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EudraVigilance access policy for medicines for human use

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Executive summary

The core responsibility of the European Medicines Agency 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 suspected adverse reactions to medicines (pharmacovigilance). The key European Union (EU) resource to support this activity is EudraVigilance, a centralised European database of suspected adverse reactions related to medicinal products authorised in the European Economic Area (EEA) and those that are subject to clinical trials.

In compliance with current EU legislation (i.e. Regulation (EC) No 726/2004, Directive 2001/83/EC as amended and Directive 2001/20/EC) the European Medicines Agency has developed this Access Policy to provide stakeholders such as Medicines Regulatory Authorities, healthcare professionals, patients and consumers, as well as the pharmaceutical industry and research organisations with certain levels of access to suspected adverse reactions reported to EudraVigilance. The Agency considers the proactive and reactive disclosure of Individual Case Safety Reports (ICSRs) as complementary by putting the principle of transparency into effect in the sense that maximum data are released proactively, that the needs of the public are met and that the requirements of personal data protection pursuant to the provisions of Regulation (EC) No 45/2001 are adhered to.

Public health concerns may materialise when Medicines Regulatory Authorities proactively communicate possible risks to the general public. The Agency believes that it is its mandate, in line with Regulation (EC) No 726/2004 to ensure that information on suspected adverse reactions are made publicly available to the extent, timing and manner that are appropriate.

Since 2007, the Agency is granting Medicines Regulatory Authorities in the EEA with unrestricted access to all ICSRs held in EudraVigilance. In the context of this Access Policy, healthcare professionals, consumers and patients, the pharmaceutical industry and research organisations will be also provided with certain levels of access to spontaneous reports held in the European pharmacovigilance database. Differences as regards the level of access for these stakeholders will only apply to the tools by which the data are made available.

Healthcare professionals, consumers and patients will have the possibility to search and screen data by means of easy to use retrieval functions provided at the Agency's website and user friendly report outputs (e.g. as aggregated summary reports or individual case report forms).

The pharmaceutical industry, which has legal obligations to continuously monitor the safety of medicines and research organisations will be provided with access to signal detection and analysis tools of the EudraVigilance Data Warehouse and Analysis System (EVDAS) with the overall objective to contribute to the protection of public health of citizens in the EU. Study protocols of research organisations will be subject to prior review by the Agency.

In summary, this Access Policy follows the approach that information related to safety signals of medicinal products will be disclosed on a systematic basis proactively with adherence to the requirements of personal data protection. The aim is to provide the highest possible degree of transparency and minimising the necessity to engage in ad-hoc reactive disclosure of information based on individual requests.

1. Background

In line with current EU legislation (i.e. Regulation (EC) No 726/2004[1], Directive 2001/83/EC[2] as amended and Directive 2001/20/EC[3]), the European Medicines Agency (hereafter referred to as the 'Agency') is in a process of implementing a policy that provides certain levels of access to Individual Case Safety Reports (ICSRs) reported to EudraVigilance, taking into account the need to protect personal data as defined by Regulation (EC) No 45/2001[4].

In 2008 a draft EudraVigilance Access Policy (hereafter referred to as 'Access Policy') was prepared by the EudraVigilance Expert Working Group (EV-EWG) in liaison with the EudraVigilance Steering Committee, Heads of Medicines Agencies and the Agency's Management Board.

The Agency released the draft Access Policy for a three months public consultation from December 2008 to March 2009 to provide interested parties the opportunity to comment. Twenty-two interested organisations and individuals provided feedback on the draft Access Policy.

All comments received were consolidated and reviewed by the Agency and the draft Access Policy was revised as applicable. An overview of the comments received and the outcome of the review of the comments by the Agency is presented in the document referenced as EMA/432253/2009.

Furthermore, on 7 September 2009, the Agency received the final Opinion[5] on "a Notification for Prior Checking regarding the data processing operations of EudraVigilance" from the European Data Protection Supervisor (EDPS). In its response dated 7 December 2009, the Agency has made proposals on how to address the recommendations of the EDPS, which have also been taken into account in the finalisation of this Access Policy.

Draft recommendations[6] of the European Ombudsman (EO) issued in April 2010 as regards the Agency's activities for stakeholders to have appropriate levels of access to information, which is easily accessible and user-friendly, are also being taken into account.

Anticipated changes to the pharmaceutical legislation have been considered in the drafting of this Access Policy, where possible. This relates in particular to the two legislative proposals[7,8] aimed at amending the current legal framework. It should be noted that further adaptations of the EudraVigilance Access Policy may be necessary once the revision of the legal framework comes into force.

1 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.
2 Of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Consolidate version : 30/12/2008).
3 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.
4 Of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data.
5 Opinion on a Notification for Prior Checking Received from the Data Protection Officer of the European Medicines Agency regarding the EudraVigilance database, Brussels, 7 September 2009 (Case 2008-402).
6 Draft Recommendation of the European Ombudsman in his inquiry into complaint 2493/2008 (BB)TS against the European Medicines Agency, April 2010.
7 Proposal for a Directive of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use:{SEC(2008) 2670}{SEC(2008) 2671}, Brussels, 10.12.2008, COM(2008) 665 final, 2008/0260 (COD).
8 Proposal for a Regulation of the European Parliament and of the Council amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency:{SEC(2008) 2670}{SEC(2008) 2671}, Brussels, 10.12.2008, COM(2008) 664 final, 2008/0257 (COD).

2. Introduction

According to the provisions laid down in article 26, paragraph (3) and article 57, paragraph (1)(d) of Regulation (EC) No 726/2004, the Agency should grant 'appropriate levels' of access to EudraVigilance to the stakeholders mentioned in article 57, paragraph (1)(d) (i.e. healthcare professionals, Marketing Authorisation Holders (MAHs) and the general public) whilst personal data protection should be guaranteed. For ICSRs originating from clinical trials the provisions of article 11, paragraph (1) of Directive 2001/20/EC apply i.e. these reports can only be shared between the Medicines Regulatory Authorities in the EEA, the Agency and the European Commission.

This Access Policy defines the overall principles of the provision of access to EudraVigilance data in line with the current legal framework and taking into account that the interest in and the use of the data may vary between stakeholders.

In addition, the requirement to protect personal data based on Regulation (EC) No 45/2001 and the overall recommendations of the EDPS as set out in his Opinion published on 7 September 2009 was also assessed and taken into account by the Agency.

Furthermore, in line with the draft recommendations of the EO issued in April 2010, the Access Policy considers proactive and reactive information disclosure as complementary i.e. the maximum possible information is proactively made available sparing the need for additional requests by stakeholders. As part of its proactive information policy, the Agency will also provide additional explanations to facilitate the understanding of the data that are made accessible.

Detailed specifications related to the technical implementation of the Access Policy are being further elaborated by the EV-EWG taking into account the overall principles set out in this document.

3. Objectives of the EudraVigilance access policy

This Access Policy has been developed to contribute to public health protection, to facilitate the implementation of the European transparency initiatives and to comply with EU personal data protection legislation. By providing proactive access to adverse reaction data collected in EudraVigilance, the following objectives should be met:

- Facilitate the monitoring of the safety of medicines during clinical trials and following their authorisation and marketing by Medicines Regulatory Authorities and the Agency;
- Support the signal detection and safety evaluation activities of Medicines Regulatory Authorities, MAHs and the Agency in the context of spontaneous reporting for authorised medicines;
- Make publicly available collated adverse reaction data related to spontaneous reports for authorised medicines and to inform healthcare professionals and the general public;
- Allow for the use of adverse reaction data for research purposes.

