EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update on preparation for Signal Management

7th industry stakeholder platform – operation of EU PV legislation

Presented by Georgy Genov on 4 April 2016
Head of Signal Management - Pharmacovigilance Department

In this talk…

- Preparing for Business process changes
- EV Signal Detection pilot
- EV Stakeholder Testing
- GVP module IX

Preparing for Business process changes

- **MAH Signal validation and management process**:

  - MAHs will have the legal obligation to monitor data available in EV and to inform the Agency and NCAs about any validated signals they identify.
  - The new process for signals validated by MAHs will be designed, discussed and consulted during the 1st revision of the GVP Module IX on signal management. Other guidance documents, including training materials, will be created and provided.
  - MAHs will be granted access to the EudraVigilance Data Analysis system in order to comply with their pharmacovigilance obligations and use the signal detection and analytical reporting functions (e.g. electronic reaction monitoring report and ICSR line listings). MAHs should put in place training for their staff concerning this new tool and register their staff to have access to it.

What training will be available?

Training should be planned for MAH staff on the new business process and new IT systems 6 months prior to implementation in order to be ready once the new EudraVigilance system is implemented.

Key Training Milestones

Training type	Training goal	Timeline	
		2016	2017
User Manual • Update of existing EV and EVDAS user manuals • Creation of new user manuals: ROR reports, Art.57 reports Data quality reports, Duplicate Detection user guide	Detailed guides to support all EVDAS and EV users	*Under Development* →	Available Online
E-Learning • New functionalities/ reports in EVDAS (including changes to the existing reports) • The move from R2 to R3 • EudraVigilance R3 Format	Support existing EVDAS and EV users	*Under Development* →	Available Online
Face to Face • Standard EVDAS training by the Signal Management Service • Regulatory and procedural aspects • EudraVigilance Access Policy • Electronic reporting principles based on new ISO ICSR standard	Support new and existing EVDAS and EV users	Standard EVDAS Training Available on Demand *EV Training Under Development* →	Standard EVDAS Training Available on Demand Available On Demand

MAH Learning Path

	Pharmacovigilance Operations	New EudraVigilance Functionalities	New EudraVigilance Functionalities - IT
E-learning	Introduction to training offering by the EMA	How to register with EudraVigilance and EVDAS	ISO ICSR standard implementation for IT system developers
	New EV functionalities and 2010 pharmacovigilance legislation	Introduction to EV system components and system functionalities	Gateway adaptations for ISO ICSR/ACK message exchange with Eudravigilance
	Implementing ISO ICSR/ICH E2B R3	Overview of reporting process for EV users	Instructions on how to test ICSR submissions to EV
	How to prepare for simplified adverse reaction reporting in the EU	EudraVigilance export manager and ICSR download	
	Revised EV Access policy – how does it impact on MAHs and NCAs	EVDAS training for MAHs	
	Revised GVP guidelines – updates and impact	Medical Literature Monitoring service	
	Medical Literature Monitoring by EMA – what's new		
Guidance	Revised Signal Detection Guideline	MAH's level 1 access via EVDAS	EV Web user manual
	Revised GVP Module VI	EVDAS Report Manual	
	Revised GVP Module IX	Webport user guide for ADR website	
Webinars	Pharmacovigilance Operations Support webinar	EV/EVDAS Functionalities webinar	

Concept of EV Signal Detection pilot

- The concept for pilot study (few MAHs, starting end 2016, proposed by Novartis) was discussed at the last meeting and presented to EV EWG
- Update: timing will not allow impact on process/GVP IX update and not feasible from technical perspective to initiate changes prior to EV audit - focus needs to remain on delivery of new EV functionalities
- Proposal: consider continuous process improvement initiative (all MAHs, starting after new process for access to EV data and signal detection/validation by MAH has started in 2017)

EV Stakeholder Testing

To provide an opportunity to EV stakeholders to use the use EV system, including EVDAS, and provide feedback, the EMA will organise stakeholder testing activities that will take place in June and July 2016. A group of NCAs and MAHs has been selected to participate through a 'Call for volunteers' in March 2016.

