3-year Report on European Union Pharmacovigilance Activities

European Medicines Agency
10th stakeholder forum on pharmacovigilance legislation

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Key principles of EU pharma law

Objectives

Protection of public health

Free movement of medicinal products within the European Union

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EU pharmaceutical legislation

Directive 2001/83/EC	**The core legislation governing the regulation of medicines in EU:** • **Title IX – Pharmacovigilance** • Article 108b – report on performance of pharmacovigilance tasks by Member States
Regulation (EC) No 726/2004	**Sets the procedures for the authorisation and supervision of medicinal products at EU level and establishes the European Medicines Agency:** • **Title II - Chapter 3 – Pharmacovigilance** • Article 29 - report on performance of pharmacovigilance tasks by Member States

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Commission Implementing legislation

- Commission Implementing Regulation (EU) No 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC
- Commission Implementing Regulation (EU) No 198/2013 of 7 March 2013 on the selection of a symbol for the purpose of identifying medicinal products for human use that are subject to additional monitoring
- Delegated Regulation (EU) No 357/2014 of 7 February 2014 specifying situations in which a post-authorisation efficacy study may be required

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Commission report

- Report from the Commission (COM(2016) 498 final) and accompanying staff working document (SWD(2016 284 final) adopted 8 August 2016
- Includes pharmacovigilance activities of Member States and the European Medicines Agency
- Mainly covering July 2012 – December 2014

EUROPEAN COMMISSION

Brussels, 8.8.2016
COM(2016) 498 final

REPORT FROM THE COMMISSION

Pharmacovigilance related activities of Member States and the European Medicines Agency concerning medicinal products for human use (2012 – 2014)

{SWD(2016) 284 final}

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Pharmacovigilance

Pharmacovigilance is the process and science of monitoring the safety of medicines and taking action to reduce the risks and increase the benefits of medicines

Related activities	• Collecting and managing data on the safety of medicines • Evaluating the data to detect 'signals' • Acting to protect public health • Communicating with/informing stakeholders and public
Stakeholders	• Users of medicines (reporting adverse drug reactions) • Healthcare professionals (HCP) working with medicines • Regulatory authorities, including the European Medicines Agency (EMA) and those in the Member States responsible for monitoring the safety of medicines • Pharmaceutical companies and companies importing or distributing medicines

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European Union Pharmacovigilance - a network approach

- Member States
- European Medicines Agency (including the Pharmacovigilance Risk Assessment Committee (PRAC)
- European Commission

The European Union

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Advantages of the network approach

- Transparency and early involvement
- Bringing together multiple experts for the benefit of public health
- Collaborative development of (scientific) guidelines taking account of the state of the art
- Facilitating communication with a variety of stakeholders including academia, patients and industry

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Functioning of the system

TRIGGERS OF THE DECISION MAKING PROCEDURE	ACTIONS BASED ON PHARMACOVIGILANCE CONCERNS
• Monitoring adverse drug reactions (ADRs) • Signal of a new adverse event, ADR • Periodic safety update reports (PSUR) • Specific procedure: referrals • Oversight of post-authorisation obligations	• Change of marketing authorisation • Suspension • Withdrawal • Revocation • Non-renewal

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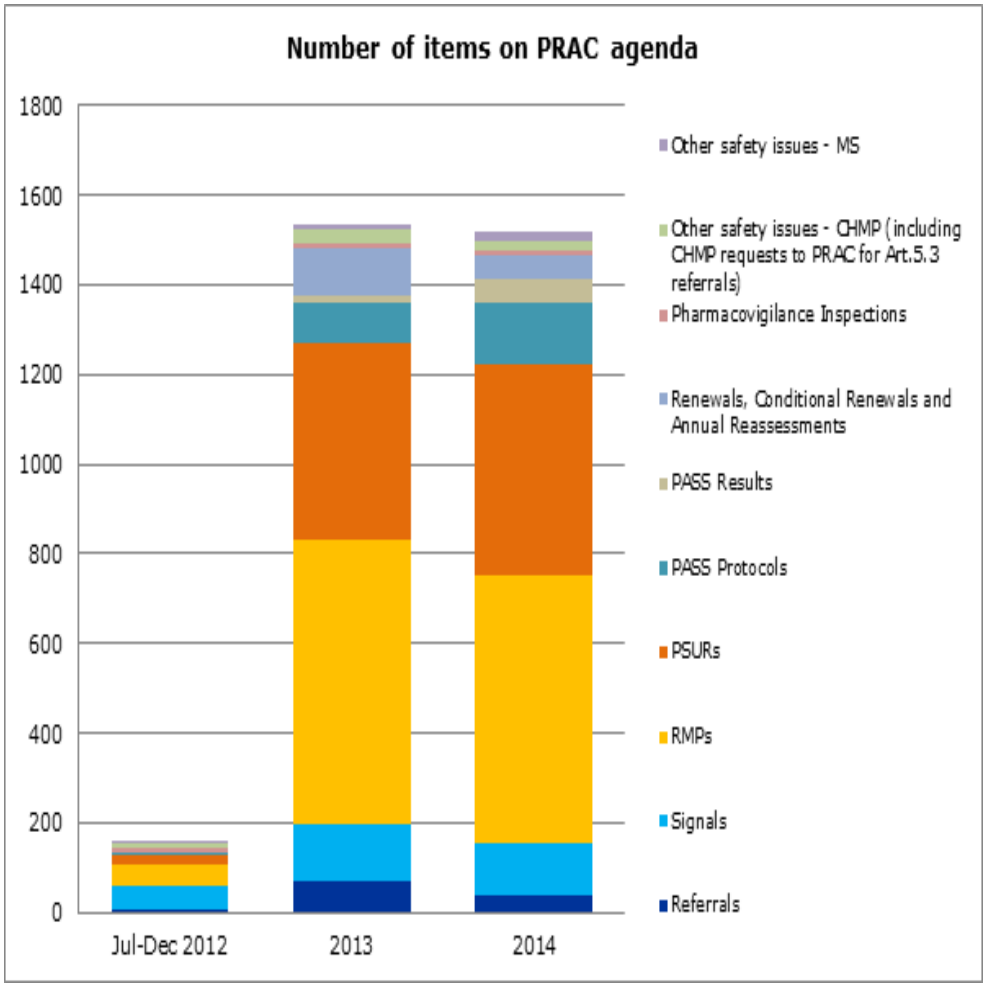
Items on the PRAC agenda



