Pharmacovigilance through the Product Lifecycle and the Central Role of the PSUR

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Periodic Safety Update Report Information Day

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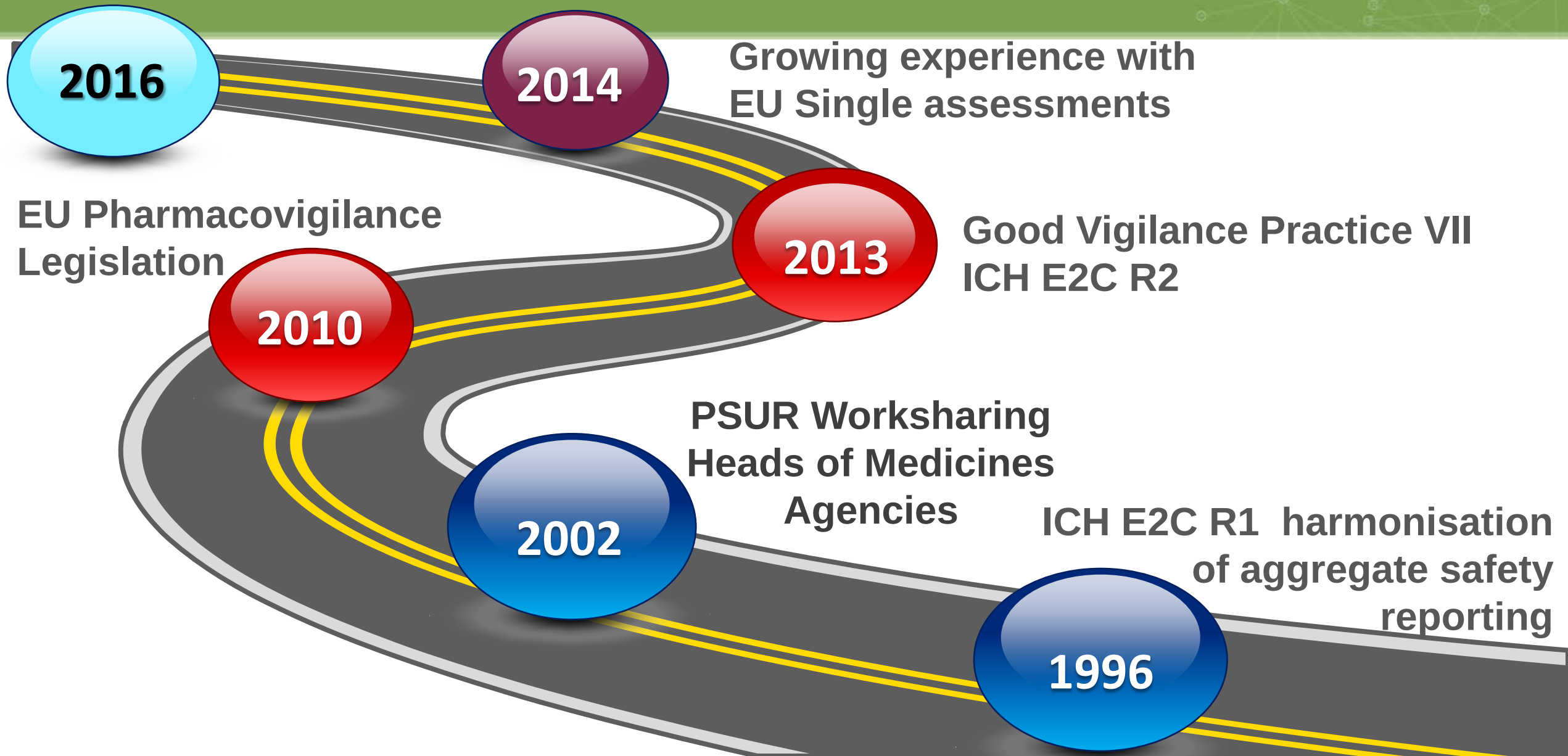
2

Outline

- **Where have we come from** – the evolution of the periodic safety update report to its current purpose and role
- **What is state of progress** - new EU regulatory approach to delivering the benefits of PSUR as central tool in lifecycle
- **How are we moving forward** – tackling today's challenges and a look ahead to the opportunities to come

Where have we come from?