4. EudraVigilance and medicinal products for human use

EudraVigilance[9] serves multiple functions, which relate to the secure electronic transmission of ICSRs, the collection and management of these reports in a centralised database and most importantly the early detection of safety issues and the medical evaluation thereof. To support these activities, EudraVigilance is composed of the following main system components:

9 http://eudravigilance.ema.europa.eu

- **Data processing and management system components**
  - **EudraVigilance Gateway**, a data-processing network for the secure exchange of adverse reaction data as referred to in Regulation (EC) No 726/2004.
  - **EudraVigilance Clinical Trial Module (EVCTM)** dedicated to the collection and management of ICSRs in the context of interventional clinical trials in line with Directive 2001/20/EC.
  - **EudraVigilance Post-Authorisation Module (EVPM)** dedicated to the collection of ICSRs related to all medicinal products authorised in the EEA in line with Regulation (EC) No 726/2004 and Directive 2001/83/EC as amended.
  - **EudraVigilance Medicinal Product Dictionary (EVMPD),** implemented to allow for the coding of medicinal product information as reported in Individual Case Safety Reports (ICSRs).
- **Data analysis and signal detection component**
  - **EudraVigilance Data Warehouse and Analysis System (EVDAS),** implemented to support the EU pharmacovigilance activities with main focus on signal detection and medical assessment of ICSRs.

Adequate quality of ICSRs as reported to EudraVigilance by Medicines Regulatory Authorities, MAHs and Sponsors is paramount in implementing this Access Policy. Following discussions at the level of Heads of Medicines Agencies in April 2008, the Agency has initiated a major data quality review and management process to ensure that high quality data are made available to stakeholders.

This refers in particular to the responsibilities of Medicines Regulatory Authorities, MAHs and Sponsors for the:

- Adequate documentation of individual cases and their follow-up in accordance with the ICH E2B(R2) guideline[10] and Volume 9A;
- MedDRA coding in line with the MedDRA Term Selection Points to Consider document;
- Local detection and management of duplicated individual cases;
- Adherence with the expedited reporting timelines of suspected (unexpected) serious adverse reactions as defined in EU legislation;

and the responsibility of the Agency for the:

- Coding of medicinal product information reported in ICSRs against the EVMPD in the absence of an international standard for the identification of medicinal products including product variants and synonyms;
- Data validation in accordance with the business rules as defined in EU guidance[11] and the ICSR electronic case management practices set out in Volume 9A;
- Detection and management of duplicated individual cases, which can occur based on current adverse reaction rules and practices as set out in EU legislation and the creation of Master Cases as referred to in EU guidance[12];

10 E2B(R2): Maintenance of the Clinical Safety Data Management including Data Elements for Transmission of Individual Case Safety Reports; the tripartite harmonized ICH guideline was finalized as E2B (Step 4) in July 1997 and amended for Maintenance as E2B(R1) on 10 November 2000. Post Step 4 editorial corrections were given on 5 February 2001 (second revision) and the guideline renamed E2B(R2).
11 Note for Guidance EudraVigilance Human – Processing of Safety Messages and Individual Case Safety Reports (ICSRs), Doc. Ref. EMEA/H/20665/04/Final, in the latest version.
12 CHMP Guideline on Detection and Management of Duplicate Individual Cases and Individual Case Safety Reports (ICSRs) (Doc. Ref. EMA/13432/2009).

- Monitoring of the adherence with the expedited reporting timelines.

5. Access to data held in EudraVigilance

5.1. Stakeholder groups

The stakeholder groups being granted access to EudraVigilance data can be summarised as follows:

- Medicines Regulatory Authorities, the European Commission and the Agency (hereafter referred to as Stakeholder Group I)
- Healthcare Professionals and the General Public (hereafter referred to as Stakeholder Group II)
- Marketing Authorisation Holders and Sponsors of Clinical Trials (hereafter referred to as Stakeholder Group III)
- Research Organisations (hereafter referred to as Stakeholder Group IV)

5.2. Overview

A summary of access to ICSRs held in EudraVigilance based on different stakeholder groups and the principles outlined in Chapters 5.1 and 5.3 is provided in Tables 1 to 4. As a general principle, the same ICSR data set is made accessible to healthcare professionals, the public, marketing authorisation holders, sponsors of clinical trials and research organisations, taking into account the need to comply with Regulation (EC) No 45/2001 on personal data protection.

This ICSR data element set is presented in Annex 1 in accordance with the ICH E2B guideline. Differences refer only to the tools by which the data are made available, taking into account the stakeholders interests' and needs.

Table 1. Access to EudraVigilance data by medicines regulatory agencies in the EEA

Stakeholder Group I	**ICSR Type**			**ICSR Type**		
	Spontaneous Report Other Not available to sender (unknown)			Report from Study		
	Disclosure	**Access Tools**	**Access Authorisation**	**Disclosure**	**Access Tools**	**Access Authorisation**
Medicines Regulatory Authorities (EEA) European Medicines Agency European Commission	All data elements for all ICSRs reported to EudraVigilance	EVDAS EVPM EVCTM	Authorised Personnel	All data elements for all ICSRs reported to EudraVigilance	EVDAS EVPM EVCTM	Authorised Personnel

Table 2. Access to EudraVigilance data by healthcare professionals and the general public

Stakeholder Group II	**ICSR Type**			**ICSR Type**		
	Spontaneous Report			Report from Study		
	Disclosure	**Data Access**	**Access Authorisation**	**Disclosure**	**Data Access**	**Access Authorisation**
Healthcare Professionals General Public	Subset of ICSR data elements in compliance with EU personal data protection legislation	European Medicines Agency's website	Not required	No disclosure	Not applicable	Not applicable

Table 3. Access to EudraVigilance data by marketing authorisation holders and sponsors

Stakeholder Group III	ICSR Type: Spontaneous Report			ICSR Type: Report from Study		
	Disclosure	**Access Tools**	**Access Authorisation**	**Disclosure**	**Access Tools**	**Access Authorisation**
Marketing Authorisation Holders Sponsors of clinical trials	Subset of ICSR data elements in compliance with EU personal data protection legislation 'Sender-based' access to complete ICSR	EVDAS incl. signal detection/ data analysis tools to facilitate compliance with pharmacovi-gilance obligations as defined in EU legislation	Authorised Personnel as designated by the EU QPPV, the Responsible Person for EudraVigilance or the appointed Deputy	Restricted 'Sender-based' access to all ICSR data elements No disclosure of ICSRs from other senders	EVDAS	Authorised Personnel as designated by the by the EU QPPV, the Responsible Person for EudraVigilance or the appointed Deputy

Table 4. Access to EudraVigilance data by research organisations

Stakeholder Group IV	ICSR Type: Spontaneous Reports			ICSR Type: Reports from Study		
	Disclosure	**Access Tools**	**Access Authorisation**	**Disclosure**	**Access Tools**	**Access Authorisation**
Research Organisations	Subset of ICSR data elements in compliance with EU personal data protection legislation	EVDAS incl. signal detection/ data analysis tools to facilitate research	Authorised Research Personnel	No disclosure	Not applicable	Not applicable

5.3. General principles

Adverse reaction data collected in EudraVigilance are derived from the legal obligations placed on Medicines Regulatory Authorities, MAHs and Sponsors in the EEA and include at present only reports which have been medically confirmed by a healthcare professional. Suspected adverse reactions directly reported by patients or consumers are currently not reportable to EudraVigilance but their

notification is proposed in the context of the legislative proposals aimed at amending the current legal framework.

The obligation of Medicines Regulatory Authorities to inform MAHs about suspected serious adverse reactions that have initially been reported to them by healthcare professionals or other sources remains as outlined in EU legislation. Since all Medicines Regulatory Authorities have access to EudraVigilance, there is no need for a MAH to notify other Medicines Regulatory Authorities in the EEA about ICSRs where their medicinal product is also reported as suspect or interacting and which have been reported by other MAHs to EudraVigilance.

The Agency grants access to EudraVigilance by taking into account the different types of ICSRs independent of the primary and the secondary source(s).

5.3.1. ICSR types

The following ICSR types are defined in the ICH E2B(R2)[13] guideline:

- Spontaneous report
- Report from study
- Other
- Not available to sender (unknown)

Reports described in the world-wide literature are not captured as a separate type of report. If a case in the literature arises from spontaneous observations, the type of report is classified as 'Spontaneous'. If the case arises from a study, the type of report is classified as 'report from study'. If it is unclear from the literature report whether or not the case(s) cited are spontaneous observations or arise from a study, then it is classified as 'Other'.

