EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Network of Centres
for Pharmacoepidemiology and Pharmacovigilance

POST-AUTHORISATION STUDIES IN EUROPE: BRIDGING THE GAP BETWEEN REGULATORY AND HEALTH TECHNOLOGY ASSESSMENT (HTA) STAKEHOLDER NEEDS BY BETTER DESIGN OF STUDIES

Luis Prieto

Risk Management Review
Scientific and Regulatory Management Department
Human Medicines Evaluation Division

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A changing scenario for post-authorisation management of medicines

Several factors are likely to shape the current/future agenda of post-authorisation medicines research in the EU:

- New pharmacovigilance (PhV) legislation
- Development of new pharmaceutical technologies
- Progress on regulatory science
- Increasing societal demands
- Globalisation and international collaboration
- IT development
- Increased interest in HTA

Impact of the new PhV legislation

- Biggest change to the legal framework for human medicines since 1995
- Product life-cycle impacted

New legislation

1. Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010. Official Journal L 348, 31/12/2010, p. 74 - 99.
http://ec.europa.eu/health/files/eudralex/vol-1/dir_2010_84/dir_2010_84_en.pdf

2. Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010. Official Journal L 348, 31/12/2010 p. 1 - 16.
http://ec.europa.eu/health/files/eudralex/vol-1/reg_2010_1235/reg_2010_1235_en.pdf

Scope of Changes of the new PhV legislation

- Coordination / lists of medicines
- Authorisation requirements
- Risk Management Plans
- **Post-Authorisation Studies (Safety and Efficacy)**
- Effectiveness of risk minimisation
- Adverse Drug Reactions reporting
- Signal detection
- Periodic Safety Update Reports
- Scientific Committees / PRAC / decision-making
- Transparency and communication
- Coordination of inspections
- Pharmacovigilance Audits

Post Authorisation Safety/Efficacy Studies (PASS/PAES)

- Implementation of the PASS procedure for protocols approval and results management
  Started July 2012 – first protocol at October PRAC

- Consultation on PAES
  Commission consultation (February 2013)

European Medicines Agency finalises first set of guidelines on good pharmacovigilance practices

News

25/06/2012

European Medicines Agency finalises first set of guidelines on good pharmacovigilance practices

The European Medicines Agency has published the first set of finalised modules of the guideline on good pharmacovigilance practices (GVP) today.

The finalisation of these seven modules is a key deliverable of the 2010 pharmacovigilance legislation, which will apply from Monday 2 July 2012. Each of the modules covers one major process in the safety monitoring of medicines. These are:

- Module I: Pharmacovigilance systems and their quality systems;
- Module II: Pharmacovigilance systems master files;
- Module V: Risk management systems;
- Module VI: Management and reporting of adverse reactions to medicinal products;
- Module VII: Periodic safety update reports;
- Module VIII: Post-authorisation safety studies;
- Module IX: Signal management.

GVP is a set of measures drawn up to facilitate the performance of pharmacovigilance in the European Union (EU). They apply to marketing-authorisation holders, the Agency and medicines regulatory authorities in EU

Related information

- Good pharmacovigilance practices
- 2010 pharmacovigilance legislation
- Commission implementing regulation No 520/2012 o June 2012
- Guide on methodological standards in pharmacoepidemiology
- Guideline on good pharmacovigilance pract Module I – Pharmacovigi systems and their qualit systems (25/06/2012)
- Guideline on good pharmacovigilance pract Module II – Pharmacovig system master file (25/06/2012)
- Guideline on good pharmacovigilance pract Module V – Risk manage

PASS 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 minimisation measures.

Examples of PASS objectives

- to quantify potential or identified risks
- to evaluate risks of a medicinal product used in patient populations for which safety information is limited or missing (eg pregnant women, specific age groups, patients with renal or hepatic impairment)
- to demonstrate the absence of risk.
- to evaluate the risks of a medicinal product after long-term use.
- to assess patterns of drug utilisation that add knowledge on the safety of the medicinal product (eg indications, dosage, co-medication, medication errors)
- to measure the effectiveness of a risk minimisation activity.

