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

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Draft
EUDRAVIGILANCE ACCESS POLICY FOR MEDICINES FOR HUMAN USE

EXECUTIVE SUMMARY

The core responsibility of the European Medicines Agency (EMEA) is the protection and promotion of public health through the evaluation and supervision of medicines. Central to this responsibility is the evaluation and coordination of the safety of medicines including the collection, management and dissemination of information on adverse reactions to medicines (pharmacovigilance). The key EU resource to support this activity is EudraVigilance, the European database of adverse reactions related to medicinal products authorised in the Community, and those which are subject to clinical trials.
In the frame of the EU Transparency Initiative and in line with recent Community legislation, the EMEA is in a process of implementing a EudraVigilance Access Policy, which will provide stakeholders such as National Competent Authorities, healthcare professionals, patients and consumers, as well as the pharmaceutical industry with access to adverse reaction data. The protection of personal data and the provision of further information upon request are important elements that are to be addressed in the implementation of the access policy.

1. INTRODUCTION

In the frame of the new Community legislation (i.e. Regulation (EC) No 726/2004, Directive 2001/83/EC as amended as well as Directive 2001/20/EC) the access to EudraVigilance data needs to be implemented taking into account the need to guarantee personal data protection.
This document has been prepared by the EudraVigilance Expert Working Group (EV-EWG) for subsequent discussion with the relevant stakeholders (EudraVigilance Steering Committee, Heads of Medicines Agencies, EMEA Management Board, Marketing Authorisation Holders, Sponsors of Clinical Trials in the EEA, Healthcare Professionals and the General Public). It should be seen as an initial step to implement the requirements within the current legal framework. From a technical point of view the possibility to revise the scope based on the initial experience gained and future revisions of the Community legislation should be taken into account.

2. EUDRAVIGILANCE HUMAN SYSTEM COMPONENTS

EudraVigilance[1] is composed of the following system components:

- **EudraVigilance Gateway**

[1] http://eudravigilance.emea.europa.eu

- The data-processing network for the exchange of adverse reaction data as defined in Regulation (EC) No. 726/2004.

- **EudraVigilance Human**

  A database consisting of two modules to collect suspected adverse reactions related to human medicinal products:
  - EudraVigilance Clinical Trial Module (EVCTM) implemented in line with the requirements defined in Directive 2001/20/EC.
  - EudraVigilance Post-Authorisation Module (EVPM) implemented in line with the requirements defined in Regulation (EC) No. 726/2004.

- **EudraVigilance Medicinal Product Dictionary**
  - Implemented to allow for the standardisation of medicinal product information as reported in Individual Case Safety Reports (ICSRs) in line with Regulation (EC) No. 726/2004, Directive 2001/83/EC as amended, as well as Directive 2001/20/EC.

- **EudraVigilance Data Warehouse and Analysis System**
  - Implemented to support the EU pharmacovigilance activities with main focus on data analysis in line with the requirements defined in Regulation (EC) No. 726/2004, Directive 2001/83/EC as amended, as well as Directive 2001/20/EC.

3. PROPOSED ACCESS TO EUDRAVIGILANCE

3.1 General Principles

3.1.1 Objective of the EudraVigilance Access Policy

According to the provisions laid down in Article 26, paragraph (3) and Article 57, paragraph (1)(d) of Regulation 726/2004, the EMEA should grant 'appropriate levels' of EudraVigilance access to the stakeholders mentioned in Article 57, paragraph (1)(d) (i.e. Healthcare Professionals, Marketing Authorisation Holders and the General Public) whereby personal data protection should be guaranteed.

The access to adverse reaction data collected in EudraVigilance should facilitate the conduct of pharmacovigilance by National Competent Authorities and Marketing Authorisation Holders at Community level and allow for the provision of collated adverse reaction information related to medicinal products to healthcare professionals and the General Public.

3.1.2 Access to EudraVigilance Data

Taking into account the various EudraVigilance system components as outlined in chapter 2, the access to EudraVigilance data will be implemented at the level of the EudraVigilance Data Warehouse and Analysis System (EVDAS) taking into account 'appropriate levels' of access to the various stakeholders and the need for the protection of personal data.

Access to EudraVigilance data will be implemented as follows:

3.1.2.1 Spontaneous Reports

- **National Competent Authorities in the EEA, the European Commission and the EMEA:**
  - The permanent access to EudraVigilance data will include **all individual cases related to spontaneous reports for all types of medicinal products independent of the authorisation procedure** and Authorised Medicinal Product (AMP) information as

collected in the EudraVigilance Medicinal Product Dictionary (EVMPD). Access will be granted to the full information available in the ICSRs.

