Erfassung von Nebenwirkungsberichten – Europäische Entwicklungen

BfArM im Dialog, 26 Februar 2016
Overview

I. The Pharmacovigilance Programme
II. ISO/ICH E2B(R3) – the new ICSR standard
III. EudraVigilance Audit – scope and timelines
IV. Eudravigilance Access Policy
V. Revision of GVP-Modul VI
Topic I.
Pharmacovigilance Programme

EU Telematics strategy and implementation roadmap 2015-2017 published August 2015

• Overview of Pharmacovigilance Systems and Services
Pharmacovigilance Programme

Projects & Outputs

- Article 57 Database
  - European database of all medicinal products

Benefits Delivered

- Support PV Procedures which facilitates coordination of regulatory decisions
- Supports the product index for EudraVigilance
- Reduction of duplication

Driven By

Effective programme management which ensures successful delivery of changes

- Set up in 2012, now established and operational with ≈ 500,000 medicinal products
- Most comprehensive database of medicinal products authorised in the EU
- EMA and the EU regulatory network continue co-operation with Industry to ensure completeness and correctness of Art57 data
- EMA Management Board in December 2015 decided that the Art57 database is functional for the purpose of notifying changes in QPPV and location of the PSMF
- Reliance on Art57 database for QPPV and PSMF location notifications delivers an important simplification for pharmaceutical industry; from 1 February 2016 Type 1A variations no longer need to be submitted for QPPV details and PSMF location
Pharmacovigilance Programme

Projects & Outputs

- **EudraVigilance Auditable Requirements**: Enhanced adverse reaction collection and management system

Benefits Delivered

- Simplified reporting delivered
- Data in ISO ICH ICSR R3 format will be higher quality, improving searchability & analysis efficiency

Driven By

- Effective programme management which ensures successful delivery of changes

- ✔ Dedicated EudraVigilance webpage launched on the Agency’s corporate website in October 2015
- ✔ Revised EudraVigilance Access Policy adopted by EMA Management Board in December 2015
- ✔ Most of IT development for new functionalities have been completed
- ✔ **EudraVigilance project training plan to be published in March 2016**
- ✔ Following internal testing by EMA, *external testing is planned for 2nd quarter 2016 with some NCAs and MAHs*
- ✔ EudraVigilance functionalities audit scheduled for 3rd quarter 2016
- ✔ **EMA Management Board will review EV system audit outcome at its December meeting.** If the functionalities agreed at the December 2014 audit have been delivered then the Management Board will announce the **launch the new EV system and start of centralised reporting in 6 months: mid 2017**
Pharmacovigilance Programme

Projects & Outputs

Medical Literature Monitoring

Delivery of literature monitoring service to MAHs

Benefits Delivered

- Improved safety monitoring of medicines
- Reduction in costs for MAH literature monitoring activities

Driven By

Effective programme management which ensures successful delivery of changes

✓ On 1st July 2015 the MLM service was launched, covering the 50 most common chemical active substance groups. The launch phase was completed on 31st August 2015

✓ The full scope of operation of the European Medicines Agency's medical literature monitoring (MLM) service was launched on 1st September 2015. The service now include 100 herbal and 300 chemical substance groups

✓ An independent audit of the service provider's internal quality management and control systems and of the service is conducted in February 2016 (and 2-yearly thereafter)
Pharmacovigilance Programme

**Projects & Outputs**

**Pharmacovigilance Fees**

*Collection of fees to cover costs of conduct of certain PV activities*

**Benefits Delivered**

- NCAs paid for certain PV assessments
- Annual fees support implementation & maintenance of measures from 2010 legislation