Non-interventional PASS: obligations and requirements

▲ legal obligation ✓ recommended in the GVP ★ optional

Management of study	PASS with MAH involvement	
	Imposed as an obligation	Conducted voluntarily
Standard formats of protocol and study report	▲	✓
PRAC oversight	▲	(if in RMP)*
Registration of study in EU PAS register	▲	✓
Study shall not to promote medicinal product	▲	▲
Payment to HCP restricted to compensation of time and expenses incurred	▲	▲
Quality systems	▲	✓
ENCePP methodological standards	✓	✓
ENCePP checklist for study protocol	✓	✓
ENCePP Code of Conduct	✓	✓
ENCePP seal	★	★

** On a voluntary basis*

Non-interventional PASS: obligations and requirements

▲ legal obligation ✓ recommended in the GVP

Reporting of study information	PASS with MAH involvement	
	Imposed as an obligation	Conducted voluntarily
Protocol and progress reports to be submitted upon request to NCA of MS where study is conducted	▲	▲
Final report to be sent to the NCA of the MS where the study is conducted, within 12 months of the end of data collection	▲	▲
Data generated in the study to be monitored with consideration to benefit-risk of product concerned	▲	▲
Any new information which might influence the evaluation of B/R balance to be reported to NCAs of MS where the product is authorised	▲	▲
Reporting of suspected adverse reactions in studies with primary data collection within 15 days (serious ADRs) or 90 days (non-serious ADRs) *	▲	▲
Final manuscript of article to be transmitted to NCAs of MS where product is authorised within 15 days after acceptance	✓	✓

* See interim and final arrangements in GVP Module VI, C.4

The “EU PAS register”

The “EU PAS Register” is based on ENCePP study registry and includes already registered studies.

What is ENCePP?

- An initiative bringing together the available expertise in the fields of pharmacovigilance & pharmacoepidemiology (Secretariat provided by EMA)

- Further strengthening of post-authorisation monitoring of medicinal products in Europe

- Facilitating conduct of post-authorisation safety and benefit risk studies (+ health outcomes)

Who are the ENCePP partners?

- research centres;
- universities, hospitals;
- owners of healthcare databases and/or electronic registries;
- existing European networks covering certain rare diseases, therapeutic fields and adverse drug events of interest.
- for-profit organisations
  - ➢ provided that they perform studies commissioned by third parties and their main focus is pharmacoepidemiology and pharmacovigilance research

123 Centres, 20 Networks, 48 Data-sources

(as of 30 September 2013)

"EU PAS Register"

(former ENCePP e-register of studies)

A free, publicly accessible resource for the registration of post-authorisation studies (currently, focus on non-interventional studies).

Its aim is to:

- ✓ Increase transparency
- ✓ Reduce publication bias
- ✓ Promote information exchange
- ✓ Facilitate collaborations within the scientific community

(http://www.encepp.eu/encepp/studiesDatabase.jsp)

PASS 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 minimisation measures*.

“Concept” paper – Seed to GVP module XVI

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY (2012)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3305

COMMENTARY

Evaluation of the effectiveness of risk minimization measures

Luis Prieto[1]*, Almath Spooner[2], Ana Hidalgo-Simon[1], Annalisa Rubino[1], Xavier Kurz[1] and Peter Arlett[1]

[1]*European Medicines Agency, London, UK*
[2]*Irish Medicines Board, Dublin, Ireland*