- Such access to individual cases will always be based on the most complete and most up to date ICSRs as reported electronically to EudraVigilance. ICSRs classified as 'error reports' are excluded.
- The data will be made accessible online via EVDAS in accordance with the detailed access policy as defined in chapter 3.2, which will allow for the use of data analysis and signal detection tools by the National Competent Authorities, the European Commission and the EMEA to monitor the safety of medicinal products.

- **Health Care Professionals and the General Public:**
  - The access to EudraVigilance data will include all individual cases related to spontaneous reports for all types of medicinal products independent of the authorisation procedure.
  - The access to individual cases related to spontaneous reports will always be based on the most complete and most up to date ICSRs reported electronically to EudraVigilance. ICSRs classified as 'error reports'[2] are excluded.
  - The data will be presented as drug analysis prints generated by EVDAS and will be published on the EudraVigilance website at regular intervals without delay after completion of the data quality review, in accordance with the access policy as defined in chapter 3.2.
  - The drug analysis prints will be published with a general guidance on the nature and the interpretation of the data. Such guidance will include general explanations addressing the following key elements:
    - Adverse reaction reports are only a subset of data being dealt with in the frame of pharmacovigilance to safeguard public health. A proper evaluation may require additional measures to assess the safety of medicines e.g., the conduct of post-authorisation studies.
    - A more detailed evaluation of adverse reaction data is mainly performed on case series taking into account other pharmacovigilance information available (e.g. sales and prescription data, pharmacoepidemiological data).
    - Individual causality assessments of adverse reaction reports are not always reliable as the degree of causality often depends on the quality of information supporting a causal association.
    - A routine evaluation of adverse reaction data is foreseen in the legislation in the frame of the EU risk management strategy as well as part of the regular preparation of periodic safety update reports (PSURs). Potential safety issues that may arise in the frame of such evaluation are addressed in form of regulatory actions, which are subsequently communicated to the stakeholders concerned (e.g., changes in the Summary of Product Characteristic (SPC); Dear Doctor Letter).

- **Marketing Authorisation Holders:**
  - The access to EudraVigilance data will include all individual cases related to spontaneous reports for all types of medicinal products independent of the authorisation procedure and AMP information as collected in the EVMPD. Access will be granted in EVDAS to a defined set of data elements as outlined in chapter 3.2, excluding case narrative and other fields which might contain information related to personal data required for pharmacovigilance.
  - The access to individual cases related to spontaneous reports will always be based on the most complete and most up to date ICSRs reported electronically to EudraVigilance. ICSRs classified as 'error reports'[2] are excluded.
  - The data will be made accessible online via EVDAS in accordance with the detailed access policy as defined in chapter 3.2, which will allow for the use of data analysis and

[2] Note for Guidance on the EudraVigilance Human version 7.0 Processing of Safety Messages and Individual Case Safety Reports (ICSRs) (Doc. Ref. EMEA/H/20665/04/Final)

signal detection tools by the Marketing Authorisation Holders to monitor the safety of medicinal products based on the aforementioned data set.

3.1.2.2 Reports from interventional and non-interventional trials

- **National Competent Authorities in the EEA, the European Commission and the EMEA:**
  - The access to EudraVigilance data will include all individual cases related to interventional and non-interventional trials and authorised and Investigational Medicinal Product (IMP) information as collected in the EVMPD. Access will be granted to the full information available in the ICSRs.
  - The access to individual cases will always be based on the most complete and most up to date ICSRs as reported electronically to EudraVigilance. ICSRs classified as 'error reports'[3] are excluded.
  - The data will be made accessible online via EVDAS in accordance with the detailed access policies as defined in chapter 3.2, which will allow for the use of data analysis and signal detection tools by the National Competent Authorities, the European Commission and the EMEA to monitor the safety of medicinal products.

- **Healthcare Professionals and General Public:**
  - There will be no access to interventional and non-interventional study data. These adverse reaction data are reported in the context of defined protocols and are subject to an overall assessment, which summarises the results at the end of the study in a study report.
  - For interventional clinical trials, this is in accordance with Article 17, paragraph (3)(a) of Directive 2001/20/EC, which states that only the National Competent Authorities of the Member States, the EMEA and the European Commission shall have access to ICSRs reported to the EudraVigilance Clinical Trial Module.
  - However, Article 57, paragraph (2) of Regulation (EC) No 726/2004 foresees that references to data on clinical trials currently being carried out or already completed which are contained in the EudraCT database provided for in Article 11, paragraph (1) and (4) of Directive 2001/20/EC, may be also accessible to the public. This is addressed in a Commission guideline published for 'public consultation on the data fields contained in the clinical trials database to be included in the EudraPharm database on medicinal products and made public'.