Heads of Medicines Agencies PSUR Worksharing Initiative

HMA

CMDh

Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

HMA

Heads of Medicines Agencies

Human Medicines | Veterinary Medicines

Human Medicines

You are here: Home > Human Medicines > CMDh > Pharmacovigilance > PSUR > PSUR Work Sharing and Synchronisation Project

CMDh

- About CMDh
- Statistics
- Agendas and Minutes
- Press Releases
- Procedural Guidance
- CMDh-Referrals

PSUR WORK SHARING AND SYNCHRONISATION PROJECT

The PSUR work sharing and synchronisation project was initiated in 2002 under the auspices of the HMA and the European Risk Management Strategy Facilitation Group (ERMS FG). The concept of the project is that substances would have harmonised birthdates allowing MAHs to submit PSURs for products containing the same substance to NCAs at the same time, thereby allowing work sharing and reducing administrative burden. The EU PSUR Work sharing Working Group (WS WG) was established to facilitate the PSUR work sharing project and became a Working Party

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International Conference on Harmonisation ICH E2C (R2)

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

PERIODIC BENEFIT-RISK EVALUATION REPORT (PBRER)

E2C(R2)

Current *Step 4* version

dated 17 December 2012

PBRER is a comprehensive, concise, critical analysis of new or emerging information on risks, and on benefit in approved indications, to enable appraisal of product's overall benefit risk profile

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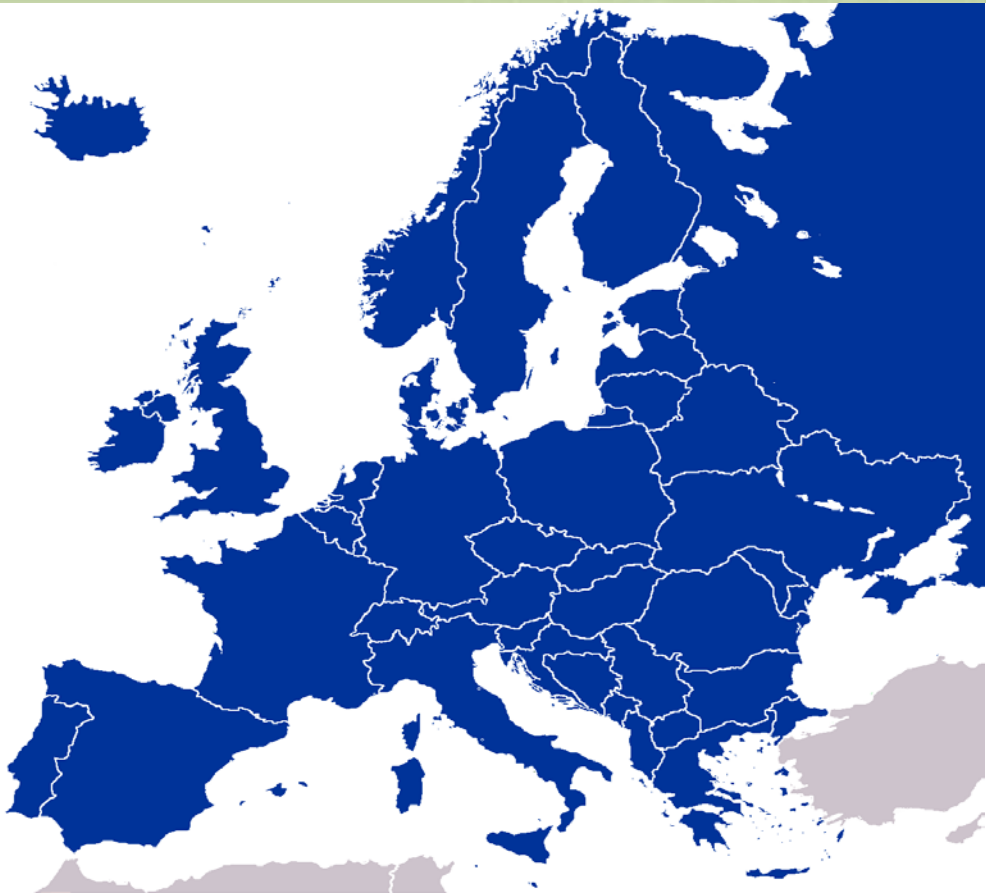
New EU Pharmacovgilance legislation

- New approach - single PSUR if medicine authorised in more than one MS
- New risk proportionate principle – routine PSURs not required for generics
- New tool for setting timing of submission and frequency of PSUR for same active – EURD list
- New Union decision-making procedure for PSURs with harmonised outcome
- New efficiency support - PSUR repository