The 'Not available to sender' option is intended for reports, where the initial sender did not specify the type of report; it differs from 'Other' which indicates the sender knows the type of report but cannot fit it into the categories provided.

5.3.2. Primary and secondary report sources

The primary source of the information is a person who reports the facts. This should be distinguished from a sender (secondary source) who is transmitting the information (e.g., MAH sending a report on to EudraVigilance). Depending on the type of ICSR as described in chapter 5.3.1. , access is granted to all reports independent of the report source.

5.3.3. Individual cases, ICSRs and classification rules

An **Individual Case** is the information provided by a primary source to describe suspected adverse reaction(s) related to the administration of one or more medicinal products (including investigational medicinal products) to an individual patient at a particular point of time.

An **Individual Case Safety Report (ICSR)** provides the most complete information related to an individual case at a certain point of time. An individual case can be associated with one or more ICSRs.

13 E2B(R2): Maintenance of the Clinical Safety Data Management including Data Elements for Transmission of Individual Case Safety Reports; the tripartite harmonized ICH guideline was finalized as E2B (Step 4) in July 1997 and amended for Maintenance as E2B(R1) on 10 November 2000. Post Step 4 editorial corrections were given on 5 February 2001 (second revision) and the guideline renamed E2B(R2).

A **Master Case** refers to a situation where information on the same individual case was reported by different primary and/or secondary sources, which has led to the creation of duplicates, which are subsequently consolidated to one single master case. In EudraVigilance all ICSRs related to the duplicates are associated with the master case, so the initial information can be traced back at all times.

All ICSRs and individual cases are classified in EudraVigilance depending on their specific characteristics (for further details refer to chapter 5.3.4.):

- Initial report
- Follow-up report
- Nullification report
- Error report

5.3.4. Access to EudraVigilance data and access tools

Taking into account the various EudraVigilance system components as outlined in Chapter 3. EVDAS serves as the data source for providing access to the stakeholder groups as referred to in EU legislation.

EVDAS is updated daily with new information reported in ICSRs proceeded by a data management process as referred to in Chapter 3. All EVDAS data are based on individual cases containing the most complete and most up to date information as reported electronically to EudraVigilance. Where a master case is generated due to confirmed duplicates, access is granted based on the consolidated information held in the master case and the associated ICSRs.

ICSRs classified as 'error reports' are excluded from the Access Policy, as they refer to incomplete or erroneous reports. If an ICSR is classified as 'Error Report', the sender is required to correct the ICSR and retransmit it before it will be further processed in EudraVigilance. The same applies to individual cases that have been nullified, as they no longer refer to a valid incident.

Access to ICSR data elements as defined in Annex 1 is granted in two ways:

- By means of EVDAS allowing for the use of signal detection and analysis tools to facilitate pharmacovigilance activities as well as research projects; the Agency provides training to support the utilisation of EVDAS to all stakeholders as applicable.
- By means of easy to use data retrieval functions and report outputs (e.g. as aggregated summary reports or individual case report forms) provided at the Agency's website.

5.4. Access by stakeholder group

5.4.1. Group I: Medicines regulatory authorities in the EEA, the European Commission and the Agency

5.4.1.1. Spontaneous reports – Other Reports – Not available to the sender (Unknown)

In accordance with the provisions of Article 26, paragraph (3) and Article 57, paragraph (1)(d) of Regulation (EC) No 726/2004 and Article 102 of Directive 2001/83/EC as amended, access is provided as follows:

- All data elements are retrievable for all individual cases where the ICSR type is spontaneous report, other report or not available to the sender (unknown). This applies to all types of medicinal products independent of the authorisation procedure and the source of the ICSR.
- All medicinal product information contained in the EVMPD.

5.4.1.2. Reports from study

In accordance with the provisions of Article 26, paragraph (3) and Article 57, paragraph (1)(d) of Regulation (EC) No 726/2004, Article 102 of Directive 2001/83/EC as amended and Article 17, paragraph (3)(a) of Directive 2001/20/EC, access is provided as follows:

- All data elements for all individual cases related to reports from interventional and non-interventional trials.
- All information related to investigational medicinal products contained in the EVMPD.

5.4.1.3. Access tools

Access is provided by means of EVDAS including the use of all available data analysis and signal detection tools.

In addition, for Medicines Regulatory Authorities the access to the transactional system components, EVCTM and EVPM is maintained for messaging and tracking purposes.

5.4.1.4. Access authorisation

Access is granted to authorised personnel of the European Commission, the Agency and Medicines Regulatory Authorities in the EEA. The identification of 'authorised personnel' is based on the EudraVigilance registration process[14]. In Member States, where regional pharmacovigilance centres are established, the responsible Medicines Regulatory Authority determines the level of access, which should be granted to these centres.

5.4.2. Group II: Healthcare professionals and the general public

5.4.2.1. Spontaneous reports

In accordance with the provisions of Article 26, paragraph (3) and Article 57, paragraph (1)(d) of Regulation (EC) No 726/2004 and Article 102 of Directive 2001/83/EC as amended, access is provided as follows:

- A restricted set of data elements as described in Annex 1 related to spontaneously reported cases taking into account the need to comply with Regulation (EC) No 45/2001 on personal data protection. This applies to all types of medicinal products independent of the authorisation procedure and the source of the ICSR (note: as outlined in Annex 1, for ICSRs access is only granted at active substance level and not at medicinal product level with the exception of centrally authorised medicinal products).
- All authorised medicinal products as represented in the EVMPD (note: this permits searching for products/product classes of interest and conducting queries for ICSRs in relation to the active substance(s) and other ingredients e.g. adjuvants of these medicinal products).

14 http://eudravigilance.ema.europa.eu/human/HowToRegister.asp

Detailed guidance on the nature and the interpretation of the data will be provided including general explanations related to the following aspects:

- Adverse reaction reports are only a subset of data being dealt with in the frame of pharmacovigilance to safeguard public health. A proper evaluation requires additional measures to assess the safety of medicines, e.g. the conduct of post-authorisation studies.
- A routine assessment of the safety of medicines is performed at regular intervals in the context of Risk Management Plans and Periodic Safety Update Reports (PSURs). Potential safety issues that may arise in the frame of such evaluation are addressed in the form of regulatory actions, which are subsequently communicated to all stakeholders concerned, e.g. by means of changes in the labelling (Patient leaflet, Summary of Product Characteristics (SPC) or Direct Communications to Healthcare Professionals).
- 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 ICSRs are not always reliable as the degree of causality often depends on the quality of information supporting a causal association.
- EudraVigilance receives reports of suspected adverse reactions that were observed after the medicines were administered. This does not mean that these reactions were caused by the medicines. They could be a symptom of another illness or they could be associated with another product taken by the patient. For example, healthcare professionals are actively encouraged to report events occurring after vaccination to facilitate the monitoring of the safety of vaccines.
- Advise to patients and consumers not to change their medication without prior consultation of their treating physician or their pharmacist.

5.4.2.2. Reports from study

Based on current EU legislation, no access to ICSRs from studies can be provided. The 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 of which the results are often published in the scientific literature.

5.4.2.3. Access tools

Access is provided by means of web-browsing and search functions on the Agency's website (for examples please refer to Annex 2). Results of queries can be downloaded and printed either in aggregated format (e.g. as tabular or graphic presentations, line listings) or as individual report forms.

5.4.2.4. Access authorisation

No specific authorisation for accessing the data on the Agency's website is required i.e. all individuals can access adverse reaction data of interest.

5.4.3. Group III: Marketing authorisation holders and sponsors

5.4.3.1. Spontaneous reports

In accordance with the provisions of Article 26, paragraph (3) and Article 57, paragraph (1)(d) of Regulation (EC) No 726/2004 and Article 102 of Directive 2001/83/EC as amended, access is provided as follows:

- A restricted set of data elements as described in Annex 1 related to spontaneously reported cases taking into account the need to comply with Regulation (EC) No 45/2001 on personal data protection. This applies to all types of medicinal products independent of the authorisation procedure and the source of the ICSR (note: as outlined in Annex 1, for ICSRs access is only granted at active substance level and not at medicinal product level with the exception of centrally authorised medicinal products).
- Where a master case is prepared due to one or more confirmed duplicates, access is provided to the data elements as described in Annex 1 for the master case and all associated duplicated cases.
- Sender-based access to all data fields for individual cases based on spontaneous reports as transmitted electronically by a MAH or a Sponsor as a sender to EudraVigilance.
- All authorised medicinal products as represented in the EVMPD (note: this permits searching for products/product classes of interest and conducting queries for ICSRs in relation to the active substance(s) and other ingredients e.g. adjuvants of these medicinal products).

