EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Overview of 3-years of operation

9th Stakeholder forum on the Pharmacovigilance legislation, 15 September 2015

Presented by Peter Arlett,
Head of Pharmacovigilance Department

An agency of the European Union

In this presentation

- Key messages
- Reminder on where we have come from
- Look back over the past three years
- Brief look to the future (more in later session)
- Some conclusions

Key messages

Working together for continuous improvement of health promotion and protection

Delivered:

- Proactive monitoring
- Faster safety issue detection
- Faster warnings to users
- Increased transparency
- Engagement of stakeholders

Renewed focus on: efficiency, process improvement, and simplification

- Key messages
- **Reminder on where we have come from**
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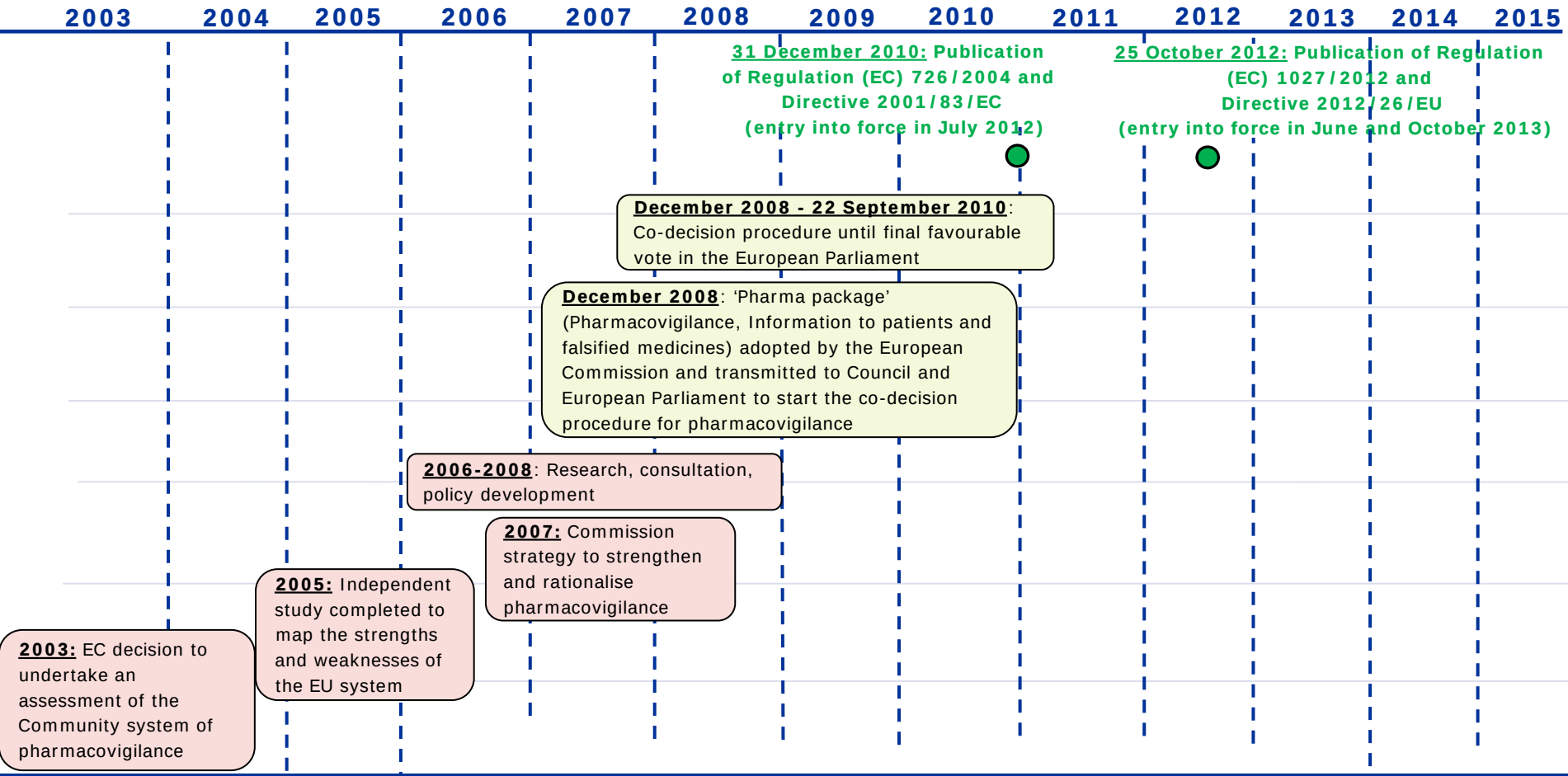
Where we have come from

- Reactive monitoring
- Overlapping roles and responsibilities
- Duplication of effort in efficient use of resource
- Exclusion of patients from safety monitoring
- Low levels of transparency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31 December 2010: Publication of Regulation (EC) 726/2004 and Directive 2001/83/EC (entry into force in July 2012)
25 October 2012: Publication of Regulation (EC) 1027/2012 and Directive 2012/26/EU (entry into force in June and October 2013)
December 2008 - 22 September 2010: Co-decision procedure until final favourable vote in the European Parliament
December 2008: 'Pharma package' (Pharmacovigilance, Information to patients and falsified medicines) adopted by the European Commission and transmitted to Council and European Parliament to start the co-decision procedure for pharmacovigilance
2006-2008: Research, consultation, policy development
2007: Commission strategy to strengthen and rationalise pharmacovigilance
2005: Independent study completed to map the strengths and weaknesses of the EU system
2003: EC decision to undertake an assessment of the Community system of pharmacovigilance

