EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Demonstrating impact for public health and stakeholders: focus on pharmacovigilance

Impact of Pharmacovigilance/Effectiveness of Risk Minimisation/Best evidence

Joint meeting: Patients and Consumers and Healthcare Professionals working parties

Peter Arlett, Corinne de Vries, Henry Fitt – 16 September 2014

Presentation Overview

- Optimising the benefits and risks of medicines and reducing the harm from ADRs
- How we achieve this
- Contribution of complementary initiatives
  - Coordination of pharmacovigilance impact measurement
  - Measuring the effectiveness of risk minimisation
  - Generating and accessing best evidence
- Looking forward

Optimising the benefits and risks of medicines and reducing the harm from ADRs

Medicines save lives and reduce suffering

But also

- 5% of all hospital admissions are for Adverse Drug Reactions (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

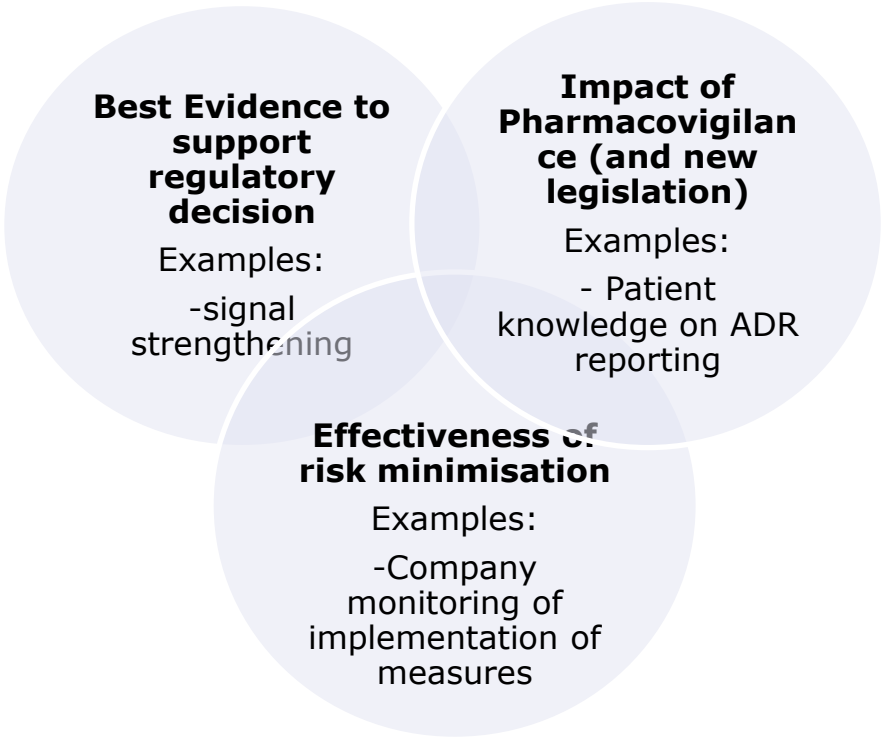
What is needed for excellent public health protection and promotion