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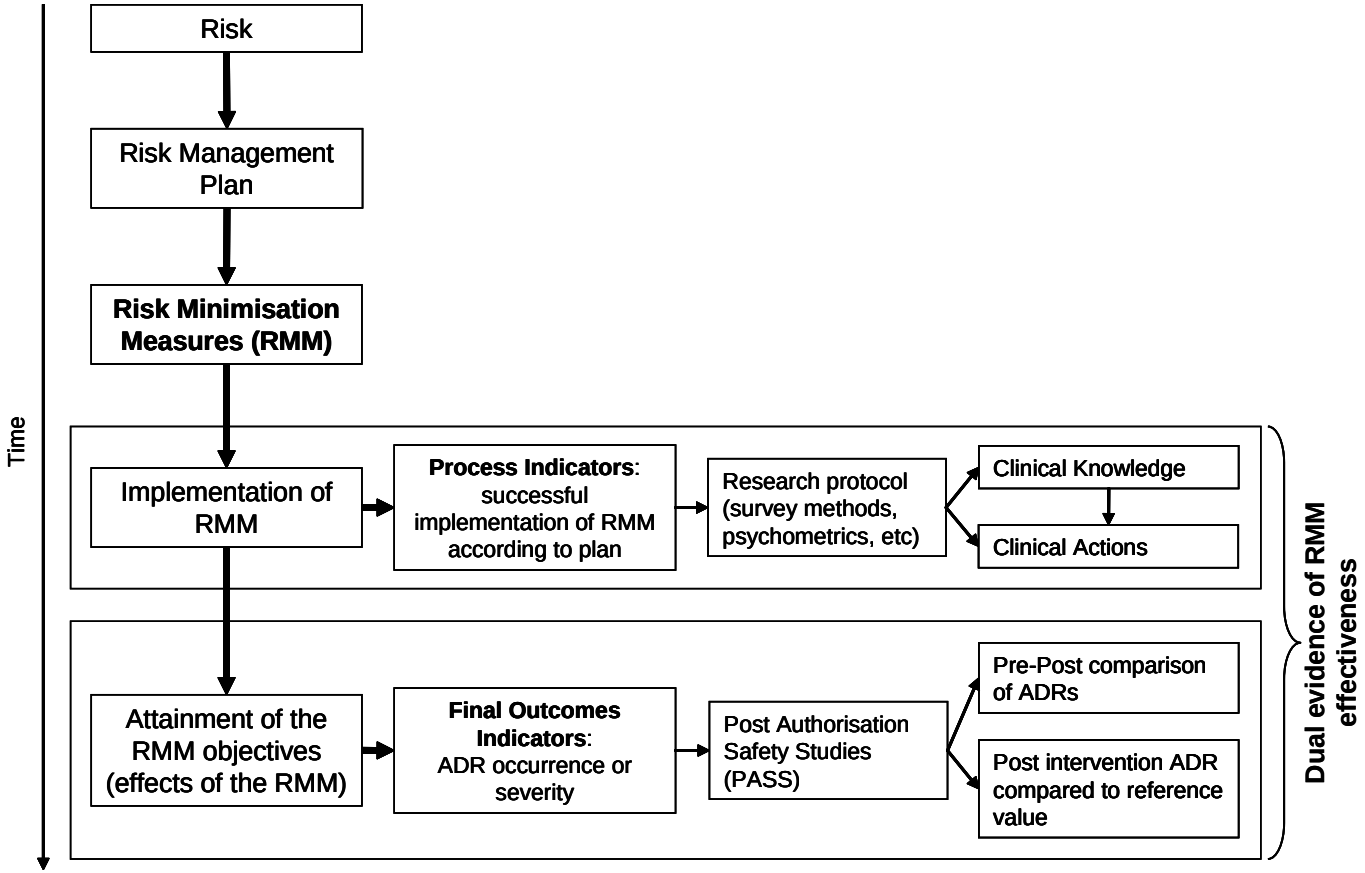
Evaluating the effectiveness of RMM by means of a dual evidence approach