5.4.3.2. Reports from study

Based on current EU legislation, no access to ICSRs from studies can be provided. Suspected adverse reactions 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 of which the results are often published in the scientific literature.

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 Sized 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). For this reason, access is granted as follows:

- Sender-based access to all data elements for cases that relate to interventional and non-interventional trials as transmitted electronically by a MAH or a Sponsor as a sender directly to EudraVigilance.
- All authorised medicinal products as represented in the EVMPD and investigational medicinal products, for which the organisation is the Sponsor and has entered the information in the dictionary.

5.4.3.3. Access tools

To facilitate pharmacovigilance activities, access is provided by means of EVDAS including the use of all available data analysis and signal detection tools. Results of EVDAS queries can be downloaded and

printed either in aggregated format (e.g. as tabular or graphic presentations, line listings) or as individual report forms.

A selection of ICSRs can be downloaded in ICH E2B format and in accordance with the ICH M2 message specifications. This is to allow pharmaceutical industry and sponsors to comply with adverse reaction reporting requirements to other Medicines Regulatory Authorities outside the EEA.

5.4.3.4. Access authorisation

Access is granted to authorised personnel of a MAH or Sponsor at headquarter level. The identification of 'authorised personnel' is based on the EudraVigilance registration process. The EU Qualified Person Responsible for Pharmacovigilance (QPPV) of the MAH/or the Person Responsible for EudraVigilance appointed by a Sponsor or their registered Deputy nominates the authorised personnel in line with the EudraVigilance Registration Process and is responsible for updating the user registration for their organisation accordingly. Access to a maximum of five signal detection and data analysis experts will be granted; these experts may reside within or outside the EEA.

5.4.4. Group IV: Research organisations

5.4.4.1. Spontaneous reports

Access to data for research purposes is granted taking into account the following principles:

1. The Agency supports in principle any efforts that aim to directly improve public health and work which is intended to improve procedures for protecting public health.
2. The data access to be granted should be sufficient to carry out work aimed at either objective named above.
3. Data access should observe EU legislation on protection of personal and commercially confidential data.
4. An ad-hoc committee will review requests for research access to data. The Agency may refuse access to the data if the committee remains unconvinced of the public health value of the proposed research or judges it to conflict with the public health and legal responsibilities of the Agency.
5. Those given access to EudraVigilance data should make appropriate efforts to publish their research.
6. The Agency has the right to view any publication resulting from EudraVigilance data before submission (maximum period for initial Agency review will be six weeks), and any issues raised by the Agency concerning incorrect analyses, unsupported inferences, misleading statements or protection of personal data must be addressed to the satisfaction of the Agency before submission for publication.
7. A standard Agency disclaimer must be added to the manuscript. The Agency reserves the right to reword the disclaimer to the manuscript in cases of unresolved disagreement over the interpretation of the data. The manuscript or its conclusions must not be disseminated in any way without the disclaimer.
8. A confidentiality agreement must be signed by the party applying for data access for research purposes. Data may not be transferred to any third party.
9. The Agency will have a standard timescale for response to requests for data.

10. The data quality will be the best available to the Agency at the time of request. Issues of data quality may be raised with the Agency but no guaranteed timescale can be given for resolution of such issues.

11. Meta data essential for interpretation of the EudraVigilance dataset will be made available.

In accordance with the provisions of Article 26, paragraph (3) and Article 57, paragraph (1)(d) of Regulation (EC) No 726/2004 and Article 102 of Directive 2001/83/EC as amended, access is provided as follows to facilitate research activities:

- A restricted set of data elements as described in Annex 1 related to spontaneously reported cases taking into account the need to comply with Regulation (EC) No 45/2001 on personal data protection. This applies to all types of medicinal products independent of the authorisation procedure and the source of the ICSR (note: as outlined in Annex 1, for ICSRs access is only granted at active substance level and not at medicinal product level with the exception of centrally authorised medicinal products).
- Where a master case is prepared due to one or more confirmed duplicates, access is provided to the data elements as described in Annex 1 for the master case and all associated duplicated cases.
- All authorised medicinal products as represented in the EVMPD (note: this permits searching for products/product classes of interest and conducting queries for ICSRs in relation to the active substance(s) and other ingredients, e.g. adjuvants of these medicinal products).

5.4.4.2. Reports from study

Based on current EU legislation, no access to ICSRs from studies can be provided. 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 of which the results are often published in the scientific literature.

5.4.4.3. Access tools

To facilitate research activities, access is normally provided by means of EVDAS including the use of all available data analysis and signal detection tools. Results of EVDAS queries can be downloaded and printed either in aggregated format (e.g. as tabular or graphic presentations, line listings) or as individual report forms.

5.4.4.4. Access authorisation

Access is granted to authorised personnel of the research organisation. The identification of 'authorised personnel' is based on the EudraVigilance registration process.

6. Implementation of the EudraVigilance access policy[15]

This Access Policy will be implemented in a stepwise approach.

- In a first phase, access was granted to the Medicines Regulatory Authorities in the EEA in July 2007.

[15] This implementation plan was amended following EMA Management Board meeting of 17 March 2011 and is documented in document reference number EMA/529383/2011

- In a second phase, access will be granted to healthcare professionals and the general public, initially for centrally authorised products, followed by a stepwise extension to include all medicinal products authorised in the EU based on the adverse reaction data described in Annex 1.
- In parallel, access will be provided to MAHs in the EEA, Sponsors and research organisations. For MAHs and Sponsors, access will initially be granted to those already registered in EudraVigilance for electronic reporting of ICSRs followed by a stepwise opening to all MAHs/Sponsors established in the EEA.

Once the revised legal framework based on the aforementioned two legislative proposals will come into force, the EudraVigilance Access Policy will be reviewed. In this context, the Agency will consider if access to MAHs can be granted for a wider ICSR data set related to those medicinal products/active substances, for which they hold a marketing authorisation in the EEA. This relates in particular to expected changes of the adverse reaction reporting rules and revised obligations in the conduct of pharmacovigilance.

To successfully implement the EudraVigilance Access Policy, a number of pre-requisites need to be fulfilled to ensure high quality and reliable data outputs. Those pre-requisites are being addressed in the context of the EudraVigilance Data Quality Management project of the Agency, which is expected to run for a period of four years starting in September 2010.

Furthermore, technical adaptations to the current EudraVigilance System are necessary to proceed with the full implementation of the EudraVigilance Access Policy. These will be addressed as part of the overall EU Telematics Master Plan and the detailed EudraVigilance project plan, which are both updated annually taking into account the Agency's annual Telematics budget and the priority deliverables as defined by the EudraVigilance Steering Committee.

Annex 1: EudraVigilance human data elements

EudraVigilance entails the processing of personal data as defined under Article. 2(a) of Regulation (EC) No 45/2001. Most of the data processed in EudraVigilance constitute health data, including medical background and a description of lifestyle of identifiable individuals, suspected adverse reactions to medicines and their outcome.

According to Article 27 of Regulation (EC) No 45/2001, on the 7 September 2009 the EDPS delivered an Opinion on the notification. for "prior" checking of EudraVigilance. Whilst recognising the legitimacy of the collection and the transfer of information related to ICSRs and suspected adverse reactions related to medicines, the EDPS made a set of recommendations to the Agency to ensure that the processing of personal data in EudraVigilance is in full compliance with Regulation (EC) No 45/2001.

Based on these recommendations, the Agency has carefully assessed all the ICSR data elements for spontaneous reports to be disclosed taking into account the need to safeguard the identity and identifiably of data subjects as defined in article 2 of Regulation (EC) No 45/2001.