- Excellent Law
- Excellent Science
- Excellent Resources

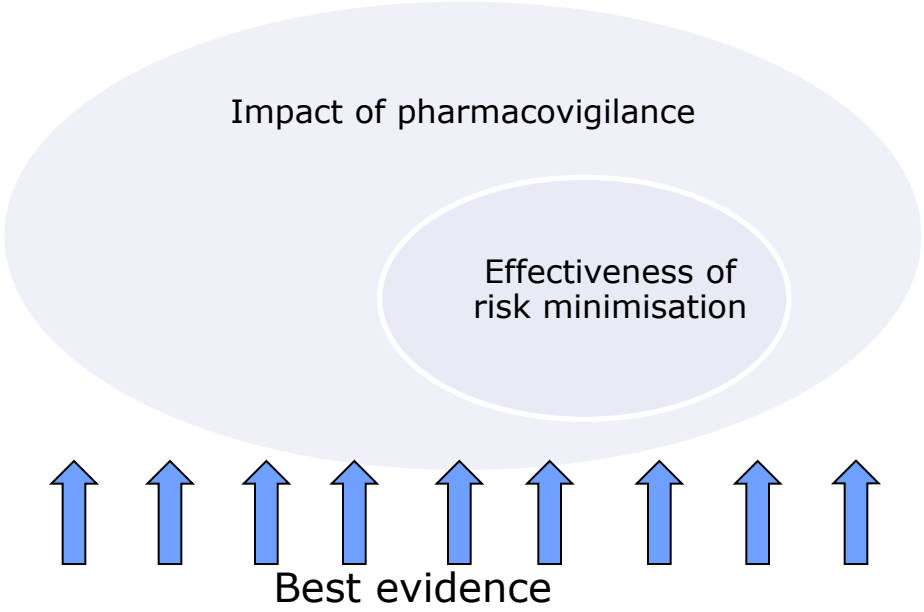
Bottom line

- Ensure we are effective in optimising the benefits and risks of medicines and reducing the harm from ADRs
- And we do this as efficiently as possible

Complementary strategies



….put another way



Impact of Pharmacovigilance

Part of EMA Work Programme 2014: commitment to:

"Develop **a programme for studying public health impact** including monitoring the effectiveness of targeted risk minimisation measures. Design methodologies for drug utilisation studies, to estimate potential public health impact of adverse drug reactions,"

Measuring performance and impact – types of measures

1. **Performance**: Structure and process measures of implementation of activities in new PhV legislation (i.e., 'outputs', e.g., implementation milestones and process measures)

2. **Impacts**:

- Behavioural change
- Outcomes (impacts on health system and industry)

Important because:

- Supports continuous improvement
- Demonstrate added value
- Justify activity and spending
- Support for future legal/audit or resourcing reviews

(Ref: C. Coglianese, Measuring Regulatory Performance, OECD Expert Paper No. 1, Aug 2012)

Measuring implementation **performance**

- Initial reporting – Commission report on the 1st year
  http://ec.europa.eu/health/files/pharmacovigilance/2014_ema_oneyear_pharmacov_en.pdf
- Publication on the first 18-months:
  http://www.nature.com/nrd/journal/vaop/ncurrent/full/nrd3713-c1.html
  - Patient reporting up
  - Transparency up
  - All new products with risk management plans
  - 128 safety signals managed
  - Faster referrals