- **Marketing Authorisation Holders and Sponsors:**
  - There will be no access to interventional and non-interventional study data. These adverse reaction data are reported in the context of defined protocols and are subject to an overall assessment, which summarises the results at the end of the study in a study report.
  - For interventional clinical trials, this is in accordance with Article 17, paragraph (3)(a) of Directive 2001/20/EC, which states that only the National Competent Authorities of the Member States, the EMEA and the European Commission shall have access to ICSRs reported to the EudraVigilance Clinical Trial Module.
  - However, in the frame of the implementation of the electronic transmission of ICSRs it has become evident that many of the smaller commercial and particularly non-commercial sponsors and Small and Medium Size Enterprises (SMEs) do not have the necessary technical tools available that would allow them to evaluate the adverse reaction data related to interventional and non-interventional trials that they conduct in the EEA. This was also discussed in the frame of the conference on the Operation of the Clinical Trials Directive (Directive 2001/20/EC) and Perspective for the Future (3 October 2007)[4]. Therefore it is proposed that for Marketing Authorisation Holders and Sponsors access to EudraVigilance data will be provided which is **restricted to those individual cases**

[3] Note for Guidance on the EudraVigilance Human version 7.0 Processing of Safety Messages and Individual Case Safety Reports (ICSRs) (Doc Ref. EMEA/H/20665/04/Final)

[4] Report on the European Commission-European Medicines Agency Conference on the Operation of the Clinical Trials Directive (Directive 2001/20/EC) and Perspectives for the Future Conference held on 3 October 2007 at the EMEA, London (Doc. Ref. EMEA/565466/2007)

related to interventional and non-interventional trials that they have transmitted electronically to EudraVigilance. Access will be granted to the full information available in the ICSRs.

- The access to individual cases will always be based on the most complete and most up to date ICSRs as reported electronically to EudraVigilance. ICSRs classified as 'error reports'[5] are excluded.
- The data will be made accessible online via EVDAS in accordance with the detailed access policy as defined in chapter 3.2. This kind of access would facilitate the Marketing Authorisation Holders' and Sponsors' undertaking in the monitoring of the patients' safety during the conduct of their trials.

3.1.3 Personal Data Protection and Anonymisation of Adverse Reaction Data

EudraVigilance should operate on the basis of anonymised reports, in a way that it is not possible to identify the patient's identity.

Appropriate rules regarding the anonymisation of data should be put in place to reach a harmonised approach with all stakeholders. These aspects have been addressed at a high level in the frame of the revision of Volume 9A. However, discussions on the detailed practicalities of data anonymisation with regard to the reporting of suspected adverse reaction should be initiated with the European Commission and/or the European Data Protection Supervisor as soon as possible. This refers in particular to patient information (such as the patient's name, date of birth, cause of death) or other identifying details especially with regard to case summary and additional information provided in adverse reaction reports.

3.2 Stakeholder Access to EudraVigilance Data

Based on initial stakeholder consultation with the EV-EWG, the following EudraVigilance Access Policy is targeted to the specific needs of the individual stakeholders, is proposed:

3.2.1 Access Category I: European Commission, EMEA and National Competent Authorities in Member States

3.2.1.1 Access Category IA: EVPM

Based on the provisions of Article 26, paragraph (3) and Article 57, paragraph (1)(d) of Regulation 726/2004 and Article 102 of Directive 2001/83/EC as amended, the following is proposed:

- Authorised personnel of the European Commission, the EMEA and National Competent Authorities in the EEA have full access to all types of ICSRs, which have been reported electronically to EudraVigilance Human – EVPM in accordance with the Community legislation. This includes information on all AMPs stored in the EVMPD.

- The identification of 'authorised personnel' is taking place through the EudraVigilance registration process (http://eudravigilance.emea.europa.eu).

- In Member States, where regional pharmacovigilance centres are established, National Competent Authorities have to determine if the same level of access is granted to these centres (CATEGORY IA). If CATEGORY IA access is not granted to these centres, the access level CATEGORY IIIA can be provided (see below).

[5] Note for Guidance on the EudraVigilance Human version 7.0 Processing of Safety Messages and Individual Case Safety Reports (ICSRs) (Doc Ref. EMEA/H/20665/04/Final)

3.2.1.2 Access Category IB: EVCTM

In line with Article 17, paragraph (3)(a) of Directive 2001/20/EC the following is proposed:

- Authorised personnel of the European Commission, the EMEA and the National Competent Authorities have full access to all types of ICSRs, which have been reported electronically to EudraVigilance Human – EVCTM in accordance with the Community legislation. This includes information on all IMPs stored in the EVMPD.

