European Legislation - Changes in the Pharmacovigilance system in the Review 2005

Sofia

18 April 2007

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Strengthening medicines safety monitoring

A public consultation shows that the current EU system of medicines safety monitoring (pharmacovigilance) needs rationalisation and strengthening.

There are unclear roles and responsibilities, complex reporting rules implemented differently by different Member States, a lack of robust safety studies and complex decision-making at EU-level. Commission Vice-President Günter Verheugen announced today a strengthening of the EU pharmacovigilance system. By making clear the roles and responsibilities for pharmacovigilance, by simplifying reporting rules and by ensuring that robust safety studies are performed to support rapid EU decision-making, the planned reform will better protect public health and support the safe use of new and innovative medicines.

Press Release DG Enterprise 26.02.07

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Improving **implementation of the current framework** will include but not be limited to:

- working with the Commission's Directorate General for Research on **funding of studies** into the safety of medicines as well as studies into the methodologies used to conduct pharmacovigilance.
- Working with the Member States to resolve implementation issues, including **administrative practices that complicate reporting** rules for industry.
- Working with the EMEA**1** to strengthen its coordinating role including supporting **full compliance and maximum utilisation** of the EU pharmacovigilance database '**Eudravigilance'**.

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Proposals for **change to the legal framework** will focus on but not be limited to:

- **Strengthen the rules on transparency** relating to pharmacovigilance data, assessment and decision-making and **involve stakeholders** (e.g. patient and healthcare professional groups) in the processes **including reporting** (including patient reporting).
- **Establish clear standards** ('Good Vigilance Practices - GVP') for the conduct of pharmacovigilance by both the industry and regulators.
- Free up resource by rationalising and **simplifying the reporting of suspected adverse drug reactions** (ADRs), both expedited and periodic reporting, making best use of current information technology (including Eudravigilance) and matching the reporting requirements with the level of knowledge about the safety of a specific product.
- Make clear the respective **roles and responsibilities and minimise duplication of effort,** while maintaining the current split of competences between the Member States and the EMEA.
- Stimulate innovation by establishing a **clear legal requirement to conduct post-authorisation safety studies** including those in risk management systems.
- Rationalise EU decision-making on drug safety issues to deliver **fast, robust decisions that are equally and fully implemented** for all relevant products and across all markets.

Directive 2004/27/EC
Whereas # 20

Pharmacovigilance and, more generally, market surveillance and sanctions in the event of failure to comply with the provisions should be stepped up. In the field of pharmacovigilance, account should be taken of the facilities offered by new information technologies to improve exchanges between Member States.

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Acronyms

ADR	Adverse Drug Reaction
DDPV	Detailed Description of the Pharmacovigilance System
DHPC	Direct Healthcare Professional Communication
GVP	Good Vigilance Practice
ICSR	Individual Case Safety Report
PASS	Post Authorisation Safety Study
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
SPS	Summary of Pharmacovigilance System

Legal Basis

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Legislative Pyramid of the EU

EU Treaty

Legal basis between the Member States of the EU

Regulation

Addressee each citizen of the EU

Directly binding, no transfer into national law necessary, no modification possible

Directive

Addressee each MS

Transfer into binding national law until a specific fixed date necessary, binding concerning the aim, modification possible

Commission Decision

Issued by the European Commission to a specially named addressee

Notes for Guidance, Guidelines, Position Papers

Documentation of the state of the art in science, reasonable differences are possible in national law

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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

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Commission Regulation (EC) No 1662/95, of 7 July 1995, laying down certain detailed arrangements for implementing the Community decision-making procedures in respect of marketing authorisations for products for human or veterinary use

*

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

*

Commission Directive 2003/63/EC of 25 June 2003 amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use

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

*

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

(Review 2004)

(OJ L136/1 of 30 April 2004)

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Major Changes

New authorisation procedure DCP

Expanded obligation to centrally authorise a medicinal product

One-time renewal after 5 years

Expiry of an authorisation after 3 years of non-marketing

(sunset clause)

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Major Changes Pharmacovigilance

Article 102
Pharmacovigilance system
Broad public database

Article 103
Obligation of the QP to stay in the EU

Article 104
Reporting obligations for ADRs
Information of the public

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Article 104 (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.

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Major Changes Pharmacovigilance

Article 102
Pharmacovigilance system
Broad public database

Article 103
Obligation of the QP to live in the EU

Article 104
Reporting obligations for ADRs
Information of the public

Article 106
Guideline about ADR reporting and electronic exchange **è** Volume 9
“Internationally recognised medicinal terminology“

Article 107
Independent referral procedure due to pharmacovigilance data
timeline concerning the urgency

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Article 107

(1)

Information of the MS about planned restrictions

(2)

Urgent measures

Opinion of the CHMP, obligatory for withdrawal from the market, on request for changes, variable timeline

Request for preliminary measures
Procedure at the Standing Committee

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Actual Guidelines of the EU concerning Pharmaco-vigilance

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The Rules Governing Medicinal Products in the European Union

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Volume 9 (A/B)

Pharmacovigilance

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EU Documents

- Conduct of Pharmacovigilance for Centrally Authorised Products (CPMP/183/97)
- Crisis Management Plan Regarding Centrally Authorised Products for Human Use (CPMP/388/97)
- Conduct of Pharmacovigilance for Medicinal Products Authorised through the Mutual Recognition Procedure
- Notice to Applicants Volume IX - Notice to Marketing Authorisation Holders - Pharmaco-vigilance Guidelines (CPMP/PhVWP/108/99 corr.)
- Referrals in Accordance with the Provisions of Council Directive 75/319/EEC in the Case of Safety Concerns Related to Medicinal Products Marketed in the European Union (EMEA/SOP/001/97)
- Revised Note for Guidance on the Rapid Alert System (RAS) and Non-Urgent Information System (NUIS) in Human Pharmacovigilance (CPMP/PhVWP/005/96, Rev.1)

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- Note for Guidance on Procedure for Competent Authorities on the Undertaking of Pharmacovigilance Activities (CPMP/PhVWP/175/95, Rev. 1)

- Compilation of Community Procedures on Administrative Collaboration and Harmonisation of Inspections (ENTR/6266/00)

VOLUME 9A

of The Rules Governing Medicinal Products in the European Union

– Guidelines on Pharmacovigilance for Medicinal Products for Human Use –

Final January 2007

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GENERAL OUTLINE OF CONTENTS

INTRODUCTION

PART I – Guidelines for Marketing Authorisation Holders

PART II – Guidelines for Competent Authorities and the Agency

1. Undertaking of Pharmacovigilance Activities by Competent Authorities in Member States

2A Conduct of Pharmacovigilance for Centrally Authorised Products

2B Crisis Management Plan regarding Centrally Authorised Products

3. Conduct of Pharmacovigilance for Medicinal Products Authorised through the Mutual Recognition or Decentralised Procedure

