EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance in the EU:

Roles and responsibilities

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An agency of the European Union

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THE CURE CAN BE WORSE THAN THE DISEASE

Actual harm caused by medicines comes from

Medication errors (2-14 % hospitalisations)

- Prescription, dispensing, preparation and administration errors, including unsubstantiated off-label use (i.v. - often more than 50 % erroneously prepared or administered)
- Errors in follow-up monitoring (anticoagulants, hepatotoxic drugs…)

Known and preventable ADRs and interactions (1.8-6.5% of hospitalisations)

Rare, or unknown ADRs

Definitions

- *Pharmacovigilance* (WHO)

The science and activities relating to the detection, understanding and prevention of adverse drug reactions or any other drug-related problems.

- *Adverse Drug Reaction*

Harmful, unintended effect which occurs at doses normally used. Can be serious or non-serious;

Types:

A- anticipated

B- bizarre

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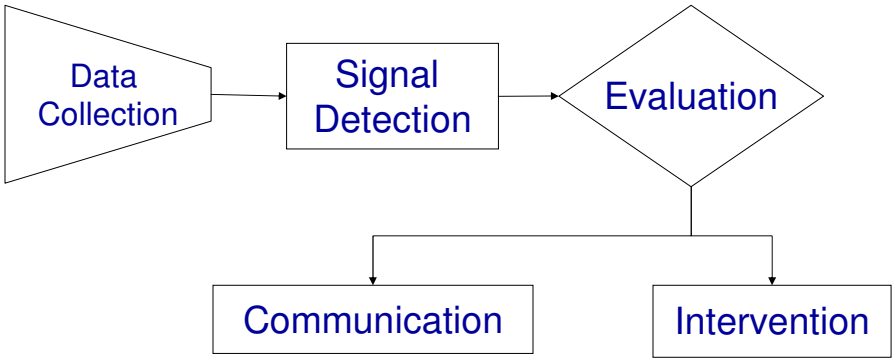
Basic pharmacovigilance process



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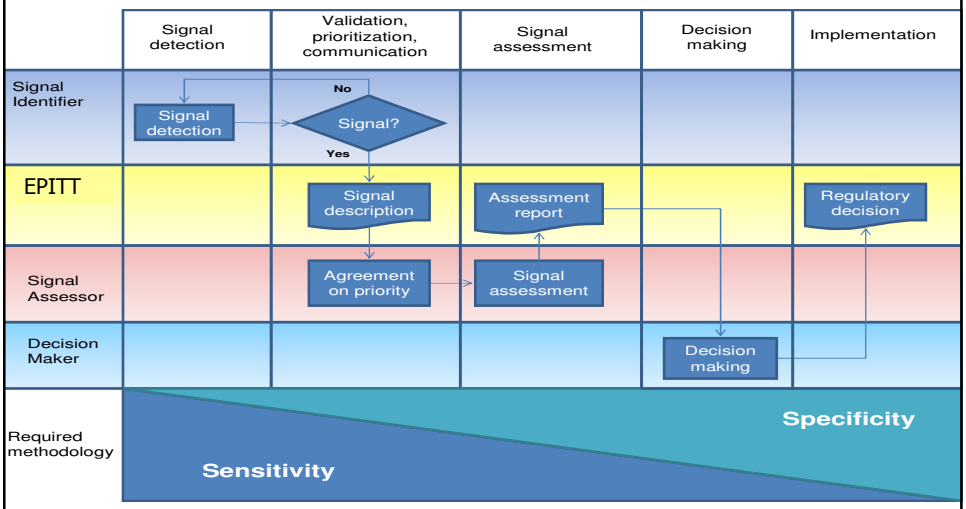
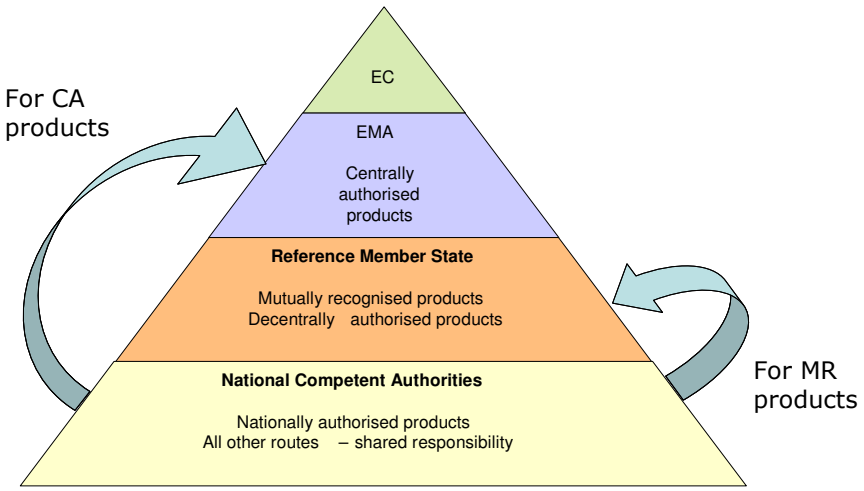
Signal Management Overview