- Identification of 'authorised personnel' is taking place through the EudraVigilance registration process (http://eudravigilance.emea.europa.eu).

3.2.2 Access Category II: Health Care Professionals and the General Public

3.2.2.1 Access Category IIA: EVPM

In relation to Article 57, paragraph (1)(d) of Regulation (EC) No. 726/2004 and Article 102 of Directive 2001/83/EC as amended, the following is proposed:

- Health Care Professionals and the General Public have access to spontaneous reports transmitted electronically to EudraVigilance Human - EVPM via an aggregated output of a subset of data. The subset of data elements is described in Annex 1. The reports, which contain aggregated data, are published without delay after completion of the data quality review on the EudraVigilance website.

3.2.2.2 Access Category IIB: EVCTM

In line with Directive 2001/20/EC, there will be no access provided to health care professionals or the general public in relation to ICSR and EVMPD data stored in EVCTM.

3.2.3 Access Category III: MAHs and Sponsors of Clinical Trials in the EEA

3.2.3.1 Access Category IIIA: EVPM

Based on Regulation (EC) No 726/2004/EC, Article 57, paragraph (1)(d), and Article 102 of Directive 2001/83/EC as amended, the following is proposed:

- Authorised personnel of the MAH have access to a subset of the ICSR data fields in EVDAS, which have been reported electronically to EudraVigilance Human – EVPM in accordance with the Community legislation. This includes information on spontaneous reports and all AMPs stored in the EVMPD. The subset of data elements is described in Annex 2.

- In this context, authorised personnel is interpreted as
  - The Qualified Person Responsible for Pharmacovigilance as defined in Regulation (EC) No 726/2004, Article 23 and in Directive 2001/83/EC, Article 103 and
  - The appointed 'EudraVigilance Deputy' at the EU company headquarters' level as defined in the frame of the EudraVigilance registration process.

- Identification of 'authorised personnel' is taking place through the EudraVigilance registration process (http://eudravigilance.emea.europa.eu).

3.2.3.2 Access Category IIIB: EVCTM

For sponsors of clinical trials conducted in the EEA, access to EVCTM is granted on the basis of the following principles:

- Authorised personnel of the sponsor have access to those ICSRs in EVDAS, which the sponsor has reported electronically to EudraVigilance Human – EVCTM in accordance with the Community legislation. This includes information on the IMPs entered by the sponsor in the EVMPD.

- In this context, authorised personnel refers to the 'Person Responsible for EudraVigilance' appointed by the sponsor in the frame of the EudraVigilance registration process (http://eudravigilance.emea.europa.eu).
  If the sponsor is also a MAH, the authorised personnel would be defined as
  - The Qualified Person Responsible for Pharmacovigilance as defined in Regulation (EC) No 726/2004, Article 23 and in Directive 2001/83/EC as amended, Article 103 and
  - The appointed 'EudraVigilance Deputy at the EU company headquarters' level as defined in the frame of the EudraVigilance registration process.

- Identification of 'authorised personnel' is taking place through the EudraVigilance registration process (http://eudravigilance.emea.europa.eu).

4. IMPLEMENTATION OF THE EUDRAVIGILANCE ACCESS POLICY

It is proposed that a stepwise approach is applied to implement the EudraVigilance Access Policy.
In a first phase access is granted to the National Competent Authorities. This has been achieved through the roll-out of EVDAS to the Member States in July 2007.

In a second phase, access will be granted to healthcare professionals and the general public, initially for centrally authorised products, and in a next phase to be stepwise extended for all active substances and medicinal products depending on the EVMPD population.

In parallel, access will be provided to Marketing Authorisation Holders and Sponsors of Clinical Trials in the EEA, initially for those Marketing Authorisation Holders and Sponsors currently registered, and in a next phase to be stepwise extended to all other Marketing Authorisation Holders and Sponsors.

However, in order to successfully implement the EudraVigilance Access Policy, a number of pre-requisites need to be fulfilled to ensure high quality and a correct output of the data.

This refers to procedural issues such as the:

- Manual recoding of medicinal product information reported in ICSRs
- EVMPD population
- Duplicate detection and management of ICSRs

As well as technical issues such as the:

- Need to update the EVMPD taking into account the scientific progress in the area of drug development. This refers in particular to the elements required to characterise biologics, herbals, advanced therapies and medicinal products designated for the use in the paediatric population.
- Full availability of the automatic and manual recoding functionalities of medicinal product information reported in ICSRs.
- Grouping functionalities, to aggregate substance and product specific adverse reaction data.
- Fully operational duplicate detection algorithm and management functions for ICSRs.