4. Rapid Alert and Non-Urgent Information System in Pharmacovigilance

5. Referrals in Case of Safety Concerns Related to Products Authorised in the EU and CHMP Opinions Following Suspension or Revocation of a Medicinal Product by a Member State

6, Principles of Collaboration with the World Health Organization in Matters of International Pharmacovigilance

PART III – Guidelines for Marketing Authorisation Holders, Competent Authorities and the Agency on Electronic Exchange of Pharmacovigilance Information in the EU

PART IV – Guidelines for Marketing Authorisation Holders and Competent Authorities on Pharmacovigilance Communication

PART V – Guidelines for Marketing Authorisation Holders and Competent Authorities on Product- or Population-Specific Pharmacovigilance

1. Guideline on Exposure to Medicinal Products During Pregnancy: Need for Post-Authorisation Data
2. Guideline on the Conduct of Pharmacovigilance for Medicines Used by the Paediatric Population

ANNEXES

1. Glossary
2. Abbreviations
3. Terminology
4. ICH Guidelines
5. Templates
6. Distribution Requirements and Address Lists for Data Submission

New Pharmacovigilance obligations in the authorisation procedures

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Directive 2001/83/EC as amended
Article 8

3. The application shall be accompanied by the following particulars and documents, submitted in accordance with Annex I:

….

(ia) A detailed description of the pharmacovigilance and, where appropriate, of the risk-management system which the applicant will introduce.

GENERAL OUTLINE OF CONTENTS

INTRODUCTION

1. Legal Basis and Structure of Volume 9A
2. Legal Framework for Pharmacovigilance
3. The Roles of the Various Parties

PART I – Guidelines for Marketing Authorisation Holders

1. General Principles
2. Requirements for Pharmacovigilance Systems, Monitoring of Compliance and Pharmacovigilance Inspections
3. Requirements for Risk Management Systems
4. Requirements for Expedited Reporting of Individual Case Safety Reports
5. Requirements for Reporting in Special Situations
6. Requirements for Periodic Safety Update Reports
7. Requirements for Company-Sponsored Post-Authorisation Safety Studies
8. Overall Pharmacovigilance Evaluation and Safety-Related Regulatory Action

Volume 9A

Part I

Section 2: Requirements for Pharmacovigilance Systems, Monitoring of Compliance and Pharmacovigilance Inspections

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GUIDELINE ON MONITORING OF COMPLIANCE WITH PHARMACOVIGILANCE REGULATORY OBLIGATIONS AND PHARMACOVIGILANCE INSPECTIONS

(INCORPORATES GUIDANCE ON THE DETAILED DESCRIPTION OF THE MAH'S PHARMACOVIGILANCE SYSTEM TO BE INCLUDED IN THE MARKETING AUTHORISATION APPLICATION)

THIS GUIDELINE WILL BE INCORPORATED IN VOLUME 9 OF EUDRALEX AFTER THE CONSULTATION PROCESS

DRAFT AGREED BY:	
- CHMP PHARMACOVIGILANCE WORKING PARTY	June 2005
- CVMP PHARMACOVIGILANCE WORKING PARTY	May 2005
- GCP INSPECTION SERVICES GROUP	June 2005
- GMP INSPECTION SERVICES GROUP	May 2005
ADOPTION BY CHMP/CVMP FOR RELEASE FOR CONSULTATION	June 2005
FURTHER DISCUSSED BY CHMP/CVMP PRIOR TO RELEASE FOR CONSULTATION	February 2006
TRANSMISSION TO COMMISSION	March 2006

This guideline replaces guideline / NfG Reference CPMP/PHVWP/1618/01 Position Paper on Compliance with Pharmacovigilance Regulatory Obligations (Adopted November 2001)

KEYWORDS	pharmacovigilance system monitoring inspection

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2. Requirements for Pharmacovigilance Systems, Monitoring of Compliance and Pharmacovigilance Inspections

2.1 Introduction

2.1.1 Roles of the Marketing Authorisation Holder

2.1.2 Roles of the Agency

2.1.3 Roles of the Competent Authorities in Member States

2.1.4 Pharmacovigilance Inspections

2.1.5 Detailed Description of the Pharmacovigilance System to Be Included in the Marketing Authorisation Application

2.1.6 Proof of the Services of a QPPV and of the Necessary Means to Notify Adverse Reactions, to be Included in the Marketing Authorisation Application

Legal Basis of Pharmacovigilance I

The MAHs should ensure that they have an appropriate system of pharmacovigilance in place in order to assure responsibility for their products on the market and to ensure that appropriate action can be taken, when necessary. This includes the MAH having at its disposal permanently and continuously an appropriately qualified person responsible for pharmacovigilance residing within the European Economic Area, and the establishment of a system for the collection, preparation and submission of all suspected adverse reactions that need to be reported promptly or at the latest within 15 days, …

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Legal Basis of Pharmacovigilance II

- Council Regulation EEC 726/2004 (Title 2, Chapter 3)
- Council Directive 2001/83/EEC (Chapter 5a)
- Commission Regulation EC 540/95

Pharmacovigilance guidelines

- Volume 9A

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Detailed description of the Pharmacovigi-lance System (DDPV)

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2.2 Detailed Description of the Pharmacovigilance System

2.2.1 Location in the Marketing Authorisation Application and Update of the Detailed Description

2.2.2 Statement of the Marketing Authorisation Holder and the QPPV Regarding their Availability and the Means for the Notification of Adverse Reactions

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2.2.3.b) Organisation

2.2.3.c) Documented Procedures

2.2.3.d) Databases

2.2.3.e) Contractual Arrangements with Other Persons or Organisations Involved in the Fulfilment of Pharmacovigilance Obligations

2.2.3.f) Training

2.2.3.g) Documentation

2.2.3.h) Quality Management System

2.2.3.i) Supporting Documentation

Modul 1.8.1

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GUIDELINE ON MONITORING OF COMPLIANCE WITH PHARMACOVIGILANCE REGULATORY OBLIGATIONS AND PHARMACOVIGILANCE INSPECTIONS

(INCORPORATES GUIDANCE ON THE DETAILED DESCRIPTION OF THE MAH'S PHARMACOVIGILANCE SYSTEM TO BE INCLUDED IN THE MARKETING AUTHORISATION APPLICATION)

THIS GUIDELINE WILL BE INCORPORATED IN VOLUME 9 OF EUDRALEX AFTER THE CONSULTATION PROCESS

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- GMP INSPECTION SERVICES GROUP	May 2005
ADOPTION BY CHMP/CVMP FOR RELEASE FOR CONSULTATION	June 2005
FURTHER DISCUSSED BY CHMP/CVMP PRIOR TO RELEASE FOR CONSULTATION	February 2006
TRANSMISSION TO COMMISSION	March 2006