**Driven By**

- Effective programme management which ensures successful delivery of changes

- Procedural fees for pharmacovigilance were first invoiced in 2014
- The 1st pharmacovigilance annual fee invoices were issued in July 2015
- **Prior to issuing an invoice for procedure-based fees or the pharmacovigilance annual fee, the Agency will provide MAHs with an opportunity to review their product information as recorded in the Art 57 database by supplying the qualified person for pharmacovigilance with an advice not**
- The next pharmacovigilance annual fee invoices for the concerned MAHs will be issued in July 2016
<table>
<thead>
<tr>
<th>Projects &amp; Outputs</th>
<th>Benefits Delivered</th>
<th>Driven By</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PSUR Repository</strong>&lt;br&gt;Centralised repository for PSURs and assessment reports</td>
<td>• Provides a simplification of PSUR submissions for industry&lt;br&gt;• Repository will include all PSURs and assessment reports</td>
<td>Effective programme management which ensures successful delivery of changes</td>
</tr>
</tbody>
</table>

- EMA launched PSUR Repository in January 2015
- Independent audit was conducted from January to March 2015
- **Based on the positive recommendation of the Pharmacovigilance Risk Assessment Committee (PRAC), on 12 June 2015 the EMA Management Board announced that PSUR Repository has achieved its full functionality**
- **The use of the PSUR repository in the European Union will become mandatory on 13 June 2016.** From then onwards, industry stakeholders no longer need to submit PSURs to National Competent Authorities, the only requirement being the submission to the PSUR Repository.
• Development of the new ISO/ICH E2B(R3) standard – some milestones
• New ISO ICSR standard - ICH E2B(R3) guideline – EU Implementation Guide the “package”
• Expected benefits
• Examples of changes moving from ICH E2B(R2) to ICH E2B(R3)
• Summary
Development of new ISO-ICH E2B(R3) standard

- 2004
  ICH initiates work on E2B(R3)

- Nov 2005
  E2B(R2) mandatory in EU

- 2006
  ICH Steering Committee decision to work with SDOs

- June 2009
  ICH Awareness publication

- Sept 2011 – March 2012
  ICH Step 3 public consultation

- Dec 2011
  Final ISO/HL7 standard published

ICH Step 4
Nov 2012
E2B(R3)

Last Release
July 2013

EU ICSR
Implementation Guide
4 Dec 2014
New ISO ICSR standard and the ICH E2B(R3) guideline

- **The standard** is based upon an HL7 ICSR model that is capable of supporting message exchange for a wide range of product types (e.g. human medicinal products, veterinary products, medical devices etc.):
  - ISO/HL7 27953-1: 2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 1: The framework for adverse event reporting
  - ISO/HL7 27953-2: 2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2: *Human pharmaceutical* reporting requirements for ICSR

- The **ICH E2B(R3) Implementation Guide (IG)** provides the core set of requirements for the content of messages i.e. the ICH agreed data elements

- The **EU ICSR IG** compliments the ICH E2B(R3) IG and defines EU specific requirements – *additional data elements, EU specific CVs, business rules*
New ISO ICSR standard and the ICH E2B(R3) guideline

Expected benefits

- Improved ICSR format (~ 10 years of operational experience)
- Alignment with new ISO Identification of Medicinal Products (IDMP) standards
- Improved quality of reports
- Interoperability with healthcare systems e.g. electronic health records
Example of changes (1/4)

• **Changes in data structure (incl. renumbering of data elements)** – new and modified ICSR sections
Examples of changes (2/4)

- Fields updated (size increased, new value)
  - H.1 Case narrative (100000AN)
  - D.2.3 Patient age group “Foetus”
  - Drug not administered (clinical trial, medication error)
  - Use of nullflavors

- Merge of fields e.g.
  - C.1.8.1 Worldwide Unique Case Identification Number
  - Updated sections e.g.
  - C.1.8.2 First Sender of This Case (value regulator; other)

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSK</td>
<td>Masked</td>
<td>There is information on this item available but it has not been provided by the sender due to security, privacy or other reasons.</td>
</tr>
<tr>
<td>UNK</td>
<td>Unknown</td>
<td>A proper value is applicable, but not known.</td>
</tr>
<tr>
<td>NA</td>
<td>Not Applicable</td>
<td>No proper value is applicable in this context (e.g. last menstrual period for a male).</td>
</tr>
<tr>
<td>ASKU</td>
<td>Asked But Unknown</td>
<td>Information was sought but not found (e.g. patient was asked but didn't know)</td>
</tr>
<tr>
<td>NASK</td>
<td>Not Asked</td>
<td>This information has not been sought (e.g. patient was not asked)</td>
</tr>
</tbody>
</table>
Examples of changes (3/4)

