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HMA/EMEA RECOMMENDATIONS ON TRANSPARENCY

RECOMMENDATIONS on the handling of requests for access to Periodic Safety Update Reports (PSURs)

Introduction

1. This document has been drafted in view of the following considerations:
 - There is a general concern about lack of transparency in the pharmaceutical field, especially on information regarding risks of medicines
 - There is an increase in requests, based on freedom of information/access to documents legislation
 - There is an increasing focus on information to patients and the general public
 - Growing media attention
 - Transparency has to be balanced with protection of confidential (sensitive) information (data) and protection of personal data
 - National agencies have to follow their national legislation
 - Recommendations of the joint HMA/EMEA group on Transparency would be useful to facilitate a common approach between national competent authorities as well as between national competent authorities and EMEA.
 - This document deals only with requests for information to PSUR data, as received from Marketing authorisation holders and does not address the request for information to assessment reports of PSURS. The handling of requests for information to assessment reports will be described in a separate document
 - Information on risks of medicines should always be presented against the benefits of the product

2. Periodic Safety Update Reports in the EU

A PSUR provides an update of the worldwide safety experience with a medicinal product and an evaluation of the risk-benefit balance of the product in the light of new safety information. According to Art 104(6) of Directive 2001/83/EC it is a legal obligation for a Marketing Authorisation holder (MAH) to submit these reports immediately upon request, or at regular intervals indicated in the legislation to the competent authorities.

Volume 9A of The Rules Governing Medicinal Products in the European Union gives detailed instructions on PSUR reports that may contain thousands of pages including detailed descriptions of individual case reports.

There is no legal obligation in the EU pharmaceutical legislation to disclose dossiers or other documentation received from MAHs as PSURs.

However, agencies receive requests for access to PSURs on the basis of national Freedom of Information Acts.

Member states have different experience with regard to requests for access to PSURs. Some have never had such a request; others have experience with these requests based on the Freedom of Information Acts. These requests are based on national legislation which may differ from country to country.

3. Information on safety of medicines

The legislation requires a proactive approach for providing information on safety of medicines. There are several provisions in Regulation (EC) No 726/2004 and Directive 2001/83/EC regarding transparency in relation with adverse events reports and safety information.

The wordings in the Regulation and Directive are not identical, but HMA and EMEA wish for a consistent approach across the European Network. Furthermore the EMEA is discussing its policy with regard to transparency on safety information and access to Eudravigilance.

Information on adverse reactions/Eudravigilance database

- Regulation (EC) No 726/2004, Article 22. Pharmacovigilance opinions of the CHMP shall be made publicly accessible;
- Regulation (EC) No 726/2004, Article 26. Data on serious adverse reactions shall be made publicly accessible, if relevant, after evaluation;
- Directive 2001/83/EC, Article 102. Information on adverse reactions shall be permanently accessible to all MSs and without delay to the public;
- Regulation (EC) No 726/2004, Article 57.1
 - (d) Health-care professionals, MAHs and the public shall have appropriate levels of access to the ADR databases (EudraVigilance), with personal data protection being guaranteed.
 - (f) task of EMEA/CHMP: distributing appropriate pharmacovigilance information to the general public.

Public assessment reports and EPARs:

Regulation (EC) No 726/2004, Article 13.3. EPARs:

- The EMEA shall immediately publish the EPAR which shall include a summary written in a manner that is understandable to the public.

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Directive 2001/83/EC, Article 21.4. The competent authorities of the MSs shall:

- draw up assessment reports. The assessment reports shall be updated whenever new information becomes available which is of importance for the evaluation of the quality, safety or efficacy of the medicinal product concerned.
- make the assessment reports publicly accessible without delay, together with the reasons for their opinion.

4. Personal data protection

Directive 95/46/EC on data protection

Article 2(a)

“Personal data” shall mean any information relating to an identified or identifiable natural person (“data subject”) ; an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity;”.

Access to periodic safety update reports (PSURs)

Access to PSURs has to be only reactive and on request, as PSURs may contain thousands of pages. National agencies have to follow their national public administration legislation. There may be some differences in national legislation, but common principles can be identified that would facilitate a consistent approach in responding to requests for information across the Network. If a decision is taken not to disclose documents or information, the agency making the decision has to justify the non-disclosure. The relevant exceptions for access to PSURs pertain to personal data and commercially confidential information.

Information on the personal data of individual persons

Right of access does not apply to information which reasonably could be traced back to individual persons.

This exception is relevant in relation to the line listings and case narratives of suspected adverse reactions reports in the PSURs recorded in the period in question. Therefore, before PSURs can be disclosed information on the health of natural persons, e.g. adverse drug reaction reports, which could be traced back to an individual person, have to be made anonymous.

EMEA has asked the advice of the European Data Protection Supervisor (EDPS)¹ about deletion of personal data. The advice confirmed the recommendation from the HMA/EMEA transparency group.

