

# Modalità di lavoro e ruolo del PRAC

Amelia Cupelli

57° Simposio AFI – Rimini

9 giugno 2017



# Dichiarazione di trasparenza/interessi\*

Le opinioni espresse in questa presentazione sono personali e non impegnano in alcun modo l'AIFA

Interessi nell'industria farmaceutica	NO	Attualmente	Da 0 a 3 anni precedenti	oltre 3 anni precedenti
<b>INTERESSI DIRETTI:</b>				
1.1 Impiego per una società: Ruolo esecutivo in una società farmaceutica	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> obbligatorio
1.2 Impiego per una società: Ruolo guida nello sviluppo di un prodotto farmaceutico	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> obbligatorio
1.3 Impiego per una società: altre attività	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
2. Consulenza per una società	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
3. Consulente strategico per una società	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
4. Interessi finanziari	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
5. Titolarità di un brevetto	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
<b>INTERESSI INDIRETTI:</b>				
6. Sperimentatore principale	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
7. Sperimentatore	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
8. Sovvenzioni o altri fondi finanziari	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo
9. Interessi Familiari	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> facoltativo

\* **Amelia Cupelli**, secondo il regolamento sul Conflitto di Interessi approvato dal CdA AIFA in data 25.03.2015 e pubblicato sulla Gazzetta Ufficiale del 15.05.2015 in accordo con la policy EMA /626261/2014 sulla gestione del conflitto di interessi dei membri dei Comitati Scientifici e degli esperti.

N.B. Il compenso ricevuto per questo intervento è regolato dalla contrattazione collettiva



# Agenda

Where have we come from – establishment of PRAC as public health focussed

What is state of progress - designing approaches for efficient operation of the public health protection tools and continuous improvement

How are we moving forward – challenges and priorities



# Pharmacovigilance Risk Assessment Committee



- public health focused committee of EMA
- undertakes PhV decisions using legislative public health protection tools
- 1<sup>st</sup> Meeting of PRAC: July 2012



# PRAC - Mandate

Responsible for assessing all aspects of risk management of human medicines, including:

- the detection, assessment, minimisation and communication of the risk of ADRs, while taking the therapeutic effect of the medicine into account
- design and evaluation of PASS
- PhV audits



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# PRAC - Responsibilities

Provides recommendations on questions on PhV and risk management systems, including the monitoring of their effectiveness, to the:

- CHMP for CAPs and referral procedures
- CMDh on the use of a medicine in MSs
- the EMA secretariat, Management Board and European Commission, as applicable



# PRAC Membership

Chair: Dr. June Raine, MHRA

## Membership:

Appointed by  
each MS:



1 member + alternate

28 + EEA countries non  
voting members

Appointed by EC:



6 members - relevant expertise  
including clinical pharmacology  
and pharmacoepidemiology

1 member/alternate representing  
patient orgs

1 member/alternate representing  
HCPs



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

3 March 2013  
EMA/PRAC/567515/2012 Rev.1<sup>1</sup>

## Pharmacovigilance Risk Assessment Committee Rules of Procedure

Agreed by the European Commission on 9 April 2014  
Date of entry into force 9 April 2014