EU Regulators: PhV responsibility and delegation



The EU pharmacovigilance system: Legal and regulatory basis

- Directive 2001/83/EEC Title IX
- Council Regulation (EC) No. 726/2004, Chapter 3 of Titles II (Human) and III (Vet)
- Vol 9 of the Rules Governing Medicinal Products in the EU
- ICH guidelines (E2B, E2C, E2D, E2E…)

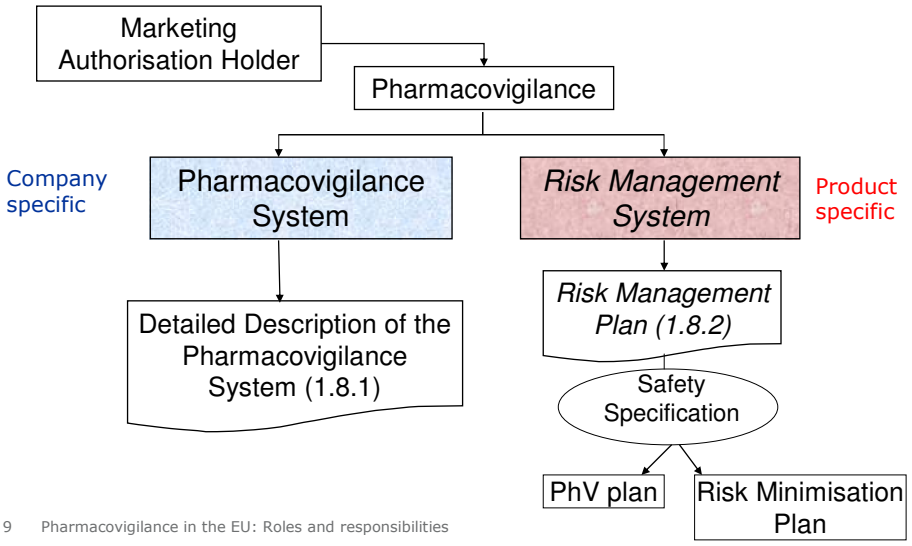
http://pharmacos.eudra.org/F2/eudralex

Obligations of MAHs & National Competent Authorities (NCAs)

National PhV systems & Networking structure

European Medicines Agency co-ordination (including Eudravigilance database)

MAH's post-marketing surveillance



Tasks of the Agency

Co-ordination of EU pharmacovigilance system

Maintenance of Rapid Alert/Non-Urgent Information System

Maintenance of EudraVigilance (electronic data processing network)

CHMP Pharmacovigilance Working Party Secretariat

Involvement in review of legislation and guideline development

Pharmacovigilance for centrally authorised products

Referral procedures for nationally authorised products

External contacts and international collaboration

EudraVigilance

- Database for the collection, verification and presentation of Adverse Drug Reaction reports
- Mandatory for transmission of ICSRs & SUSARs within EEA
- Key functionalities
  - Gateway
    - Single electronic reporting point within EEA
    - Routing of messages to specified receiver
  - EVWEB
    - Free web-based application for the creation and transmission of ICSRs
    - 3-day training courses every month at Agency and around world
  - EVMPD
    - EudraVigilance Medicinal Product Dictionary
    - Standardises medicinal product data in ICSRs
  - EVDAS
    - EudraVigilance Data Analysis System
    - Statistical analysis of data in EudraVigilance
- Achievements
  - All NCAs in production with EV
  - >500 MAHs & Sponsors in production with EV
  - >2 million individual case safety reports in EV

CHMP Pharmacovigilance Working Party

Expert Group to the CHMP

Mandate

To provide advice on the safety of medicinal products authorised in the EU and the investigation of ADRs, to enable effective identification, assessment and management of risk, at any phase in the product life cycle.

