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HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems, medical products and innovation
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PHARM 755

PHARMACEUTICAL COMMITTEE
23 October 2018

Subject: **Overview of Member States biennial reports on audits of their pharmacovigilance systems (2017 reporting year)**

Agenda item 2ii

Action to be taken:
For information
If there are any comments on the draft please send before 19th October 2018.

October 2018

This document is a Health and Food Safety Directorate General document for information purposes. It does not represent an official position of the Commission on this issue, nor does it anticipate such a position.

Overview of Member States biennial reports on audits of their pharmacovigilance systems (2017 reporting year)

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1. Introduction and background

All medicinal products for human use have to be authorised either at Member State or Union level before they can be placed on the EU market. They are subject to a strict testing and assessment of their quality, safety and efficacy before being authorised. Once placed on the market they continue to be monitored to assure that aspects which could impact the safety profile of a medicine are detected and assessed and that necessary measures are taken.

The legal framework of pharmacovigilance for medicines marketed within the EU is provided for in Regulation (EC) No 726/2004[1] with respect to centrally authorised medicinal products and in Directive 2001/83/EC[2] with respect to nationally authorised medicinal products (including those authorised through the mutual recognition and decentralised procedures).

The pharmacovigilance legislation places an obligation on Member States to operate a pharmacovigilance system for the fulfilment of their pharmacovigilance tasks and their participation in Union pharmacovigilance activities[3]. The legislation also obliges Member States to perform a regular audit of their pharmacovigilance system and report the results to the Commission every 2 years[4] (Article 101(2) of the Directive 2001/83/EC).

This report provides an overview of the audit activities reported by the Member States, in general covering the reporting period September 2015 to September 2017, based on the audit reports submitted by Member States. The national competent authorities that submitted information on their audits activities are given in the Annex. The information provided by the national competent authorities is not presented in a harmonised way and is not directly comparable. This overview focuses on changes and updates of the activities between 2015 to 2017, however, it does not provide a detailed description of audit findings.

2. Pharmacovigilance systems of the Member States

2.1. Overview of the pharmacovigilance systems of the Member States

According to the Member States' reports, the majority conducted Risk Assessment exercises, followed by updates of the national audit programmes in line with the results from the Risk Assessments. The national audit programmes are adopted by the Heads of Agencies and senior managers in the competent authorities. In one case the pharmacovigilance tasks are outsourced to another national competent authority..

2.2. Audit programmes

The development of each national competent authority's **audit strategy** takes account of past audits and on-going implementation of corrective actions, as well as the outcome of a risk assessment exercise. The strategies are generally reviewed within a rolling programme with varying durations of audit strategies. During the reporting period more than half of the competent authorities reviewed their audit strategy.

A wide range of pharmacovigilance activities has been audited across the Member States. The

[1] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1)

[2] 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 (OJ L 311, 28.11.2001, p. 67)

[3] Article 101(1) of the Directive 2001/83/EC

4 Article 101(2) of the Directive 2001/83/EC

findings are documented with different levels of detail, for example with respect to the audit scope, and findings description.

2.3. Organisation structure, responsibilities and resources

Organisational structures across the Member States have been described in different ways, varying from matrix to more vertical organisations. The majority of Member States submitted that there were no major changes in the organisational structures since the last reporting period. Some Member States implemented changes in the organisational structure, e.g. the establishment of an independent agency. The organograms and details of the organisational structures are published by some Member States.

In addition all Member States finalised the implementation of relevant changes in the EU legislation concerning pharmacovigilance and emphasised full compliance thereof. Most of the Member States further stated that the majority of changes in their pharmacovigilance system consisted of updates of existing standard operating procedures (SOP) as well as the establishment of new standard operating procedures.

Management of **human resources** is important as the implementation and operation of pharmacovigilance systems that comply with EU and national legislative requirements have had an impact on resource needs. The majority of Member States stated that competent and specialised personnel are available and specifically hired for the various pharmacovigilance tasks in line with the relevant legislative requirements. Where possible, additional personnel was recruited. Nevertheless, some Member States also pointed out a decrease of personnel and a minority of Member States noted an issue with a shortfall in human resources.

2.4. Training

Overall, the organisation of activities related to training and personal development in the Member States follows a structured set of common principles and Member States pointed out no major changes during the reporting period. A majority of Member States indicated that regularly reviewed and harmonised training programmes are in place. With regard to internal trainings, Member States have structures for the training of new employees, as well as continuing education for already trained employees. Most Member States further referred to the participation of their personnel specifically in European Medicines Agency trainings and webinars.