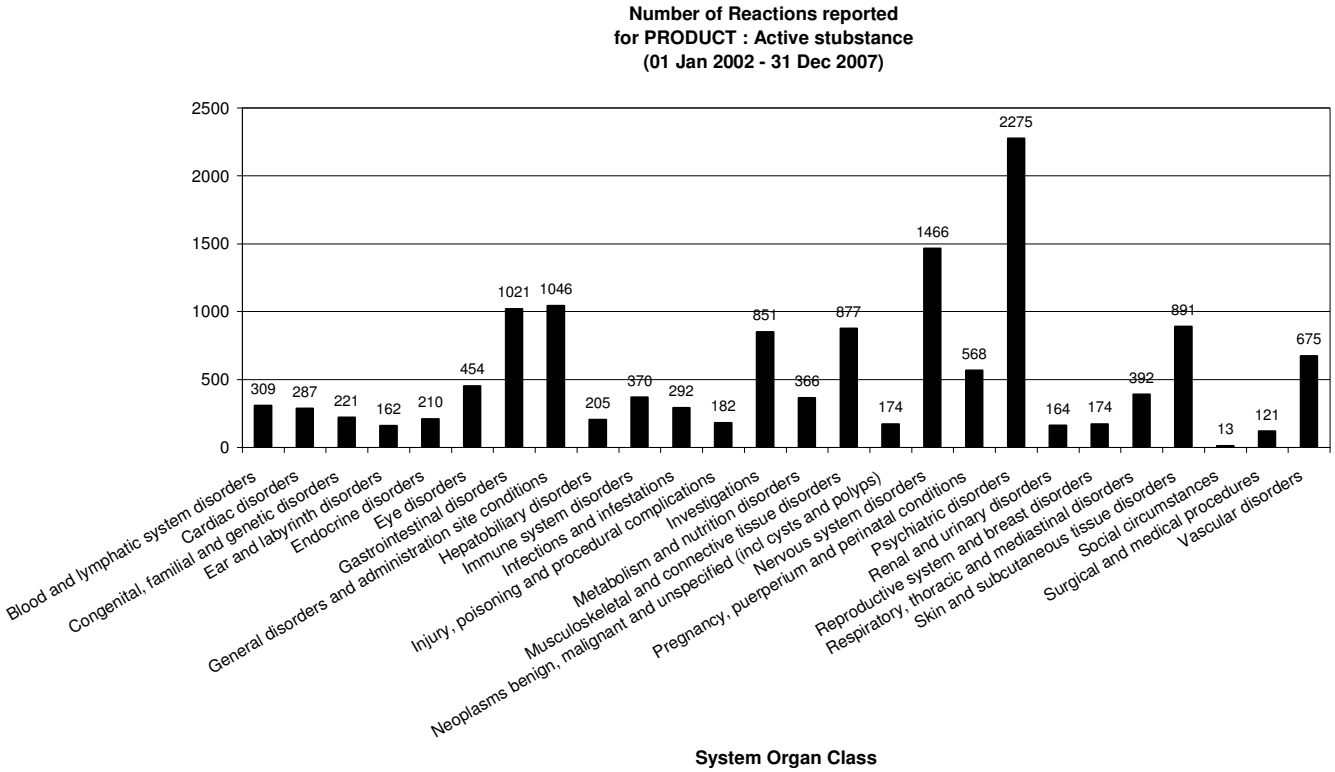
ANNEX 1: DATA ELEMENTS EVPM ACCESS CATEGORY II

The search function provided on the EudraVigilance website will allow in a first step e.g. to select an active substance or a fixed combination of several active substances for centrally authorised medicinal products; in a 2nd step this functionality will be further extended to active substances of all other types of medicinal products (depending on the population of the EVMPD).

Examples for a possible data output are provided as follows:

- For single ingredient medicinal products, the name of the active substance and the related medicinal product name (e.g. PRODUCT: Active substance(s)). If the active substance is also part of a fixed combination product, the data available on the fixed combination will be also displayed separately. Total number of spontaneous reports received for which the selected active ingredient(s) is/are suspected or interacting. Only the valid reports with the most recent information are counted, excluding nullification reports.
- Age of the patient expressed as age groups in accordance with E2B(R2)
- Gender of the patient (male, female, unspecified, unknown)
- Total number of reactions reported
- Presentation of System Organ Classes (SOCs) Number of reactions reported at PT level per SOC; each adverse reaction will be presented at PT level and will only be displayed once at the level of the Primary SOC

a) Number of reactions reported to EudraVigilance for PRODUCT: Active substance(s) during a specified period of time, stratified by System Organ Class