Benefit risk throughout the product lifecycle

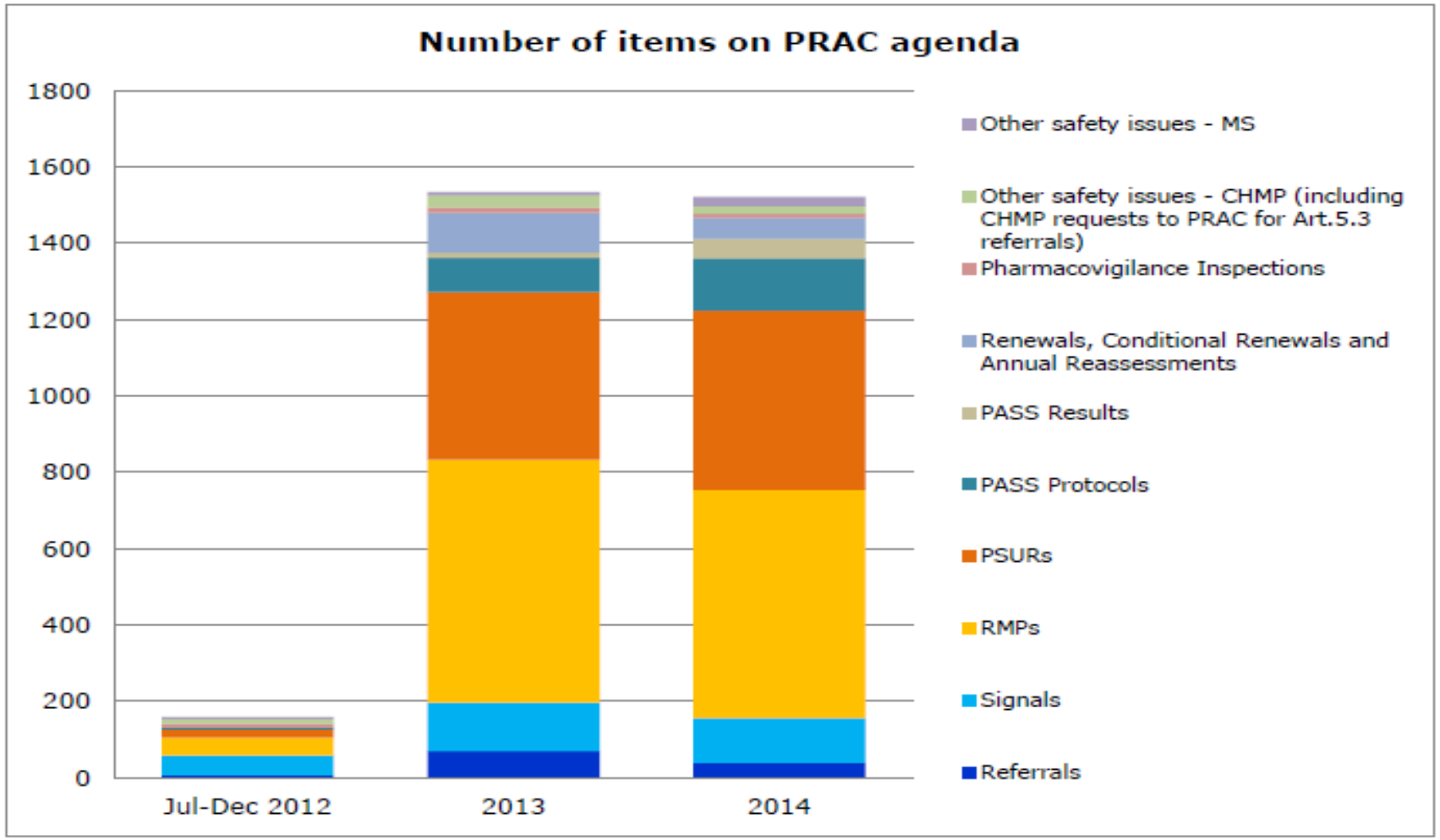
Periodic safety update report is now…

- A scientific evaluation of benefit risk
- Based on all available data (including data from clinical trials in unauthorised indications and populations)
- In context of usage – sales volumes, prescriptions and estimate of population exposure