Impact measurement vs. objectives of pharmacovigilance legislation

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

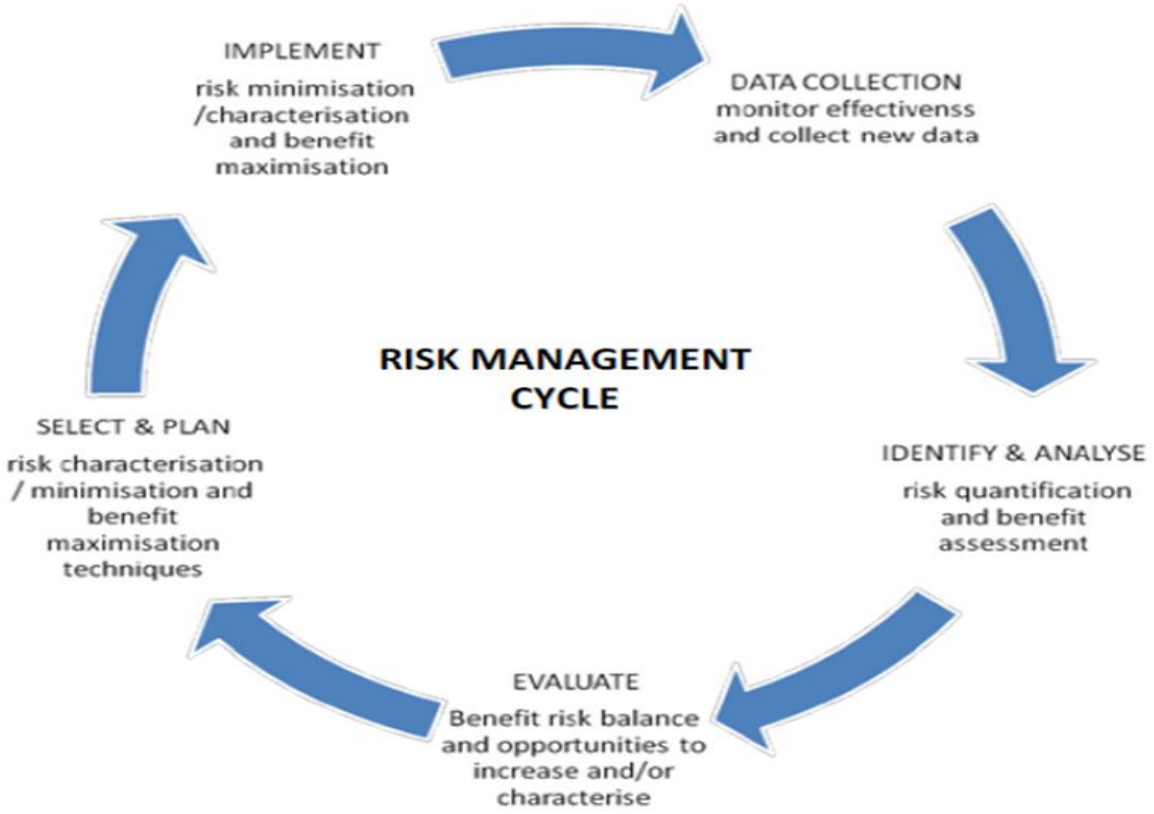
- Robust and rapid EU decision-making
- Engage patients and healthcare professionals
- Science based - integrate benefit and risk
- Risk based/proportionate
- Increased proactivity/planning
- Reduced duplication/redundancy
- Increase transparency and provide better information on medicines

Impact measurement – *examples* vs. objectives

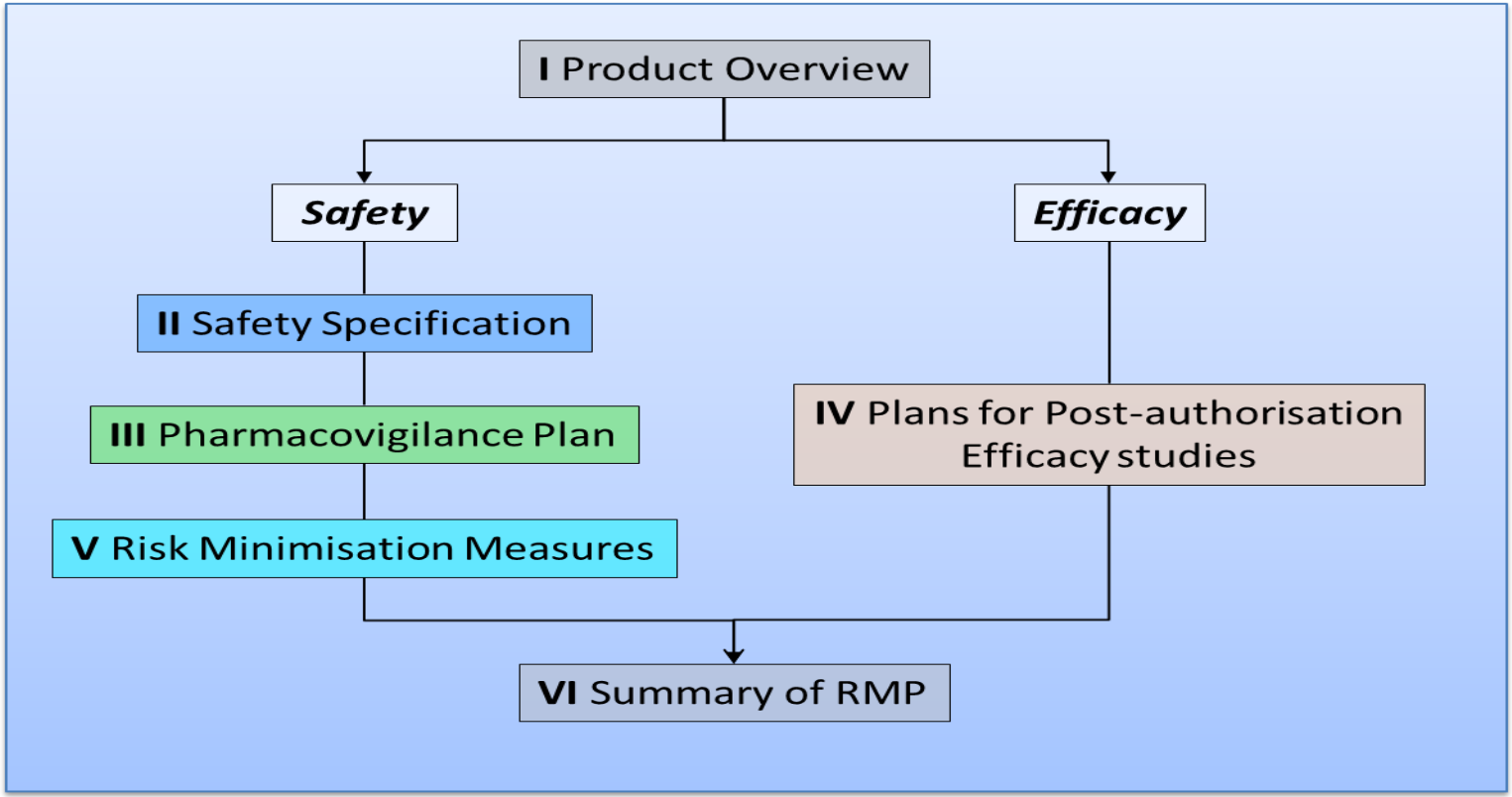
- Robust and rapid EU decision-making – do healthcare professionals and patients following restrictions and monitoring (drug utilisation)?
- Engage patients and healthcare professionals – knowledge of reporting, increased reporting rates, ability to access reliable medicines information
- Reduced duplication/redundancy - reduced industry costs on duplicative reporting
- Provide better information on medicines - healthcare professionals and patients' understanding of warnings
- Reducing burden of ADRs and optimising the use of medicines – incidence and prevalence of adverse reactions (health outcome studies - surveys, studies of heath records)