New pharmacovigilance legislation: Implementation priorities from 2011 to 2015

1. Health promotion and protection
2. Transparency and communication
3. Simplification

- Key messages
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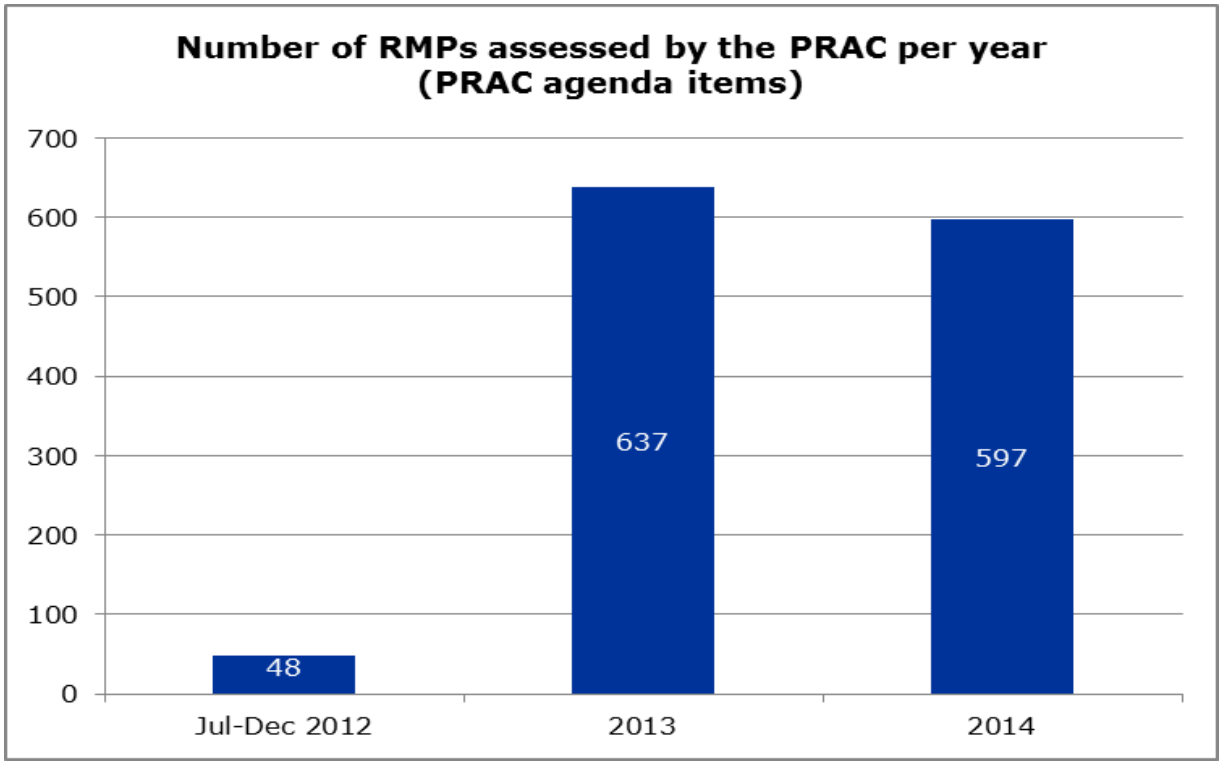
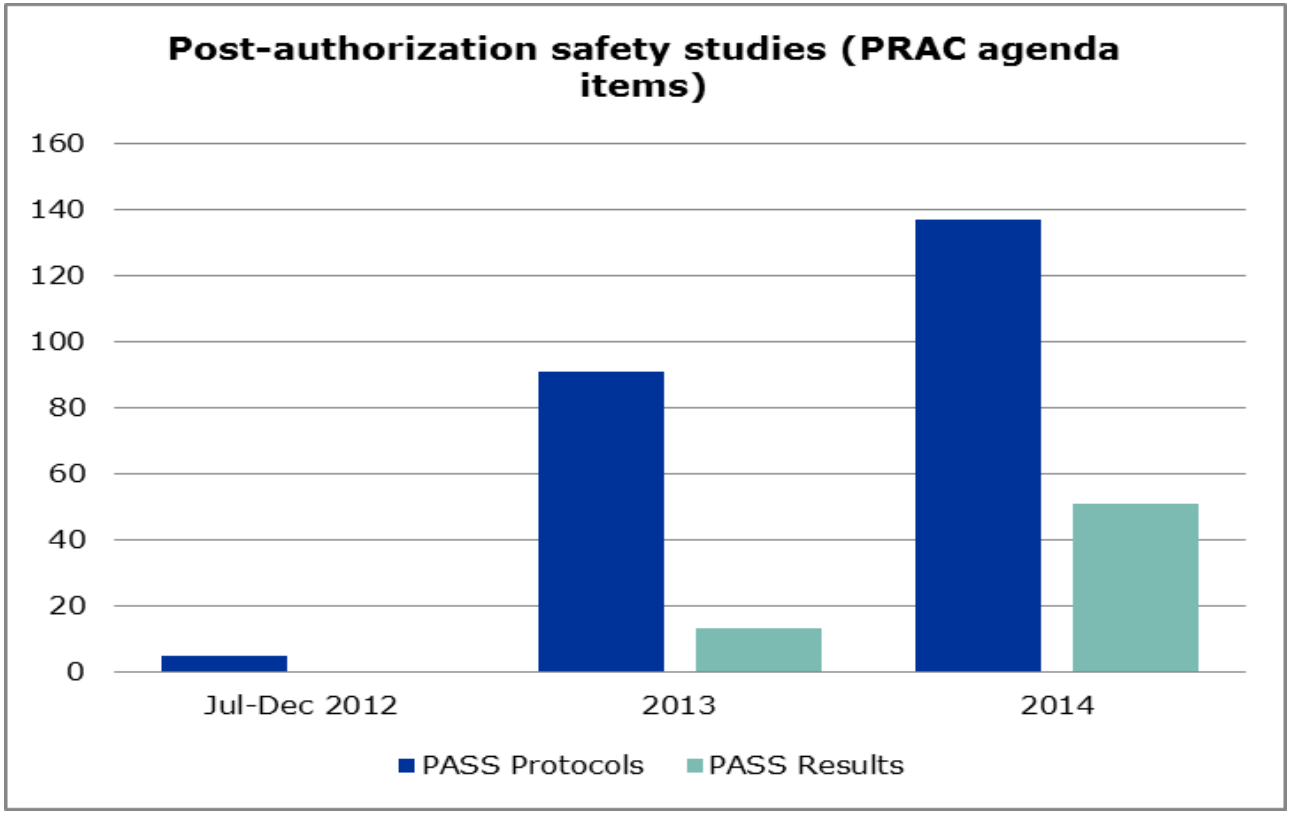
Strengthened expert advice, assessment and decision-making

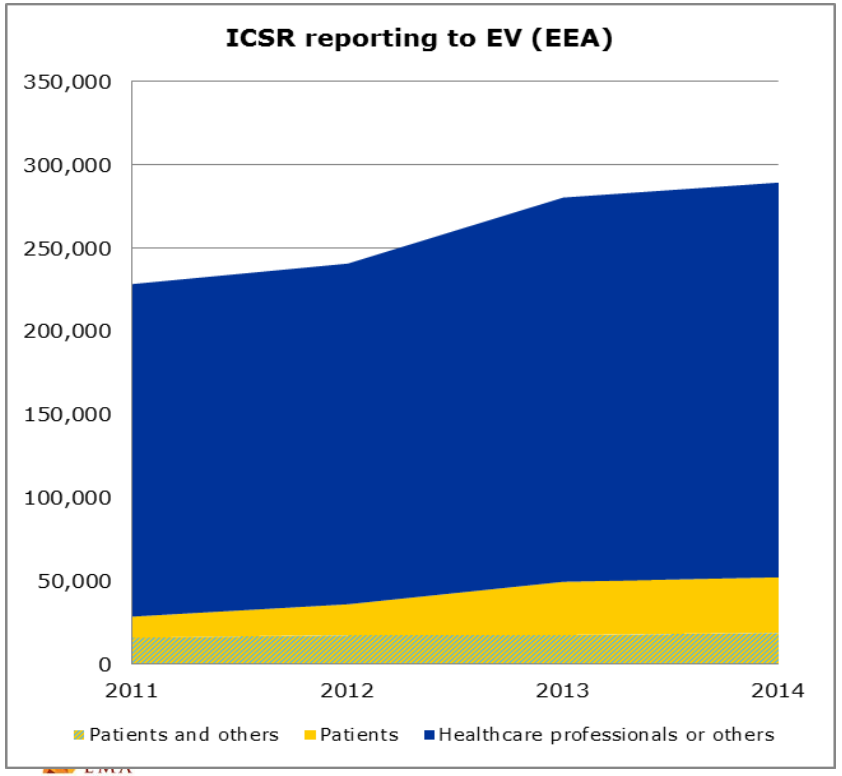
Risk Management planning: Planning of data collection and risk minimisation – supports protection and innovation