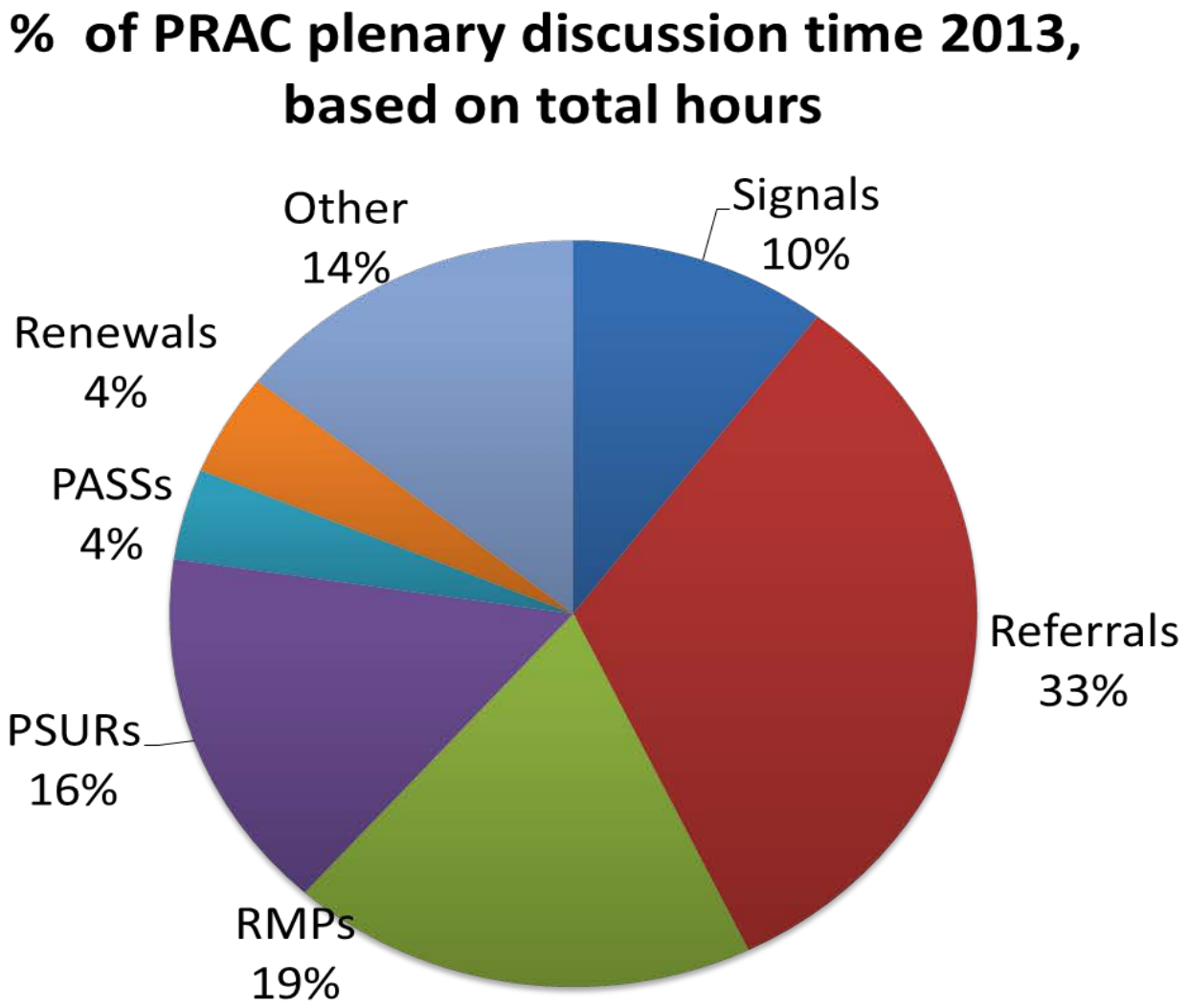
Pharmacovigilance Risk Assessment Committee

All aspects of the risk management of the use of medicinal products including the detection, assessment, minimisation and communication relating to the risk of adverse reactions, having due regard to the therapeutic effect of the medicinal product, the design and evaluation of post-authorisation safety studies and pharmacovigilance audit