This annex provides an overview of all those ICH E2B/M2 ICSR data elements that are made accessible to healthcare professionals, the public, MAHs, sponsors of clinical trials and research organisations.

To safeguard the identity of individuals in relation to ICSRs, the following approach has been followed:

- No specific EU/EEA country information is disclosed;
  - Country information is grouped by EU/EEA and non-EU/EEA, whereby the latter allows for further sub-categorisation according to the United Nations Geoscheme, including macro-geographical regions (continents) and sub-regions.
- No world-wide unique case identifiers or sender identifiers are disclosed;
  - The EudraVigilance Local Number (EV Master Reference Number in case of duplicates) is displayed instead to allow for the unique reference to an individual case.
- No medicinal product name is disclosed with the exception of centrally authorised medicinal products;
  - This is to avoid the identification of a specific EU/ EEA country; since centrally authorised medicinal products are licensed at EU level and as such do not allow for the identification of a specific country, this information will be displayed.
- No information on specific dates will be provided;
  - The only reference date that will be displayed refers to the EudraVigilance Gateway date i.e. the date by which the report was transmitted electronically to EudraVigilance.
- No information in relation to personal identifiers will be provided;
  - This includes initials, date of birth, medical record or hospital numbers, weight or height of the patient etc.
- No narrative text elements will be disclosed;
  - Narrative text elements may contain personal information.
- No information on the receiver is disclosed;
  - The receiver is implicit as being EudraVigilance.

All data elements will be presented in English language. As a nature of spontaneous reports, not all data are always provided. Certain information may therefore not always be available and the corresponding elements may appear blank in the data output results.

Data outputs can be presented in aggregated format (e.g. as tabular or graphic presentations, line listings) or as individual report forms.

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
	M.1	ICH ICSR Message Header	
1	M.1.1	Message Type (Type of information being transmitted e.g. ICSR, PSUR)	**YES**
2	M.1.2	Message Format Version (Version number of message format)	**NO**
3	M.1.3	Message Format Release (Release number of the message format)	**NO**
4	M.1.4	Message Number	**NO**
5	M.1.5	Message Sender Identifier	**NO**
6	M.1.6	Message Receiver Identifier	**NO**
7	M.1.7a	Message Date Format	**Displayed as EV Gateway Receipt Date**
8	M.1.7b	Message Date	**Displayed as EV Gateway Receipt Date**
	ICH ICSR M2 Data Processing Specifications		
9		Safety Report Version Number	**NO**
	ICH E2B ICSR Specifications		
	A.1	**Identification of the case safety report**	
10	A.1.0.1	Sender's (Case) Safety Report Unique Identifier	**NO but** displayed as EudraVigilance LOCAL NUMBER (EV Master Reference Number in case of duplicates)
11	A.1.1	Identification of the country of the primary source	**NO but** grouped by EU/EEA and Non-EU/EEA; for Non-EU a grouping

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
			according to the United Nations Geoscheme, including macro-geographical regions (continents) and sub-regions is also applied
12	A.1.2	Identification of the country where the reaction/event occurred	**NO but** grouped by EU/EEA and Non-EU/EEA; for Non-EU/EEA a grouping according to the United Nations Geoscheme, including macro-geographical regions (continents) and sub-regions is also applied
13	A.1.3a	Date format of this transmission	**NO**
14	A.1.3b	Date of this transmission	**NO**
15	A.1.4	Type of report (Spontaneous, report from study, Other Not available to sender)	**YES but** Restricted to Report Type 'Spontaneous Report'
	A 1.5	Seriousness[16]	
16	A.1.5.1	Serious (Yes, No)	**YES**
17	A.1.5.2	Seriousness criteria (Results in death, Life threatening, Caused/prolonged hospitalisation, Disabling/Incapacitating, Congenital anomaly/birth defect, Other medically important condition)	**YES**
18	A.1.6a	Date format report was first received from source	**NO**
19	A.1.6b	Date report was first received from source	**NO**
20	A.1.7a	Date format of receipt of the most recent information for this report	**NO**
21	A.1.7b	Date of receipt of the most recent information for this report	**NO**
	A.1.8	Additional available documents held by sender	
22	A.1.8.1	Are additional documents available (Yes, No)	**NO**
23	A.1.8.2	List of documents held by sender	**NO**
24	A.1.9	Does this case fulfil the local criteria for an expedited report? (Yes, No)	**NO**

[16] For definitions, please refer to the ICH E2A guideline 'Clinical Safety Data Management: Definitions and Standards for Expedited Reporting'; adopted by CPMP, November 94, issued as CPMP/ICH/377/95.

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
	A.1.10	Worldwide unique case identification number	
25	A.1.10.1	Regulatory authority's case report number	**NO but** displayed as EudraVigilance LOCAL NUMBER (EV Master Reference Number in case of duplicates)
26	A.1.10.2	Other sender's case report number	**NO but** displayed as EudraVigilance LOCAL NUMBER (EV Master Reference Number in case of duplicates)
	A.1.11	Other case identifiers in previous transmissions	
30	A.1.11.1	Source(s) of the case identifier	**NO**
31	A.1.11.2	Case identifiers	**NO**
32	A.1.12	Identification number of the report which is linked to this report	**NO**
	A.1.13	Report nullification	
33	A.1.13.1	Reason for nullification	**NO**
34	A.1.14	Was the case medically confirmed, if not initially from health professional?	**YES**
	A.2	Primary source(s) of information	
	A.2.1	Primary source(s)	
35	A.2.1.1a	Reporter identifier (Reporter title)	**NO**
36	A.2.1.1b	Reporter identifier (Reporter given name)	**NO**
37	A.2.1.1c	Reporter identifier (Reporter middle name)	**NO**
38	A.2.1.1d	Reporter identifier (Reporter family name)	**NO**
39	A.2.1.2a	Reporter identifier (Reporter organization)	**NO**
40	A.2.1.2b	Reporter identifier (Reporter department)	**NO**
41	A.2.1.2c	Reporter's address (Reporter street)	**NO**
42	A.2.1.2d	Reporter's address (Reporter city)	**NO**
43	A.2.1.2e	Reporter's address (Reporter state or province)	**NO**
44	A.2.1.2f	Reporter's address (Reporter postcode)	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
45	A.2.1.3	Country	**NO but** grouped by EU/EEA and Non-EU/EEA; for Non-EU/EEA a grouping according to the United Nations Geoscheme, including macro-geographical regions (continents) and sub-regions is also applied
46	A.2.1.4	Qualification (Physician, Pharmacist, Other Health Professional, Lawyer, Consumer or other non health professional)	**YES**
47	A.2.2	Literature reference(s)	**YES**
	A.2.3	Study identification	
48	A.2.3.1	Study name	**NO**
49	A.2.3.2	Sponsor study number	**NO**
50	A.2.3.3	Study type in which the reaction(s)/event(s) were observed (Clinical trials, Individual patient use, Other studies)	**NO**
	A.3	Information on Sender and Receiver of Case Safety Report	
	A.3.1	Sender	
51	A.3.1.1	Type Pharmaceutical Company, Regulatory Authority, Health professional, Regional Pharmacovigilance Center, WHO Collaborating Center for International Drug Monitoring, Other)	**YES**
52	A.3.1.2	Sender Identifier (Sender organization)	**NO**
53	A.3.1.3a	Sender Identifier (Sender department)	**NO**
54	A.3.1.3b	Sender Identifier (Title)	**NO**
55	A.3.1.3c	Sender Identifier (Given name)	**NO**
56	A.3.1.3d	Sender Identifier (Middle name)	**NO**
57	A.3.1.3e	Sender Identifier (Family name)	**NO**
58	A.3.1.4a	Sender's Address (Street address)	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
59	A.3.1.4b	Sender's Address (City)	**NO**
60	A.3.1.4c	Sender's Address State or Province)	**NO**
61	A.3.1.4d	Sender's Address (Postcode)	**NO**
62	A.3.1.4e	Sender's Address (Country)	**NO but** grouped by EU/EEA and Non-EU/EEA; for Non-EU/EEA a grouping according to the United Nations Geoscheme, including macro-geographical regions (continents) and sub-regions is also applied
63	A.3.1.4f	Sender's Telephone Number (Telephone)	**NO**
64	A.3.1.4g	Sender's Telephone Number (Telephone extension)	**NO**
65	A.3.1.4h	Sender's Telephone Number (Telephone country code)	**NO**
66	A.3.1.4i	Sender's Fax Number (Fax)	**NO**
67	A.3.1.4j	Sender's Fax Number (Fax extension)	**NO**
68	A.3.1.4k	Sender's Fax Number (Fax country code)	**NO**
69	A.3.1.4l	Sender's E-mail Address	**NO**
	A.3.2	Receiver	
70	A.3.2.1	Type (Pharmaceutical Company, Regulatory Authority, Health professional, Regional Pharmacovigilance Center, WHO Collaborating Center for International Drug Monitoring, Other)	**NO**
71	A.3.2.2a	Receiver identifier (Receiver organization)	**NO**
72	A.3.2.2b	Receiver identifier (Receiver department)	**NO**
73	A.3.2.2c	Receiver identifier (Title)	**NO**
74	A.3.2.2d	Receiver identifier (Given name)	**NO**
75	A.3.2.2e	Receiver identifier (Middle name)	**NO**
76	A.3.2.2f	Receiver identifier (Family name)	**NO**
77	A.3.2.3a	Receiver's Address (Street address)	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
78	A.3.2.3b	Receiver's Address (City)	**NO**
79	A.3.2.3c	Receiver's Address (State or Province)	**NO**
80	A.3.2.3d	Receiver's Address (Postcode)	**NO**
81	A.3.2.3e	Receiver's Address (Country)	**NO**
82	A.3.2.3f	Receiver's Telephone Number (Telephone)	**NO**
83	A.3.2.3g	Receiver's Telephone Number (Telephone extension)	**NO**
84	A.3.2.3h	Receiver's Telephone Number (Telephone country code)	**NO**
85	A.3.2.3i	Receiver's Fax Number (Fax)	**NO**
86	A.3.2.3j	Receiver's Fax Number (Fax extension)	**NO**
87	A.3.2.3k	Receiver's Fax Number (Fax country code)	**NO**
88	A.3.2.3l	Receiver's E-mail Address	**NO**
	B	Information on the Case	
	B.1	Patient characteristics	
	B.1.1	Patient	
89	B.1.1.1a	Patient medical record number(s) and source(s) of the record number (GP medical record number)	**NO**
90	B.1.1.1b	Patient medical record number(s) and source(s) of the record number (Specialist record number)	**NO**
91	B.1.1.1c	Patient medical record number(s) and source(s) of the record number (Hospital record number)	**NO**
92	B.1.1.1d	Patient medical record number(s) and source(s) of the record number (Investigation number)	**NO**
	B.1.2	Age information	