- New fields e.g.
  - C.1.2 Date of creation (timestamp replacing version number)
  - C.1.6.1.r.2 Included Documents (incl specification of media types allowed)
  - D.7.3 Concomitant Therapies – flag to indicate other therapies at time of the reaction (radiotherapy, drug class)
  - C.2.r.5 Primary Source for Regulatory Purposes - this source identifies where the case occurred

- Fields have become repeatable e.g.
  - C.1.6.1.r.1 Documents Held by Sender
  - G.k.7.r Indication for Use in Case
  - Study registration

Note that 'EU' is permitted as a country code
Examples of changes (4/4)

- New concepts/principles
  - E.i.3.2 Seriousness Criteria at Event Level
  - C.1.11 Amendment e.g. correction of adverse event/reaction terms, seriousness, seriousness criteria or causality assessment
  - One MedDRA version in a single ICSR
  - G.k.4.r Dosage information

- HL7 messages sent as batch e.g.
  - N.1 ICH ICSR Transmission Identification (batch wrapper) – each batch has a header
  - N.2 ICH ICSR Message Header (message wrapper) – each ICSR in the batch is its own message with its own message header

<table>
<thead>
<tr>
<th>Field</th>
<th>R2 value</th>
<th>R3 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.k.4.r.1a</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>G.k.4.r.1b</td>
<td>mg</td>
<td>mg</td>
</tr>
<tr>
<td>B.4.k.5.3</td>
<td>3</td>
<td>element removed</td>
</tr>
<tr>
<td>G.k.4.r.2</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>G.k.4.r.3</td>
<td>day</td>
<td>hours</td>
</tr>
</tbody>
</table>
New ISO ICSR standard and the ICH E2B(R3) guideline

Reference documentation

• ICH documentation (http://estri.ich.org)
  ➢ ICH Implementation guide package
  ➢ ICH E2B(R3) Questions & Answers (Q&As)

Step 4 ICH IG Package  UPDATED

To download the package click here

ICH E2B(R3) Questions & Answers (Q&As)

To download the Q&As click here
New ISO ICSR standard and the ICH E2B(R3) guideline

Reference documentation

- EU Documentation (http://www.ema.europa.eu)
  - EU Individual Case Safety Report (ICSR) Implementation Guide (EMA/51938/2013) plus supporting documents

<table>
<thead>
<tr>
<th>Documentation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU ICSR Implementation Guide</td>
<td>A guide describing the additional EU-specific requirements to generate a valid ICSR and message acknowledgment to implement EN ISO ICSR in accordance with ICH E2B(R3).</td>
</tr>
<tr>
<td>EU ICSR implementation guide business rules spreadsheet</td>
<td>This spreadsheet includes all the ICH E2B(R3) and EU specific business rules in a format to help system developers.</td>
</tr>
<tr>
<td>EU backwards forwards conversion element mapping spreadsheet</td>
<td>This document describes the relationship between EU specific data elements in E2B(R3) and E2B(R2). This document is an addition to the ICH backwards-forwards conversion rules. It covers additional EU-specific rules for the conversion back and forth between E2B(R2) and E2B (R3).</td>
</tr>
<tr>
<td>Draft EU BFC conversion</td>
<td>The ICH backwards-forwards conversion tool updated to include additional EU-specific data fields.</td>
</tr>
<tr>
<td>EU E2B(R3) code lists</td>
<td>The list of codes for EU-specific data fields.</td>
</tr>
<tr>
<td>EU reference instances</td>
<td>ICH reference instances amended to include EU-specific data fields.</td>
</tr>
<tr>
<td>EU example instances</td>
<td>Additional example instances to be used for testing E2B(R3) transmissions to the EudraVigilance system.</td>
</tr>
</tbody>
</table>
• The ISO/ICH E2B(R3) ICSR standard will bring benefits to all stakeholders