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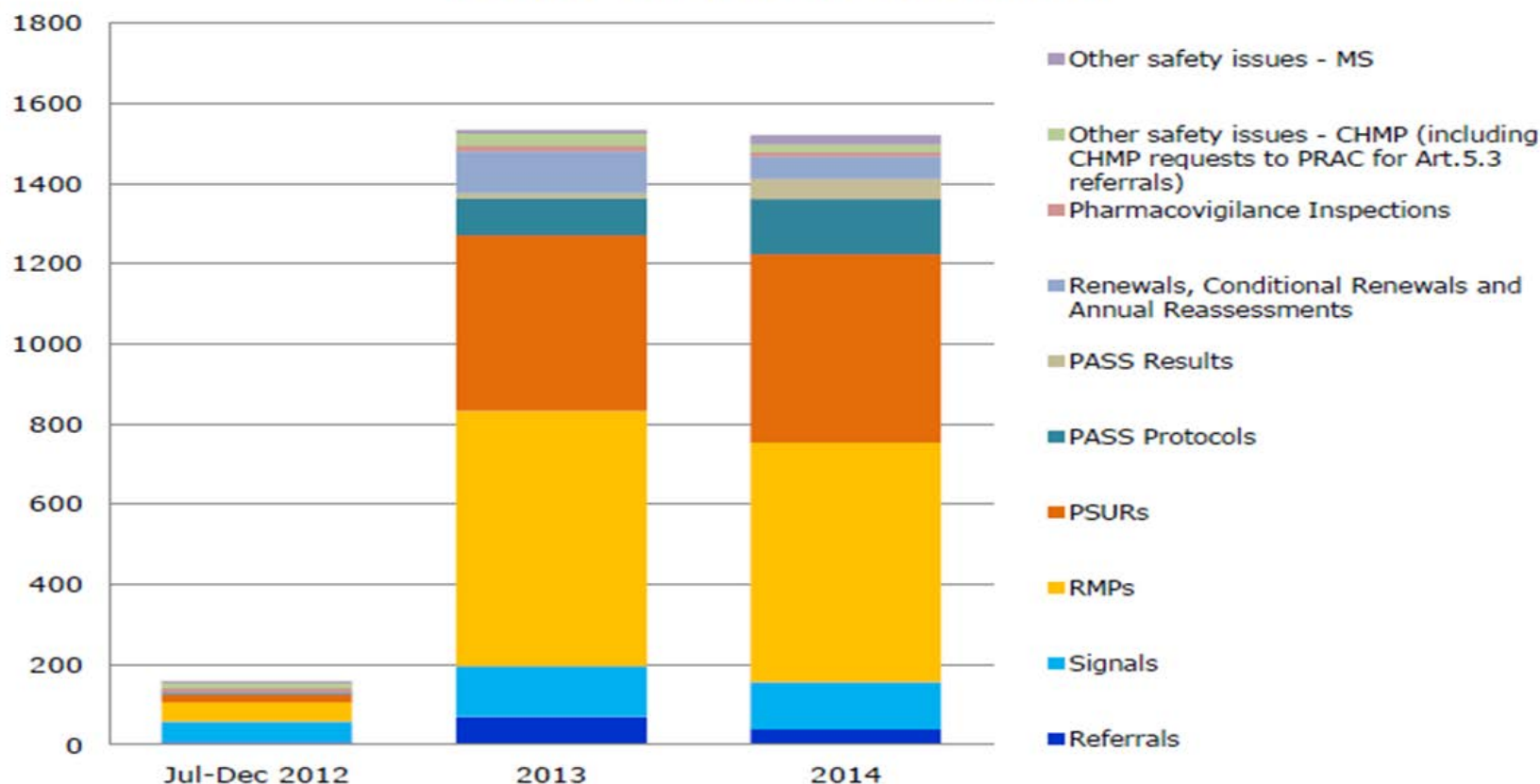
# PRAC's main goals for public health

- Proactively investigating drug safety  
continuous signal detection, filling knowledge gaps  
via PASS
- Responding to safety and benefit risk issues  
risk-proportionate decisions to rigorous timescales,  
effectiveness of risk minimisation
- Driving forward the new era in transparency  
real time access to information on PRAC activities
- Increasing involvement of stakeholders  
health professionals, patients and public