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
93	B.1.2.1a	Date of birth (Date format)	**NO**
94	B.1.2.1b	Date of birth	**NO but** Age is calculated at time of onset of reaction (if available). If several reactions/events are in the report, the age at the time of the first reaction/event is used. For foetal reaction(s)/event(s) B.1.2.2.1 "Gestation period when reaction/event was observed in the fetus" is used (if available). A validation is performed to ensure that all dates of onset of reactions –in case of multiple reactions- fall within a 12 months period. If the dates are beyond a 12 months onset period, age is not calculated.
95	B.1.2.2a	Age at time of onset of reaction/event (Age value)	**YES**
96	B.1.2.2b	Age at time of onset of reaction/event (Age unit)	**YES**
97	B.1.2.2.1a	Gestation period when reaction/event was observed in the fetus (value)	**NO**
98	B.1.2.2.1b	Gestation period when reaction/event was observed in the fetus (Unit)	**NO**
99	B.1.2.3	Patient age group	**YES** Age and patient age group are mapped to a defined age grouping scheme applied in EudraVigilance
100	B.1.3	Weight (kg)	**NO**
101	B.1.4	Height (cm)	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
102	B.1.5	Sex	**YES**
103	B.1.6a	Last menstrual period date (format)	**NO**
104	B.1.6b	Last menstrual period date	**NO**
	B.1.7	Relevant medical history and concurrent conditions	
105	B.1.7.1a.1	MedDRA version for Medical History	**NO**
106	B.1.7.1a.2	Structured information as coded in MedDRA (Disease / surgical procedure / etc.)	**NO**
107	B.1.7.1b	Start Date (format)	**NO**
108	B.1.7.1c	Start Date	**NO**
109	B.1.7.1d	Continuing	**NO**
110	B.1.7.1e	End Date (format)	**NO**
111	B.1.7.1f	End Date	**NO**
112	B.1.7.1g	Comments	**NO**
113	B.1.7.2	Text for relevant medical history and concurrent conditions	**NO**
	B.1.8	Relevant past drug history (repeat as necessary)	
114	B.1.8a	Name of Drug as Reported	**NO**
115	B.1.8b	Start Date (format)	**NO**
116	B.1.8c	Start Date	**NO**
117	B.1.8d	End Date (format)	**NO**
118	B.1.8e	End Date	**NO**
119	B.1.8f.1	MedDRA version for indication	**NO**
120	B.1.8f.2	Indication as coded in MedDRA	**NO**
121	B.1.8g.1	MedDRA version for reaction	**NO**
122	B.1.8g.2	Reaction	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
	B.1.9	In case of death	
123	B.1.9.1a	Date of death (format)	**NO**
124	B.1.9.1b	Date of death	**NO**
125	B.1.9.2.a	MedDRA version for reported cause(s) of death	**NO**
126	B.1.9.2.b	Reported cause(s) of death (repeat as necessary)	**NO**
127	B.1.9.3	Was autopsy done?	**NO**
128	B.1.9.4a	MedDRA version for autopsy-determined cause(s) of death	**NO**
129	B.1.9.4b	Autopsy-determined cause(s) of death (repeat as necessary)	**NO**
	B.1.10	For a parent-child/fetus report, information concerning the parent	**NO**
130	B.1.10.1	Parent identification	**NO**
	B.1.10.2	Parent age information	
131	B.1.10.2.1a	Date of birth of parent (format)	**NO but** Age is calculated (if birth date is available)
132	B.1.10.2.1b	Date of birth of parent (Value)	**NO but** Age is calculated (if birth date is available)
133	B.1.10.2.2a	Age of parent	**YES**
134	B.1.10.2.2b	Age of parent (Unit)	**YES**
135	B.1.10.3a	Last menstrual period date (format)	**NO**
136	B.1.10.3b	Last menstrual period date	**NO**
137	B.1.10.4	Weight (kg) of parent	**NO**
138	B.1.10.5	Height (cm) of parent	**NO**
139	B.1.10.6	Sex of parent	**YES**
	B.1.10.7	Relevant medical history and concurrent conditions of parent	
140	B.1.10.7.1a.1	MedDRA version for parent medical history	**NO**
141	B.1.10.7.1a.2	Structured information coded in MedDRA	**NO**
142	B.1.10.7.1b	Start Date (format)	**NO**
143	B.1.10.7.1c	Start Date	**NO**
144	B.1.10.7.1d	Continuing	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
145	B.1.10.7.1e	End Date (format)	**NO**
146	B.1.10.7.1f	End Date	**NO**
147	B.1.10.7.1g	Comments	**NO**
148	B.1.10.7.2	Text for relevant medical history and concurrent conditions of parent (not including reaction/event)	**NO**
	B.1.10.8	Relevant past drug history	
149	B.1.10.8a	Name of drug as reported	**NO**
150	B.1.10.8b	Start date (format)	**NO**
151	B.1.10.8c	Start date	**NO**
152	B.1.10.8d	End date (format)	**NO**
153	B.1.10.8e	End date	**NO**
154	B.1.10.8f.1	MedDRA version for indication	**NO**
155	B.1.10.8f.2	Indication as coded in MedDRA	**NO**
156	B.1.10.8g.1	MedDRA version for reaction	**NO**
157	B.1.10.8g.2	Reactions (if any and known) as coded in MedDRA	**NO**
	B.2	Reaction(s)/Event(s)	
158	B.2.i.0	Reaction/event as reported by primary source	**NO**
159	B.2.i.1.a	MedDRA version for reaction/event term LLT	**NO**
160	B.2.i.1.b	Reaction/event in MedDRA terminology LLT	**NO**
161	B.2.i.2.a	MedDRA version for reaction/event term PT	**YES**
162	B.2.i.2.b	Reaction/event MedDRA term PT	**YES**
163	B.2.i.3	Term highlighted by the reporter	**NO**
164	B.2.i.4a	Date of start of reaction/event (format)	**NO**
165	B.2.i.4b	Date of start of reaction/event	**NO**
166	B.2.i.5a	Date of end of reaction/event (format)	**NO**
167	B.2.i.5b	Date of end of reaction/event	**NO**
168	B.2.i.6a	Duration of reaction/event (value)	**YES but** Duration is calculated based on B.2.i.4a/b and B.2.i.5a/b