• The use of the new ICSR standard will require changes on how ICSRs are currently created, reported, processed and analysed

• Detailed ICH and EU guidance is published, which should be carefully reviewed and assessed to assist in the necessary adaptations of phv systems and business processes
Topic III. EudraVigilance Audit

- Changes to EudraVigilance
- Audit of EudraVigilance and planning
- Training
- Further guidance and information
- Summary

Enhanced adverse reaction collection and management system
Changes to EudraVigilance (1/2)

Pharmacovigilance legislation

• Simplification of adverse reaction reporting in the EU (Dir 2001/83/EC Art 107/107a)
• Reporting to WHO UMC of suspected adverse reactions occurring in the EU by the Agency (Reg (EC) 726/2004, Art 28c)
• Provision of access to EudraVigilance – EEA medicines regulatory authorities, Commission, EMA, healthcare professionals, public, research institutions and marketing authorisation holders (Reg (EC) 727/2004, Art 24)
• Signal detection and validation based on EudraVigilance data (Commission IR (EU) 520/2012, chapter III)
• Monitoring of selected literature for a selected number of substances by EMA (Reg (EC) 726/2004, Art 27)
• Use of internationally agreed formats, standards and terminology (Commission IR (EU) 520/2012, chapter IV)
Changes to EudraVigilance (2/2)

Clinical trials legislation

• Electronic database for safety reporting to be module of EudraVigilance = EudraVigilance Clinical Trial Module (EVCTM) (Reg (EU) No 536/2014, Art 40)

• Reporting of suspected unexpected serious adverse reactions (SUSARs) by sponsor to EVCTM (Reg (EU) No 536/2014, Art 42)

• Development of a standard web-based structured form for the SUSARs reporting by sponsors to EudraVigilance (Reg (EU) No 536/2014, Art 42)

• Re-routing of SUSARs to concerned to Member States (Reg (EU) 536/2014, Art 44)
Audit of EudraVigilance and planning (1/4)

- Functional specifications were prepared by the Agency in collaboration with Member States and the Commission to address required changes.
- Functional specifications were endorsed by EMA Management Board in December 2013 and are subject to an independent audit ("auditable requirements").
- EMA Management Board is to announce when Eudravigilance database has achieved full functionality and the system meets the functional specifications based on:
  - Independent audit report
  - Recommendation of the Pharmacovigilance Risk Assessment Committee
- Simplification of adverse reaction reporting will apply six months following the announcement by the Board.
Audit of EudraVigilance and planning (2/4)

Delivery of new EV functionalities

High level plan of changes

<table>
<thead>
<tr>
<th>Key milestones</th>
<th>2016</th>
<th>2017</th>
<th>Post ISO IDMP Implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>Revised EV Access Policy published</td>
<td>6 months post announcement of successful audit</td>
<td>EV stop accepting R2 format messages</td>
</tr>
<tr>
<td>Q3</td>
<td>EudraVigilance Audit</td>
<td>Mid 2017</td>
<td>Implement new EVDAS/eRMR functionalities</td>
</tr>
<tr>
<td>Q4</td>
<td>Announcement of successful EudraVigilance Audit</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Changes to legislation of:
- Post-authorisation
- Clinical trials

Results in changes to:
- EudraVigilance system
- Reporting of ICSRs and SUSARs

Change Management Plan to detail IT & business changes which affect EMA, NCAs, MAHs and Clinical Trials Sponsors

Stakeholders to develop individual internal detailed plans to manage the changes.
Audit of EudraVigilance and planning (3/4)
High level EMA Stakeholder Communication Plan

- EMA will work closely with stakeholders at each step of the process to ensure everyone is informed and prepared
- Communication Plan will be routinely updated
What training will be available?

Timely training of staff is critical to ensure readiness and preparedness for new business processes and new IT functionalities of local phv systems and EV

Flexible training paths

- Main focus will be on *module based* online training for all users (accessible through the dedicated EMA webpage)

- The online learning will comprise the use of:
  - User Manuals
  - Information videos and quick guides
  - Demo videos
  - Competency assessments

- Limited face to face trainings based on train the trainer approach may be offered.
Where to find further guidance and detailed information?