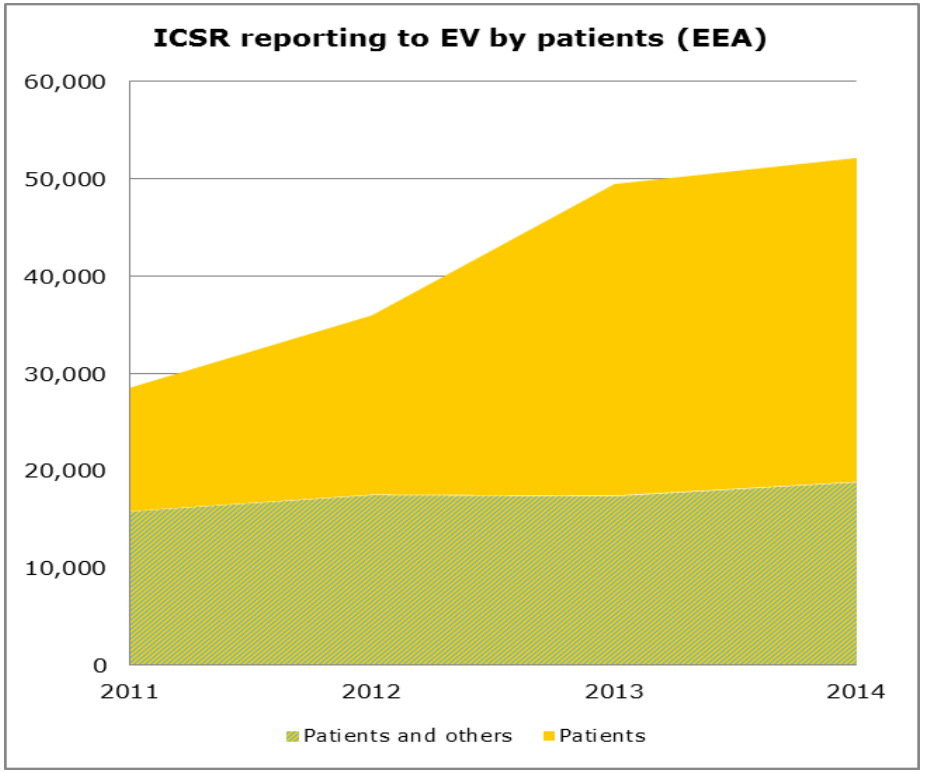


Post-authorisation studies: better planned and better scrutinised

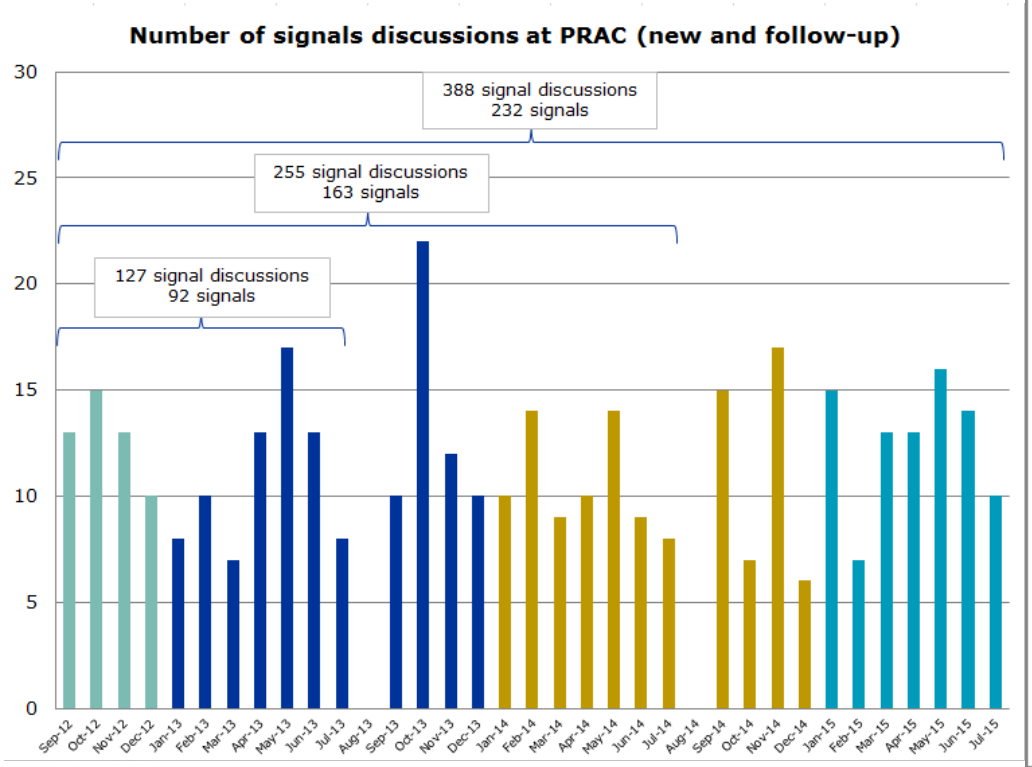


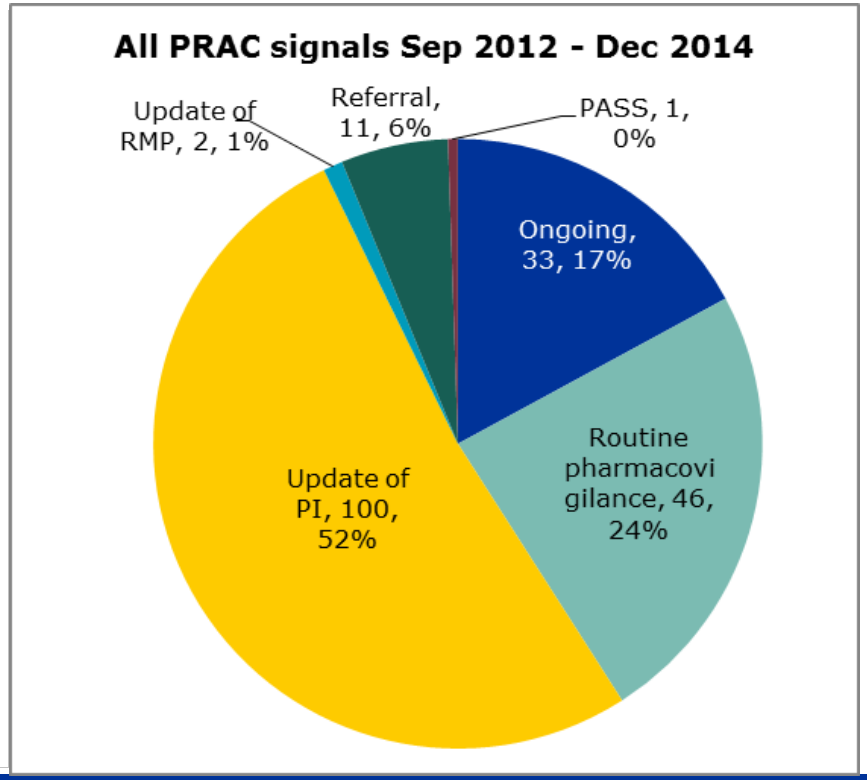
Increased reporting of suspected side effects and reporting by patients