Effectiveness of Risk Minimisation

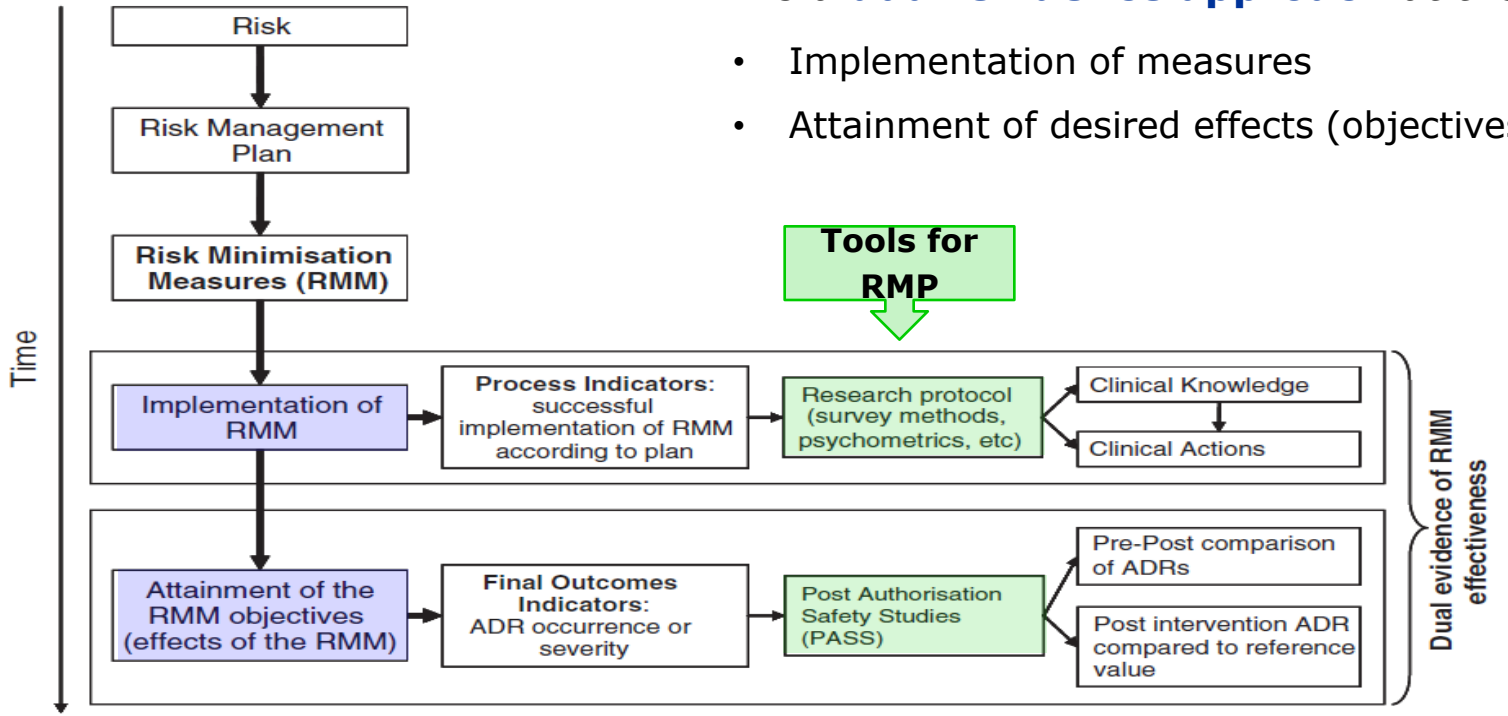
Principles of risk management



Information flow in risk management plans



Evaluating effectiveness of RM measures



…is a **dual-evidence approach** at the level of

- Implementation of measures
- Attainment of desired effects (objectives)