This guideline replaces guideline / NfG Reference CPMP/PHVWP/1618/01 Position Paper on Compliance with Pharmacovigilance Regulatory Obligations (Adopted November 2001)

KEYWORDS	pharmacovigilance system monitoring inspection

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Guideline on monitoring of compliance with pharmacovigilance regulatory obligations and pharmacovigilance inspections

Draft

14. April 2005
EMEA/INS/PhV/119149/2005

(Incorporates Guidance on the detailed description of the MAH's Pharmacovigilance System to be included in the marketing authorisation application)

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5. Detailed description of the Pharmacovigilance System to be included in the marketing authorisation application and proof that the applicant has the services of a qualified person and the necessary means for the notification of adverse reactions

5.1 Statement of the MAH and the qualified person regarding their availability and the means for the notification of adverse reactions

5.2 Location of the Pharmacovigilance system that should be described in the Marketing Authorisation Application

5.3 Elements of the Pharmacovigilance system that should be described in the MAA

5.3.1 Qualified person responsible for Pharmacovigilance

5.3.2 Organisation

5.3.3 Procedures in place which are documented in writing

5.3.4 Databases

5.3.5 Links with other organisations

5.3.6 Training

5.3.7 Documentation

5.3.8 Quality management system

Volume 9A
Part I
(1)

The Marketing Authorisation Holders should ensure that they have an appropriate system of pharmacovigilance in place in order to assure responsibility for their products on the market and to ensure that appropriate action can be taken, when necessary. This includes the Marketing Authorisation Holder having at its disposal permanently and continuously an appropriately qualified person responsible for pharmacovigilance residing within the European Economic Area, and the establishment of a system of pharmacovigilance.

Volume 9A
Part I
(2)

The detailed description should comprise an overview of the pharmacovigilance system providing information on the key elements of that system. Where aspects of the system such as the organisational arrangements are particular to the product rather than the main system of the Marketing Authorisation Holder/company (Marketing Authorisation Holder or a group of Marketing Authorisation Holders sharing the same pharmacovigilance system) this should be indicated in a product-specific addendum.

The detailed description should be supported by documentation maintained by the company.

Updates to the information provided in the detailed description of the pharmacovigilance system should be made as type II variations.

Proposal

Only one submission to the CA as a „Pharmacovigilance Master File“.

No submission with every MAA necessary.

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English Deutsch

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Bundesinstitut für Arzneimittel und Medizinprodukte

Mitteilung zur Einreichung von Unterlagen gemäß § 22 Abs. 2 Nr. 5 und Nr. 6 AMG (Pharmakovigilanz- und Risikomanagement-System; qualifizierte Person für Pharmakovigilanz)

Stand: 09.01.2007

Das BfArM bittet darum, die Einreichung von Unterlagen nach § 22 Abs. 2 Nr. 5 (Beschreibung des Pharmakovigilanz-Systems) und Nr. 6 (qualifizierte Person nach § 63a) AMG bereits jetzt nach den Vorgaben der im Entwurf vorliegenden „Guideline on Monitoring of compliance with pharmacovigilance regulatory obligations and pharmacovigilance inspections" (Kapitel „Guidance on the detailed description of the MAHs pharmacovigilance system to be included in the marketing authorisation application") vorzunehmen. Danach müssen die im Folgenden aufgelisteten Elemente in der Beschreibung enthalten sein. Insgesamt sollte die Beschreibung 20 Seiten nicht überschreiten (ohne Anlagen). Die folgenden Kapitelnummern entsprechen der o.g. Guideline.

5.1
Unterschriebene Erklärung des Zulassungsinhabers und der Qualified Person für Pharmakovigilanz über deren Verfügbarkeit und die der notwendigen Mittel zur Erfüllung der Meldeverpflichtungen.

5.3
Beschreibung der Elemente des Pharmakovigilanz-Systems

5.3.1
Qualified Person für Pharmakovigilanz

- Name, Adresse, Erreichbarkeit
- Lebenslauf
- Arbeitsplatzbeschreibung
- Beschreibung der Vertretungsregelung

5.3.2
Organisation

- Namen und Adressen der Organisationen, wo Pharmakovigilanz-Aktivitäten (national, EU-weit, global) durchgeführt werden
- Punkte in der EU, an denen Pharmakovigilanz-Daten gesammelt werden und abrufbar sind
- Organigramme der verschiedenen Pharmakovigilanz-Einheiten

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Monitoring of Compliance by the Competent Authorities

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2.3 Monitoring of Compliance by the Competent Authorities

2.3.1 Qualified Person Responsible for Pharmacovigilance

2.3.2 Availability of Pharmacovigilance Data

2.3.3 Change in the Evaluation of the Risk-Benefit Balance of a Product

2.3.4 Expedited Adverse Reaction Reporting

2.3.5 Periodic Safety Update Reports

2.3.6 Information Requested by Competent Authorities

2.3.7 Submission of Safety Variations

2.3.8 CHMP Commitments in Respect of Centrally Authorised Products

2.3.9 Post-Authorisation Safety Studies

2.3.10 Provision of Additional Data on Studies

EEA Competent Authorities have been working for many years to facilitate Marketing Authorisation Holders in meeting pharmacovigilance regulatory obligations. This has included the development of guidelines, education programmes, responding to enquiries and the development of electronic reporting. Competent authorities should monitor Marketing Authorisation Holders for compliance with pharmacovigilance regulatory obligations. Furthermore, Competent Authorities exchange information in cases of non-compliance and will take appropriate regulatory action as required. It should be noted that enforcement action is within the competency of individual Member States.

Article 84 of Regulation (EC) 726/2004 sets out the roles of the Member States, the Agency and the Commission with respect to the imposition of penalties for infringement of that Regulation or regulations adopted pursuant to it.

Monitoring Compliance

Methods available to regulatory authorities for prospective monitoring of compliance with expedited reporting of adverse reactions could be:

- Monitoring adverse reaction reports received against a complete list of MAs or MAHs to determine complete failure to report.
- Monitoring the time between receipt by MAH and submission to competent authorities to detect late reporting.
- Monitoring the quality of reports, including comparison of the quality of duplicate reports. Submission of reports judged to be of poor quality may result in the follow-up procedures of MAHs being scrutinised.
- Checking Periodic Safety Update Reports (PSURs) to detect under-reporting (e.g. of expedited reports).