2.5. Compliance management and record management

No major changes were noted regarding the systems for compliance management. All Member States request an initial declaration of conflicts. In addition, a majority of Member States requests an annual update of the declarations of interest. With regard to record management, Member States have secure systems in place and the majority has a regularly updated data back-up system.

2.6. Documentation of the quality system

The national competent authorities reported that the quality systems for pharmacovigilance activities are described in various documents. Overall, when specified, the hierarchy of quality system documents refers to EU and national legislations, good pharmacovigilance practice (GVP) and relevant guidelines, overarching quality manual (sometimes referred to as quality handbook), SOPs (sometimes grouped by categories), working instructions, process charts, decision chains, lists and decision logs. The majority of the national competent authorities stated that SOPs were reviewed and new SOPs implemented. Additionally, most of the quality systems are in line with the relevant, updated ISO standards.

2.7. Business continuity arrangements

The majority of Member States submitted that there are sufficient and detailed Business Continuity arrangements in place, which are regularly reviewed and supervised. Some Member States stated that there are dedicated employees specifically responsible for the business continuity arrangements

2.8 Monitoring of performance and effectiveness

National competent authorities have reported having adequate tools and mechanisms to monitor the performance and effectiveness of their pharmacovigilance systems. The system of monitoring can vary including peer review, business management reports. The key performance indicators might be included in the operational plans. There were no major changes since the last reporting period.

3. Overview of audits

Most competent authorities reported on their activities between September 2015 to September 2017. One smaller Member State did not submit a report.

Where audit reports had been completed, the national competent authorities reported between 1 and 13 audits having been undertaken. The scope of the individual audits varied, in some Member States there were audits of their pharmacovigilance system overall whilst others had audited specific activities within the system. The template used for the biennial reporting indicates that the number of critical or major findings should be noted. More than half of the national competent authorities stated that there were no major or critical findings in the audit outcomes. Where areas for improvement had been identified in the audits generally actions had already been taken or were in progress to address the issue. The majority of national competent authorities implemented outstanding actions from the outcomes from the last report findings although in a few cases where there is a need for the development of new systems the implementation of these were in progress.

4. Summary

The Member States are obliged to submit reports on the results of the audits of their pharmacovigilance system every 2 years. This document provides an overview of the reports submitted for the reporting period September 2015 – September 2017.

The Member States plan the audit of their pharmacovigilance system according to a risk assessment of the various activities. Areas for improvement were identified in some audits. Where information was provided, follow up actions had been implemented or were in progress.

ANNEX

The following designated competent authorities submitted information on their audit activities to the European Commission.

Member State	Competent Authorities
Belgium (BE)	Federal Agency for Medicines and Health Products
Bulgaria	Bulgarian Drug Agency
Czech Republic (CZ)	State Institute for Drug Control
Denmark (DK)	Danish Medicines Agency
Germany (DE)	- Federal Institute for Drugs and Medical Devices - Paul-Ehrlich-Institute, Federal Institute for Vaccines and Biomedicines
Estonia (EE)	State Agency of Medicines
Ireland (IE)	Health Products Regulatory Authority
Greece (EL)	National Organization for Medicines
Spain (ES)	Spanish Agency for Medicines and Medical Devices
France (FR)	French Medicines and Health Products Safety Agency
Croatia (HR)	Agency for Medicinal Products and Medical Devices of Croatia
Italy (IT)	Italian Medicines Agency
Cyprus (CY)	Pharmaceutical Services, Ministry of Health
Latvia (LV)	State Medicines Agency
Lithuania (LT)	State Medicines Control Agency
Hungary (HU)	National Institute of Pharmacy and Nutrition
Malta (MT)	Medicines Authority
Netherlands (NL)	- Medicines Evaluation Board - Netherlands Pharmacovigilance Centre Lareb
Austria (AT)	Austrian Federal Office for Safety in Health Care/ Austrian Medicines and Medical Devices Agency
Poland (PL)	Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
Portugal (PT)	National Authority of Medicines and Health Products
Romania (RO)	National Agency for Medicines and Medical Devices
Slovenia (SI)	Agency for Medicinal Products and Medical Devices of the Republic of Slovenia
Slovakia (SK)	State Institute for Drug Control
Finland (FI)	Finnish Medicines Agency
Sweden (SE)	Medical Products Agency
United Kingdom (UK)	Medicines and Healthcare products Regulatory Agency

In addition the Icelandic Medicines Agency (IC), the Norwegian Medicines Agency (NO) and the Liechtenstein Office of Public Health (LI) submitted reports on their pharmacovigilance audit activities.