L Prieto et al., Pharmacoepidemiol Drug Saf 2012; 21: 896–899

Overview of risk minimisation activities for CAPs

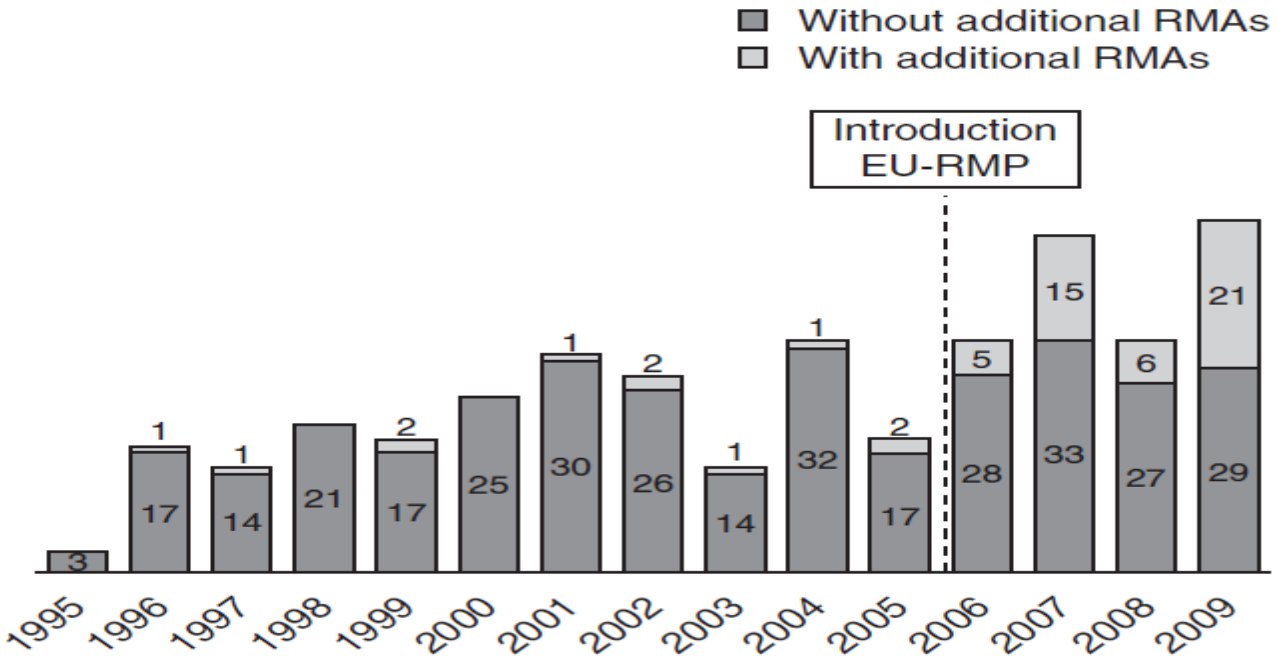


Fig. 1. Active substances with and without additional RMAs, stratified by year of authorization. **EU-RMP** = EU Risk Management Plan; **RMAs** = risk management activities.

Best evidence

- Who we are
- Why the need for Best Evidence
- EMA steps to stimulate generation of best evidence for pharmacovigilance:
  - ENCePP
  - EMA-funded studies
  - Use of Electronic Health Records