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Non-Compliance

- Poor quality reports: poor documentation of adverse reaction reports or insufficient information provided to perform a thorough assessment in the Presentation of Individual Case Histories section, new safety signals not or poorly assessed in the Overall Safety Information section, misuse not highlighted, absence of standardised medical terminology (e.g. MedDRA/VEDDRA).
- Company core data sheet (CCDS) or Summary of Product Characteristics (SPC): where changes have been made to the CCDS or SPC since the submission of the last PSUR, for human medicinal products - the covering letter does not highlight the differences between the CCDS and the EU SPC. Previous requests from regulatory authorities not addressed: submission of a report where previous requests from competent authorities have not been addressed (e.g. close monitoring of specific safety issues).

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Non-Compliance

- Non-submission: complete non-submission of PSURs, submission outside the correct cycle or outside the correct time frames (without previous submission of a type II variation), non-restart of the cycle of submission when necessary.
- Incorrect format of the document: report not in accordance with Notice to Marketing Authorisation Holders contained in Volume 9 A of The Rules Governing Medicinal Products In The European Union.
- Concealment of information particularly in the following sections of the report: Update of Regulatory Authority or MAH Actions taken for Safety Reasons, Changes to Reference Safety Information, Patient Exposure, Presentation of Individual Case Histories.

Risk Management System

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Date of authorisation

Check for security strongly limited

Small number of subjects in clinical trials

Exclusion criteria

Limited co-medication

Relatively short period of studies

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Modul 1.8.2

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Establishing a European Risk Management Strategy

Summary report of the heads of agencies ad hoc working group

January 2003

http://heads.medagencies.com/heads/docs/summary.pdf

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ICH

E2E

Step 5
(Implementation)

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INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

PHARMACOVIGILANCE PLANNING
E2E

Current *Step 4* version
dated 18 November 2004

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and USA.

Legal Basis

Article 6 of the Regulation (EC) Nr. 726/2004

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Article 8 of the Directive 2001/83

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Guideline on Risk Management Systems for Medicinal Products for Human Use

14. November 2005
Coming into force 20.11.05

(EMEA/CHMP/96268/2005)

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Implementation of ICH E2E

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VOLUME 9A

of The Rules Governing Medicinal Products in the European Union

– Guidelines on Pharmacovigilance for Medicinal Products for Human Use –

Final January 2007

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3. Requirements for Risk Management Systems

Risk Management System

4 Steps

Detection

Assessment

Minimisation

Communication

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Risk Management System

Definition

A risk management system is a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicinal products, including the assessment of the effectiveness of those interventions.

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Description of the Risk Management System → EU Risk Management Plan (EU-RMP)

Part I

A Safety Specification

Compilation of the security profile (non-clinical, clinical) at a given point of time.

Contains important identified risks, potential risks as well as important missing information.

Potential for overdose

Transmission of infections

Abuse

Off-label use

Paedriatric use (off-label)

Basis for → Pharmacovigilance Plan

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Description of the Risk Management Systems→ EU Risk Management Plan (EU-RMP)

A Pharmacovigilance Plan

Based on the Safety Specification.
Proposes measures which can further clarify the identified security concerns.

Contents

Safety concern

Objective of proposed action

Action proposed

Rationale for proposed action

Monitoring by the MAA/MAH

Milestones for evaluation and reporting

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Description of the Risk Management System → EU Risk Management Plan (EU-RMP)

Part II

An evaluation of the need for risk minimisation measures

and if there is such a need:

→ **A risk minimisation plan**

Only necessary, if additional risk minimising actions are needed

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Risk minimisation plan

Contents

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Methods for Risk Minimisation
Table I.3.A

Risk minimisation activities can be divided into those where a reduction in risk is achieved primarily through the provision of information and education and those which seek to control the use of the medicine. When it is obvious that a risk minimisation activity will be needed post authorisation, consideration should be given to piloting the activity during the development phase to see the effectiveness and suitability. When this is done, the outcome should be provided in the risk minimisation plan under the appropriate action.

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Methods for Risk Minimisation
Table I.3.A

Provision of Information

Provision of information to Healthcare Professionals and/or Patients on the specific risks of a product and the measures on how to reduce them is an essential activity of risk management. This provision of information may be confined to information contained within the Summary of Product Characteristics (SPC) and Package Leaflet (routine risk management) or may be through the use of additional educational material (additional risk management). The need for additional material beyond the Summary of Product Characteristics and Package Leaflet will depend upon the risk and should be considered on a case-by-case basis. Experts in risk communication should be consulted as appropriate.

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Methods for Risk Minimisation
Table I.3.A

Additional Educational Material

- Direct Healthcare Professional Communications;
- Physician's Guide to Prescribing;
- Pharmacist's Guide to Dispensing;
- Checklists for assessing comprehension, knowledge, attitudes, and/or desired safety behaviours about the risk(s). These should be tailored to the target audience (e.g. physicians, pharmacists or patients);
- Checklists for actions before prescribing or dispensing;
- Patient Information Brochures;
- Specific training programmes.

Methods for Risk Minimisation
Table I.3.A

Control at Pharmacy Level

Control of Prescription Size or Validity

Informed Consent and other Patient Aspects

Restricted Access Programmes

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When is an RMP necessary?

Not only before authorisation, but also after.

Along with the authorisation for

- any product containing a new active substance;
- a similar biological medicinal product;
- a generic/hybrid medicinal product where a safety concern requiring additional risk minimisation activities has been identified with the reference medicinal product.

With an application involving a significant change in a marketing authorisation (e.g. new dosage form, new route of administration, new manufacturing process of a biotechnologically derived product, significant change in indication) unless it has been agreed with the Competent Authority that submission is not required.

On request from a Competent Authority (both pre- and post-authorisation).

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Routine Pharmacovigilance

When no safety concern, routine Pharmacovigilance should be sufficient, without the need for additional actions.

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Practical action

If necessary, timely scientific advise, especially with CA

Usually submission in the MAA.

On request also after authorisation.

Decision about RMP with authorisation, changes possible.