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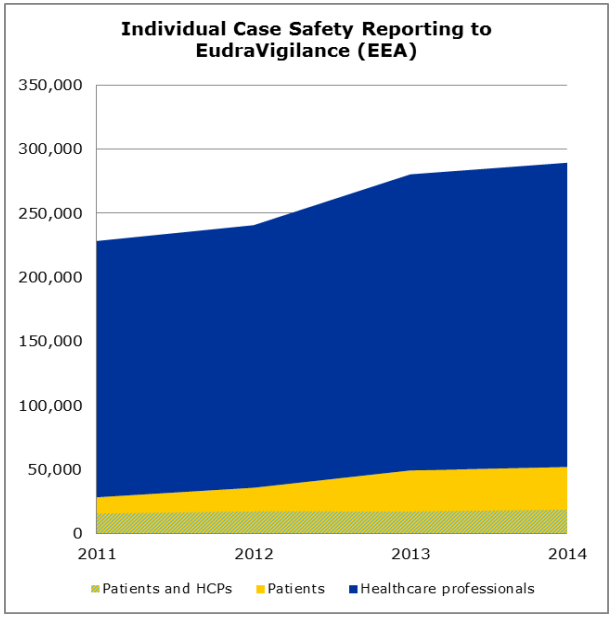
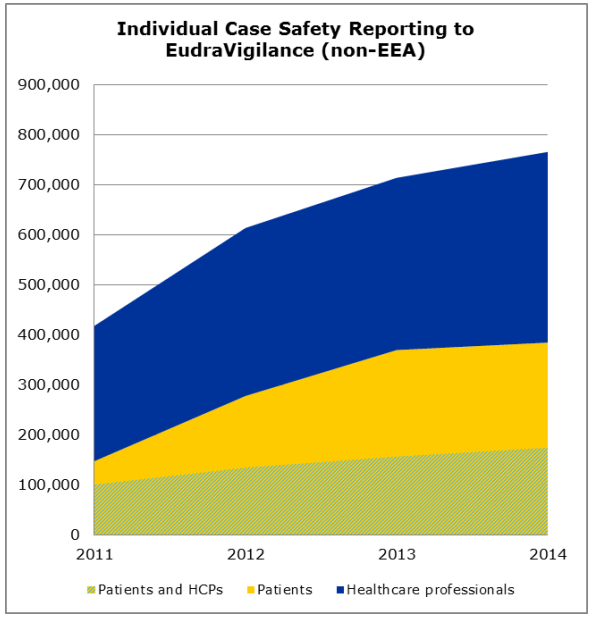
Monitoring adverse drug reactions

- Increasing number of reports
- Patient reporting increased by around 50%





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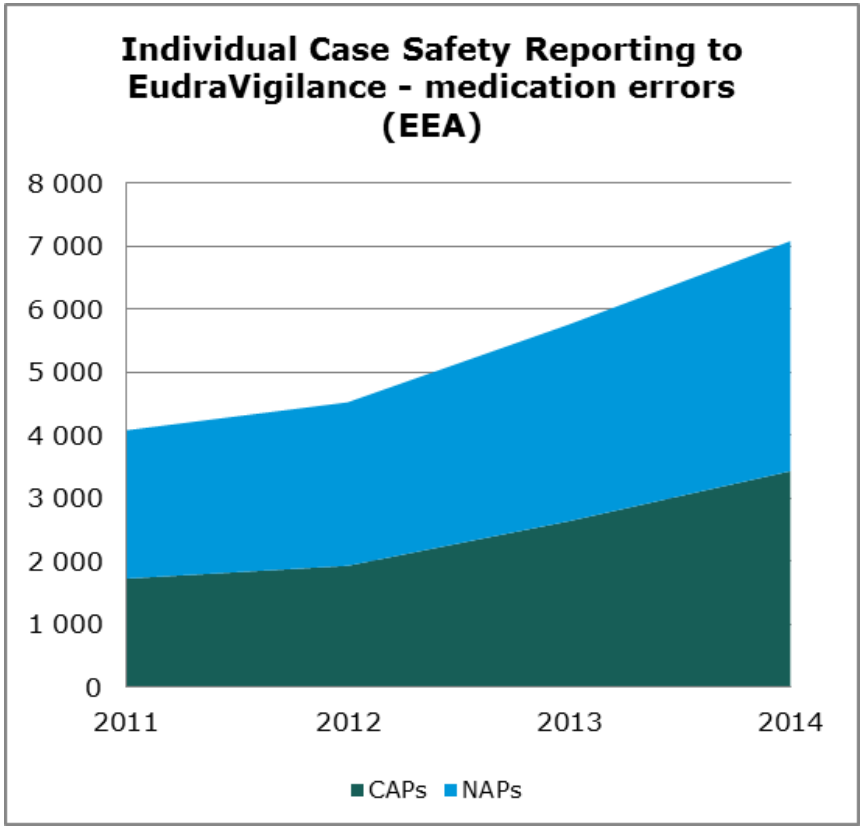
Medication errors

- Increasing level of reporting
- 2013 workshop on prevention of medication errors



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Additional monitoring - Black symbol

- 2013 black symbol – black inverted triangle - introduced
- Included in information to HCPs and patients
- For biological medicines or medicines containing a new active substance authorised after 1 January 2011 until 5 years after authorisation
- For medicines with certain additional obligations
- List published by EMA and updated monthly
- End 2014 – 193 centrally authorised medicines, 8 nationally authorised medicines, 1 269 medicines with conditions

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Signal management

Aim	• Signal detection, validation, confirmation, analysis and prioritisation, assessment and recommendation for action
Process	• Through **signal detection** signals are identified. The data is evaluated during **signal validation** to verify the existence of a new potentially causal association or a new aspect of a known association. **Confirmed signals** are **analysed and prioritisation** by PRAC. Following the scientific evaluation of all the evidence available through the **signal assessment** by PRAC a **recommendation** is made.

