EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

New Pharmacovigilance legislation

Post-authorisation safety studies

ENCePP Plenary meeting

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Why ?

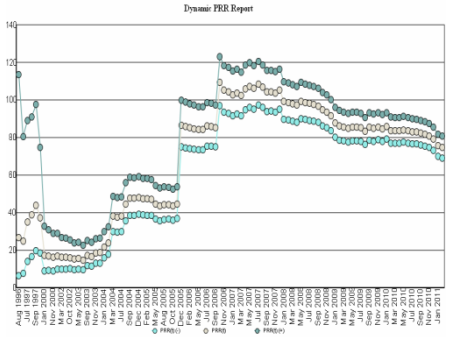
Public health impact of adverse drug reactions in the EU

- 5% of all hospital admissions are for ADRs
- 5% of all hospital patients suffer an ADR
- ADRs are the 5th most common cause of hospital death
- Estimated 197,000 deaths per year in EU from ADRs
- EU societal cost of ADRs amounts to Euro 79 billion per year

Source: Annex 2 of the Report on the impact assessment of strengthening and rationalising EU Pharmacovigilance COMMISSION OF THE EUROPEAN COMMUNITIES Sept 2008

Strengthening pharmacovigilance requires:

Resources



Law

New pharmacovigilance legislation

Regulation (EU) No 1235/2010

Directive 2010/84/EU

Good Vigilance Practice (GVP)

Science

ENEPP – Independence, Standards, Transparency

PROTECT

EU-ADR

and many other projects…

The new pharmacovigilance legislation

High level objectives

Promote and protect public health by reducing burden of ADRs and optimising the use of medicines:

- Clear roles and responsibilities
- Science based (move up hierarchy)
- Risk based/proportionate
- Increased proactivity/planning
- Reduced duplication/redundancy
- Integrate benefit and risk
- Communication and transparency

The new pharmacovigilance legislation

Addresses almost all pharmacovigilance activities

- Authorisation requirements
- Risk Management Plans
- PSURs
- Scientific Committees
- Transparency and communication
- Coordination of inspections
- Audits
- Effectiveness of risk minimisation
- ADR reporting
- Post-autorisation safety studies

Post-authorisation safety studies

Definition

Any study relating to an authorised medicinal product conducted with the aim of:

- identifying, characterising or quantifying a safety hazard,
- confirming the safety profile of the medicinal product, or of
- measuring the effectiveness of risk management measures.

The Good Vigilance Practice guidance

Guidance for the implementation of the new pharmacovigilance legislation

Guidance divided by Module (PASS: Module VIII)

Each Module divided in three sections:

- A. Introduction
- B. Structures and processes
- C. Operation of the EU Network

General guidance and requirements for PASS in Module VIII.B. of the Good Pharmacovigilance Practice

Guiding principles:

- Scientific standards
- Transparency
- Harmonisation
- Quality control

Applies to all PASS

Level of enforcement depends of type of studies (voluntarily/imposed) and topic

Post-authorisation safety study

- Clinical trial
- Non-interventional study

If the PASS is a clinical trial, Directive 2001/20/EC and Volume 10 of The Rules Governing Medicinal Products in the European Union shall apply

GVP Module VIII mainly applies to non-interventional trials

General guidance and requirements

General principles

- Consideration to relevant scientific guidance (eg ISPE, ENCePP)
- Investigators qualified by education, training and experience
- Research contract
  - compliance to regulatory requirements
  - investigator's scientific expertise to be excercised
  - ENCePP Code of Conduct recommended

General guidance and requirements

Study protocols

- Transmission to relevant competent authorities
- Involvement of QPPV
- Registration into EU public registry of PASS (i.e. ENCePP registry, to be up-graded)
- Change control
    - substantial amendments to protocol to be notified

General guidance and requirements

Reporting of pharmacovigilance data

- data relevant to the risk benefit balance
- Reporting of ADRs:
  - serious and non serious ADRs to be reported within 15 and 90 days respectively *(see current GVP Module VI, subject to final approval)*
  - for studies with secondary use of data
    - → no requirement for reporting; events/reactions summarised in final study report
  - for studies with primary use of data
    - → reporting where possible relationship between an event and a suspected medicinal product considered by reporter or MAH

General guidance and requirements

Study reports

- Progress reports
  - may be requested before study commences or any time during study conduct – timing to be agreed
- Final study report
  - to be submitted as soon as possible after finalisation within 12 months
  - transmission to competent authorities
- Publication of results by investigators
- Submission of published study results

General guidance and requirements

Format and content of study protocols and study reports

- Described in Implementing measures and GVP
- Obligation for studies imposed as an obligation
- Recommendation for studies conducted voluntarily
- Technical contribution from EMA to European Commission
- Based on international guidance, e.g.
  - ISPE
  - STROBE, CONSORT
  - ENCePP Checklist for Study Protocols
  - ENCePP Guide for standards in pharmacoepidemiology

General guidance and requirements

Registration of studies in EU registry of non-interventional post-autorisation safety studies (« ENCePP » registry)

- Recommended for all post-authorisation safety studies
- Transparency
- Tool for obligation to EMA to publish study protocols and final results of imposed PASS concerning Centrally-authorised products
- Tool for communication and exchange of information
- Minimisation of administrative procedures and duplication of work.

General guidance and requirements

Quality systems, audit and inspections

- Fulfilment of obligations in relation to study can be audited, inspected and verified.
- Traceability and documentation of any change to data.
- Analytical dataset and statistical programme used to generate results to be kept in electronic format and available for auditing and inspection
- MAH should ensure that external investigators are qualified by education training or experience to perform their tasks.

General guidance and requirements

Data protection

- MAH should ensure that all study information is handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of the study subjects remains protected.
- Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data.
- Relevant legislation and guidance of Member States where the study is conducted.

Implementing Measures: Post-Authorisation Safety Studies

Art 36 (4)– Scope

"The marketing authorisation holder shall ensure that all study information is handled and stored as to allow accurate reporting, interpretation and verification of that information and shall ensure that the confidentiality of the records of the study subjects remains protected. The marketing authorisation holder shall ensure that the analytical dataset and statistical programmes used for generating the data included in the final study report are kept in electronic format and are available for auditing and inspection"

Implementing Measures: Annex III

Protocol, abstracts and final study report for post-authorisation studies

- Format of the study protocol
- Format of the abstract of the final study report
- Format of the final study report

Thank you !