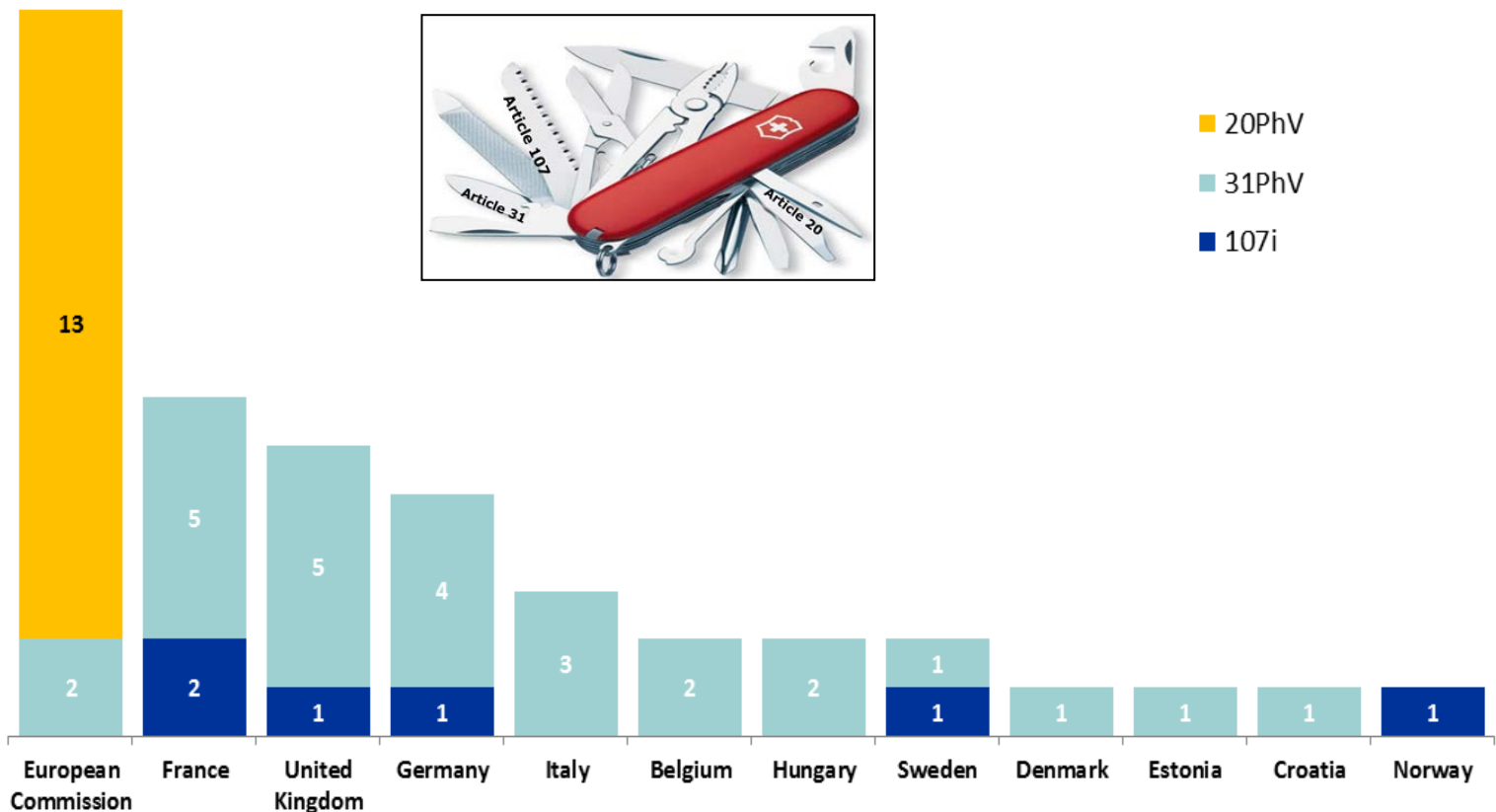
# Procedures on the PRAC Agenda

Number of items on PRAC agenda



*Report from the EC - Pharmacovigilance related activities  
(2012 – 2014)*

# Referral at PRAC by triggering party per article July 2012 – March 2017





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SCIENCE MEDICINES HEALTH

8 July 2016  
EMA/459912/2016

## EMA starts review of retinoid medicines

Effectiveness of measures for pregnancy prevention and for minimising possible risk of neuropsychiatric disorders to be evaluated

SCIENCE MEDICINES HEALTH

5 May 2017  
EMA/153837/2017

PRAC concludes there is no clear and consistent evidence of a difference in inhibitor development between classes of factor VIII medicines

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed its review of factor VIII medicines to evaluate the risk of developing inhibitors in patients with haemophilia A who have not previously been treated with these medicines. Having reviewed the available evidence, the PRAC concluded that there is no clear and consistent evidence of a difference in the incidence of inhibitor development between the two classes of factor VIII medicines: those derived from plasma and those made by recombinant DNA technology.