Determined if there are new risks identified for a medicine and if changes to the marketing authorisation are required

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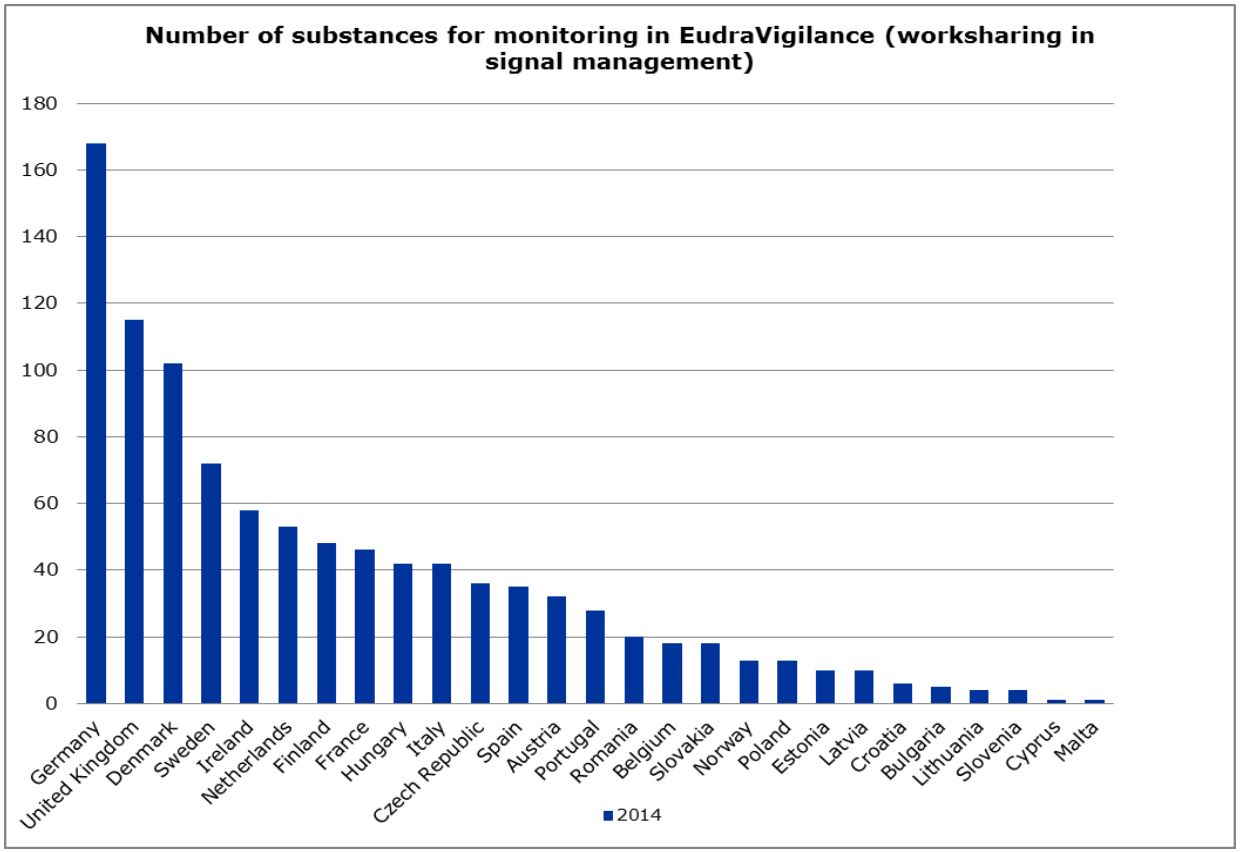
Signal detection – sharing the work



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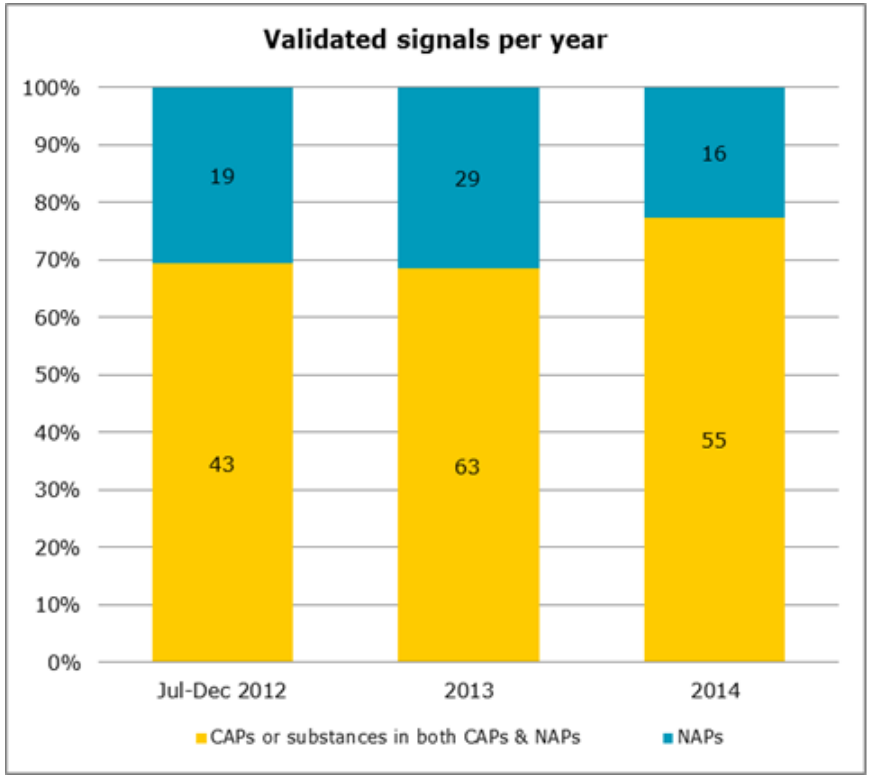
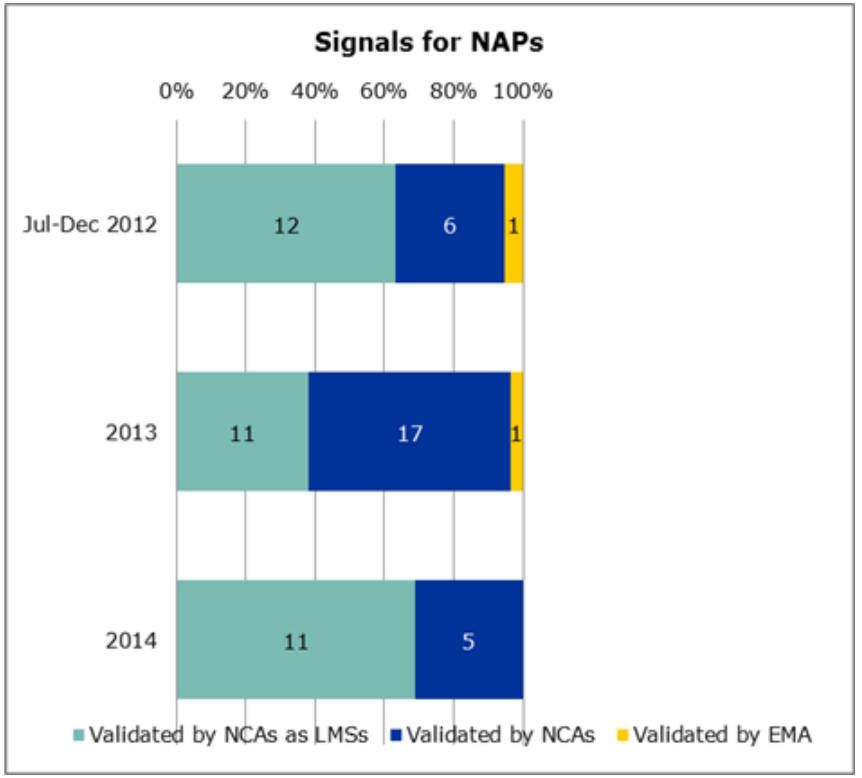
Signals - collaborative validation