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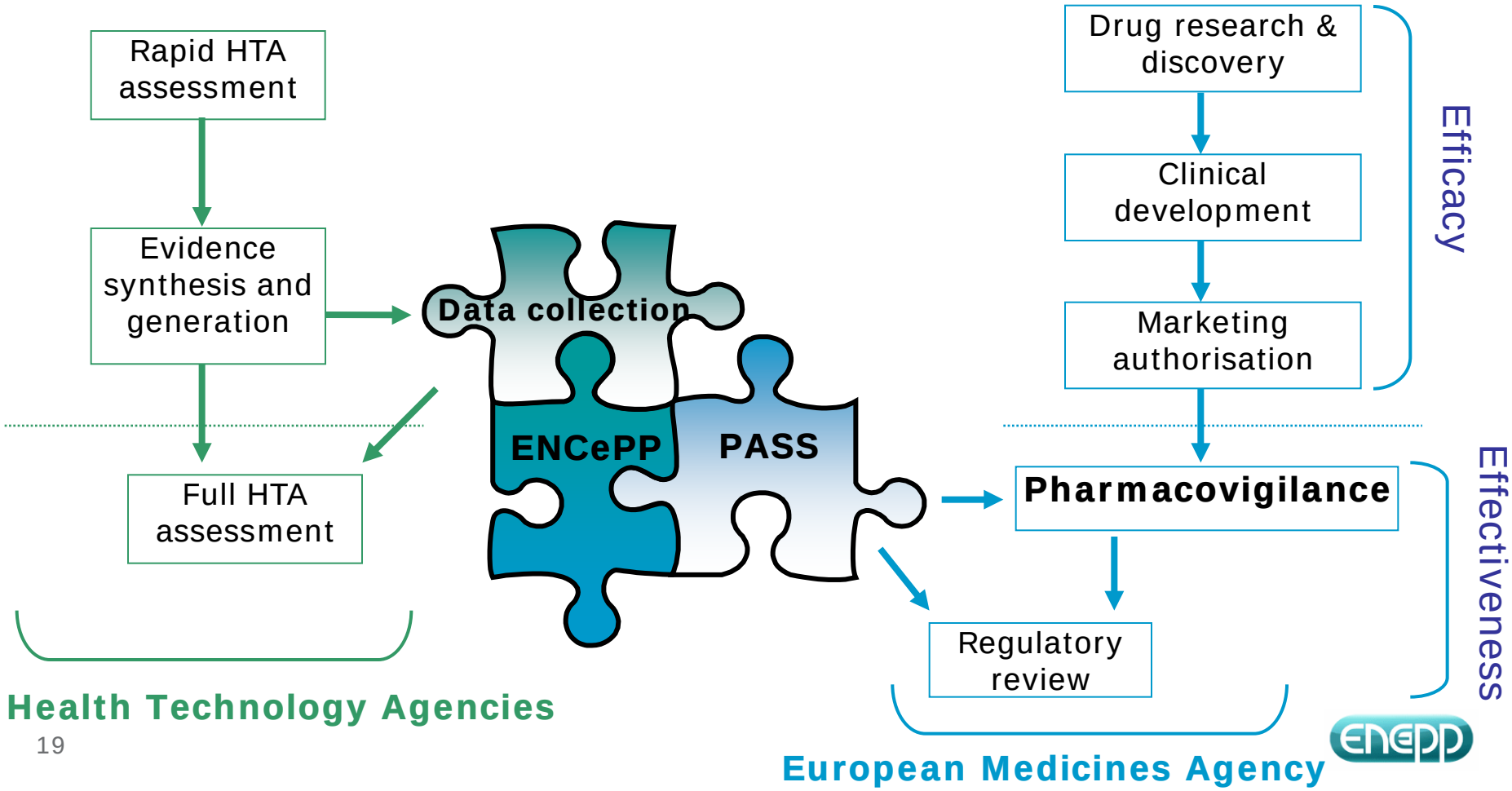
Post-authorisation data collection: the potential for a bridge from medicines regulation to HTA

A potential bridge from medicines regulation to HTA



ENCePP Working Group on HTA

- To support and build capacity for studies that can be used by both regulators and HTA.
- To provide a forum of academics and service providers for consultation as appropriate to support the development of guidance by ENCePP, EMA and EUnetHTA, including on PASS/PAES and HTA.
- To develop good practice guidance (e.g. in conducting post authorisation studies (PAS) that might meet the needs of regulators and HTA)

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***TF Observers**:* David Haerry, Ulf Bergman
***EMA support**: Luis Prieto, Kevin Blake*

THANK YOU
for your attention

luis.prieto@ema.europa.eu

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