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SCIENCE MEDICINES HEALTH

10 February 2017  
EMA/85325/2017

## EMA to review persistence of side effects known to occur with quinolone and fluoroquinolone antibiotics

Review to focus on long-lasting effects mainly affecting musculoskeletal and nervous systems

[Home](#) ▶ [Find medicine](#) ▶ [Human medicines](#) ▶ [Referrals](#)

### Valproate and related substances

[Summary](#)

[Key facts](#)

[Public hearing](#)

[All documents](#)

Procedure  
started

Under  
evaluation

PRAC  
recommendation

CMDh  
Position

European  
Commission  
final decision

### New review of valproate use in pregnancy and women of childbearing age

#### EMA to consider if risks of these medicines require further restrictions of use

The European Medicines Agency (EMA) has started a review looking at the use of valproate-containing medicines in the treatment of women and girls who are pregnant or of childbearing age. These medicines are approved nationally in the EU to treat epilepsy, bipolar disorder and in some countries, migraine, and have been previously reviewed by the Agency.

# PRAC Work Plan 2017 - Overview

1. Optimising management and utility of adverse reactions
2. Lifecycle approach to pharmacovigilance and risk management
3. Process improvements and simplification
4. Special populations and product guidance
5. Partners and stakeholders - engagement
6. Strengthening links between assessment and inspection
7. Measuring the impact of pharmacovigilance activities
8. Fostering international collaborations



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

23 March 2017  
EMA/PRAC/213230/2017  
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC):  
Work Plan 2017

Adopted by the Committee on 23 March 2017



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# 1. Optimise mgmt & utility of reported ADRs



- EudraVigilance functionalities

PRAC adoption of recommendation on audit results

- Signal detection

- IMI-WEB-RADR project

review relevant outputs

# EudraVigilance Auditable Requirements (PV-ADR)

***Independent audit of new EudraVigilance system***

**Feb 2017**

***Progress update to EMA Management Board***

**Mar 2017**

***PRAC recommendation on final audit report***

**May 2017**

***EMA Management Board adoption of final audit outcome -***

Final audit report to be presented for adoption by written procedure, supported if needed by a dedicated Management Board teleconference

**May 2017**

***Release of new EudraVigilance functionalities*** – Including adoption of revised Access Policy, and the move to simplified reporting.