Composition

Chairperson (Dr June Raine)

+ 1 member per Member State, Norway, Iceland and Liechtenstein

+ 8 Co-opted members (expertise in risk management, communication, pharmacoepidemiology)

+ 2 Observers: 1 from European Commission, 1 from Patient Organisations

+ EMEA

Output

Recommendations to CHMP/CMD(h)/NCAs, and published Monthly report

External contacts and international collaboration

European Medicines Agency/PhVWP

European Economic Area

Co-operation with Accession Countries

World Health Organization (WHO) and Collaborating Centres

Non-EEA regulatory authorities, including US Food and Drug Administration (FDA) - PhVWP videoconferences, and visiting experts

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

Consultation with industry associations at EU level

Consultation with other interested parties and learned societies

EPITT (European Pharmacovigilance Issues Tracking Tool)

- Database facilitating the sharing of safety information of the medicinal products for human use between the National Competent Authorities (NCAs) and the Agency.
- 4 "main modules" : Safety Issues, Safety Signals, PSURs, RMPs
- Objectives:
  - Tracking of the Safety Issues and Signals "live cycles" (independently of the authorisation type)
  - Monitoring of the implementation of PhVWP recommendations and SPC wordings within the EU
  - Tracking and monitoring of the PSURs cycles and Risk Management Plans together with the implementation of the regulatory actions they require
  - Support to the European Incident Management Plan procedure
  - Easy retrieval of the documents related to the safety of a medicinal product
- EPITT is :
  - 250 users within the EU (Agency and 27 NCAs)
  - Around 65 users per week working in about 20 different NCAs

Rapid Alert and Non-Urgent Information System

System for exchange of information and communication.

e-mail based system within EudraNet, sent from EPITT.

Participants

Competent authorities of Member States and EEA States, including the European Commission

European Medicines Agency

ENCePP: European Network of Centres for PhV & Pharmacoepidemiology

Capacity building

•EMEA-led project to bring together the **available expertise and research experience** in the fields of **PhEpi** and **PhV** scattered across Europe in a **Network of Excellence**, [research and medical-care centres, healthcare databases, electronic registries and existing networks].

• The aim is to further **strengthen the post-authorisation monitoring of medicinal products in Europe** by facilitating the conduct of high quality, multi-centre, independent post-authorisation studies focusing on safety and benefit:risk.

ENCePP – what is happening?

- Capacity building in EU academia - fostering partnerships and new networks and consortia for funded projects
- Sharing best practice and developing standards for studies
- Developing information resources:
  - Public database of service providers (released 29/1)
  - Public database of available data sources
  - Public database of non-interventional studies

The present and future…

New therapeutic areas (advanced therapies)

Increasing importance of harmonisation in drug safety

Improved Public communication and transparency

Increasing communication within and outside the EU

EudraVigilance (improve signal detection, access policy)

Patient reports

Product-specific risk management programmes and epidemiological tools

Review of PhV legislation – Pharma package

Conclusion: advantages of EU collaboration

- Pooling / sharing of expertise
- Peer review of each other's work
- Benchmarking
- Sharing standards
- Bigger population from which to collect data
- Bigger databases – greater power to detect (e.g. EudraVigilance)
- Bigger market – reduced cost of monitoring relative to market size
- Different healthcare systems – allows comparisons of use and impact of risk minimisation measures

Risk Minimisation Tools: Examples

Education:

Labelling

Education materials

- Written, sound, video, cards

Training

Reminders (letters, alert cards, check lists, IT alerting mechanisms…)

Distribution:

Legal status (OTC, Rp…)

Hospital/speciality only

Controlled distribution system

- Only registered and trained physicians/pharmacists/patients