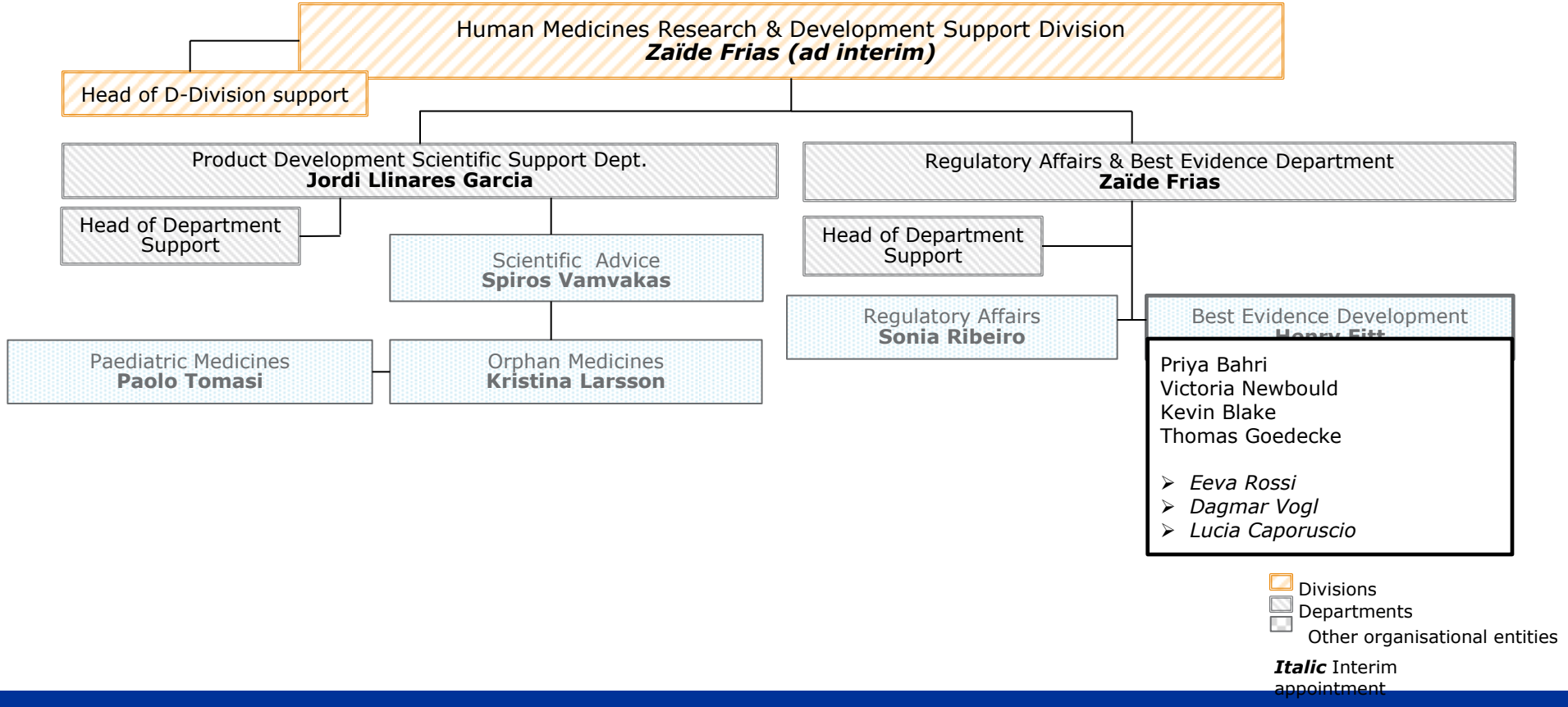
Who we are

Newly created Office, stemming from Review and Reconnect exercise.

Responsibilities include

- Obtaining best evidence for regulatory decision making (in collaboration with other EMA offices)
- Liaison with research funding bodies (H-2020 and IMI)
- ENCePP secretariat

Who we are


Human Medicines Research & Development Support Division
Zaïde Frias (ad interim)
Head of D-Division support
Product Development Scientific Support Dept.
Jordi Llinares Garcia
Head of Department Support
Scientific Advice
Spiros Vamvakas
Paediatric Medicines
Paolo Tomasi
Orphan Medicines
Kristina Larsson
Regulatory Affairs & Best Evidence Department
Zaïde Frias
Head of Department Support
Regulatory Affairs
Sonia Ribeiro
Best Evidence Development
Priya Bahri
Victoria Newbould
Kevin Blake
Thomas Goedecke