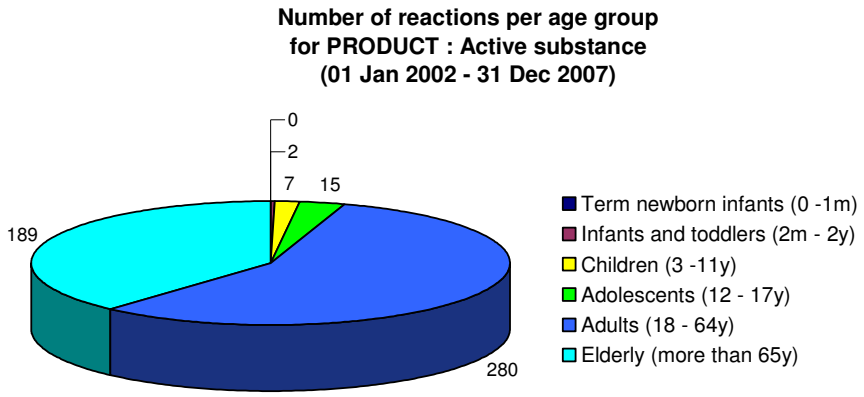


b) Number of suspected adverse reactions (MedDRA Preferred Terms reported to EudraVigilance) for PRODUCT: Active substance(s) during a specified period of time, stratified by System Organ Class and origin (EEA, non-EEA).

Number of reactions reported at Preferred Term level per System Organ Class (SOC) for PRODUCT: Active substance (01 Jan 2002 - 31 Dec 2007)

SOC	Reaction Preferred Term	Total	EEA	Non EEA
Blood and lymphatic system disorders				
	Aplastic anaemia	6	2	3
	Autoimmune thrombocytopenia	3	2	1
	Bone marrow failure	9	6	3
	Coagulopathy	90	20	70
	Coombs negative haemolytic anaemia	1	0	1
	Disseminated intravascular coagulation	52	12	40
	Eosinophilia	28	14	14
	Factor V inhibition	1	0	1
	Factor VIII inhibition	1	1	0
	Febrile neutropenia	4	1	3
Cardiac disorders				
	Acute myocardial infarction	6	0	6
	Angina pectoris	1	0	1
	Arrhythmia	19	5	14
	Arteriosclerosis coronary artery	3	0	3
	Atrial fibrillation	22	2	20
	Atrioventricular block	5	2	3
	Cardiac failure	14	11	3
	Cardiotoxicity	10	0	10
	Hypertensive heart disease	2	0	2
	Myocardial fibrosis	1	0	1
	Myocardial infarction	36	11	25
	Myocardial ischaemia	2	1	1
	Nodal arrhythmia	1	0	1
Congenital, familial and genetic disorders				
	Cleft lip and palate	1	1	0
	Congenital anomaly	2	1	1
	Congenital aortic stenosis	1	0	1
	Congenital eyelid malformation	1	1	0
	Dysmorphism	3	2	1
	Epidermolysis	1	1	0
	Intestinal malrotation	1	0	1
	Limb reduction defect	1	1	0
Ear and labyrinth disorders				
	Deafness	3	0	3
	Deafness transitory	1	0	1
	Ear discomfort	1	0	1
	Ear pain	4	0	4
	Ear pruritus	1	0	1
	Hearing impaired	1	0	1
	Hypoacusis	1	0	1
	Middle ear effusion	1	0	1
	Otorrhoea	1	0	1
	Sudden hearing loss	1	0	1
	Tinnitus	4	1	3
	Vertigo	11	7	4

c) Number of suspected adverse reactions reported to EudraVigilance for PRODUCT: Active substance(s) during a specified period of time, stratified by age group



ANNEX 2: ICH E2B(R2) DATA ELEMENTS EVPM ACCESS CATEGORY III

1 A. ADMINISTRATIVE AND IDENTIFICATION INFORMATION

1.1 *A.1 Identification of the case safety report*

A.1.0.1 Sender's (case) safety report unique identifier
A.1.1 Identification of the country of the primary source
A.1.2 Identification of the country where the reaction/event occurred

A.1.4 Type of report
- *Spontaneous report*

A.1.5 Seriousness
A.1.5.1. Serious
- *Yes/no*

A.1.5.2. Seriousness criteria (more than one can be chosen)
- *Results in death*
- *Is life-threatening*
- *Requires inpatient hospitalization or prolongation of existing hospitalization*
- *Results in persistent or significant disability/incapacity (as per reporter's opinion)*
- *Is a congenital anomaly/birth defect*
- *Other medically important condition*