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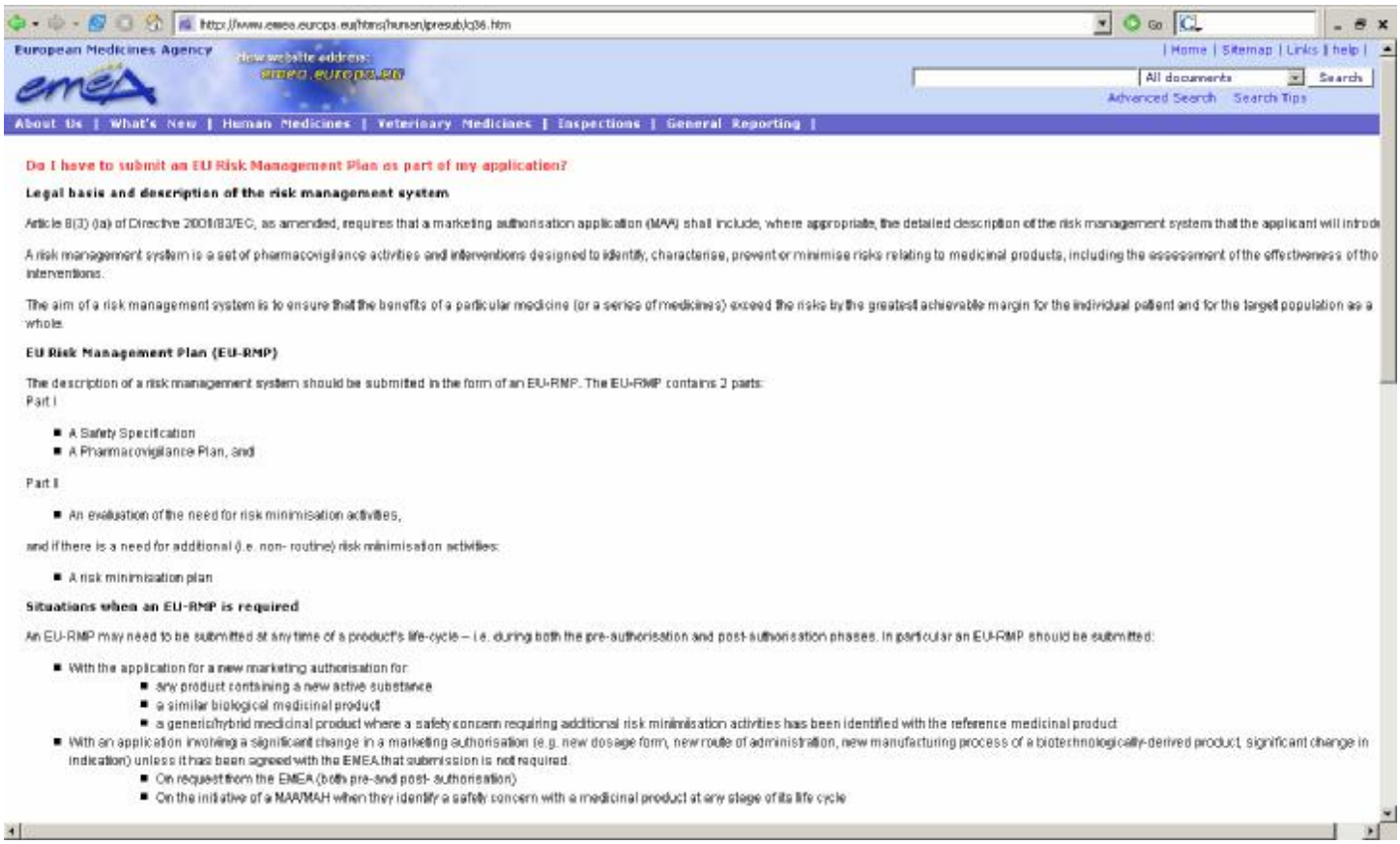

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Do I have to submit an EU Risk Management Plan as part of my application?

Legal basis and description of the risk management system

Article 8(3) (ia) of Directive 2001/83/EC, as amended, requires that a marketing authorisation application (MAA) shall include, where appropriate, the detailed description of the risk management system that the applicant will introd

A risk management system is a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicinal products, including the assessment of the effectiveness of the interventions.

The aim of a risk management system is to ensure that the benefits of a particular medicine (or a series of medicines) exceed the risks by the greatest achievable margin for the individual patient and for the target population as a whole.

EU Risk Management Plan (EU-RMP)

The description of a risk management system should be submitted in the form of an EU-RMP. The EU-RMP contains 2 parts:
Part I

- A Safety Specification
- A Pharmacovigilance Plan, and

Part II

- An evaluation of the need for risk minimisation activities,

and if there is a need for additional (i.e. non- routine) risk minimisation activities:

- A risk minimisation plan

Situations when an EU-RMP is required

An EU-RMP may need to be submitted at any time of a product's life-cycle – i.e. during both the pre-authorisation and post-authorisation phases. In particular an EU-RMP should be submitted:

- With the application for a new marketing authorisation for:
  - any product containing a new active substance
  - a similar biological medicinal product
  - a generic/hybrid medicinal product where a safety concern requiring additional risk minimisation activities has been identified with the reference medicinal product
- With an application involving a significant change in a marketing authorisation (e.g. new dosage form, new route of administration, new manufacturing process of a biotechnologically-derived product, significant change in indication) unless it has been agreed with the EMEA that submission is not required.
  - On request from the EMEA (both pre-and post- authorisation)
  - On the initiative of a MAA/MAH when they identify a safety concern with a medicinal product at any stage of its life cycle

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European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 27/09/2006
Doc.Ref. EMEA/192632/2006

Annex C: TEMPLATE FOR EU RISK MANAGEMENT PLAN (EU – RMP)

This template provides advice on how the data requested in the Guideline, if available, should be presented. It is anticipated that, particularly in section 1, all the information will not be available for all drugs and that the type of product and where it is in its lifecycle will affect how much information can be provided.

Overview of EU Risk Management Plan Template	
Section	
	Product information
1	Safety Specification
2	Pharmacovigilance Plan
3	Evaluation of the need for risk minimisation activities
4	Risk Minimisation Plan
5	Summary of the EU-RMP
6	Contact person details
Annex 1	Interface between EU-RMP and Eudravigilance *To be provided in electronic form only*
Annex 2	Current (or proposed if initial EU-RMP) SPC, Package Leaflet
Annex 3	Synopsis of ongoing and completed clinical trial programme
Annex 4	Synopsis of ongoing and completed pharmacoepidemiological study programme
Annex 5	Protocols for proposed and ongoing studies in pharmacovigilance plan
Annex 6	Newly available study reports
Annex 7	Other supporting data
Annex 8	Details of proposed educational programme (if applicable)

To be valid an EU-RMP MUST contain sections 1,2 & 3. With the exception of section 4 (which must be completed if additional risk minimisation activities are proposed) all sections should be provided. Annex 1 should be provided in electronic form only.

Please ensure that the data provided in this document are coded in MedDRA terms where appropriate and are consistent with those submitted electronically in the template attached in Annex 1.