PRAC agenda items 2012-2014



PRAC time allocation to procedures



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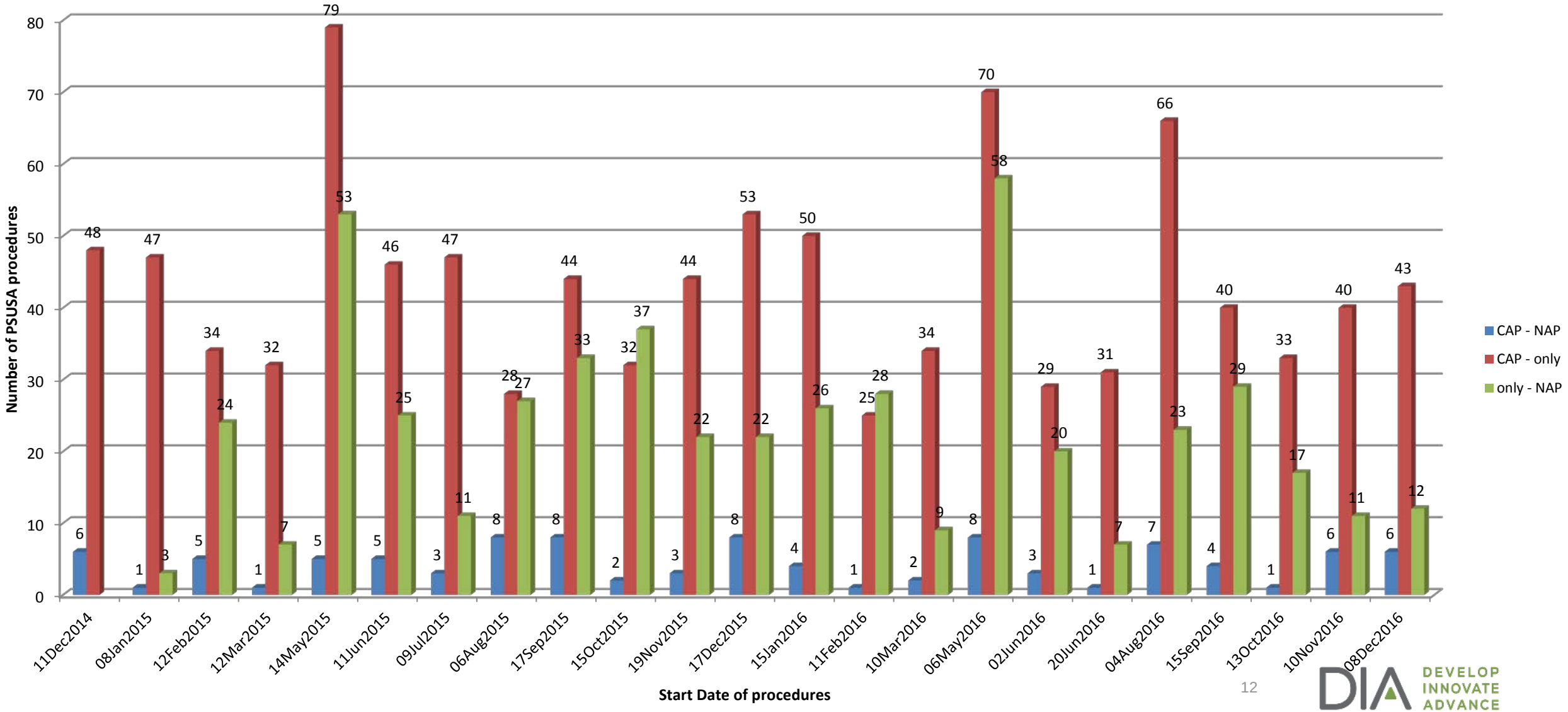
PSUSAs