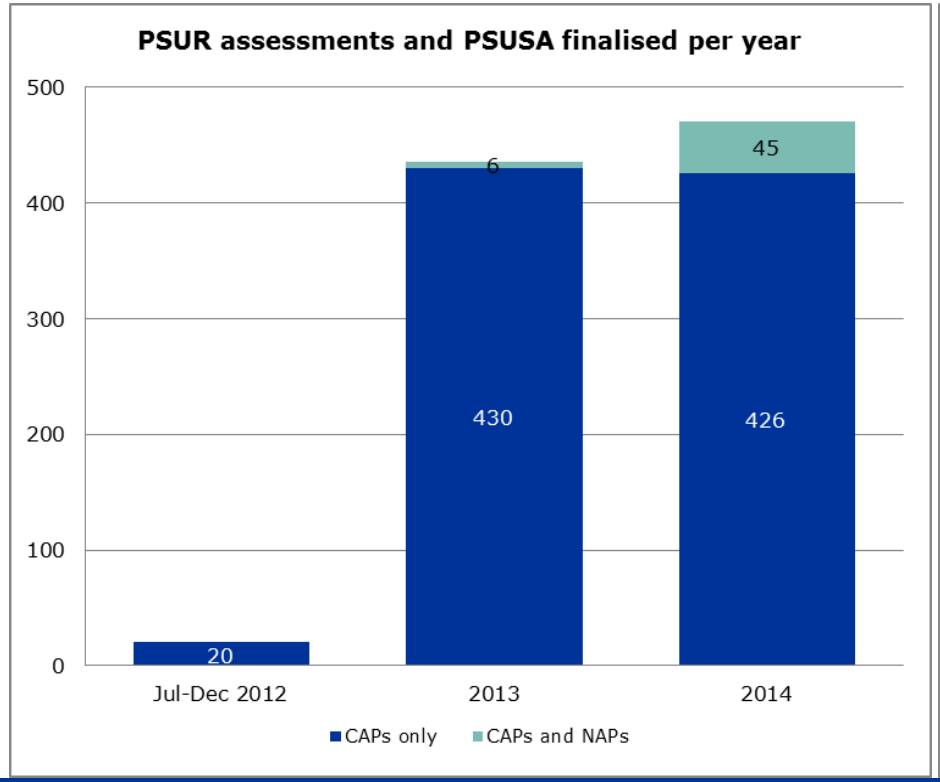


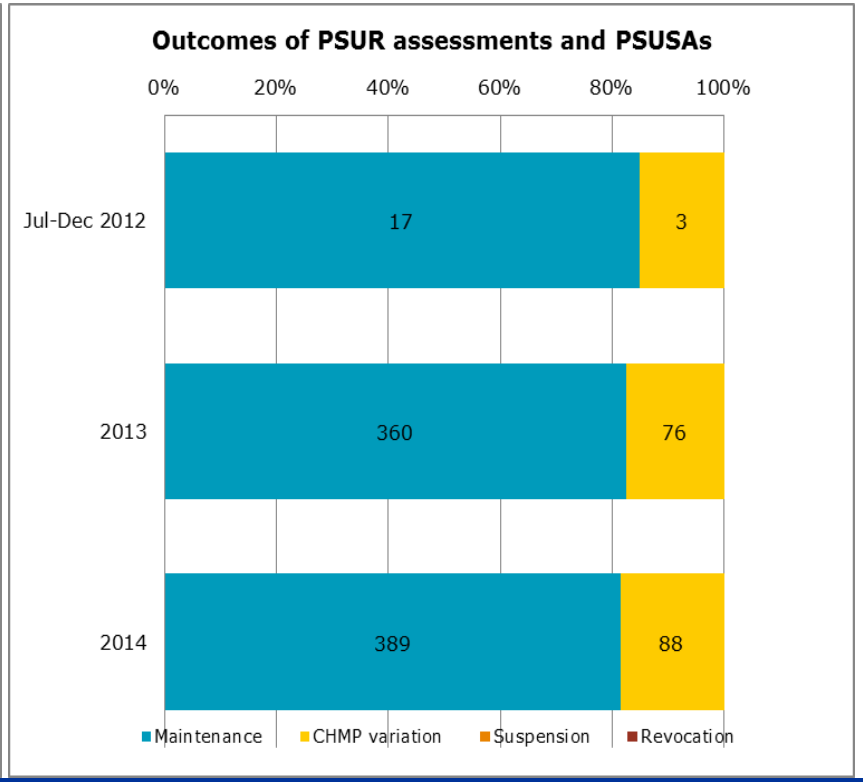
Safety signals: Faster detection and management of new and changing safety issues



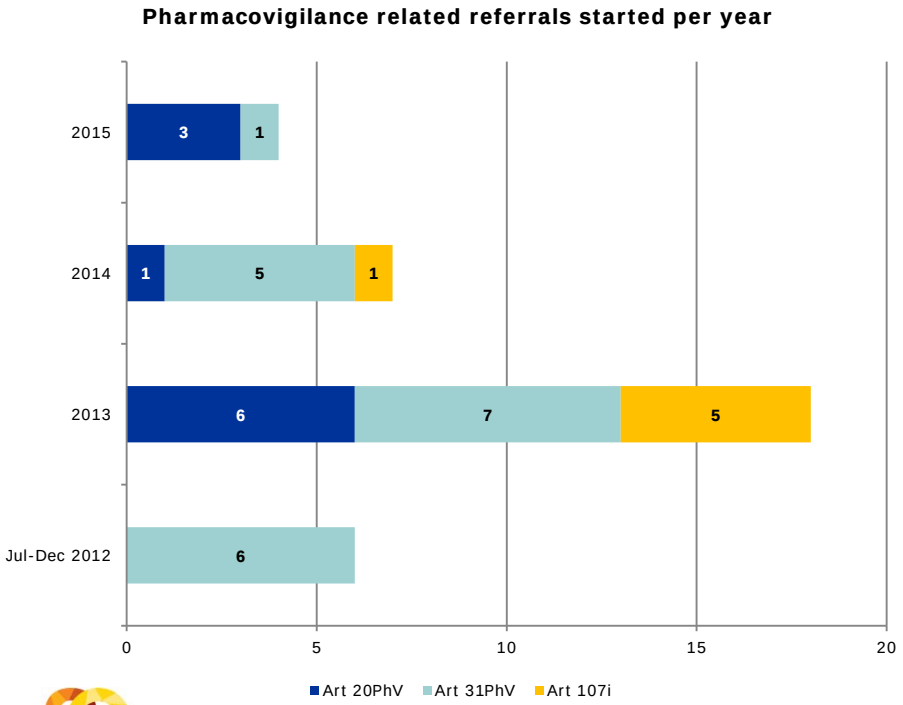


Periodic Safety Update Reports: integration of benefit and risk and direct application of new labelling (faster impact)





Referrals to PRAC: major assessments delivering labelling for safe and effective use of medicines



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30 May 2013 Last updated at 00:40

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Common painkillers 'pose heart risk'

By James Gallagher
Health and science reporter, BBC News

Two common painkillers, ibuprofen and diclofenac, can slightly increase the risk of heart problems if taken in high doses for a long time, data suggests.

