on trade in medicinal products (hereafter AMG), in the version of the Notice of 11 December 1998 [2]. Pursuant to sentence 2 of Section 29(1) AMG, the applicant shall notify the competent national autorities of any suspected case of serious adverse reaction or serious case of interaction with other products known to him and also of certain cases of abuse immediately and in any case within 15 days of notification. Without further restrictions in the text, this obligation exists irrespective of whether the suspected case occurred inside or outside the Federal Republic of Germany and of whether the adverse effect has been confirmed or not. Senctences 3 to 8 of Section 29(1) AMG contain further provisions relating to the documentation on adverse reactions and its presentation to the competent authorities.

3. **Comparison between the German provisions and the Community legal provisions**

(8) The obligation to report adverse reactions of a medicinal product under sentence 2 of Section 29(1) AMG differs from the obligation under the amended Article 29d of Directive 2000/38/EC in two respects.

(9) Firstly, sentence 2 of Section 29(1) AMG requires the applicant to report any suspected case of serious adverse reaction notified to him, in other words irrespective of whether the suspected case occurred inside or outside Germany. Under the new version of Article 29d(2), the marketing authorisation holder is required to report the adverse reactions only to the competent authority of the Member State in which the adverse reaction took place.

(10) To the extent that the suspected serious adverse reaction took place in a non-Member country, i.e. outside the Community, the new version of Article 29d(4) establishes an obligation to report the suspected case only where the adverse reaction is unexpected. Such a restriction is not contained in the second sentence of Section 29(1) AMG.

II. **PROCEDURE**

(11) By letter of 18 January 2001, received on 25 January 2001, the Permanent Representation of the Federal Republic of Germany to the European Union applied to the Secretariat-General of the Commission to be allowed to maintain the provisions of sentences 2 to 8 of Section 29(1) AMG regarding the obligation to report adverse reactions. In Germany's opinion, this is justified on the grounds of major needs within the meaning of Article 30 of the EC Treaty, i.e. the protection of health and lives of humans.

(12) By letter of 2 March 2001, the Commission informed the German authorities that it had received the notification pursuant to Article 95(4) of the EC Treaty and that the period of six months provided under Article 95(6) of the EC Treaty to examine the notification had begun to run from 26 January 2001, the day after it was received.

(13) By letter of 17 April 2001 the Commission informed the other Member States about the notification of the Federal Republic of Germany and gave them an opportunity to express an opinion within one month. Notice of the notification was also published in the *Official Journal of the European Communities* [3] in order to inform other interested parties of the provisions notified and to be maintained by Germany.

[1] In the light of the corrigendum in OJ L 262, 10.7.2000, p. 46.
[2] BGBl. I p. 3586; as last amended by Article 2 of the Law of 20 July 2000, BGBl. I p. 1045.
[3] OJ C 130, 1.5.2001, p. 2.

III. **ASSESSMENT**

1. **Consideration of admissibility**

(14) The notification submitted by the German Government aims to maintain the obligations to report adverse reactions contained in Section 29 AMG, which derogate from those of Directive 2000/38/EC. This Directive was adopted on the basis of Article 29i of Directive 75/319/EEC, which in turn is based on ex-Article 100a (current Article 95) of the EC Treaty. Directive 2000/38/EC thus represents a harmonisation measure adopted by the Commission within the meaning of Article 95(4) of the EC Treaty.

(15) In accordance with the requirements of Article 95(4) of the EC Treaty, Germany has notified the Commission of the text of the national provisions it wishes to maintain as well as the grounds which, in Germany's opinion, justify the application.

(16) Accordingly, it is the Commission's opinion that the notification with which Germany requests the Commission to approve maintenance of the provisions of sentences 2 to 8 of Section 29(1) AMG, derogating from Directive 2000/38/EC, is admissible on the basis of the provisions of Article 95(4) of the EC Treaty.

2. **Assessment of merits**

(17) The Commission can only approve a notification pursuant to Article 95(4) of the EC Treaty if all of the conditions listed in Article 95 of the EC Treaty are met. In particular, maintaining the national provisions must be justified on grounds of major needs referred to in Article 30 of the EC Treaty, or relating to protection of the environment or the working environment (Article 95(4) of the EC Treaty). In addition the national provisions may neither be a means of arbitrary discrimination or a disguised restriction on trade between Member States; neither can they constitute an obstacle to the functioning of the internal market (Article 95(6) of the EC Treaty).