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
			(if available) if duration is not specified
169	B.2.i.6b	Duration of reaction/event (unit)	**YES but** Duration is calculated based on B.2.i.4a/b and B.2.i.5a/b (if available) if duration is not specified
170	B.2.i.7.1a	Time interval between beginning of suspect drug administration and start of reaction/event	**YES**
171	B.2.i.7.1b	Time interval unit between suspect drug administration and start of reaction/event	**YES**
172	B.2.i.7.2a	Time interval between last dose and start of reaction/event	**NO**
173	B.2.i.7.2b	Time interval unit between last dose and start of reaction/event	**NO**
174	B.2.i.8	Outcome of reaction/event at the time of last observation	**YES**
	B.3	Results of tests and procedures relevant to the investigation of the patient:	
175	B.3.1a	Structured information (repeat as necessary)	**NO**
176	B.3.1b	Date	**NO**
177	B.3.1c	Test	**NO**
178	B.3.1d	Result as coded in MedDRA	**NO**
179	B.3.1e	Unit	**NO**
180	B.3.1.1	Normal low range	**NO**
181	B.3.1.2	Normal high range	**NO**
182	B.3.1.3	More information available (Yes/No)	**NO**
183	B.3.2	Results of tests and procedures relevant to the investigation of the patient:	**NO**
	B.4	Drug(s) Information	
184	B.4.k.1	Characterization of drug role	**YES**
	B.4.k.2	Drug identification	
185	B.4.k.2.1	Proprietary medicinal product name	**NO** with the exception of centrally authorised medicinal products, for which the name is displayed
186	B.4.k.2.2	Active Drug substance names	**YES** As coded against the

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
			EVMPD; where the reported substance (concomitant medication) cannot be recoded due to data quality issues, the information is not displayed in coded format
		Medicinal product classification/grouping	**YES**
187	B.4.k.2.3	Identification of the country where the drug was obtained	**NO but** grouped by EU/EEA and Non-EU/EEA; for Non-EU/EEA a grouping according to the United Nations Geoscheme, including macro-geographical regions (continents) and sub-regions is also applied
188	B.4.k.3	Batch/lot number	**NO**
	B.4.k.4	Holder and authorization/application number of drug	
189	B.4.k.4.1	Authorization/Application Number	**NO**
190	B.4.k.4.2	Country of authorization/application	**NO**
191	B.4.k.4.3	Name of holder/applicant	**NO**
	B.4.k.5	Structured Dosage Information:	
192	B.4.k.5.1	dose (number)	**YES**
193	B.4.k.5.2	dose (unit)	**YES**
194	B.4.k.5.3	number of separate dosages	**YES**
195	B.4.k.5.4	number of units in the interval	**YES**
196	B.4.k.5.5	definition of the interval	**YES**
197	B.4.k.5.6	cumulative dose to first reaction (number)	**YES**
198	B.4.k.5.7	cumulative dose to first reaction (unit)	**YES**
199	B.4.k.6	Dosage text	**NO**
200	B.4.k.7	Pharmaceutical form (Dosage form)	**YES**
201	B.4.k.8	Route of administration	**YES**
202	B.4.k.9	Parent route of administration (in case of a parent child/fetus report)	**YES**
203	B.4.k.10a	Gestation period at time of exposure (value)	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
204	B.4.k.10b	Gestation period at time of exposure (unit)	**NO**
205	B.4.k.11a	MedDRA version for indication	**NO**
206	B.4.k.11b	Indication for use in the case as coded in MedDRA	**NO**
207	B.4.k.12a	Date of start of drug (format)	**NO**
209	B.4.k.12b	Date of start of drug	**NO**
	B.4.k.13	Time interval between drug administration and start of reaction/event	
210	B.4.k.13.1a	Time interval between beginning of drug administration and start of reaction/event (value)	**YES**
211	B.4.k.13.1b	Time interval between beginning of drug administration and start of reaction/event (unit)	**YES**
212	B.4.k.13.2a	Time interval between last dose of drug and start of reaction/event (value)	**YES**
213	B.4.k.13.2b	Time interval between last dose of drug and start of reaction/event (unit)	**YES**
214	B.4.k.14a	Date of last administration (format)	**NO**
215	B.4.k.14b	Date of last administration	**NO**
216	B.4.k.15a	Duration of drug administration	**YES** If duration is not provided it is calculated based on B.4.k.12a/b and B.4.k.14a/b

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
			(if available)
217	B.4.k.15b	Duration of drug administration unit	**YES**
218	B.4.k.16	Action(s) taken with drug	**YES**
	B.4.k.17	Effect of rechallenge (or re-exposure), for suspect drug(s) only	
219	B.4.k.17.1	Did reaction recur on readministration?	**YES**
220	B.4.k.17.2a	MedDRA version for reaction(s)/event(s) recurred	**YES**
221	B.4.k.17.2b	If yes, which reaction(s)/event(s) recurred?	**YES**
	B.4.k.18	Relatedness of drug to reaction(s)/event(s) (repeat as necessary)	
222	B.4.k.18.1a	MedDRA version for Reaction assessed	**NO**
223	B.4.k.18.1b	Reaction assessed	**NO**
224	B.4.k.18.2	Source of assessment	**NO**
225	B.4.k.18.3	Method of assessment	**NO**
226	B.4.k.18.4	Result	**NO**
	B.4.k.19	Additional information on drug	
227	B.5	Narrative case summary and further information:	
228	B.5.1	Case narrative including clinical course, therapeutic measures, outcome and additional relevant information.	**NO**
229	B.5.2	Reporter's comments	**NO**
230	B.5.3a	MedDRA Version for Sender’s diagnosis	**NO**

	ICH E2B/M2 Data Element	ICH E2B/M2 Data Element Title	Stakeholder Groups II, III and IV Access to ICH ICSR E2B(R2) Data Elements
231	B.5.3b	Sender's diagnosis/syndrome and/or reclassification of reaction/event	**NO**
232	B.5.4	Sender's comments	**NO**