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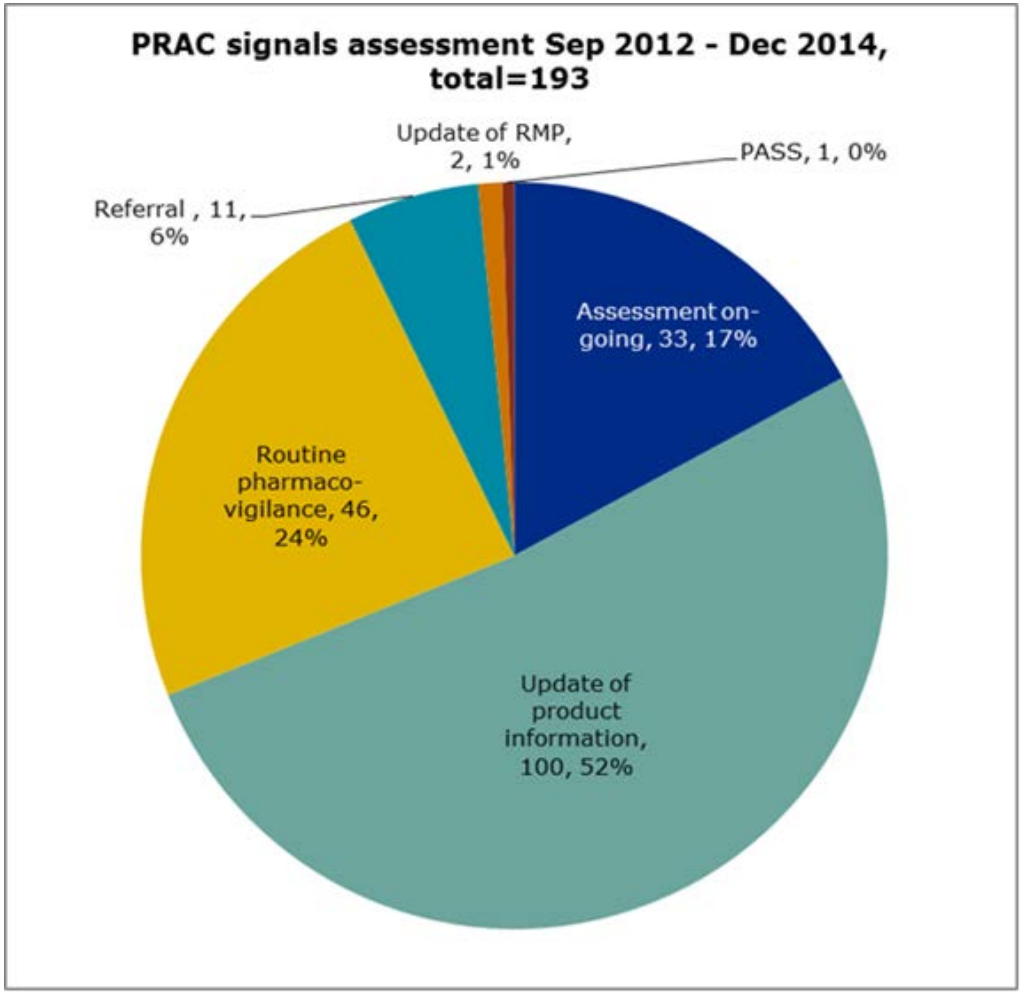
Signal detection
recommendations