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Pharmacovigilance Inspections

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Th/179/75

VOLUME 9A

of The Rules Governing Medicinal Products in the European Union

– Guidelines on Pharmacovigilance for Medicinal Products for Human Use –

Final January 2007

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Th/179/76

2.4 Pharmacovigilance Inspections

2.4.1 Conduct of Inspections

2.4.2 Routine Inspections

2.4.3 Targeted Inspections

2.4.4 Pharmacovigilance System Inspections

2.4.5 Product-Specific Inspections

2.4.6 Requesting and Reporting of Inspections

2.4.7 Inspections of Contractors and Licensing Partners

2.4.8 Inspections in European Economic Area

2.4.9 Inspections in Third Countries

2.4.10 Fees for Inspections Requested by the CHMP

2.4.11 Procedures for Coordination of Pharmacovigilance Inspection for Centrally Authorised Products

2.4.12 Procedures for Pharmacovigilance Inspections

2.4.13 Unannounced Inspections

2.4.14 Inspection Reports

2.4.15 Follow-up of Inspection Findings

2.4.16 Sharing of inspection information

2.5 Regulatory Action

The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

London, 15 November 2001
CPMP/PhVWP/1618/01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

POSITION PAPER ON COMPLIANCE WITH PHARMACOVIGILANCE REGULATORY OBLIGATIONS

DISCUSSION IN THE PHARMACOVIGILANCE WORKING PARTY	March 2001
TRANSMISSION TO CPMP	March 2001
RELEASE FOR CONSULTATION	June 2001
DEADLINE FOR COMMENTS	September 2001
DISCUSSION OF COMMENTS BY THE PHARMACOVIGILANCE WORKING PARTY	October 2001
ADOPTION BY CPMP	November 2001
DATE OF COMING INTO OPERATION	January 2002

Note:

The first version of this document was developed by the CPMP Pharmacovigilance Working Party (PhVWP), following consultation with the EMEA and national Competent Authorities through the PhVWP Members, including consultation with Good Clinical Practice and Good Manufacturing Practice Inspectorates. It was adopted by the CPMP in May 2001 and endorsed by the Heads of Agencies at their meeting in June 2001. This version was agreed by the PhVWP in October 2001 and adopted by the CPMP in November 2001, taking into account comments received from interested parties during the consultation phase. It was endorsed by the Heads of Agencies at their meeting in November 2001 for coming into operation in January 2002.

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GUIDELINE ON MONITORING OF COMPLIANCE WITH PHARMACOVIGILANCE REGULATORY OBLIGATIONS AND PHARMACOVIGILANCE INSPECTIONS

(INCORPORATES GUIDANCE ON THE DETAILED DESCRIPTION OF THE MAH'S PHARMACOVIGILANCE SYSTEM TO BE INCLUDED IN THE MARKETING AUTHORISATION APPLICATION)

THIS GUIDELINE WILL BE INCORPORATED IN VOLUME 9 OF EUDRALEX AFTER THE CONSULTATION PROCESS

DRAFT AGREED BY:	
- CHMP PHARMACOVIGILANCE WORKING PARTY	June 2005
- CVMP PHARMACOVIGILANCE WORKING PARTY	May 2005
- GCP INSPECTION SERVICES GROUP	June 2005
- GMP INSPECTION SERVICES GROUP	May 2005
ADOPTION BY CHMP/CVMP FOR RELEASE FOR CONSULTATION	June 2005
FURTHER DISCUSSED BY CHMP/CVMP PRIOR TO RELEASE FOR CONSULTATION	February 2006
TRANSMISSION TO COMMISSION	March 2006

This guideline replaces guideline / NfG Reference CPMP/PHVWP/1618/01 Position Paper on Compliance with Pharmacovigilance Regulatory Obligations (Adopted November 2001)

KEYWORDS	pharmacovigilance system monitoring inspection

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Legal Background

Directive 2001/83/EC

Article 111

1. The competent authority of the Member State concerned shall ensure, by means of repeated inspections, that the legal requirements governing medicinal products are complied with.

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Directive 2004/27/EC of 31 March 2004 amending Directive 2001/83/EC

Amendment of Article 111:

"*(1)* The competent authority of the Member State concerned shall ensure, by means of repeated inspections, and if necessary **unannounced inspections**, … , that the legal requirements governing medicinal products are complied with. ..."

(continued)

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Directive 2001/83/EC as amended

“Such inspections shall be carried out by officials representing the competent authority who shall be empowered to:

...

(d) inspect the **premises, records and documents** of marketing authorisation holders or any firms employed by the marketing authorisation holder to perform the activities described in Title IX *, … .“

* Pharmacovigilance

(continued)

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Directive 2001/83/EC as amended

“3. After every inspection …, the officials representing the competent authority shall report on whether the manufacturer complies with the principles and guidelines of good manufacturing practice … or, … , with the requirements laid down in Articles 101 to 108 *. ...“

* Titel IX

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Th/179/84

Regulatory Action

In the event of non-compliance, regulatory options include the following:

• *Education and Facilitation*

MAHs may be informed of non-compliance and advised on how this can be remedied.

• *Inspection*

Non-compliant MAHs may be inspected to determine the extent of non-compliance and then reinspected to ensure compliance is achieved.

• *Warning*

Competent authorities may issue a formal warning reminding MAHs of their pharmacovigilance regulatory obligations.

• *Naming non-compliant MAHs*

Competent authorities will consider a policy of making public a list of MAHs found to be seriously or persistently non-compliant.

• *Urgent Safety Restriction*

• *Variation of the Marketing Authorisation*

• *Suspension of the Marketing Authorisation*

• *Revocation of the Marketing Authorisation*

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Pharmacovigilance Inspections

To ensure that MAHs comply with pharmacovigilance regulatory obligations and to facilitate compliance, competent authorities may conduct pharmacovigilance inspections. There should be collaboration between competent authorities to minimise duplication and maximise coverage. Inspections will be random and systematic, as well as targeted to MAHs suspected of being noncompliant. …

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Targeted Inspections

• Triggers for the inspection are identified which do not relate to specific concerns about a product safety or actual non-compliance e.g.:

o The MAH has not previously been inspected.

o The MAH has placed their first product (or only a few) on the market in the EEA.

o The MAH has recently been or are involved in a merger or takeover process.

o The MAH has changed their system significantly – new database system, contracting out of reporting activities etc.

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Targeted Inspections

- Triggers for the inspection are identified which relate to specific concerns about a product's safety or actual non-compliance e.g. significant issues relating to:

o Specific Obligations relating to the monitoring of product safety, identified at the time of the marketing authorisation.

o Follow-Up Measures relating to the monitoring of product safety, identified at the time of the marketing authorisation.

o Delays in expedited or periodic reporting.

o Incomplete reporting.

o Submission of poor quality or incomplete PSURs

o Inconsistencies between reports and/or other information sources.

o Change in risk-benefit balance.

o Failure to communicate change in risk-benefit balance.

o Previous inspection experience.

o Information received from other authorities.

o Poor follow-up to requests for information from the competent authorities.

o Product withdrawal with little or no advance notice to the EEA competent authorities.

Conduct of inspections

The competent authority, for inspection of the MAH's pharmacovigilance system will be the competent authority of the Member State in whose territory the MAH's qualified person responsible for pharmacovigilance is located. Where an additional facility in another Member State requires inspection (e.g. a database) the inspection will be carried out by the competent authority of the Member State in whose territory the facility is located.