(a) *Major needs*

(18) When examining whether the national measures notified under Article 95(4) are justified by major needs, the Commission has to take as a basis 'the grounds' put forward by the Member State to justify the maintenance of its national provisions. This means that, according to the provisions of the Treaty, the responsibility for proving that these measures are justified lies with the requesting Member State. Given the procedural framework established by Article 95 of the EC Treaty, in principle the Commission has to limit itself to examining the relevance of the elements which are submitted by the requesting Member State, without itself having to seek possible grounds of justification.

(19) Germany invokes major needs to protect the health and life of humans and consequently one of the circumsances referred to in Article 30 of the EC Treaty. Maintaining the obligations to report as provided for in the current provisions of sentences 2 to 8 of Section 95(1) AMG would attain the highest possible level of health protection for the population in their use of medicinal products. This high national level of protection was endangered by Directive 2000/38/EC since, firstly, adverse reactions will in future only be reported to the Member state in which they take place and, secondly, adverse reactions which take place in a non-member country are only covered by the obligation to report when they are 'unexpected'.

(aa) Reporting adverse reactions from Member States

(20) Germany considers that it is 'not acceptable on health grounds' to report adverse reactions only to the Member State in which the suspected case occurred. As justification Germany points out that the data network to be established under Directive 2000/38/EC does not yet exist. Therefore, on the basis of the restricted notification requirements, it could not be guaranteed in the foreseeable future that the authorities of all Member States would receive information of equivalent quality and at the same time.

(21) Major needs within the meaning of Article 30 of the EC Treaty cannot be invoked on this basis for two reasons.

(22) Firstly, the statement of the Federal Republic of Germany that the data network referred to in Directive 2000/38/EC does not yet exist and cannot be established in the foreseeable future, at least not by 5 December 2001, is incorrect. In so far as the establishement of the data network provided for in the new version of Article 29f requires preliminary work on the part of the EMEA and the Commission, this will be completed on schedule by 5 December 2001. According to the current timetable, the EMEA, will make the basic version of the central bank databank available by 1 December 2001. From that date individual case reports within the meaning of the new Article 29d(2) to (5) can be entered in the databank and shared by the authorities of all Member States. Contrary to Germany's statement therefore, the technical and procedural preconditions for establishing and using the data network will exist by the end of the transposition period for Directive 2000/38/EC.

However, account must be taken of the fact that the establishment of the databank is not the task of the EMEA alone. Rather it is the responsibility of the authorities of the Member States, pursuant to the new version of Article 29f(2), to use the newly established data network to forward the reports of adverse reactions transmitted to them to the EMEA and to the other Member States. However, for this the information must first be entered by the Member States and subsequently transmitted to the EMEA databank, where it is automatically fed into the central databank and is retrievable. To ensure that the reports are generally comparable and to make them more intelligible, the participants have agreed to use the standards developed in the framework of the International Conference on Harmonisation of Technical Requirements for Registration of Medicinal products for Human Use when collecting and entering data.

It is only in the course of 2002 that most Member States will be able to convert their national computer systems to the uniform standard and begin electronic data transmission to the EMEA using this standard. Where a Member State has not yet made the conversion and in the event of a suspected case in this Member State, only the basic information on the product concerned, the patient and the type of adverse reaction will be entered in the central databank of the EMEA and be electronically retrievable. However, this will not interfere with the overall dissemination of pharmacovigilance information within the Community. Where the Member States have not converted their systems by the due date of 5 December 2001, they are required under the new version of Article 29f(2) to transmit the relevant reports in another appropriate form. The restricted operating capacity of the data network will therefore not have any adverse consequences on health protection.

(23) Secondly, the legal position in most Member States counters Germany's argument that major needs of health protection require it to maintain the obligation to report also adverse reactions from other Member States. According to the current legal position, only four Member States require that their own authorities should also be informed when the suspected case of a serious adverse reaction occurs in another Member State. In addition to Germany, this is the case in Austria, Portugal and the United Kingdom. All other Member States require such a communication to the national authorities only when the adverse reaction occurred on their national territory. With regard to information on adverse reactions in other Member States, the information network which already exists within the Community is for the most part evidently considered to be adequate. This must be even more true for the markedly improved data network to be established on the basis of Directive 2000/38/EC.

(24) Altogether therefore no major needs within the meaning of Article 30 of the EC Treaty can be recognised which could justify maintaining the obligation to report adverse reactions from other Member States. Rather the restriction contained in the new version of Article 29d(2) represents a logical conclusion to the establishment of the new data network. This will make the same information available to the Member States as previously, but presentation will be improved. Maintaining the previous obligations to report would place an unnecessary and unjustifiable burden on the respective marketing authorisation holders.