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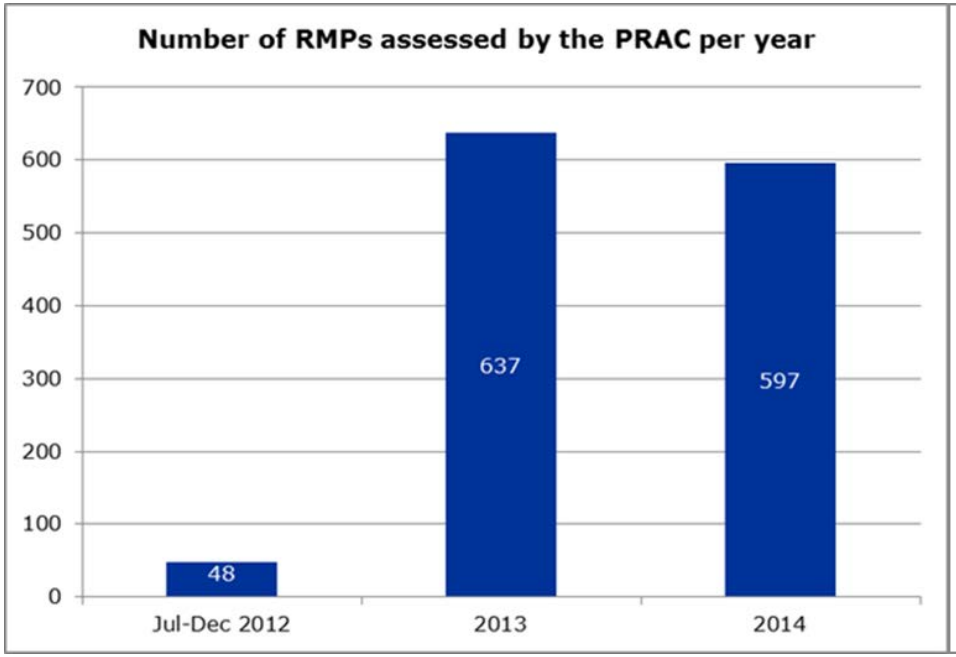
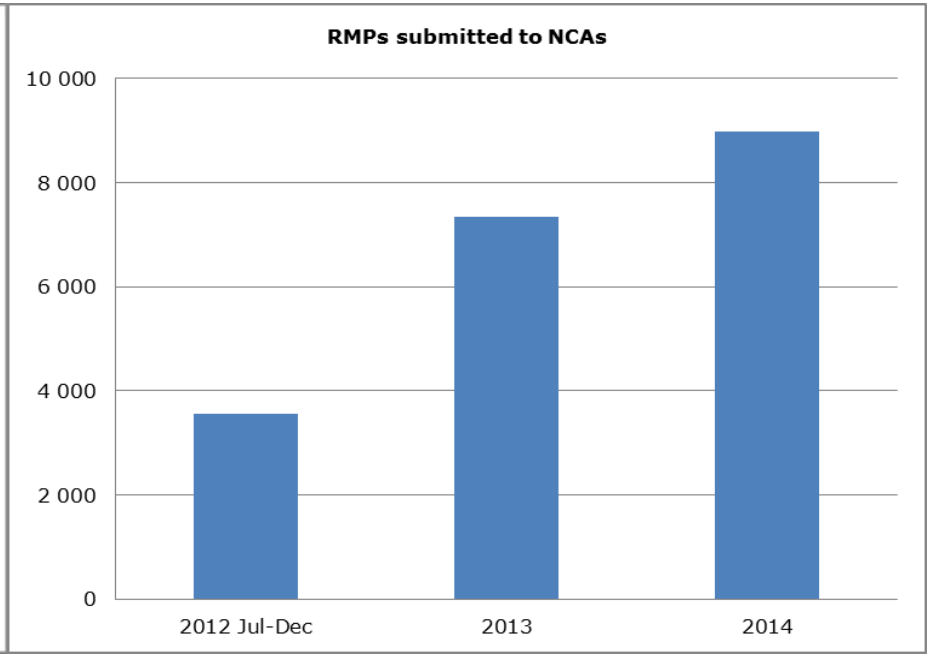
Risk management plans





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Periodic Safety Update Reports

Aim	• Periodic safety update reports (PSURs) are reports providing an evaluation of the benefit-risk balance of a medicine • Marketing authorisation holders must submit PSURs at defined time points following a medicine's authorisation
Scope	• Cumulative data - focus on the new information • Scientific assessment and integrated benefit-risk evaluation • Single PSUR for all products containing the same active substance

Determined if there are new risks identified for a medicine or whether the balance of benefits and risks has changed

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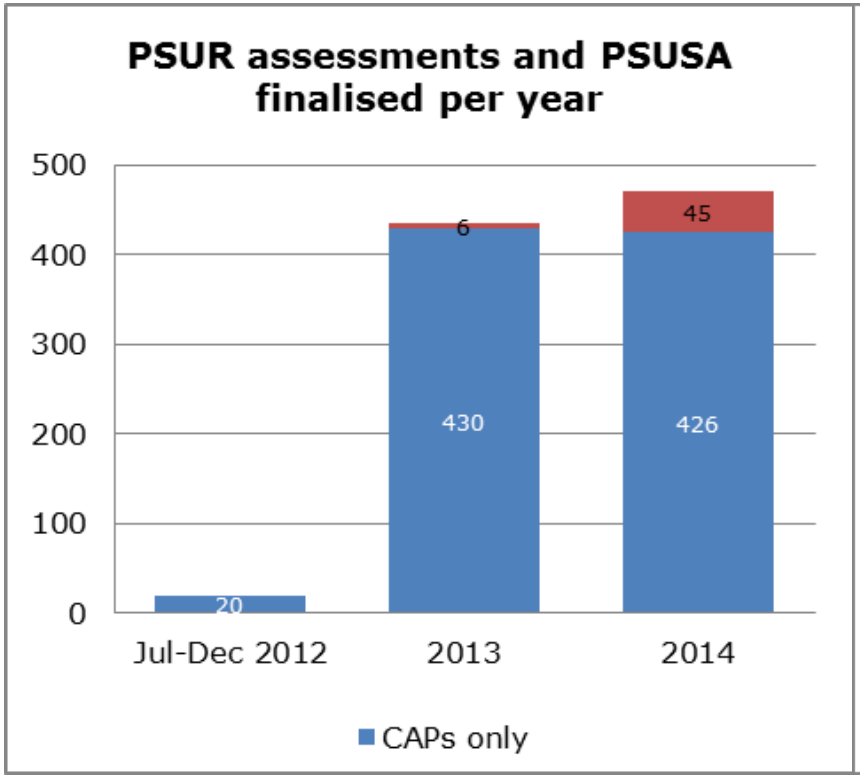
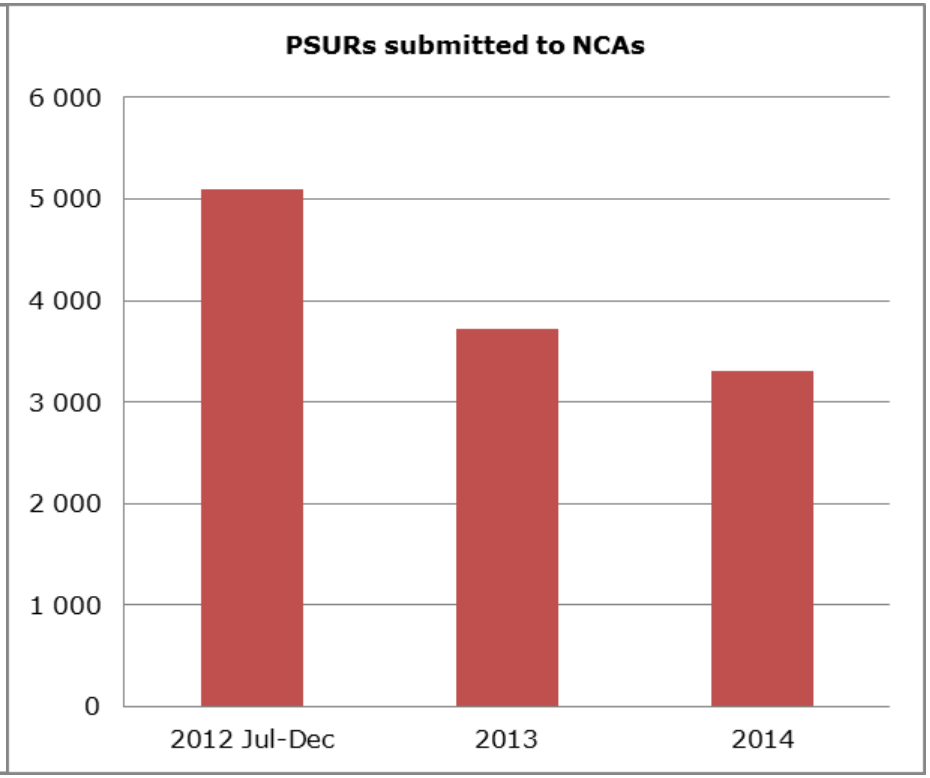
PSUR assessments