The minimum personal data to be deleted to ensure anonymisation of the information would require the deletion of information on

- 1) Date of birth
- 2) (Reporting) country
- 3) Patient identification code

In addition, case-by-case assessment should be made whether additional information should be deleted in any other part of the documentation of PSURs. This is particularly relevant concerning case narratives where much detailed personal information may appear.

It should never be possible to identify a natural person from the information disclosed, so in case of reports related to patients suffering from a rare disease it may be needed to delete further information.

Commercially confidential information

The right of access to documents does not apply to ‘commercially confidential information’. In the “Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents” (EMEA/45422/2006) the following description is given of “Commercially confidential information”:

“Commercially confidential information” is generally considered to fall broadly into two categories:

- Confidential intellectual property, “know-how”, and trade secrets (including e.g. formulas, programs, process or information contained or embodied in a product, unpublished aspects of trade marks, patents, etc).
- Commercial confidences (e.g. structures and development plans of a company).

¹ Reference is made to the website of EDPS for further information: <http://www.edps.europa.eu/EDPSWEB>

Three elements of commercial information of the PSUR will be reviewed below:

a) The worldwide list of marketing authorisations for the medicinal product

In all EU Member States, information on registration status is publicly available, but not necessarily in non-EU countries. There are no grounds for assuming that the granting of access to the information in the worldwide list on marketing authorisations *granted* for the medicinal product will inflict a financial loss on a company.

Therefore, as a general rule, such information cannot be considered commercially confidential.

b) The sales figures stated in the PSUR for calculation of an estimated number of patients or animals that have been exposed to the medicinal product.

A PSUR must contain information on *global* sales and a justified estimate of the number of patients or animals that have been treated with the medicinal product in the period in question.

The total global sales figures may, thus, give an indication of a pharmaceutical company's size globally, and the potential sales of the medicinal product.

Such information is (publicly) available from different providers and therefore cannot be considered commercially confidential

c) The presentation in the PSUR of safety studies performed, ongoing and planned as well as relevant scientific literature

The content and level of detail of such safety studies may vary. It should not always be considered confidential but assessed on a case by case basis.

Non-published safety studies are assessed specifically for the level of detail and sensitivity of the information. However, when such studies, their results and their timelines are part of the conditions for marketing authorisations, specific obligations or follow up measures, they are not regarded as commercially confidential information.

Procedural steps

As a general rule access to documents will only be granted when the evaluation of the data by the responsible agency has been finalised and not during the assessment process.

Before a competent authority grants access to a PSUR, it is good administrative practice that the MAH is heard in relation thereto.

The agency forwards a copy of the PSUR fully anonymised and with deletion of commercially confidential information to the MAH. As a starting point, the company is only asked whether there is any commercially confidential information not satisfactorily deleted. The MAH can raise objections thereto if he finds the anonymisation to be unsatisfactory. As a rule the company should be allowed to comment, within the given deadline of the agency, otherwise it is assumed that they have no objections.

The agency will assess the objections raised by the MAH, but take the final decision in case of disagreement.

Public assessment report of a PSUR

In the PSUR, the MAH has to provide a summary of the safety data with a conclusion whether the new data have any consequences for the benefit risk balance of the product.

When making the PSUR available, the agency may also, as an option, provide a public assessment report on the PSUR. The assessment of a PSUR can be concluded with the request to update the SPC and PIL via a Type II Variation. The assessment report of the Type II variation can be added to the public assessment report when this is already available in the public domain. The EMEA will propose a template for such an update.

The handling of requests for access to a PSUR assessment reports will be discussed in a separate document

SUMMARY/ RECOMMENDATIONS

HMA/EMEA subgroup on transparency recommends the following common principles to facilitate a consistent approach:

If a decision on access to documents provides non-disclosure of documents, the agency making the decision has to justify the non-disclosure. The relevant exceptions for access to PSURs pertain to personal data and commercially confidential information.

Information on personal data of individual persons

The minimum personal data to be deleted to ensure anonymisation of the information are:

- Date of birth
- (Reporting) country
- Patient identification code

In addition, case-by-case assessment should be made whether additional information should be deleted in any other part of the documentation of the PSUR.

Commercially confidential information

The worldwide list of marketing authorisations is not considered to be commercial confidential information that should be deleted.

The *global sales* figures are (publicly) available from different providers and therefore cannot be considered commercially confidential.

Safety studies, ongoing and planned as well as relevant scientific literature; the content and level of detail of such studies may vary; therefore it should be assessed on a case by case basis.

Procedural steps

Before a competent authority grants access to a PSUR, it is good administrative practice that the MAH is heard in relation thereto.

The agency forwards a copy of the PSUR fully anonymised and with deletion of commercially confidential information to the MAH. The MAH should be allowed to comment within a given deadline of the agency. The agency will assess the objections raised by the MAH, but take the final decision.

Format of dataset

The recommendations on the handling of requests for access to PSURs are based on the current format of the dataset. It should be discussed with industry how the layout and format of a PSUR could be amended to separate confidential and personal data from the scientific data to facilitate the handling of these requests and so reduce the workload of the agencies.