Eeva Rossi
Dagmar Vogl
Lucia Caporuscio
Divisions
Departments
Other organisational entities
Italic Interim appointment

Why the need for "Best Evidence"

Traditional model of regulating medicines:

- Companies submit data ➲ regulators assess data ➲ based on this evidence, regulators decide on B:R ratio and on proposed labelling.
- Post-authorisation: besides company-generated data (studies), ✔ access to spontaneous reports ✔ published articles.

While valid scientific evidence generated by an MAH remains at the core of regulatory evaluation, the timing and quality of evidence is over-reliant on individual MAHs and their resources.

There may be additional relevant data and information available from alternative sources that can inform decision-making.

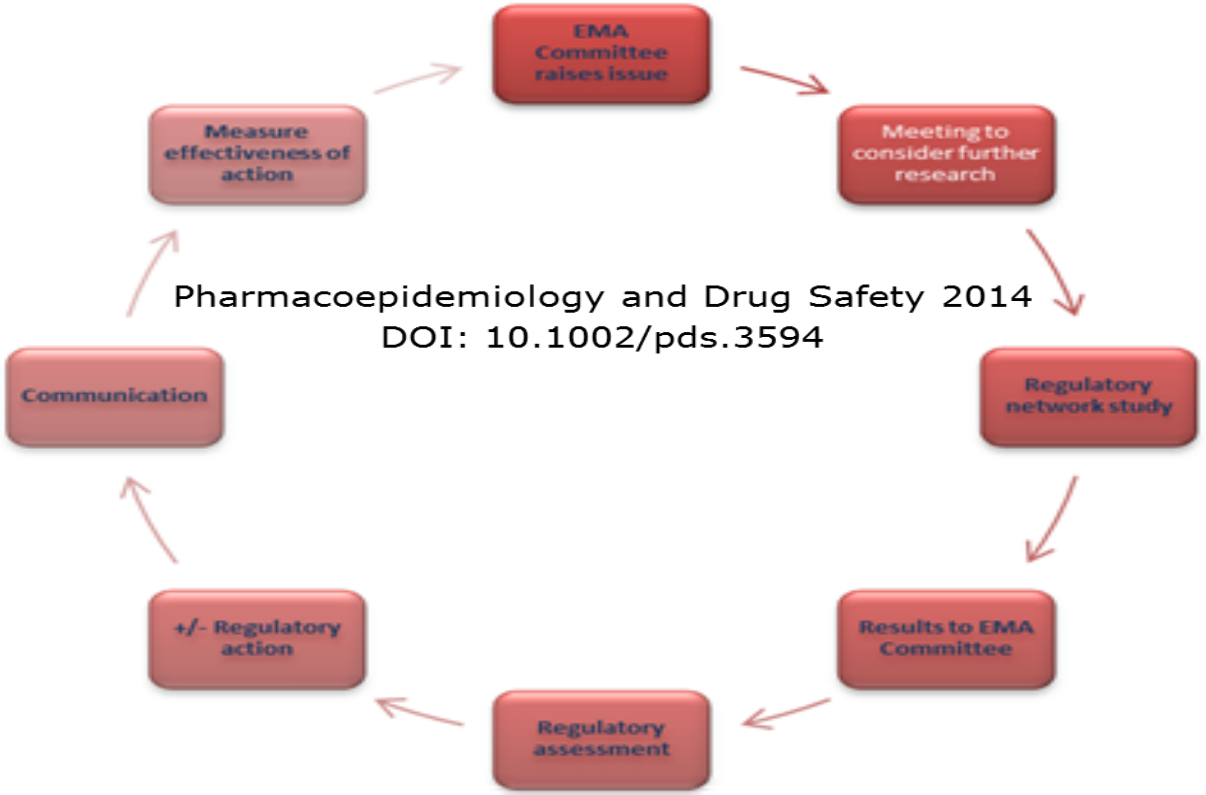
Why the need for “Best Evidence”