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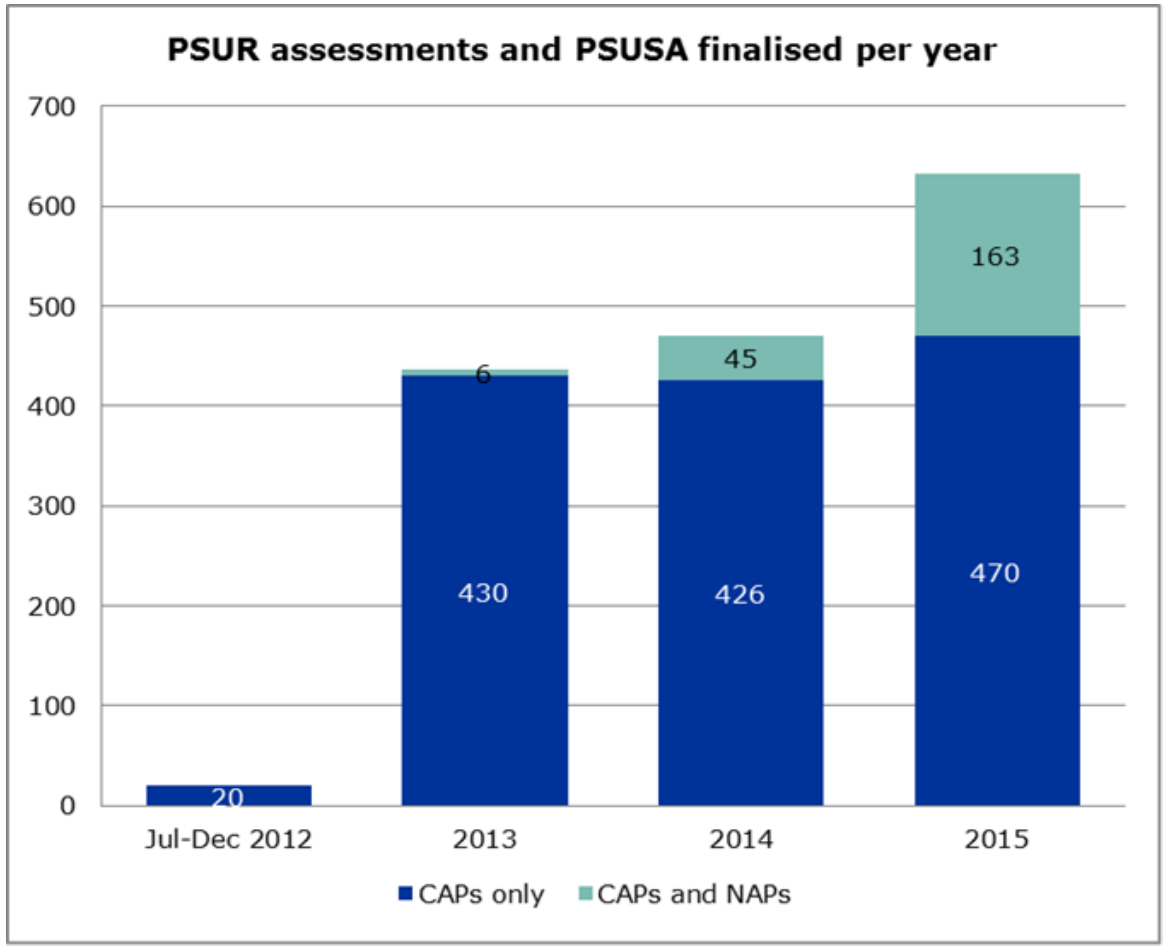
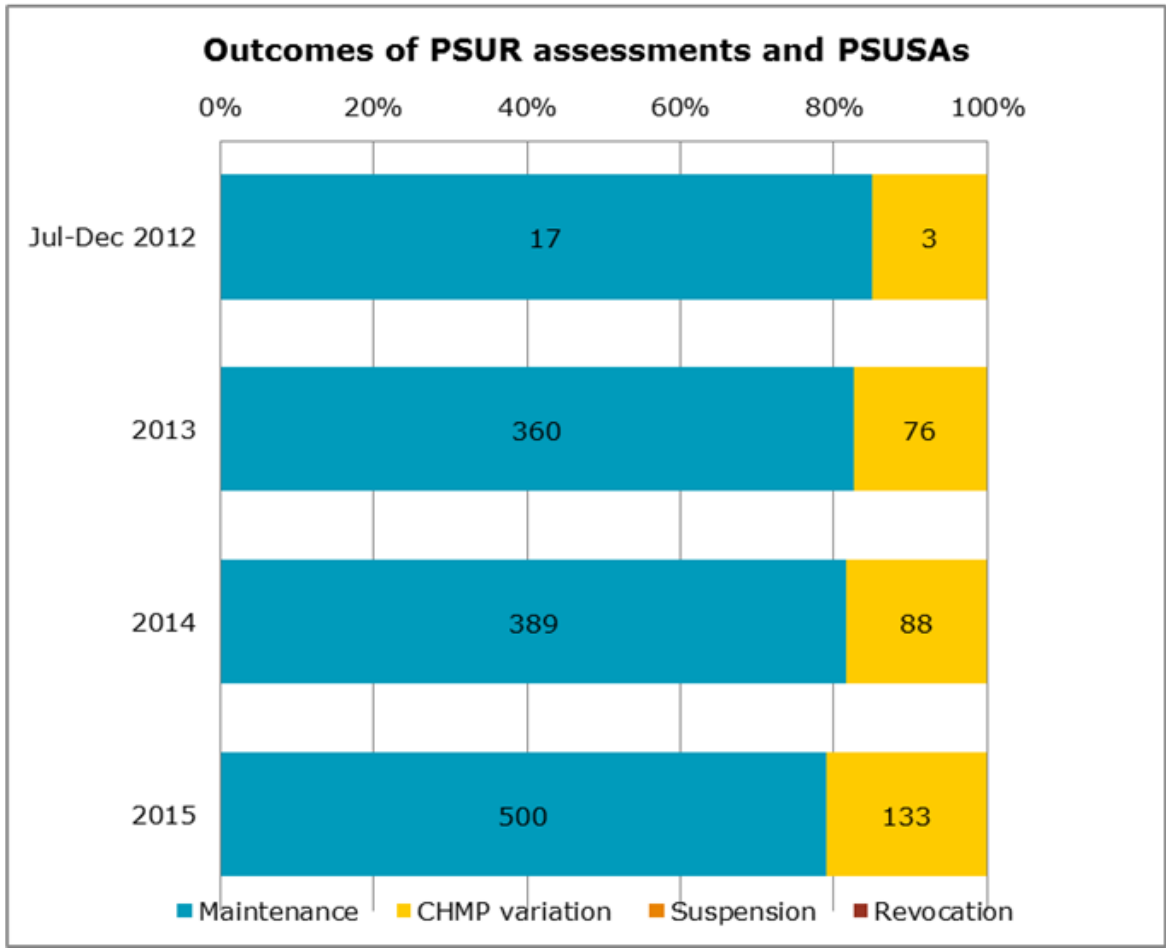
Periodic Safety Update Report outcomes