People with severe arthritis often take the drugs, which also calm inflammation, to go about daily life.

The researchers said some patients would deem the risk acceptable, but they should be given the choice.

A study, **published in the Lancet**, showed the drugs posed even greater risks for smokers and the overweight.

The risks have been reported before, but a team of researchers at the University of Oxford analysed the issue in unprecedented detail in order to help patients make an informed choice.

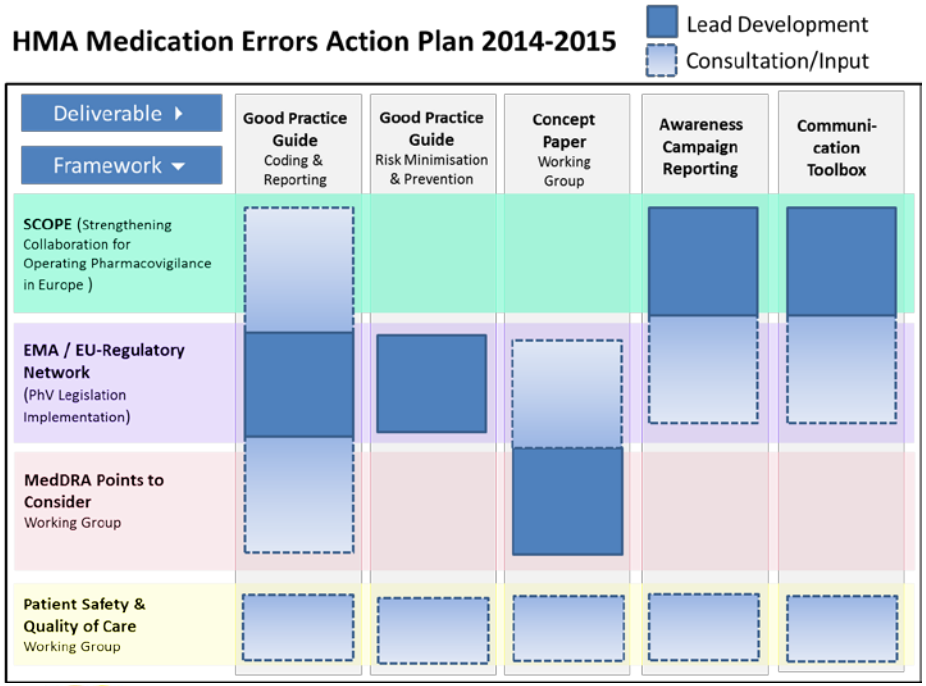
Related Stories

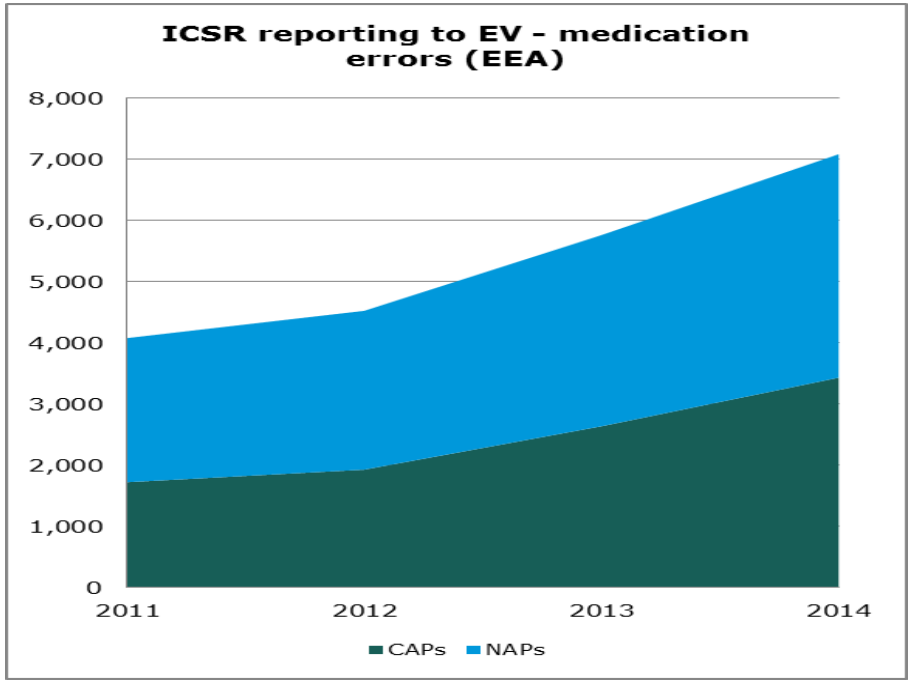
Drug 'overused' despite heart risk

Painkillers linked to heart risk

Q&A: Vioxx lawsuit

Medication errors: improvements to reduce the burden of harm





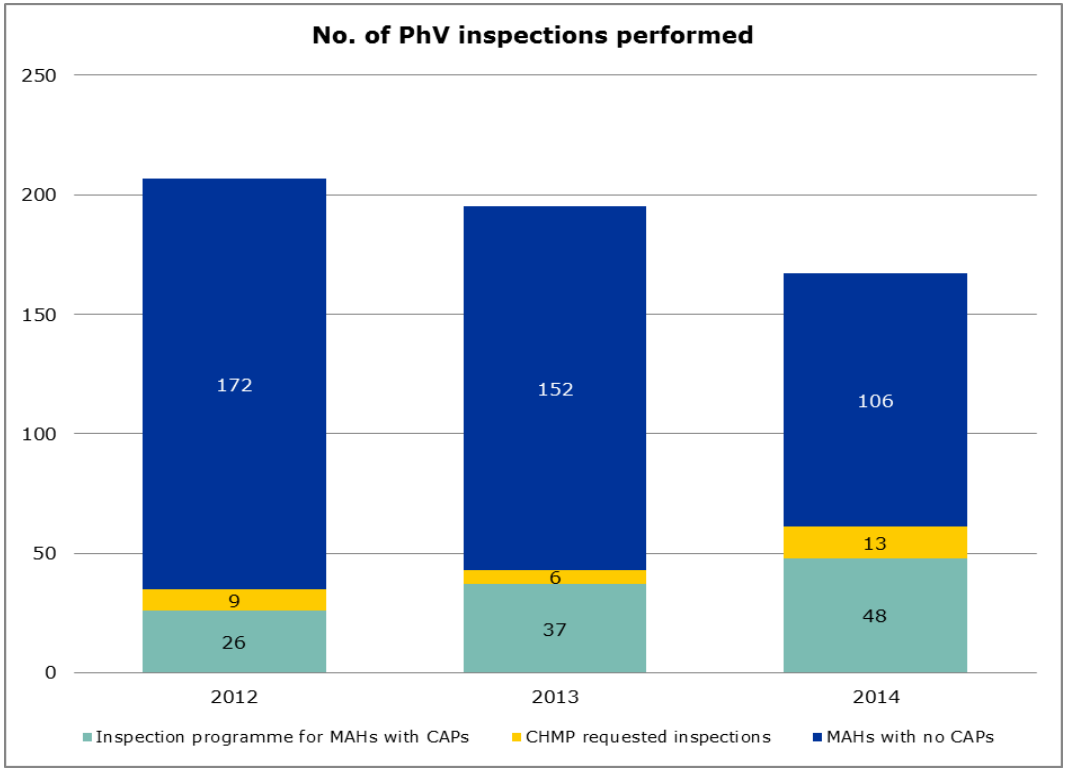
EU pharmacovigilance guidance and standards: Supporting excellence in health promotion and protection