- Dedicated EudraVigilance webpage at the Agency’s corporate website

http://www.ema.europa.eu
Where to find further guidance and detailed information?

http://www.ema.europa.eu

| Consultation of Project Maintenance Group 1 | 15 July 2015 |
| Consultation of EudraVigilance Expert Working Group | 23 September 2015 |
| Consultation of Signal Management Review Technical Working Group (SMART WG) – Work Stream 1 | 7-10 September 2013 |
| Consultation of the Pharmacovigilance Risk Assessment Committee (PRAC) | 7-10 September 2013 |
| Implementation Group (IG) for Information | 14 September 2015 |
| IT Directors for Information | 22 October 2015 |
| EU Telematic Management Board (EUTMB) for Information | 15 September 2015 |
| Endorsement by European Risk Management Facilitation Group (ERM-FG) | 12 October 2015 |
| Heads of Medicines Agencies (HMA) for Information | 22 October 2015 |
• Agreed enhancements to EudraVigilance are being progressed according to project plan
• Regular updates at each project milestone will be provided to stakeholders according to published communication plan
• Modular and easy accessible training will be provided
• EudraVigilance stakeholder change management plan provides instructions on how to prepare for system and business process changes
Topic IV Revised EudraVigilance Access Policy

Access to ICSRs held in EudraVigilance by Marketing Authorisation Holders

Adopted in December 2015

- 2010 PV legislation - extended access to EudraVigilance
- Principles of the Access Policy
- Policy highlights
- References
- Summary
2010 PV legislation - extended access to EudraVigilance

• Article 24(2) of the Regulation defines the level of EudraVigilance access as follows:
  
  – EudraVigilance shall be fully accessible to the competent authorities of the Member States and to the Agency and the European Commission.
  
  – It shall also be accessible to MAHs to the extent necessary for them to comply with their pharmacovigilance obligations.
  
  – The Agency shall ensure that healthcare professionals and the public have appropriate levels of access to the EudraVigilance database, while guaranteeing personal data protection.

• Article 28(c) of Regulation (EC) No 726/2004 further states that
  
  – The Agency shall make available promptly all suspected adverse reaction reports occurring in the Union to the WHO.

  **N.B.**  – Changes do not relate to Clinical Trial reports (suspected unexpected serious adverse reactions - SUSARs)
Principles of the Access Policy

- The policy takes into account the legal requirement of broadening stakeholder access to EudraVigilance data;
- The policy drives to enable pharmacovigilance monitoring for public health;
- The policy is fully in line with EU data protection law;
- The policy recognises the applicable ISO ICSR standard/ICH E2B(R3) guideline;
- All stakeholders have the responsibility to apply appropriate technical and organisational measures to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss.
Policy highlights (1/4) – stakeholder groups

- Six Stakeholder Groups
  - Stakeholder Group I - Medicines regulatory authorities in EEA Member States, European Commission and the Agency
  - Stakeholder Group II - Healthcare Professionals and the Public
  - **Stakeholder Group III - Marketing Authorisation Holders**
  - Stakeholder Group IV - Academia
  - Stakeholder Group V - WHO Uppsala Monitoring Centre
  - Stakeholder Group VI- Medicines regulatory authorities in third countries
### Policy highlights (2/4) - Stakeholder Group III – MAH access