13

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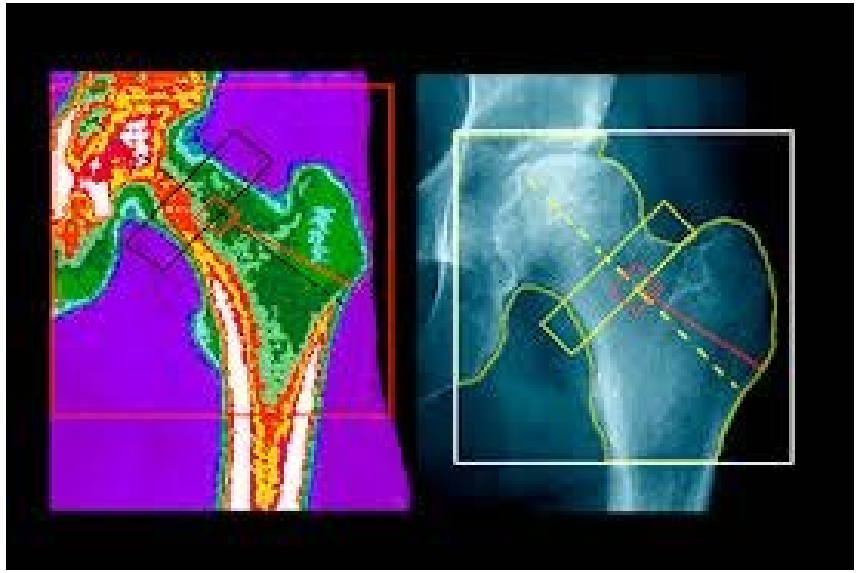
Example – Strontium ranelate & CVS risk

PSUR procedure enabled full review following concerns about cardiovascular risk

Scientific assessment of benefit risk in context of other therapeutic options for osteoporosis

Debate focussed on feasibility and likely effectiveness of risk minimisation measures

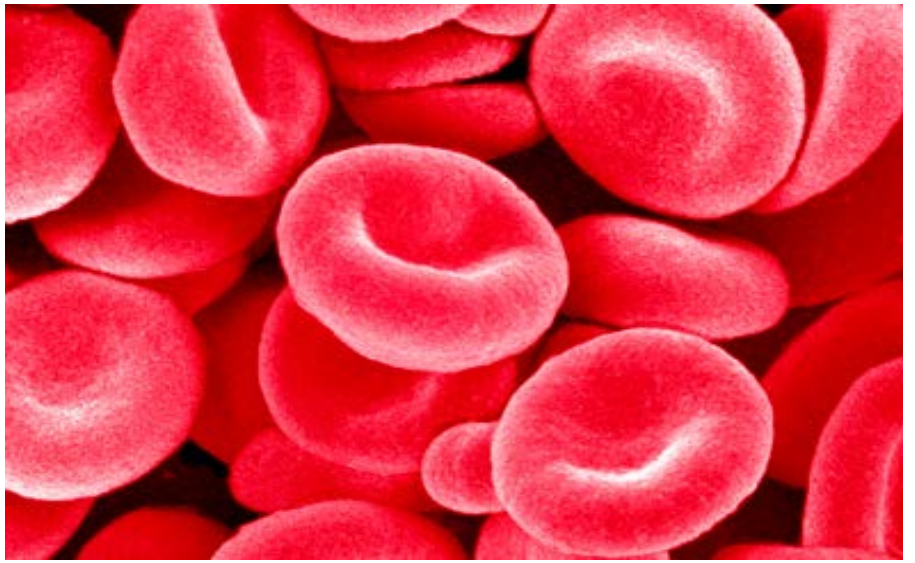


Example – colloidal iron & hypersensitivity reactions

PSUR review of serious hypersensitivity reactions associated with Rienso

Healthcare professional communications on new slower administration regime, contra-indications & warnings

Drug utilisation study to monitor effectiveness of risk minimisation measures



Example - iv paracetamol & accidental overdose

Accidental overdose in children following confusion between mg & ml led to product information updates, national communications and ongoing monitoring

Based on cumulative reported cases, safety concern of medication errors considered “important identified risk” in risk management plan

Effectiveness of risk minimisation measures by MAHs and cumulative analysis in the next PSUR