Building knowledge throughout the product lifecycle is pivotal in fully characterising the B/R profile of the product.

- New data sources, new methodologies + technologies, and
- the proactive mandate to regulators in the new PhV legislation
- enable gathering of additional scientific evidence to supplement the contribution of the pharmaceutical industry.

This may be generated by academic research centres and the EU Regulatory Network itself, providing information to support decision making by EMA’s scientific committees.

Evidence-decision cycle



ENCePP (European Network of Centres for Pharmacoepidemiology & Pharmacovigilance)

- Established in response to increasing number of PASS requested and the need to leverage e-health resources and take Pharmacoepidemiology to next level
- Brings together expertise in the fields of pharmacovigilance & pharmacoepidemiology across Europe.
- The aim is to improve the quality, ease, speed, transparency and reliability of post-authorisation benefit:risk evidence feeding into regulatory decision making (PRAC/CHMP)
- Currently includes 141 centres, 22 networks, 50 data source owners

EMA-funded studies on authorised products

- Initiated in 2010
- Aim: to enable EMA to obtain fast and reliable answers to questions on safety or BR of medicines needing urgent elucidation by means of observational research, ultimately facilitating regulatory decision-making.
- Initial scope
  - research topics with high public health relevance
  - necessitating rapid regulatory consideration
  - with a EU impact.
- 8 studies performed to date, all publicly available

In-house analysis of e-Health data (1)

Procurement of 2 databases of electronic medical records (THIN and IMS) enables EMA to conduct drug utilisation studies related to specific concerns identified in (pre)referral procedures.

- The Health Improvement Network (THIN) is a primary care medical research database of anonymised patient records (> 3.7 million active UK patients)
- THIN includes Diagnoses, Symptoms, Prescriptions Tests and results, demographic information, information on death and outcomes of conditions and treatments.

Examples:

- Self-controlled case series study in THIN on fluoroquinolones and retinal detachment. http://www.encepp.eu/encepp/viewResource.htm?id=6709
- August 2010 (prior to rosiglitazone suspension Sept 2010), Retrospective cohort study to estimate adherence to rosiglitazone contraindications . Suggested that about 8% of patients were prescribed rosiglitazone despite presence of cardiac contraindications.

Looking forward

Impact

- Strategy and work plan to deliver indicators and studies to measure the impact (behaviour change[s] and outcomes in health system and industry) – collaborative approach
- Work to develop the scientific methods

Effectiveness of risk minimisation

- Continuous oversight through risk management plans

Best evidence

- Further establish best evidence through EMA committees

Good opportunity to collaborate with patients, consumers and healthcare professionals.

Thank you for your attention

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