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Conduct of inspections

In general, companies have a pharmacovigilance centre in the Community covering multiple products that are on the market, in the Community. These centres may also be the global pharmacovigilance centres, or the latter may be located in third countries. Where the global centres, databases, etc are located in third countries the same competent authority, as above, will be responsible for purposes of inspection on behalf of the community, if such an inspection is considered necessary. Where relevant or on request, and in particular for product specific issues, they may be assisted, or the inspection may be conducted, by an inspector and/or expert from the Rapporteur/Co-Rapporteur agency (for CAPs) or the Reference Member State agency (for MRPs/Decentralised Procedures).

Ad Hoc GCP PhV Session – 13 September 2006
Agenda Item 5.1.3 – For Discussion

European Medicines Agency
Inspections

Procedure no.: INS/GCP/6

GUIDANCE FOR CONDUCTING PHARMACOVIGILANCE INSPECTIONS REQUESTED BY THE EMEA

Ad Hoc Meeting of GCP Inspection Services

Applies to: EMEA, EU/EEA Inspectorates	
Summary of scope: This SOP provides unified standards on the conduct of Pharmacovigilance inspection that are applicable for any site to be inspected at the request of the EMEA	
Keywords: : Conduct, Phv inspection	**Restricted**
Supersedes: N/A	

Preparation	**Date**
Concept	
Draft	
Deadline for comments	
[Draft 2]	

Finalisation	**Date**
Adoption	
[Transmission to other (Ad Hoc) WP, CPMP, Standing Committee, public etc.]	
[Adoption by other (Ad Hoc) WP, CPMP, Standing Committee, public etc.]]	
Effective date	

Document maintenance	**Date**
Review	
[Reviewed]	

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Guidance on the Conducting Pharmacovigilance Inspections

Conduct of a Pharmacovigilance Inspection

Opening meeting

Legal and Administrative Aspects

Organisational Structure

- Quality systems and SOPs
- Resources and training of Personnel

Facilities and equipment

MAH audit and quality assurance system

Qualified person (QP)

Safety information from clinical investigations

Source Data Verification

Quality defects

Closing meeting

Preparation of Inspection report

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Th/179/92

GUIDANCE FOR CONDUCTING PHARMACOVIGILANCE INSPECTIONS

Conduct of the inspection /
collecting information

- Legal and administrative aspects
- Organisational structure
- Facilities and equipment
- MAH audit and QA
- Qualified person (QP)
- Safety information from clinical investigations
- Source document verification
- Quality defects

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Th/179/93

GUIDANCE FOR CONDUCTING PHARMACOVIGILANCE INSPECTIONS

Legal and administrative aspects

- Documentation of the responsible parties for PhV activities
- QP
- Availability of information on all suspected ARs at least at a single point within the community;
- Systems to assure appropriate insurance cover for MAH's products when used in clinical trials before marketing
- Contractual documentation in respect of any out-sourced MAH responsibilities
- Co-marketing agreements
- Commitments for ADR reporting to the Agency/EMEA in relation to Centrally Authorised Products;
- Post-authorisation commitments and follow-up measures for centrally authorised products
- Preparation and submission of PSURs / SPCs (including revisions) / CIBs (including revisions)
- Documentation of responsibilities in relation to PhV of products undergoing clinical trials;
- Collection and reporting of SAEs in clinical trials and of spontaneous ADRs.

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GUIDANCE FOR CONDUCTING PHARMACOVIGILANCE INSPECTIONS

Organisational structure

- Quality system and SOPs
- Do SOPs cover all aspects of PhV?
  - ADRs
  - Data management
  - Quality defects
  - PSURs
  - Signal generation
- Organisational charts
- Generation, update and approval of SOPs
- Resources and training of personal (job descriptions, qualifications, deputies)

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GUIDANCE FOR CONDUCTING PHARMACOVIGILANCE INSPECTIONS

Source Data Verification

- Consistency and correctness of coding
- Quality and completeness of the medical review
- Quality of the information included in case summaries
- Adequacy of follow-up measures taken
- Determination of seriousness / listedness / expectedness
- Submission of expedited reports to authorities. Have all relevant reports been submitted?
- Have all relevant cases been discussed or included in the line listings of the PSUR covering the relevant time period?
- Have expedited reports been submitted within correct timeframes?
- Have qualifying serious reports from clinical trials been reported expedietly and included in PSURs?
- Can specific literature cases be retrieved from the database?

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Classification of EU PhV Inspection Findings

Critical

A deficiency in PhV systems, practices and/or processes that adversely affects the rights, safety and well being of patients or that poses a potential risk to public health and/or might represent a serious and direct violation of applicable legislation and guidelines.

Major

A deficiency in PhV systems, practices and/or processes that **might** adversely affect the rights, safety and/or well being of patients and/or that **might** pose a potential risk to public health and/or **might** represent a serious and direct violation of applicable legislation and guidelines.

Minor

A deficiency in PhV systems, practices or processes that **would not be expected** to adversely affect the rights, safety or well being of patients

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Th/179/97

Ad Hoc GCP PhV Session – 13 September 2006
Agenda Item 5.1.1 – For Discussion

The European Medicines Agency
Inspections

Procedure no: INS/PhV/1

PROCEDURE FOR COORDINATING PHARMACOVIGILANCE INSPECTIONS REQUESTED BY THE CXMP

Ad Hoc Meeting of GCP Inspection Services

Applies to: EMEA, EU/EEA Inspectorates	
Summary of scope: This SOP describes the different steps of the PhV inspection process and particularly the interfaces between Member States inspection services and CXMP/EMEA	
Keywords: PhV Inspection, Coordination, CXMP (CHMP/CVMP)	**Restricted**
Supersedes: N/A	

Finalisation	**Date**
Adoption by Ad Hoc Meeting of GCP Inspection Services	
Adoption by CXMP	
Revision	

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Th/179/98

Ad Hoc GCP PhV Session – 13 September 2006
Agenda Item 5.1.2 – For Discussion

The European Medicines Agency
Inspections

Procedure no: INS/PhV/4

PROCEDURE FOR REPORTING OF PHARMACOVIGILANCE INSPECTIONS REQUESTED BY THE CXMP

Ad Hoc Meeting of GCP Inspection Services

Applies to: EMEA, EU/EEA Inspectorates	
Summary of scope: This SOP describes the content of PhV inspection reports and the process of their approval and the distribution to the EMEA and	
Keywords: PhV Inspection, Reporting, IR, CXMP (CHMP/CVMP)	**Restricted**
Supersedes: N/A	

Finalisation	**Date**
Adoption by Ad Hoc Meeting of GCP Inspection Services	
Adoption by CXMP	

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Th/179/99

Example
of a
PhV Inspection Report

TABLE OF CONTENTS

8. Conclusions and Recommendations of the Inspection Team

The NAM has inspected the pharmacovigilance systems of [redacted]-Finland. The inspection revealed critical and major findings in key pharmacovigilance activities of [redacted]Finland, partly due to quality control and quality assurance. The inspectors reviewed these findings with the company at the closing meeting at the site of the inspection.