Challenges

- Reaching a shared understanding and putting this into practice
- “Old” medicines with established place in therapeutics
- Diversity of EU national MAs and medical practices
- Maximising improvements - driving up efficiencies
- Delivering the public health benefit

Optimising PSURs as lifecycle benefit risk tool

- Improving clarity around all regulatory requests
- Building on experience with PSUSAs for mixed CAPs and NAPs as NAPs-only PSUSAs come to the fore
- Granularity and Periodicity Advisory Group in place including PRAC and CMDh members
- Maximising use of PSUR repository

Building effective collaboration

Resourceful use of tools
Early dialogue

Use of Inter-Committee Scientific Advisory groups

EU Member States

European Commission

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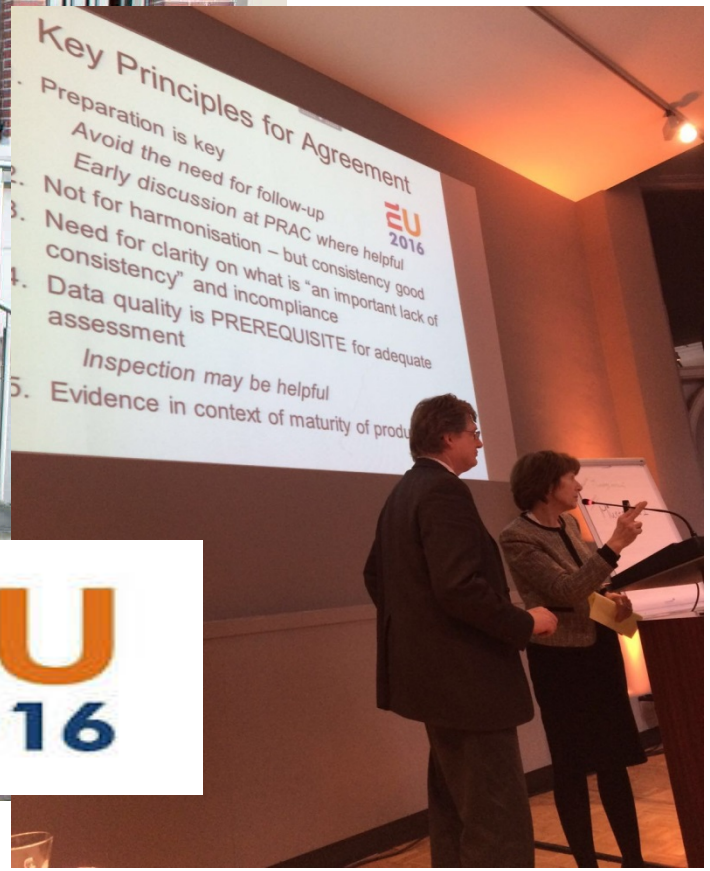
CMDh - PRAC agreement on PSUR principles



Key Principles

1. Preparation is key
   - *Avoid the need for follow-up actions*
   - *Early discussion at PRAC where helpful*
2. Not for harmonisation – but consistency good
3. Need for clarity on what is “an important lack of consistency” and incompliance
4. Data quality is PREREQUISITE for adequate assessment
   - *Inspection may be helpful*
5. Evidence in context of maturity of product

Key Principles

6. Updates to MAs are applicable to all medicinal products containing the active
7. If important new risk, update safety specification of all products
8. Implementation of outcome – common guidance document to be published
9. Follow-up request (if ANY) should be scientifically justified, identifying the procedure and lead MS
10. An updated template allows for “other considerations” eg interactions, FDCs etc

Opportunities

- Cross-committee action group in place with clear Road Map
- Improved guidance & templates to support alignment – update of GVP VIII
- Joint regulator – industry training planned

Opportunities

- New ways for delivering updated information on benefit risk to patients

Measuring the impact of pharmacovigilance activities

- ✓PRAC adopted a strategy for measuring the impact of pharmacovigilance activities
- ✓To allow regulators to determine which activities are most successful, to identify enablers and barriers for generating positive impacts which will contribute to the development of proactive pharmacovigilance systems and to promote best practice across the EU
- ✓A workshop on pharmacovigilance impact, with a particular focus on methodologies for measuring impact will be held on 5-6 December 2016 at EMA

25

Conclusions

PRAC is committed to optimising PSURs as the lifecycle benefit risk tool

Delivering updated information to all medicines users to support decisions

Alignment of approaches by industry and regulators is still “work in progress”

Key to success is collaboration by all stakeholders

- Theme for today’s InfoDay

Quote

"Coming together is a beginning. Keeping together is progress. Working together is success."

Henry Ford

Thank you for your attention!

Ask