I PhV and QS	Published	XI Participation	Consult on Public Hearings
II PSMF	Published	XII Regulatory action	Consult:2015
III Inspections	Rev 1 published	XIV International	Referred to 2016
IV Audits	Rev 1 published	XV Communication	Rev 1 in preparation
V RMP	Rev 2 in preparation	XVI RMM	Rev 1 published
VI ICSR	Rev 2 under public consultation	P.I Vaccines	Published
VII PSUR	Rev 1 published	P.II Biologicals	Consult:2015
VIII PASS	Rev 1 in preparation	P.III Pregnancy	Drafting
IX Signals	Rev 1 in preparation	P.IV Geriatrics	Drafting
X Add Monitoring	Published	Annex I Definitions	Rev published

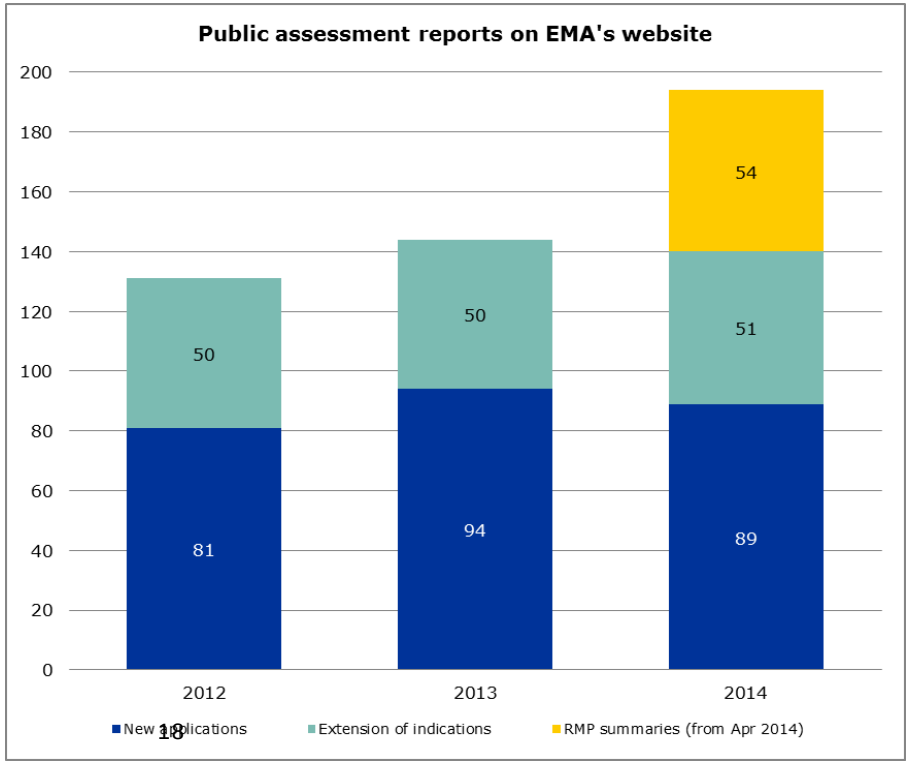
Ensuring pharmacovigilance systems work: audit and inspection

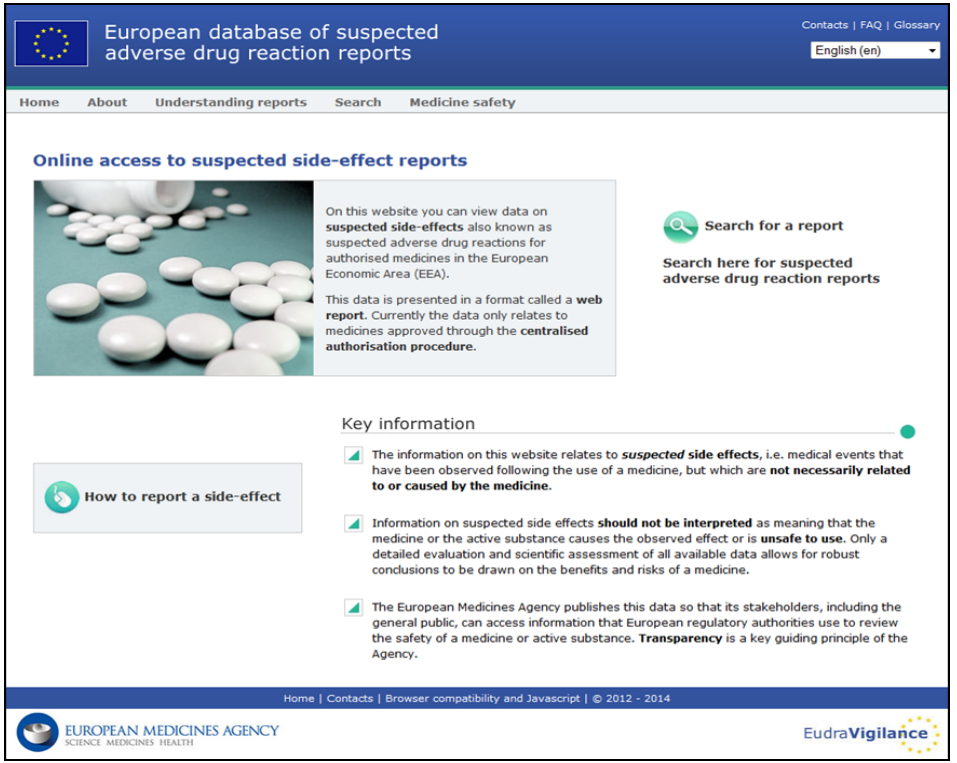
Audit of pharmacovigilance systems:

- EMA
- National agencies
- Pharmaceutical companies



Major increase in transparency: committee proceedings, side effect data, RMP summaries, PSUR assessment conclusions





Coordinated EU communications on pharmacovigilance

HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 January 2013
EMA/118465/2012

Guideline on good pharmacovigilance practices (GVP)

Module XV – Safety communication

Draft finalised by the Agency in collaboration with Member States and submitted to ERMS FG	12 July 2012
Draft agreed by ERMS FG	20 July 2012
Draft adopted by Executive Director	25 July 2012
Start of public consultation	26 July 2012
End of consultation (deadline for comments)	21 September 2012
Revised draft finalised by the Agency in collaboration with Member States	10 January 2013
Revised draft agreed by ERMS FG	16 January 2013
Revised draft adopted by Executive Director as final	22 January 2013
Date for coming into effect	24 January 2013

XV.C. Operation of the EU regulatory network

XV.C.1. Coordination of safety announcements in the EU

In the EU, patients and healthcare professionals increasingly look at competent authorities as providers of important information on medicines. For safety communication to be effective, adequate coordination and cooperation is required within the EU regulatory network[3]. A good level of coordination of safety communication is of particular importance so that healthcare professionals and patients receive consistent information on regulatory decisions in the EU.