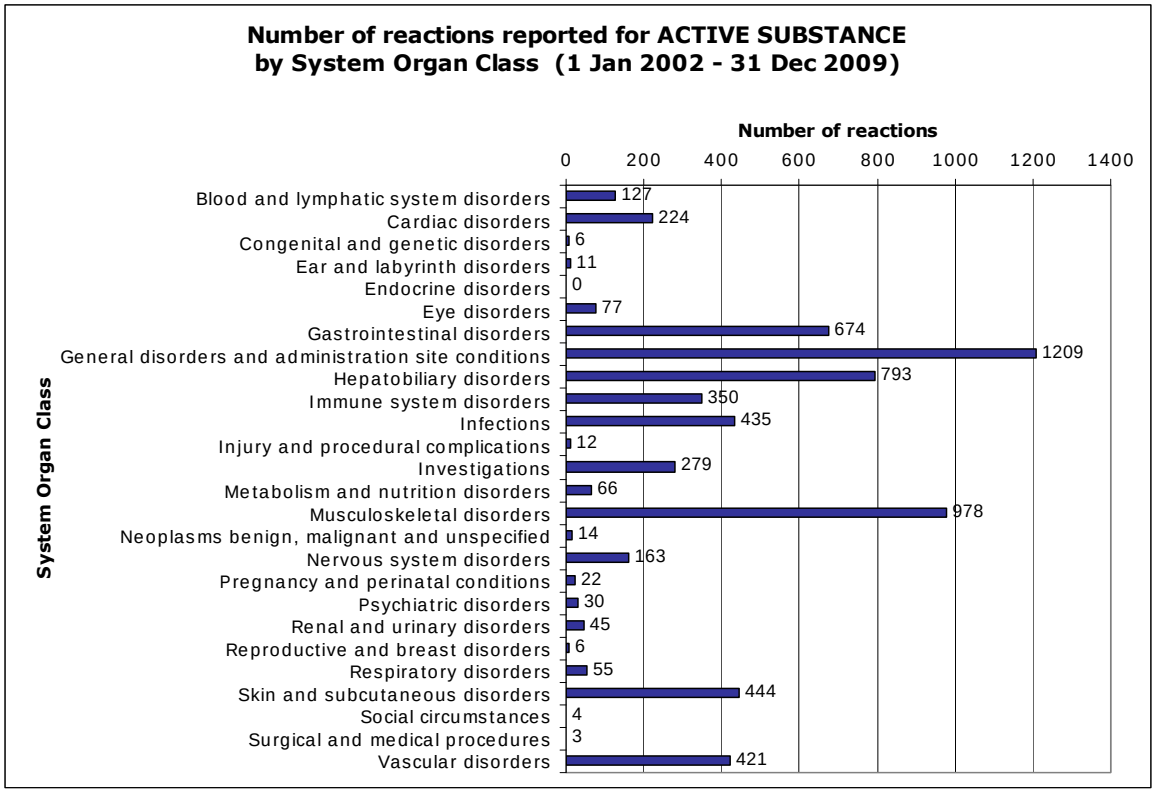
Annex 2: Examples for aggregated data outputs

Examples for data outputs based on the following core information:

Active substance (where the role of the medicinal product is indicated as suspect or interacting):

- For single ingredient medicinal products, the name of the active substance (e.g. Active substance A).
- For a fixed combination medicinal product (i.e. more than one active substance), the name of the combination of the active substances (e.g. Active substance A and Active substance B).
- The total number of individual cases received as spontaneous reports.
- Age of the patients expressed as age groups in accordance with ICH E2B(R2) or ICH E1117.
- Gender of the patient (male, female, unknown).
- Total number of suspected adverse reactions reported:
  - Presented by MedDRA Primary System Organ Classes (SOCs),
  - Number of suspected adverse reactions reported at PT level per Primary SOC.

a) Number of suspected adverse reactions reported to EudraVigilance for an active substance or a combination of active substances during a specified period of time, stratified by System Organ Class



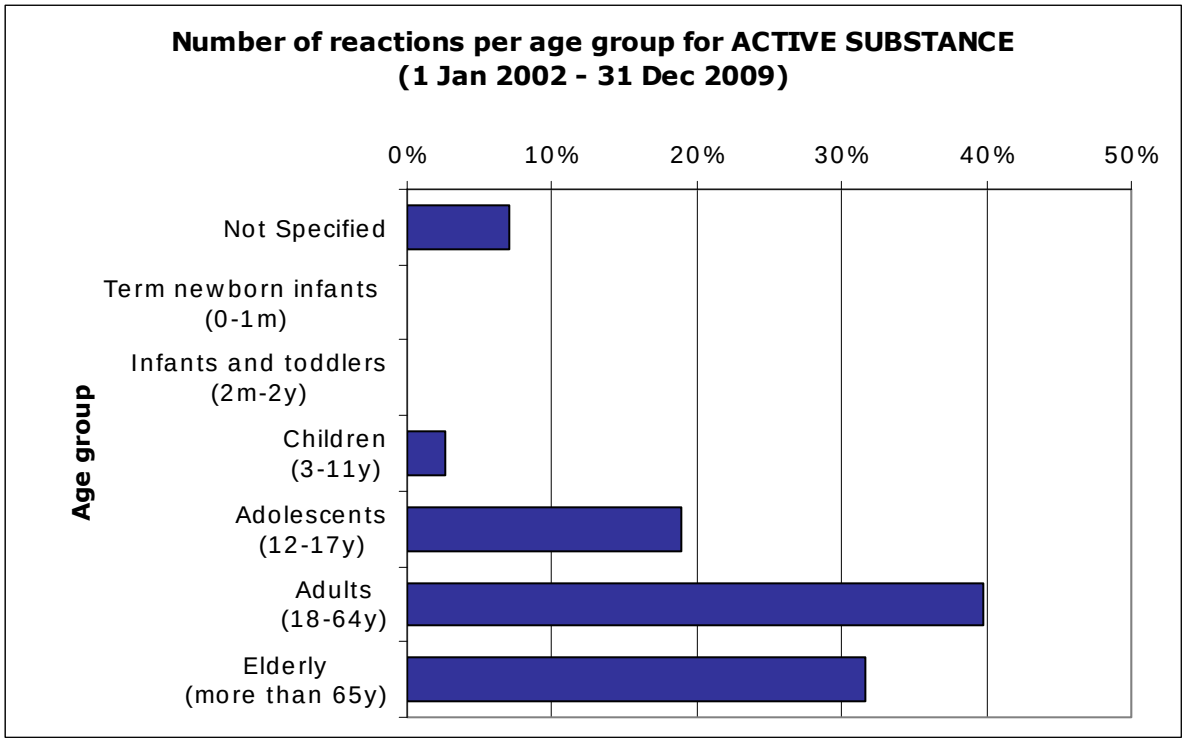
17 Clinical Investigation of Medicinal Products in the Pediatric Population, adopted by CPMP, July 2000, issued as CPMP/ICH/2711/99.

b) Number of suspected adverse reactions (MedDRA Preferred Terms) for an active substance or a combination of active substances 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)
Active substance

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 an active substance or a combination of active substances during a specified period of time, stratified by age group.



Annex 3: Acronyms

EEA	European Economic Area
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
EU	European Union
ICSR	Individual case safety report
IMP	Investigational medicinal product
MAH	Marketing authorisation holder
MedDRA	Medical Dictionary for Regulatory Activities[18]
PSUR	Periodic safety update report
PT	Preferred term
QPPV	Qualified person responsible for pharmacovigilance
SMEs	Small and medium-sized enterprises
SOC	System Organ Class
SPC	Summary of product characteristics

18 http://www.meddramsso.com

References

- 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).
- Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data (Official Journal of the European Communities 12/1/2001, L 8 p. 1-22).
- Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents (Official Journal of the European Communities 31/5/2001 L 145/43-48).
- 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).
- Draft EMEA Policy on the Practical Operation of Access to EMEA Documents (EMEA/110196/2006/Final).
- Opinion on a Notification for Prior Checking Received from the Data Protection Officer of the European Medicines Agency regarding the EudraVigilance database, Brussels, 7 September 2009 (Case 2008-402).
- European Ombudsman response to the Public Consultation on the European Medicines Agency's Draft Transparency Policy, Strasbourg, 9 October 2009.
- Draft Recommendation of the European Ombudsman in his inquiry into complaint 2493/2008 (BB)TS against the European Medicines Agency, April 2010.
- Proposal for a Directive of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use:{SEC(2008) 2670}{SEC(2008) 2671}, Brussels, 10.12.2008, COM(2008) 665 final, 2008/0260 (COD).
- Proposal for a Regulation of the European Parliament and of the Council amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency:{SEC(2008) 2670}{SEC(2008) 2671}, Brussels, 10.12.2008, COM(2008) 664 final, 2008/0257 (COD).
- 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 Agency, London (Doc. Ref.: EMEA/565466/2007).
- Note for Guidance EudraVigilance Human – Processing of Safety Messages and Individual Case Safety Reports (ICSRs), Doc. Ref. EMEA/H/20665/04/Final, in the latest version.

- Draft CHMP Guideline on Detection and Management of Duplicate Individual Cases and Individual Case Safety Reports (ICSRs) (Doc. Ref. EMA/13432/2009).