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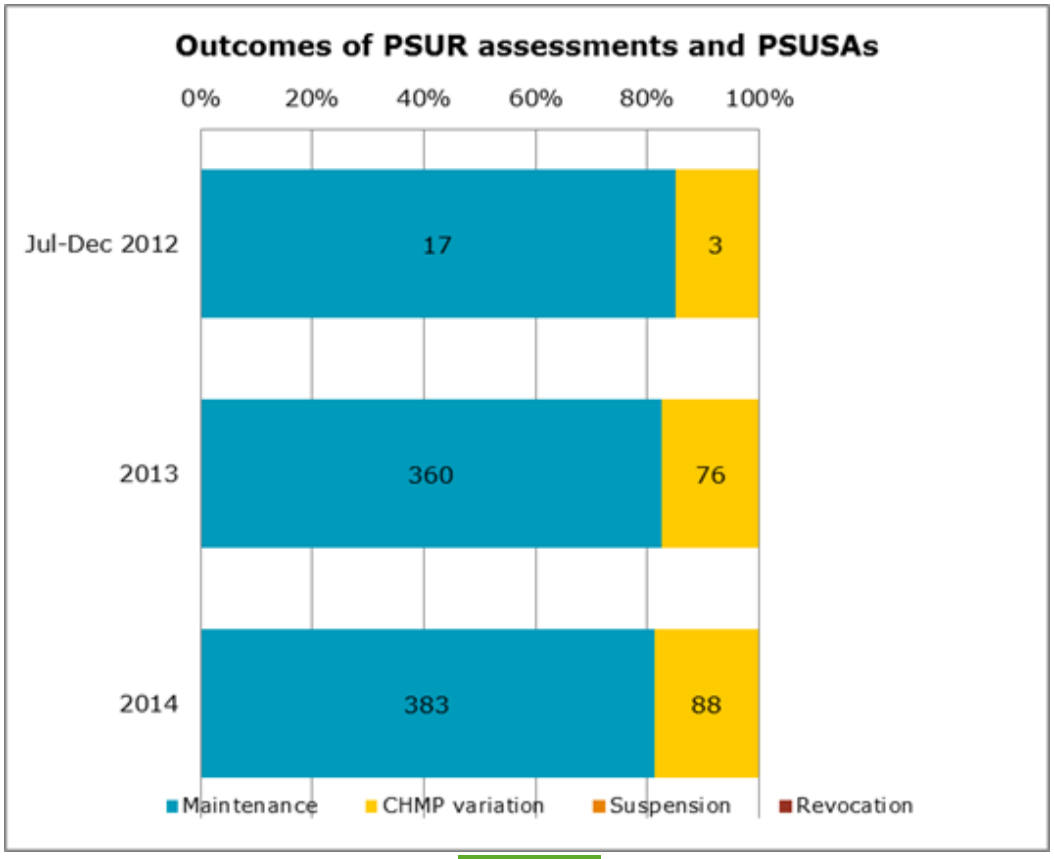
PRAC PSUR assessments outcomes



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Referral procedures

Aim	• Resolves issues such as concerns over the **safety** or **benefit-risk balance** of a medicine or a class of medicines • EMA conducts a **scientific assessment** on behalf of the EU and makes a **recommendation** for a harmonised position across the EU
Safety-related referrals	• **Based on evidence from pharmacovigilance** – assessment and recommendation by PRAC, then: • **Centrally authorised or centrally and nationally authorised medicines:** ➢ Assessed by the Committee for Medicinal Products for Human Use (CHMP) • **Only nationally authorised medicines** ➢ Assessed by the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)
Procedure	• **Can be started by the European Commission or any Member State** • For most referrals, the **European Commission issues a decision to all Member States** reflecting the measures to take to implement the Agency's recommendation

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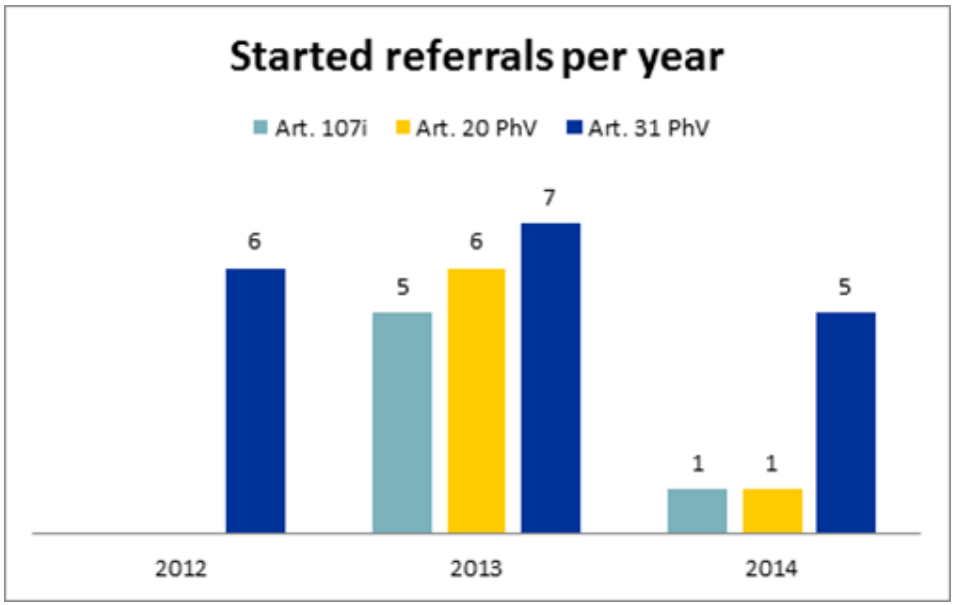
Pharmacovigilance referrals