When issuing safety announcements, competent authorities may make use of the different tools and channels described in XV.B.5. Prior to the publication of a safety announcement, the Member States, the Agency or the European Commission shall inform each other not less than 24 hours in advance, unless urgent public announcements are required for the protection of public health [DIR Art 106a(2)].

For active substances contained in medicinal products authorised in more than one Member State, the Agency shall be responsible for the coordination between national competent authorities of safety announcements [DIR Art 106a(3)].

For practical reasons, considering the potential for overlap between transparency measures and active communications and in order to focus on those topics of major health relevance, not all safety information made public by a Member State or the Agency will be subject to systematic exchange and coordination. Only safety announcements that relate to the following and that pertain to active substances contained in medicinal products authorised in more than one Member State require coordination within the EU regulatory network:

- the suspension, withdrawal or revocation of a marketing authorisation due to changes to its risk-benefit balance;
- the start or finalisation of an EU referral procedure for safety reasons;
- restriction of indication or treatment population or the addition of a new contraindication;
- dissemination of a DHPC agreed by relevant competent authorities of a Member State or the Agency (see XV.C.2.1.);
- other emerging safety concerns judged by a national competent authority or the Agency to be likely to give rise to public or media interest in more than one Member State (e.g. a publication of important safety findings in a (scientific) journal, safety related regulatory action taken in a

Engagement of stakeholders

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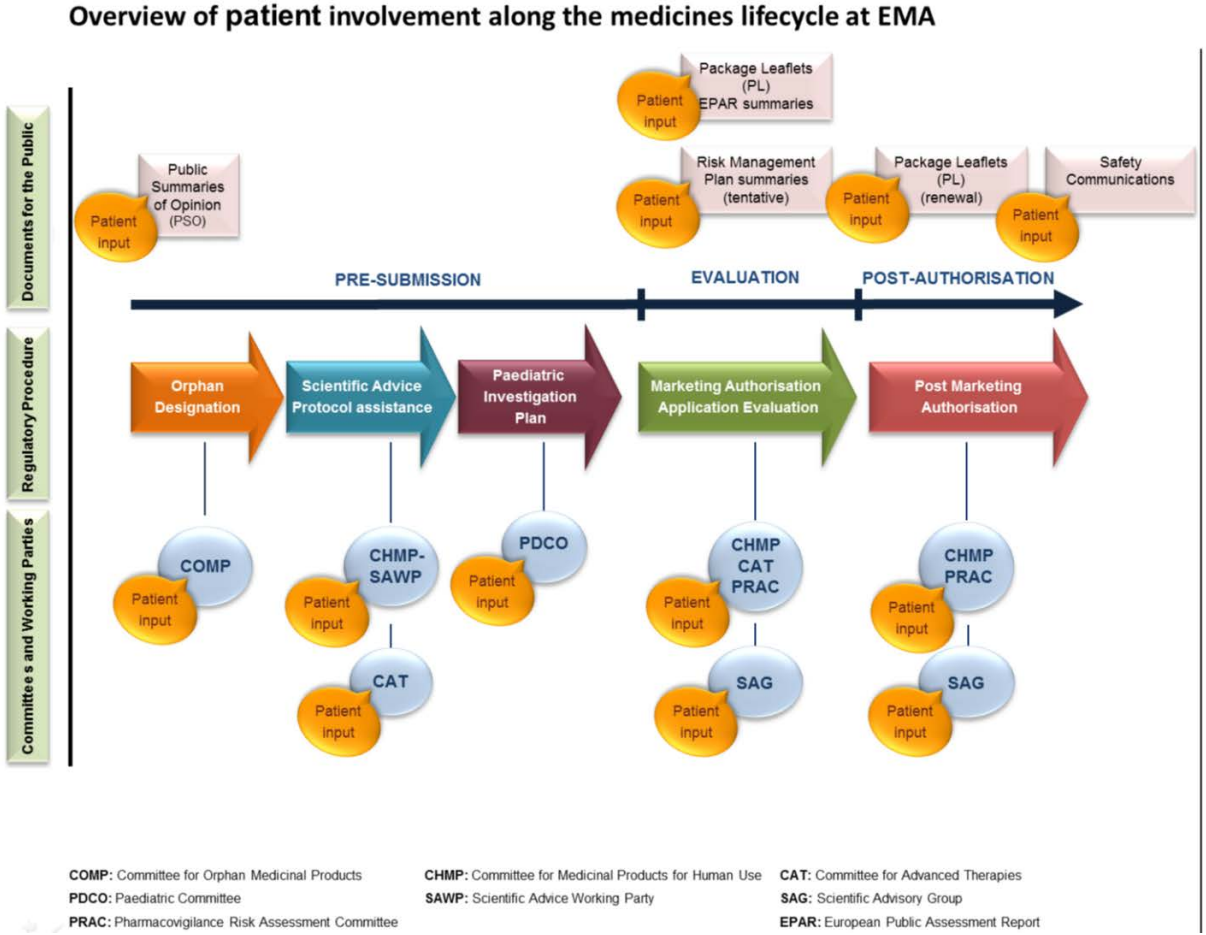
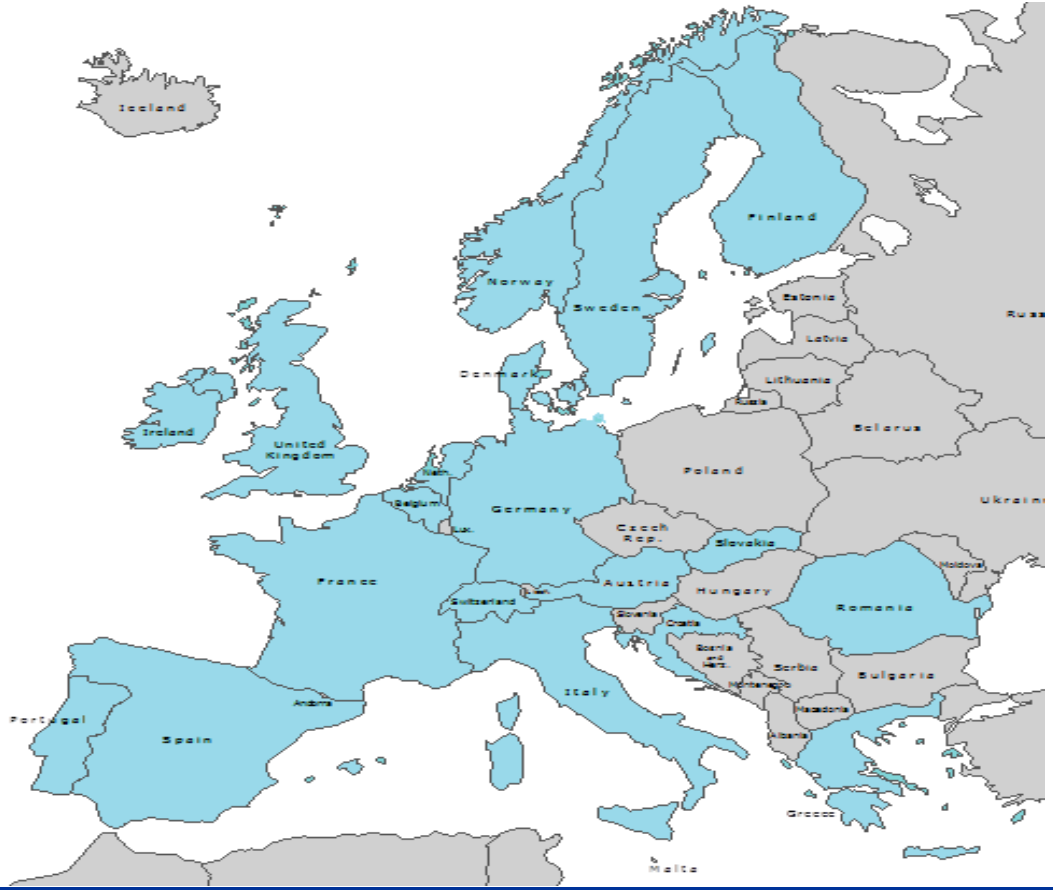