<table>
<thead>
<tr>
<th>EV System Component</th>
<th>Report Type</th>
<th>ICSR Data Element Access</th>
</tr>
</thead>
</table>
| **Stakeholder Group III** | • For ICSR that do not contain suspect drug owned by the MAH  
  • Spontaneous report | • **Level 1** = for case overview  
  ‒ Access to addrepts.eu website and EVDAS |
| | • For ICSRs that contain suspect drug owned by the MAH  
  • Spontaneous report  
  • Report from study  
  ‒ Individual patient use  
  ‒ Other studies  
  • Other  
  • Not available to sender | • **Level 2A** = Extended subset of ICSR data elements for signal detection and validation  
  ‒ **Level 2B** = 2A including case narrative  
  ‒ Access authorisation based on EV registration and signature of Confidentiality Undertaking for signal validation and other phv obligations  
  ‒ Access to EVWEB and EVDAS based on users registration |
| | • For ICSRs sent by the MAH  
  • Spontaneous report  
  • Report from study  
  ‒ Individual patient use  
  ‒ Other studies  
  • Other  
  • Not available to sender | • **Level 3** = All ICSR data elements  
  ‧ Sender-based  
  ‧ MLM reports based on Article 27 of REG 726/2004 for signal detection and validation  
  ‒ Access to EVWEB and EVDAS based on users registration |
### Policy highlights (3/4) – defined mechanism of access

<table>
<thead>
<tr>
<th>EV System Component</th>
<th>Stakeholder Group</th>
<th>Data Formats and Purpose</th>
</tr>
</thead>
</table>
| EVWEB incl. ICSR Export Manager | III               | • ICSR XML format – electronic case processing  
• ICSR form – individual case review |
| EVDAS                        | III               | • e-RMRs/substance groupings – signal detection  
• ICSR line listings – overview of individual cases - signal validation  
• ICSR forms - individual case review - signal validation  
• Aggregated data outputs based on query parameters – signal detection/validation and case administration |
| Adrreports.eu web portal     | III               | • Aggregated data outputs  
• ICSR line listings – overview of individual cases  
• ICSR forms - individual case summary |
Policy highlights (4/4) - ICH E2B(R3) data elements access defined

<table>
<thead>
<tr>
<th>ICH E2B(R3) ICSR Implementation Guide ICSR sections</th>
<th>Total</th>
<th>Stakeholder Group I</th>
<th>Stakeholder Group II-VI</th>
<th>Stakeholder Group III &amp; IV</th>
<th>Stakeholder Group III</th>
<th>Stakeholder Group V &amp; VI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Level 3</td>
<td>Level 1</td>
<td>Level 2A</td>
<td>Level 2B</td>
<td>Level 3</td>
</tr>
<tr>
<td>C.1 Identification of the case safety report</td>
<td>20</td>
<td>20</td>
<td>3</td>
<td>18</td>
<td>18</td>
<td>20</td>
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<tr>
<td>C.2.r Primary source(s) of information</td>
<td>15</td>
<td>15</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>C.3 Information on sender of case safety information</td>
<td>16</td>
<td>16</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>16</td>
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<td>C.4.r Literature reference(s)</td>
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<td>2</td>
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<tr>
<td>C.5 Study identification</td>
<td>6</td>
<td>6</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>D. Patient characteristics</td>
<td>96</td>
<td>96</td>
<td>4</td>
<td>87</td>
<td>87</td>
<td>96</td>
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<td>E.1 Reaction(s)/event(s)</td>
<td>21</td>
<td>21</td>
<td>11</td>
<td>21</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>F.r Results of tests and procedures relevant to the investigation of the Patient</td>
<td>13</td>
<td>13</td>
<td>0</td>
<td>13</td>
<td>13</td>
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<tr>
<td>G.k Drug(s) information</td>
<td>76</td>
<td>76</td>
<td>23</td>
<td>72</td>
<td>72</td>
<td>76</td>
</tr>
<tr>
<td>H. Narrative case summary and further information</td>
<td>7</td>
<td>7</td>
<td>0</td>
<td>4</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Grand Total</td>
<td>272</td>
<td>272</td>
<td>53</td>
<td>228</td>
<td>230</td>
<td>272</td>
</tr>
</tbody>
</table>
### Policy highlights – summary