A.1.9 Does this case fulfill the local criteria for an expedited report?
- *yes/no*

A.1.10 Worldwide unique case identification number
A.1.10.1 Regulatory authority's case report number
A.1.10.2 Other sender's case report number
A.1.11 Other case identifiers in previous transmissions
- *yes*

A.1.11.1 Source(s) of the case identifier (e.g., name of the company, name of regulatory agency)
A.1.11.2 Case identifier(s)
A.1.12 Identification number of the report which is linked to this report (repeat as necessary)
A.1.13 Report nullification
- *yes*

A.1.13.1 Reason for nullification
A.1.14 Was the case medically confirmed, if not initially from a health professional?
- *yes/no*

1.2 *A.2 Primary source(s) of information*

A.2.1.3 Country
A.2.1.4 Qualification
- *Physician*
- *Pharmacist*
- *Other health professional*
- *Lawyer*
- *Consumer or other non health professional*

A.2.2 Literature reference(s)

1.3 *A.3 Information on sender and receiver of case safety report*

A.3.1 Sender
A.3.1.1 Type
- *Pharmaceutical company*
- *Regulatory authority*
- *Health professional*
- *Regional pharmacovigilance center*
- *WHO collaborating center for international drug monitoring*
- *Other* (e.g. distributor, study sponsor, or contract research organization)

A.3.1.2 Sender identifier

2 B. INFORMATION ON THE CASE

2.1 *B.1 Patient characteristics*

B.1.2 Age information
B.1.2.1 Date of birth (To be expressed as age)
B.1.2.2 Age at time of onset of reaction/event (To be expressed as age)
B.1.2.2.1 Gestation period when reaction/event was observed in the fetus
B.1.2.3 Patient age group (to be specified as age based on the distribution of overall age in EVDAS)
- *Neonate*
- *Infant*
- *Child*
- *Adolescent*
- *Adult*
- *Elderly*

B.1.3 Weight (kg)
B.1.4 Height (cm)
B.1.5 Sex
B.1.6 Last menstrual period date
B.1.7 Relevant medical history and concurrent conditions (not including reaction/event)
B.1.7.1 Structured information on relevant medical history including onset and resolution date as well as relevant comments
B.1.8 Relevant past drug history (repeat the line as necessary)
Name of drug as reported, Start date, End date, Indication, Reactions
B.1.9 In case of death
B.1.9.2 Reported cause(s) of death (repeat as necessary)
B.1.9.3 Was autopsy done?
- *Yes/No/Unknown*

B.1.9.4 Autopsy-determined cause(s) of death (repeat as necessary)
B.1.10 For a parent-child/fetus report, information concerning the parent
B.1.10.2 Parent age information
B.1.10.2.1 Date of birth of parent (to be specified as age)
B.1.10.2.2 Age of parent
B.1.10.3 Last menstrual period date
B.1.10.4 Weight (kg) of parent
B.1.10.5 Height (cm) of parent
B.1.10.6 Sex of parent
B.1.10.7 Relevant medical history and concurrent conditions of parent (not including reaction/event)
B.1.10.7.1 Structured information (parent)
Disease/surgical procedure/ etc., Start date, Continuing Y/N/U, End date, Comments
B.1.10.8 Relevant past drug history of parent
Name of drug as reported; Start date, End date, Indication, Reactions (if any and known)

2.2 *B.2 Reaction(s)/event(s)*

B.2.i.0 Reaction/event as reported by the primary source
B.2.i.1 Reaction/event in MedDRA terminology (Lowest Level Term)
B.2.i.2 Reaction/event MedDRA term (Preferred Term)
B.2.i.3 Term highlighted by the reporter
1= Yes, highlighted by the reporter, NOT serious
2= No, not highlighted by the reporter, NOT serious
3= Yes, highlighted by the reporter, SERIOUS
4= No, not highlighted by the reporter, SERIOUS
B.2.i.4 Date of start of reaction/event
B.2.i.5 Date of end of reaction/event
B.2.i.6 Duration of reaction/event
B.2.i.7 Time intervals between suspect drug administration and start of reaction/event
B.2.i.7.1 Time interval between beginning of suspect drug administration and start of reaction/event
B.2.i.7.2 Time interval between last dose and start of reaction/event
B.2.i.8 Outcome of reaction/event at the time of last observation
- recovered/resolved
- recovering/resolving
- not recovered/not resolved
- recovered/resolved with sequelae
- fatal
- unknown

2.3 *B.3 Results of tests and procedures relevant to the investigation of the patient*

B.3.1 Structured information (repeat as necessary)
Date Test, Result, Unit, Normal low range, Normal high range, More information available (*Y/N*)
B.3.2 Results of tests and procedures relevant to the investigation