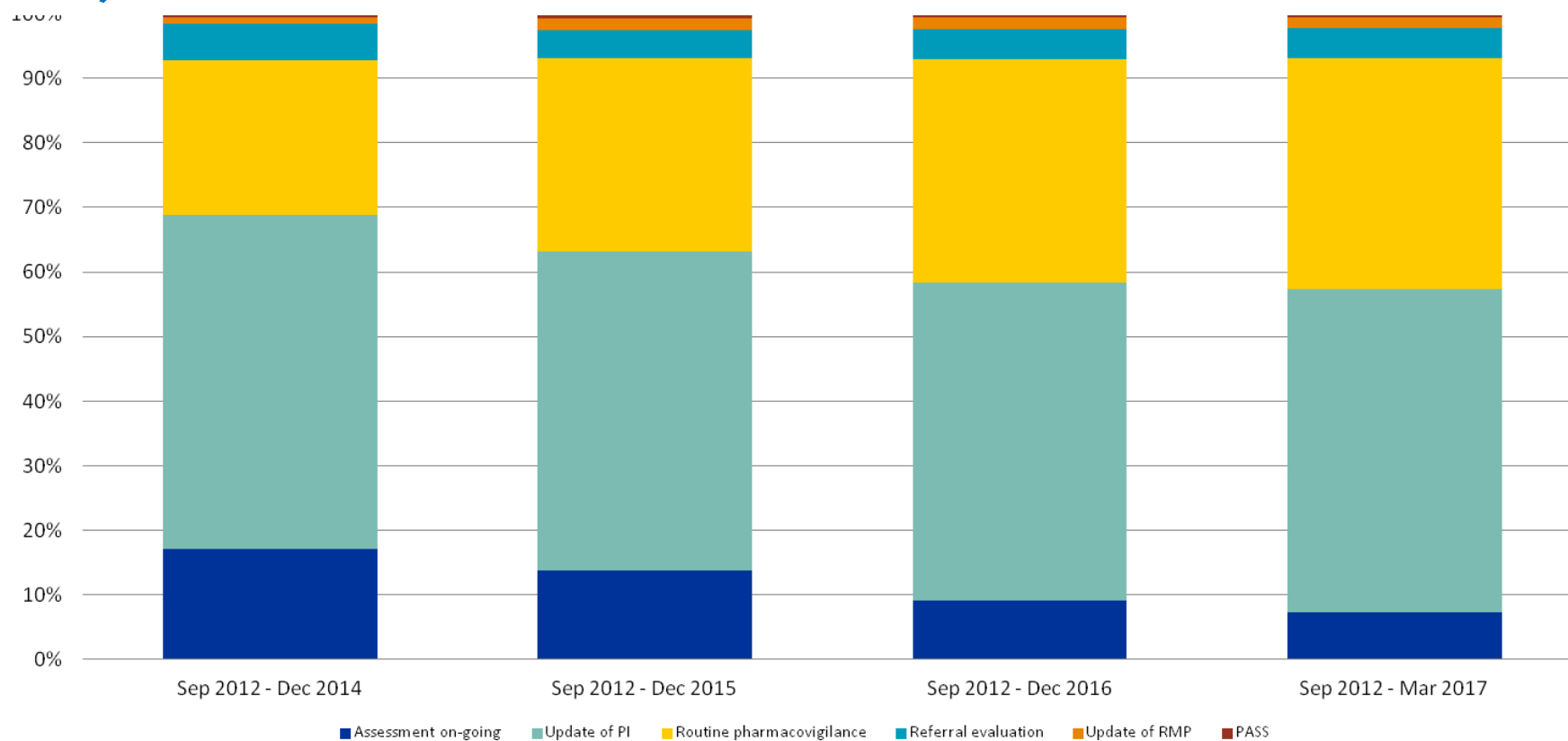
**Nov 2017**



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# Overview of signal outcomes (Sept 2012 – March 2017)



# Signals - Proactive & planned PhV

- PRAC focus on signal detection
- SMART (Signal Management Review Team) – tools, processes, methods

- 2017 priority? Avoid duplication, ensure efficiency

Apply evidence-based new methodologies for SD

Improve processes based on experience

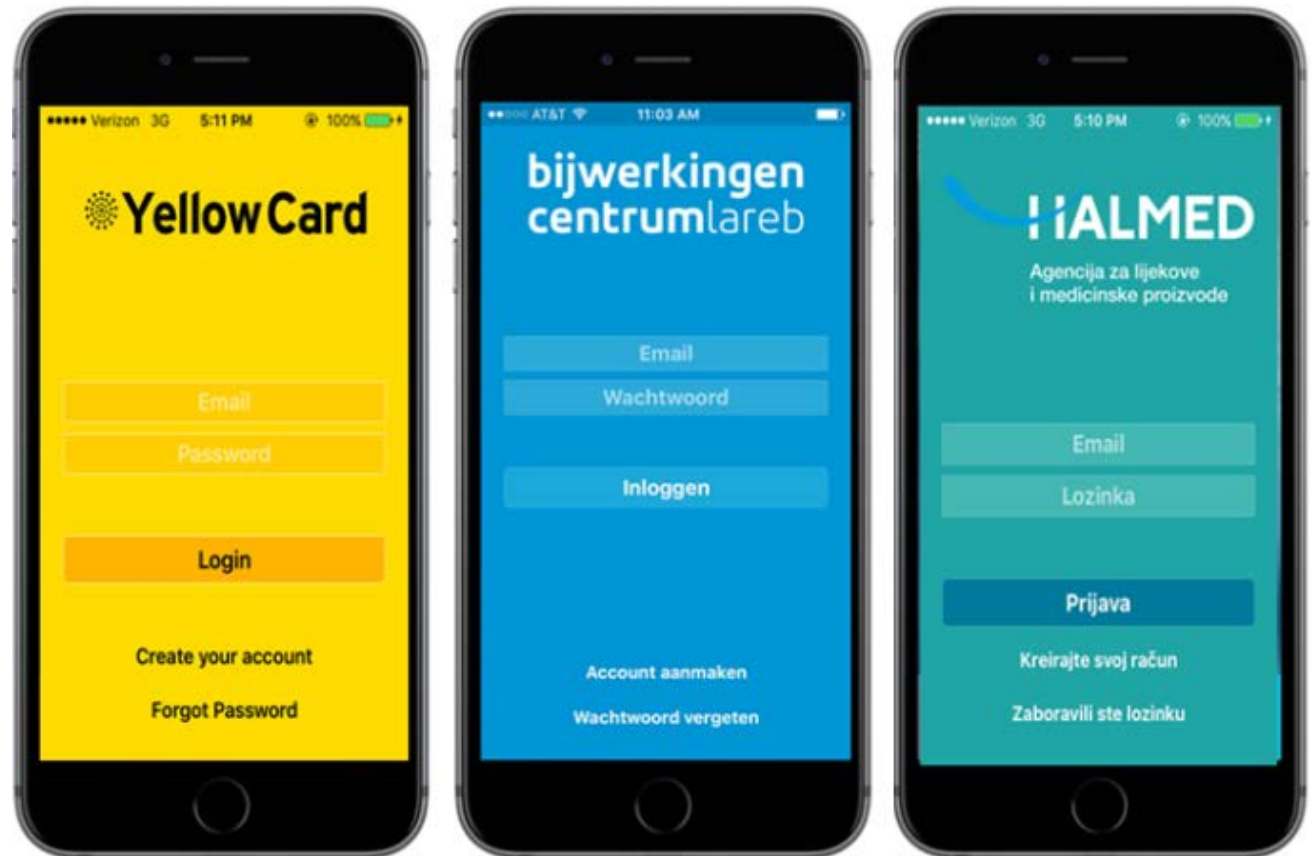
Handling of MAHs' signals after the go-live of the new EudraVigilance system