July 2012 – December 2014

- 6 Art. 107i - urgent safety referrals for nationally authorised medicines
- 7 Art. 20 - related to centrally authorised medicines only
- 18 Art. 31 - related to nationally or nationally and centrally authorised medicines

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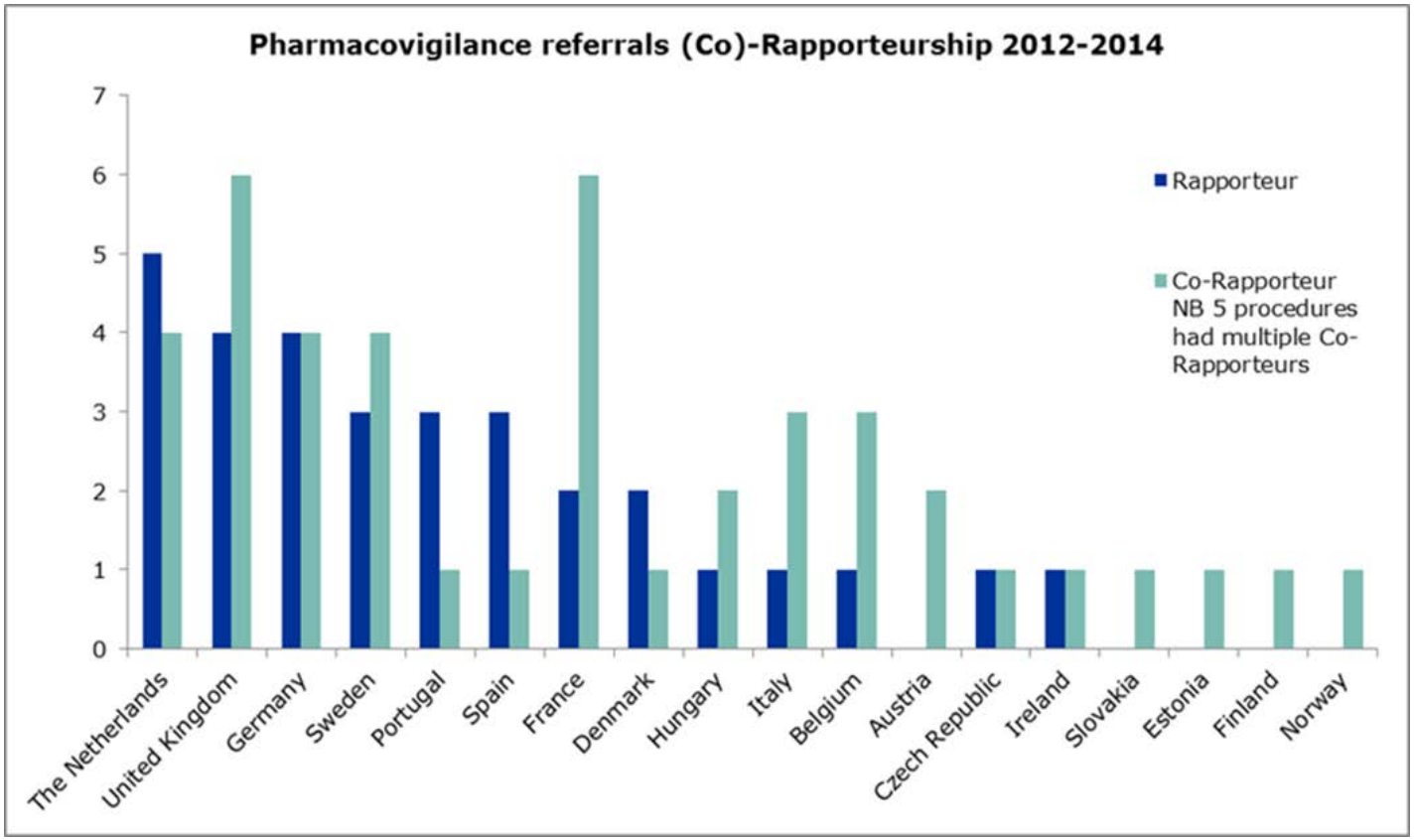
Referrals - collaborative effort



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Referrals outcomes

- 24 variations of marketing authorisation (MA)
- 6 suspensions of indication or MA
- 4 revocations of indication or MA