The critical findings of the inspection were:

- *poor quality and integrity of pharmacovigilance data*
- *lack of access to pharmacovigilance data in ADR databases*

The major findings of the inspection were:

- *non-compliance of the MAH to meet the regulatory timelines in expedited reporting (≤15 days of initial receipt) of serious ADRs*

There are no procedures for quality control of ADR reporting of [redacted]-Finland, nor checking the CIOMS I form produced by Global [redacted] or other contractual parties against source data to confirm that the information in the CIOMS form is complete and correct. The defects in the CIOMS forms influence also the quality of safety information in the PSURs.

The lack of availability of the ADR information and access to the ADR databases blocks or potentially limits the ability of the ASO and the pharmacovigilance unit of the MAH to perform signal detection activities and to respond promptly e.g. to queries from the NAM. The rapid and effective identification and assessment of drug safety issues is dependent on early access to complete information. This is fundamental to Competent Authorities and MAHs ability to protect public health in taking appropriate action swiftly. In addition, it is against EU legislation that the ADR database is not accessible for the MAH at least at one point within the Community, as is the case with [redacted] database for [redacted] (and possibly with [redacted].

It should be noted that in spite of any contractual arrangements on pharmacovigilance activities with other parties, the legal responsibility in respect of pharmacovigilance of its authorised products rests with the MAH.

These findings represent serious deficiencies and in some cases are direct violations of applicable legislation and/or guidelines. The inspection team considers that the critical and major findings could have a potentially serious public health impact.

As these deficiencies mentioned here are within the pharmacovigilance systems of [redacted]Finland, the issues identified have potential impact on all products of the company, not just on the products selected for specific review as part of this inspection.

The inspection team recommends that [redacted]-Finland should

1. *Revise its SOPs in order to integrate the concept of quality assessment and criteria*
2. *Review the procedures for follow-up of reported cases*
3. *Correct the defective CIOMS forms of [redacted] (and other medicinal products, where defects have been identified)*
4. *Send all expedited reports to the NAM in required timeframe*
5. *Review the mechanisms used to determine the reportability of individual reports (including the determination of expectedness)*

6. *Provide the NAM with all of the expedited reports that have not been submitted within an appropriate time frame*
7. *Notify the NAM in writing of those arrangements for meeting pharmacovigilance obligations that have been made with contractual partners. The notification should be made at the time of marketing authorisation is granted and subsequently, when any changes to the arrangements are made*
8. *Ensure continuous availability of medical cover, experienced in the field of pharmacovigilance, to ensure adequate medical support to the pharmacovigilance activities*

In addition, the company should clarify the following open issues:

9. *Accessibility to the ADR database for* [redacted]
10. *The tracking list of EU cases, submitted by the MAH after the inspection on 31 December 2003) indicates that there are at least 83 EU cases from intensified monitoring programmes or from clinical trials that have not been submitted to the NAM. The MAH should clarify, which of these serious ADRs have occurred in non-interventional post-authorisation studies where the medicinal product is prescribed in the usual manner in accordance with the terms of the marketing authorisation. If so, these ADRs should also be reported on an expedited basis to the NAM (both expected and unexpected ADRs)*

[redacted] responded to the recommendations of the inspection team as follows:

.....

Inspectors' conclusions:

During the pharmacovigilance inspection in December 2003, the NAM identified lack of compliance of [redacted]-Finland with several pharmacovigilance obligations. In the written reply of [redacted]-Finland, the company has committed to make a number of corrective actions to its general procedures for pharmacovigilance. These changes, if implemented, should resolve many of the identified deficiencies. The effectiveness of these actions will be closely monitored by the NAM.

The NAM note that [redacted]-Finland is an affiliate of global [redacted] corporate. However, [redacted]-Finland is the MAH for several dozens of medicinal products and therefore legally responsible for the pharmacovigilance obligations, despite any delegation of pharmacovigilance tasks within the global [redacted] sites or with other contractual partners. The Qualified Person in charge of pharmacovigilance for [redacted]-Finland must ensure that the company fulfils the legal responsibilities according to national and EU legislation.

One critical issue still remains unresolved: the ASO, i.e. the Qualified Person responsible for pharmacovigilance or any other of the personnel of the [redacted]-Finland has no access of the pharmacovigilance databases that contain the ADR data of products for which the company is the MAH in Finland. In their reply to the preliminary inspection report, the company state that the ASO has a key role in the signal detection. The inspection team, however, is not convinced that the ASO or the other pharmacovigilance staff of [redacted] Finland have complete information as a basis for their decisions on safety signals. The same doubt is with the ability of the ASO to respond promptly e.g. to queries from the NAM. The rapid and effective identification and assessment of drug safety issues is dependent on early access to complete information in order to protect public health in taking appropriate action rapidly when needed.

This inspection report is formally informing the company that its pharmacovigilance monitoring and reporting systems are considered to be in a state of serious non-compliance with national and European requirements and require prompt action to correct the system and other faults. The company is warned that failure to rectify this situation in a prompt manner will result in regulatory action.

The inspection team considers that the pharmacovigilance system of [redacted] Finland should be re-inspected after an appropriate time has been allowed for implementation of the suggested changes (e.g. in late 2004).

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Frequent findings (BfArM)

Sales Representatives

Training

Documentation

Archiv

Data Base

Late Cases

Tracking

Th/179/105

Requirements, that the companies have to meet

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Th/179/106

Guideline on monitoring of compliance with pharmacovigilance regulatory obligations and pharmacovigilance inspections

Draft

14. April 2005
EMEA/INS/PhV/119149/2005

(Incorporates Guidance on the detailed description of the MAH's Pharmacovigilance System to be included in the marketing authorisation application)

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Th/179/107

5.1 Statement of the MAH and the qualified person regarding their availability and the means for the notification of adverse reactions

5.2 Location of the Pharmacovigilance system that should be described in the Marketing Authorisation Application

5.3 Elements of the Pharmacovigilance system that should be described in the MAA

5.3.1 Qualified person responsible for Pharmacovigilance

5.3.2 Organisation

5.3.3 Procedures in place which are documented in writing

5.3.4 Databases

5.3.5 Links with other organisations

5.3.6 Training

5.3.7 Documentation

5.3.8 Quality management system

Summary of Pharmacovigilance System (SPS)

Company details

General information

Pharmacovigilance system

Databases and IT systems

Links with other organisations

Quality management system

Personnel

Training records

Documentation

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Th/179/109