Engagement, dialogue, training - EMA Industry Platform meeting on June 2<sup>nd</sup>



# Innovative Medicines Initiative IMI-WEB-RADR project

Mobile technologies and social media as new tools in PhV



UK (Yellow Card) – launched 14 July 2015  
Netherlands (LAREB) – launched 29 January 2016  
Croatia (HALMED) – launched 18 May 2016



## 2. Lifecycle approach to PhV and risk management



Optimal PRAC input on risk management planning (robust, feasible and risk proportionate) incl high value, high uncertainty products

- Support innovation and the fulfilment of unmet medical needs of patients (accelerated assessment and PRIME scheme)


Contribute to the collection and utilisation of real-world data in PRAC procedures or via scientific advice, important in supporting assessment and decision-making on how medicines are used, their effectiveness and their safety

- Contribute to task force on EMA patient registries
- Improve PRAC-SAWP interaction in SA process for PASS and others



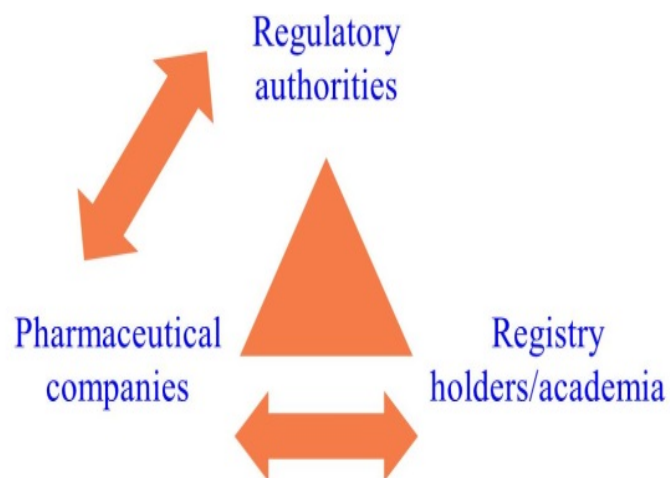
# Patient Registry Initiative - Background

- Launched in September 2015
- Explore ways of expanding the use of patient registries by introducing and supporting a more systematic and standardised approach to their contribution to the benefit-risk evaluation of medicines within the EEA
- Stakeholder feedback encourages an active role of EU network in supporting collaboration on the establishment and maintenance of disease registries
- 28th October 2016 - Patient Registries workshop