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Access given (summary)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulators in EEA</td>
<td>Complete access to all data via data Warehouse</td>
</tr>
<tr>
<td>General public</td>
<td>All spontaneous reports as aggregated data + line listings based on restricted data elements via adreports.eu</td>
</tr>
<tr>
<td>MAHs</td>
<td>1. Access to all data elements for cases sent</td>
</tr>
<tr>
<td></td>
<td>2. Access to restricted data set for substances in their products (for signal detection)</td>
</tr>
<tr>
<td></td>
<td>3. Access to extended data set based on confidentiality undertaking (for signal validation. N.B. includes free text narratives)</td>
</tr>
<tr>
<td>Academia</td>
<td>Aggregated access as general public + access on request + study protocol to extended data set based on confidentiality undertaking. No pre-scrutiny of publications</td>
</tr>
<tr>
<td>WHO-UMC</td>
<td>Extended data set – agreed with WHO – sent electronically every day</td>
</tr>
<tr>
<td>3rd country regulators</td>
<td>Data set as WHO but reactive access (i.e. on request)</td>
</tr>
</tbody>
</table>
Where to find further information?

Increasing access to reports on adverse reactions to medicines

10/12/2015

Increasing access to reports on adverse reactions to medicines

Revised EudraVigilance access policy is adopted by EMA Management Board

The EMA will give increased access to reports on suspected adverse reactions to medicines authorised in the European Union (EU), while guaranteeing that personal data will be fully protected. This is the outcome of a revision of EudraVigilance Access Policy, which was adopted by EMA’s Management Board at its December 2015 meeting. The adoption followed a broad public consultation generating close to 400 comments which have been taken into account in the final policy.

EudraVigilance is the European database of all suspected adverse reactions reported with medicines authorised in the European Economic Area (EEA). Managed by EMA on behalf of the EU medicines regulatory network, EudraVigilance receives over one million adverse drug reaction (ADR) reports per year. The large database included in the database provide the backbone for the continuous safety monitoring of medicines in the EU.

The Agency has made data from EudraVigilance publicly available since 2011. At the time, EMA defined levels of access to information on ADR reports for medicines in

• Revised EudraVigilance Access Policy to be implemented as part of the enhancements of EudraVigilance

• Unprecedented access to currently $\approx 10$ million reports/$6$ million cases

• Full protection of personal data based on detailed analysis of data elements related to identifiability of patients/reporters

• Better functionality in the EV data warehouse for regulators

• New access for MAHs incl eRMRs, line listings and ICSR forms to support signal detection and validation

• Access for academia to support research
Topic V. Revision 2 of GVP Module VI

Guideline on good pharmacovigilance practices: Module VI – Management and reporting of adverse reactions to medicinal products

- Key areas to be addressed
- Summary
Revision 2 GVP Module VI- key areas to be addressed

- Electronic reporting modalities of ICSRs and new ICSR format
  - Update in line with new/changed R3 data elements and ICH guidance
  - Provide guidance on new principles e.g. seriousness at reaction level, additional drug role characterisation, amendment reports, handling of additional documents etc.
  - Update references to ICH/EU guidance documents

- Process changes in relation to simplified adverse reaction reporting and implementation of the revised EudraVigilance Access Policy

- Clarification of roles and responsibilities for follow-up, data quality, and duplicate detection (‘shared responsibilities’ of the Agency, NCAs and MAHs)
Revision 2 GVP Module VI- key areas to be addressed

- Management of suspected adverse reactions reported in scientific and medical literature
  - Incorporate literature monitoring and ICSR reporting activities of the Agency (Art 27, REG (EC) 726/2004)
  - Clarify reporting of individual cases from post-authorisation studies published in the literature as regards identifiable patients presented in tables or short summaries
  - Clarify literature monitoring in local journals (substances for which MA assessment is ongoing)
- Management of adverse events originating in non-interventional efficacy studies
  - Provide guidance on management of individual cases of lack of efficacy with no other associated events
Revision 2 GVP Module VI- key areas to be addressed

Under discussion

- Reporting rules for clinical trials and post-authorisation studies
  - Alignment of definitions and reporting modalities based on REG (EU) 536/2014 “Clinical Trials Regulation”

- Off-label use
  - Guidance on managing information on off-label use without harm
**Summary**

- Topics for revision 2 of GVP Module are defined
- Drafting has been initiated – EV-EWG involved
- Public consultation envisaged for end of 2nd quarter 2016
Thank you for your attention

Further information

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