The scope of the EV stakeholder testing is to ensure on a high level that the required functionalities have been implemented and that users are able to perform their required role as originally specified in the requirements.

Testing will include:

- EV web
- EVDAS system (including eRMR for MAH)

Any feedback will be analysed by EMA and prioritised for implementation.

Scope of EV stakeholder testing (1)

Not all the 'EudraVigilance Functionalities to be audited' can be tested by external stakeholders, however the main functionalities part of the EV stakeholder testing are:

EVWEB functionalities

- Creating and sending of ICSRs, each data field will be completed to ensure that the requirements of the EU ISO ICSR implementation guide are supported
- Import of XML E2B(R2) and E2B(R3) files is correctly supported
- Export of files in different formats is supported
- Acknowledgements to ICSRs received can be created and sent
- Previous submissions by the same user/organisation can be retrieved and followed up through the WEBTRADER functionality
- Access to ICSR via EV Web search and ICSR export manager, including MLM cases only
- Re-routing of ICSRs to NCAs

Scope of EV stakeholder testing (2)

EVDAS functionalities

- This will include:
  - The enhancements to the existing EVDAS reports.
  - The new EVDAS reports
  - The eRMR for MAH
- Reports will be prioritised to focus on they key functionalities supporting signal detection, ICSR compliance monitoring and access to art.57 data.

Notes:
- eRMR for NCAs is not part of the testing as no new functionalities other than rebuilding the eRMR in the new R3 format are being implemented (same format, same columns).
- For NCAs, the additional detailed requirements collected during the user survey in July/August 2014 will be circulated to the participants to the EV stakeholder testing.

GVP module IX - revision 1

- Highlights:
  - Guidance on MAH-validated signals:
    - MAH signals from EV and/or other sources to feed into general EU SM process
    - Template for validated signals + central mailbox accessible to EMA and Member States
    - Handling of some signals in PSURs or variations
    - 'Emerging safety issues' for urgent safety concerns only
    - Minimum requirements for access to EV case narratives
  - Frequency of EV monitoring (risk-based)
  - Clarifications on definitions and responsibilities throughout process

- EV-EWG consultation on first revised draft: 11/12/2015 – 05/02/2016

=> Contributions from EFPIA (Abbvie, Eli Lilly, GSK, Janssen, Merck KGa, MSD, Novartis, Novo Nordisk, Roche, Sanofi, Takeda) and Baxter

GVP module IX - revision 1

Main comments:

- IR terminology (e.g. confirmation) vs. e.g. CIOMS VIII
- Roles and responsibilities
- Interface between MAH established processes and EU process with PRAC involvement

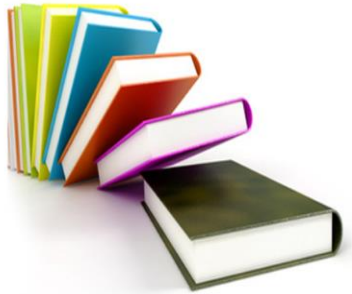
Updated draft:

- Dedicated section on IR terminology
- Roles and responsibilities further clarified
- Revised structure (scientific vs EU procedural aspects)
- Flowcharts

Next steps:

- PRAC consultation: Q2 2016
- Public consultation: Q3 2016

Module IX Addendum I – Methodological Aspects of Signal Detection from Spontaneous Reports



- General principles and components of an effective system for routine signal detection
- The approaches to signal detection discussed have been tested in a number of large and medium sized reporting databases (PROTECT outcomes)

Timeframe: aligned with GVP IX

- ➢ Under development: User guide on how to screen Adverse Drug Reactions in EudraVigilance
- Methodological Aspects of Signal Detection in EudraVigilance;
- User manuals on how to use Data Analysis System (EVDAS) and the electronic Reaction Monitoring Report (eRMR) for Signal Detection will also be updated;

Thank you for your attention

Further information

Contact me at (georgy.genov@ema.europa.eu)

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
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