2.4 *B.4 Drug(s) information*

B.4.k.1 Characterization of drug role
- Suspect
- Concomitant
- Interacting
B.4.k.2 Drug identification
B.4.k.2.1 Proprietary medicinal product name (as reported)
Proprietary medicinal product name (as recoded by the EMEA)
B.4.k.2.2 Active substance name(s) (as reported)
Active substance name(s) (as recoded by the EMEA)
B.4.k.2.3 Identification of the country where the drug was obtained
B.4.k.3 Batch/lot number
B.4.k.4 Holder and authorization/application number of drug
B.4.k.4.1 Authorization/Application Number
B.4.k.4.2 Country of authorization/application
B.4.k.4.3 Name of holder/applicant
B.4.k.5 Structured Dosage Information
B.4.k.5.1 dose (number)
B.4.k.5.2 dose (unit)
B.4.k.5.3 number of separate dosages
B.4.k.5.4 number of units in the interval
B.4.k.5.5 definition of the interval unit
B.4.k.5.6 cumulative dose to first reaction (number)
B.4.k.5.7 cumulative dose to first reaction (unit)
B.4.k.6 Dosage text
B.4.k.7 Pharmaceutical form (Dosage form)
B.4.k.8 Route of administration

B.4.k.9 Parent route of administration (in case of a parent child/fetus report)
B.4.k.10 Gestation period at time of exposure
B.4.k.11 Indication for use in the case
B.4.k.12 Date of start of drug
B.4.k.13 Time intervals between drug administration and start of reaction/event
B.4.k.13.1 Time interval between beginning of drug administration and start of reaction/event
B.4.k.13.2 Time interval between last dose of drug and start of reaction/event
B.4.k.14 Date of last administration
B.4.k.15 Duration of drug administration
B.4.k.16 Action(s) taken with drug
- *Drug withdrawn*
- *Dose reduced*
- *Dose increased*
- *Dose not changed*
- *Unknown*
- *Not applicable*

B.4.k.17 Effect of rechallenge (or re-exposure), for suspect drug(s) only
B.4.k.17.1 Did reaction recur on readministration?
-*yes/no/unknown*

3 ADDITIONAL DATA ELEMENTS NOT INCLUDED IN ICH E2B(R2) BUT TO BE ACCESSIBLE

- EudraVigilance LOCAL NUMBER EU-EC-XXXXXX
  (as returned by EudraVigilance in the Acknowledgment Message)
- Case Classification (e.g. Initial, Follow-up, Report Nullification)
- Internal EMEA field Message Official Receive Date (as captured at the level of the EudraVigilance Gateway)
- Document type that specifies the type of transmission
- Sex of the patient (B.1.5) ICH E2B(R2) values are: 1 Male, 2 Female. Unknown and unspecified are maintained due to backwards compatibility with ICH E2B (R1) version 2.0)

DEFINITIONS

AMP	Authorised Medicinal Product
EEA	European Economic Area
EMEA	European Medicines Agency
EudraCT	European Clinical Trials Database
EudraPharm	Website with information on all medicinal products for human or veterinary use that have been authorised in the European Union (EU) and the European Economic Area (EEA)
EVCTM	EudraVigilance Clinical Trial Module
EVDAS	EudraVigilance Data Warehouse and Analysis System
EV-EWG	EudraVigilance Expert Working Group
EVMPD	EudraVigilance Medicinal Product Dictionary
EVPM	EudraVigilance Post-Authorisation Module
ICSR	Individual Case Safety Report
IMP	Investigational Medicinal Product
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities[6]
PSUR	Periodic Safety Update Report
PT	Preferred Term
SME	Small and Medium Size Enterprises
SOC	System Organ Class
SPC	Summary of Product Characteristic

[6] http://www.meddramsso.com

REFERENCES (scientific and / or legal)

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 (*Official Journal L 136, 30/4/2004 p. 1 - 33*).

Consolidated 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 as amended by Directive 2002/98/EC, Directive 2004/24/EC and Directive 2004/27/EC.

Directive 2001/20/EC OF the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (*Official Journal L 121, 1/5/2001 p. 34 - 44*).

Note for Guidance on the EudraVigilance Human version 7.0 Processing of Safety Messages and Individual Case Safety Reports (ICSRs) (Doc. Ref. EMEA/H/20665/04/Final)

Report on the European Commission-European Medicines Agency Conference on the Operation of the Clinical Trials Directive (Directive 2001/20/EC) and Perspectives for the Future Conference held on 3 October 2007 at the EMEA, London (Doc. Ref.: EMEA/565466/2007)