(bb) Reporting adverse reactions from non-member countries

(25) With regard to restricting the obligation to report adverse reactions from non-member countries to those which are unexpected, as contained in the new version of Article 29d(4), Germany claims that this could lead to a substantial increase in the risk of transmitting infectious pathogens via medicinal products with biological components. It claims that the product information mentions the risk of virus transmission via medicinal products obtained from human body parts. Thus, in the event of a suspected case of virus transmission, for example of the HIV or hepatitis viruses through such a medicinal product, then the adverse reaction could not be classified as 'unexpected' and for this reason would not have to be reported if it occurs in a non-member country. This could interfere with batch recalls and efforts to identify other possibly infected patients and with follow-up measures such as diagnosis and therapy.

(26) To the extent that Germany's remarks relate to the specific example of a transmission of HIV or hepatitis viruses, they are based on a misconception. Germany assumes that contamination of a medicinal product with the HIV or hepatitis virus is to be classified as an 'expected' adverse reaction and consequently to be excluded from the obligation to report which, in accordance with Directive 2000/38/EC, is restricted to 'unexpected' adverse reactions. This interpretation is not correct. Blood products are examined for such viruses as part of the manufacturing and authorisation process. In principle therefore they are used on the understanding that the medicinal products are not infected. However, if such an infection does exist, then it is an unexpected adverse reaction, which under the new legal position is fully covered by the notification requirement.

(27) Irrespective of whether virus infections in medicinal products can ever be classified as expected adverse reactions, there is a further reason why Germany's arguments are not grounds for major needs within the meaning of Article 30 of the EC Treaty. This consideration is based on the fact that any expected adverse

reactions have to be taken into account during the testing and authorisation of a product, while obviously this is not possible when these are unexpected, During the subsequent monitoring of a medicinal product in the framework of pharmacovigilance, special significance is thus attached to unexpected as opposed to expected adverse reactions. For this reason, the general reporting and evaluation of adverse reactions, even when they occur outside the Community, appears necessary only when these are unexpected.

(28) This conclusion is based on scientific evidence acquired in recent years relating to the medicinal products approved as part of the centralised Community procedure pursuant to Regulation (EEC) 2309/93. This procedure is obligatory for certain products of the biotechnology and high technology industries, which are regarded as particularly complex and sensitive. None the less the second subparagraph of Article 22(1) of Regulation (EEC) 2309/93 restricts the obligation to report the adverse reactions of such medicinal products which occur in non-member countries to those which are unexpected. Analyses and evaluations of the information on adverse reactions generated from centrally authorised medicinal products have confirmed that it is also not necessary to report and evaluate information on expected adverse reactions from non-member countries.

(29) This assessment is further supported by the fact that the Federal Republic of Germany is the only Member State which does not restrict the obligation to report adverse reactions occurring in non-member countries to those which are unexpected, but extends this obligation to adverse reactions which are expected. This highlights the fact that none of the other Member States considers it necessary, in order to protect the health and life of humans, to include reports of suspected serious expected adverse reactions from non-member countries in the pharmacovigilance systems.

(30) Consequently, in maintaining an obligation to report suspected serious expected adverse reactions from non-member countries, Germany is not able to invoke major needs within the meaning of Article 30 of the EC Treaty. The provision of the new version of Article 29d(4) applies new scientific evidence without prejudicing the high level of health protection in the Community.

(b) *Arbitrary discrimination, disguised restriction on trade, an obstacle to the functioning of the internal market*

(31) Pursuant to Article 95(6) of the EC Treaty the Commission is required to approve the national provisions or reject them after it has ensured that they do not constitute a means of arbitrary discrimination or a disguised restriction on trade between the Member States and are not an obstacle to the functioning of the internal market.

(32) Since, in the light of the conditions referred to in Article 95(4) of the EC Treaty, Germany's application is unfounded, the Commission does not need to examine whether the said national provisions constitute a means of arbitrary discrimination and a disguised restriction on trade between the Member States nor whether they are an obstacle to the functioning of the internal market.

IV. **CONCLUSION**

(33) In the opinion of the Commission Germany's application is therefore

— admissible,

— but unfounded.

(34) The Commission has therefore decided to reject this application pursuant to Article 95(6) of the EC Treaty,

HAS ADOPTED THIS DECISION:

Article 1

The national provisions on the obligation to report the adverse reactions of medicinal products notified to the Commission by the Federal Republic of Germany by letter of 18 January 2001, and which derogate from Directive 2000/38/EC are rejected.

Article 2

This Decision is addressed to the Federal Republic of Germany.

Done at Brussels, 18 July 2001.

For the Commission

Erkki LIIKANEN

Member of the Commission