COMP: Committee for Orphan Medicinal Products
PDCO: Paediatric Committee
PRAC: Pharmacovigilance Risk Assessment Committee
CHMP: Committee for Medicinal Products for Human Use
SAWP: Scientific Advice Working Party
CAT: Committee for Advanced Therapies
SAG: Scientific Advisory Group
EPAR: European Public Assessment Report

Building capacity for data collection: ENCePP as an example

- **153 centres**
- **23 networks**
- **51 data sources**



Building capacity through good practice: SCOPE

Share expertise and best practice

Deliver practical tools and guidance

Operate pharmacovigilance

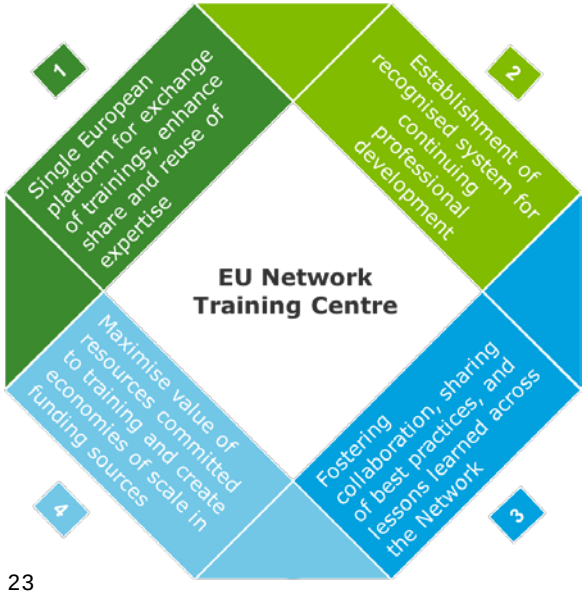
By Member States

For Member States

With Member States

Building capacity through training

More than 10,000 stakeholders trained by EU network in recent years



Evidence based process improvements: investment in regulatory science

PROTECT

imi efpia

Pharmacoepidemiological Research on Outcomes of The

Selection of 20 outputs among 101 PROTECT deliverables	
Recommendations for pharmacoepidemiology	
Output 1	Inventory on drug utilisation data
Output 2	Comparison of methods to control for confounding
Output 3	Balance measures for propensity score models
Output 4	Comparison of covariate adjustment methods
Output 5	Recommendations for pharmacoepidemiological
Methods for signal detection	
Output 6	Evaluation of disproportionality analysis
Output 7	Adverse Drug Reaction Repository
Output 8	Lessons learnt from a characterisation of databases used for signal detection
Output 9	Grouping of existing adverse drug reaction terminologies
Output 10	Novel groupings for adverse drug reactions
Output 11	Subgrouping and stratification in statistical signal detection
Output 12	Statistical signal detection from clinical trials
Output 13	Statistical signal detection from electronic health records
Benefit risk integration and representation	
Output 14	Methodologies for benefit-risk evaluation
Output 15	Methodologies for graphical representation
Output 16	Final tools for graphical B:R representation
Output 17	Recommendations on methodologies for B-R integration and representation
Output 18	Development of accessible material to patients
Output 19	Repository of training material
Output 20	Enhanced ADDIS software

Simplification through efficient systems and services

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Projects & Outputs	Benefits Delivered
Article 57 Database *European database of all medicinal products*	• Support PV Procedures which facilitates coordination of regulatory decisions • Supports the product index for EudraVigilance • Reduction of duplication
EudraVigilance Auditable Requirements *Enhanced adverse reaction collection and management system*	• Simplified reporting delivered • Data in ISO ICH ICSR R3 format will be higher quality, improving searchability & analysis efficiency
Medical Literature Monitoring *Delivery of literature monitoring service to MAHs*	• Improved safety monitoring of medicines • Reduction in costs for MAH literature monitoring activities
Pharmacovigilance Fees *Collection of fees to cover costs of conduct of certain PV activities*	• NCAs paid for certain PV assessments • Annual fees support implementation & maintenance of measures from 2010 legislation
PSUR Repository *Centralised repository for PSURs and assessment reports*	• Provides a simplification of PSUR submissions for industry • Repository will include all PSURs and assessment reports

Driven By

Effective programme management which ensures successful delivery of changes

Provides public health benefits across Europe

1995 2015 EMA

Funding of processes and systems through fees

SCOPE:

- The newly adopted Pharmacovigilance fees regulation allows the EMA to **collect fees from MAHs for PV activities** conducted at EU level for medicinal products for human use.
- The income will be used to **remunerate national competent authorities** (NCAs) of the EU for the scientific assessment carried out by the rapporteurs and to **contribute to the Pharmacovigilance-related costs of the Agency**.

✓ Pharmacovigilance annual fee advice notes were sent to QPPVs on the 20th April 2015;

✓ **The 1st annual pharmacovigilance fee invoices were issued in July 2015;**

✓ The EMA invoicing portal has been launched (enables customers to get instant access to their account, view and print invoices, raise invoice queries and make payments via SEPA direct debit).

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- Brief look to the future (more in later session) **- Priorities for the next years**
- Some conclusions

Priorities for the next years

- Working together for continuous improvement of health promotion and protection
- Renewed focus on: efficiency, process improvement, and simplification
- Harness the opportunities of new technology and real-world evidence
- Ensure we make a positive impact

Highlights of the years to come

- Improvement of processes: use of scientific advice, signal detection by industry, proportionate risk management planning……
- Guidance informed by experience: biologics, pregnancy, geriatrics, regulatory action, efficacy studies……
- Better use of mobile technology and social media: IMI WebRADR
- Better organisation of EU capacity for studies: IMI ADVANCE
- Better use of real world data: Registries, electronic health records, inter-stakeholder collaboration
- Information technology for simplification: EudraVigilance, EU database of medicines, PSUR repository
- Continuous improvement and ensuring effectiveness: measuring impact of pharmacovigilance

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Conclusions

Working together for continuous improvement of health promotion and protection

Delivered:

- Proactive monitoring
- Faster safety issue detection
- Faster warnings to users
- Increased transparency
- Engagement of stakeholders

Renewed focus on: efficiency, process improvement, and simplification

A few thanks

- Colleagues in the Member States who run national systems and contribute to the EU system
- Committees and working parties
- EMA staff contributing to achieving our goals
- Patient and healthcare professional colleagues that report and support the governance and the decision-making
- Industry for engagement and feedback


1995
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Thank you

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