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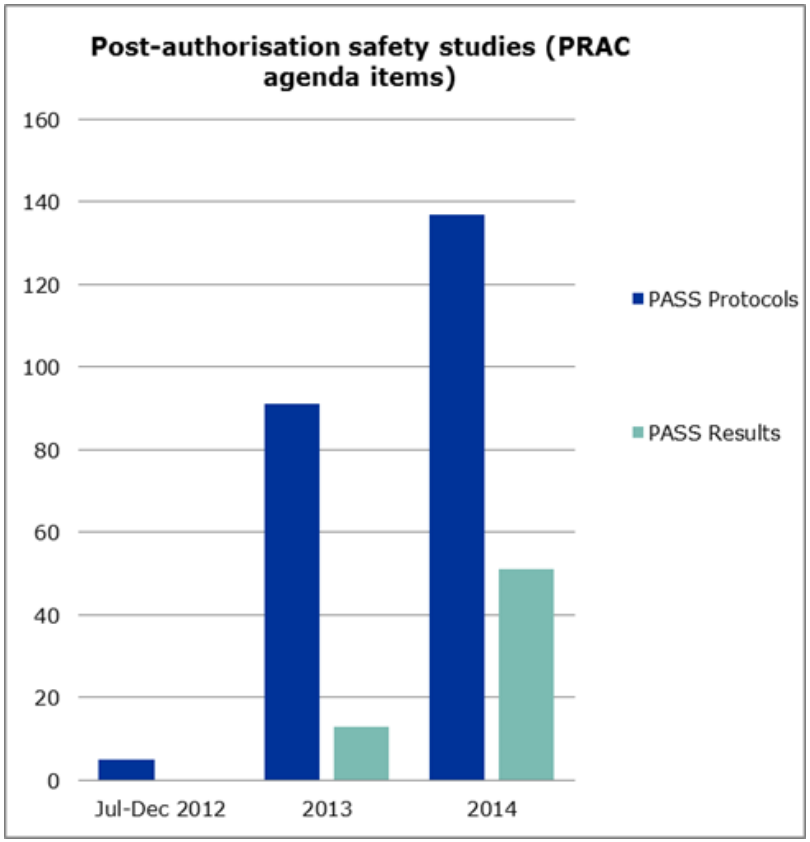
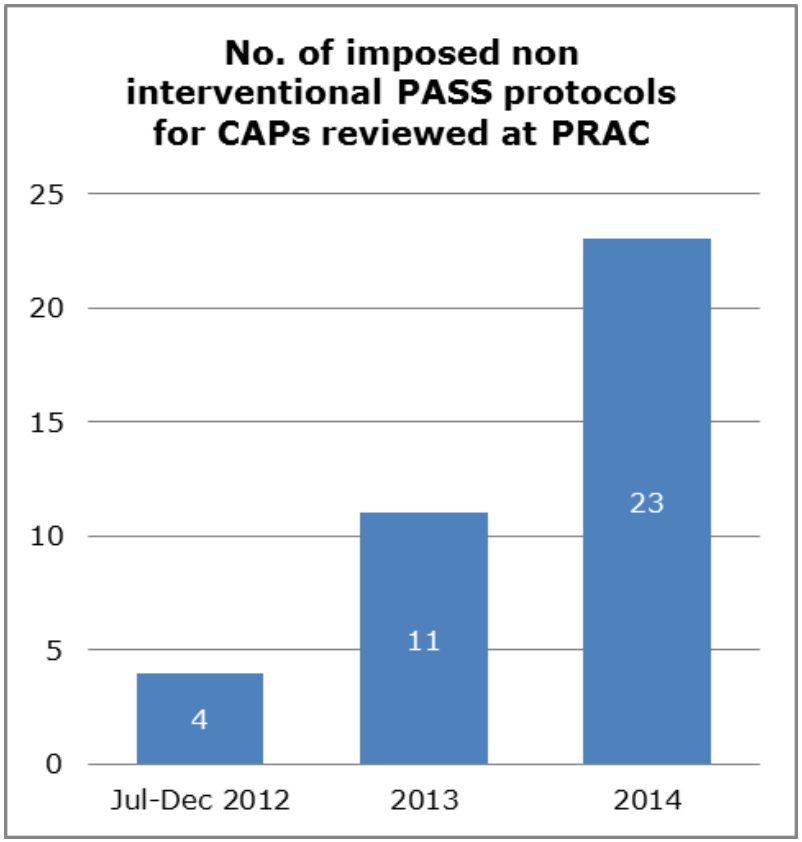
Post-authorisation studies





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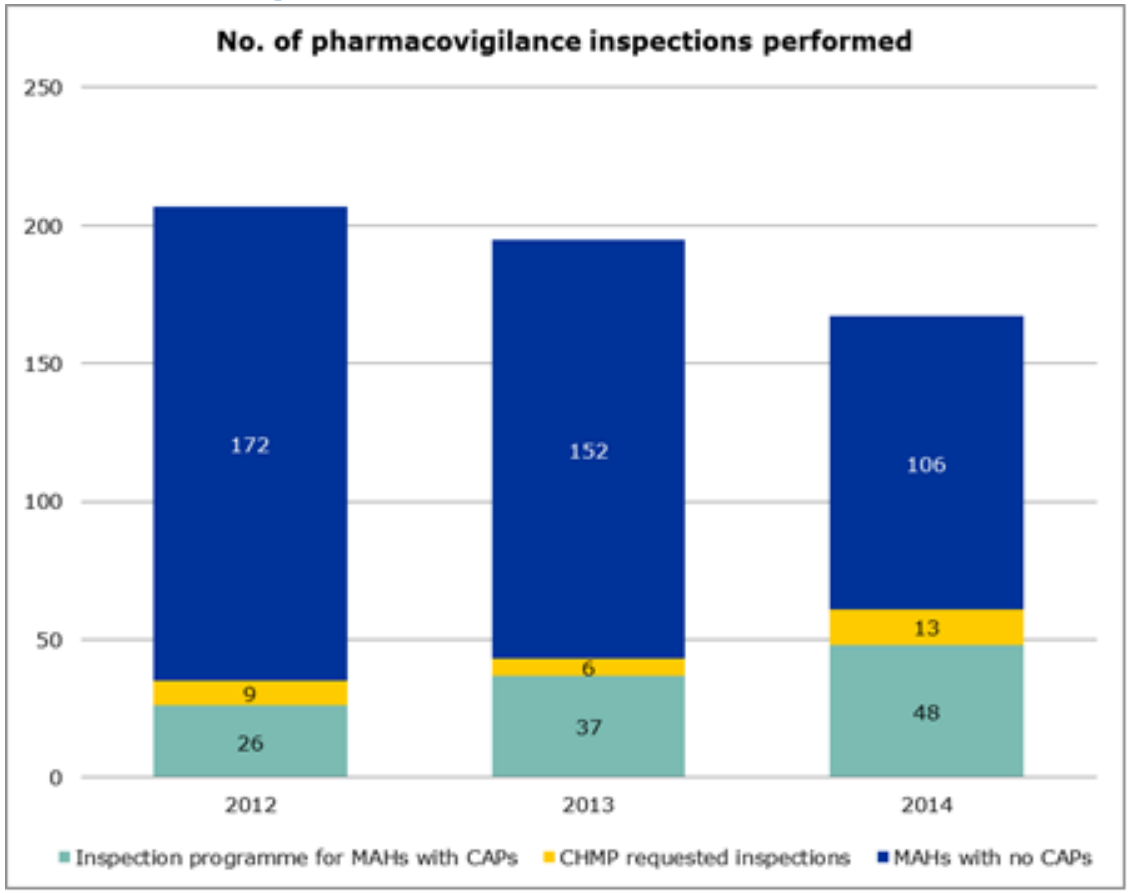
Pharmacovigilance inspections



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Communications and information

- Information related to the PRAC – agendas, minutes
- Public safety communications – e.g. concerning referrals
- European database of suspected ADRs
- European Network of Centres in Pharmacoepidemiology and Pharmacovigilance
  e.g. outcomes of imposed PASS
- Risk management plan summaries

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Systems and services

- Database of medicinal products authorised in the EU (Article 57 database)
- EudraVigilance enhancements
- Literature monitoring service
- PSUR repository

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Future deliverables

- Continuing process improvements and complete implementation of systems and services
  (e.g. EudraVigilance, extension of literature monitoring, dedicated European medicines web portal)

- Continue training network

- Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action

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Thank you for your attention

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Public Health information:

http://ec.europa.eu/health/index_en.htm

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