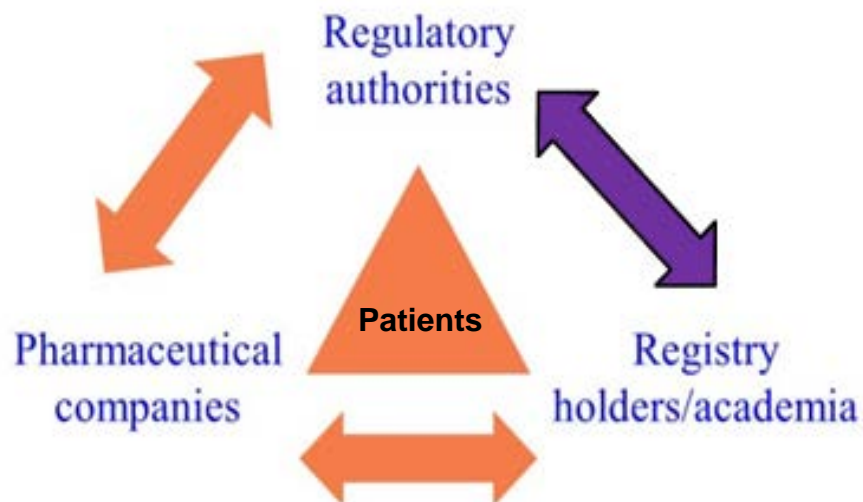
 <b>EUROPEAN MEDICINES AGENCY</b> SCIENCE • MEDICINES • HEALTH	
13 February 2017	
DRAFT/EDLY	
Regulatory, Human Medicines, Pharmaceuticals and Consumer Division	
<b>Patient Registries Workshop, 28 October 2016</b> Observations and recommendations arising from the workshop	
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# Interactions - regulators and registry holders

Present... 'the broken triangle'



Future... MORE COOPERATION



# PRAC role - Patient Registry Initiative

Contribute to develop:

- guidance for stakeholders on common methodological aspects and governance of patient registries
- core data set common to all registries
- disease-specific core data sets



**Cystic Fibrosis Workshop: 14<sup>th</sup> June**

**Multiple-Sclerosis Workshop: 7<sup>th</sup> July**



### 3. Process improvements and simplification



- GVP module V on RMPs
- PSURs – continue implementation of PSUR Road Map including revision of GVP mod VII – Joint PRAC/CMDh initiative
- Continuous support from PRAC efficiency group (review of quarterly workload and performance measures)
- SCOPE Joint Action – advise on implementation and maintenance of SCOPE output, training, sustainability



# Process improvement, tools to enhance consistency of PSUSA assessment

Optimising safety information for medicines in Europe throughout product lifecycle

Email Print Help Share

News

06/04/2017

**Optimising safety information for medicines in Europe throughout product lifecycle**

**New guidance and process improvement for periodic safety update reports**

Following two years of experience with safety monitoring of nationally authorised medicines via the single assessment of periodic safety update reports (PSURs), the European Medicines Agency (EMA) has issued additional guidance and recommendations as part of its commitment to continuous process improvement.

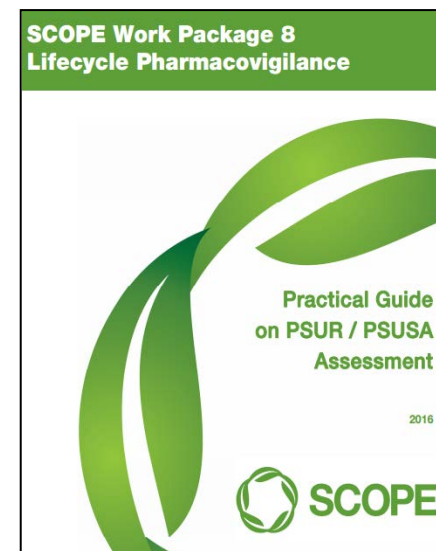
PSURs are reports that evaluate the benefit-risk balance of a medicine as evidence is gathered in clinical use. They are submitted by marketing authorisation holders at defined time points following a medicine's authorisation. The Agency uses the information in PSURs to determine if there are new risks linked to a medicine or if the

**Related content**

- ▶ Periodic safety update reports
- ▶ Good pharmacovigilance practices (GVP)

**Related documents**

- 📄 Guideline on good pharmacovigilance practices (GVP): Module VII – Periodic safety update report - Explanatory note (06/04/2017)
- 📄 Questions and answers on PSUSA: Guidance document for assessors (06/04/2017)



## Next steps:

Joint assessors' & industry training  
Revision of GVP Module VII

[About](#)[Outputs & Results](#)[Work Packages](#)

# SCOPE Joint Action

The Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action was aimed to help medicine regulators operate pharmacovigilance systems to the EU legislative requirements. Regulators have worked together to improve the skills and capability in the pharmacovigilance network to help safeguard public health in both national territories and the EU as a whole.

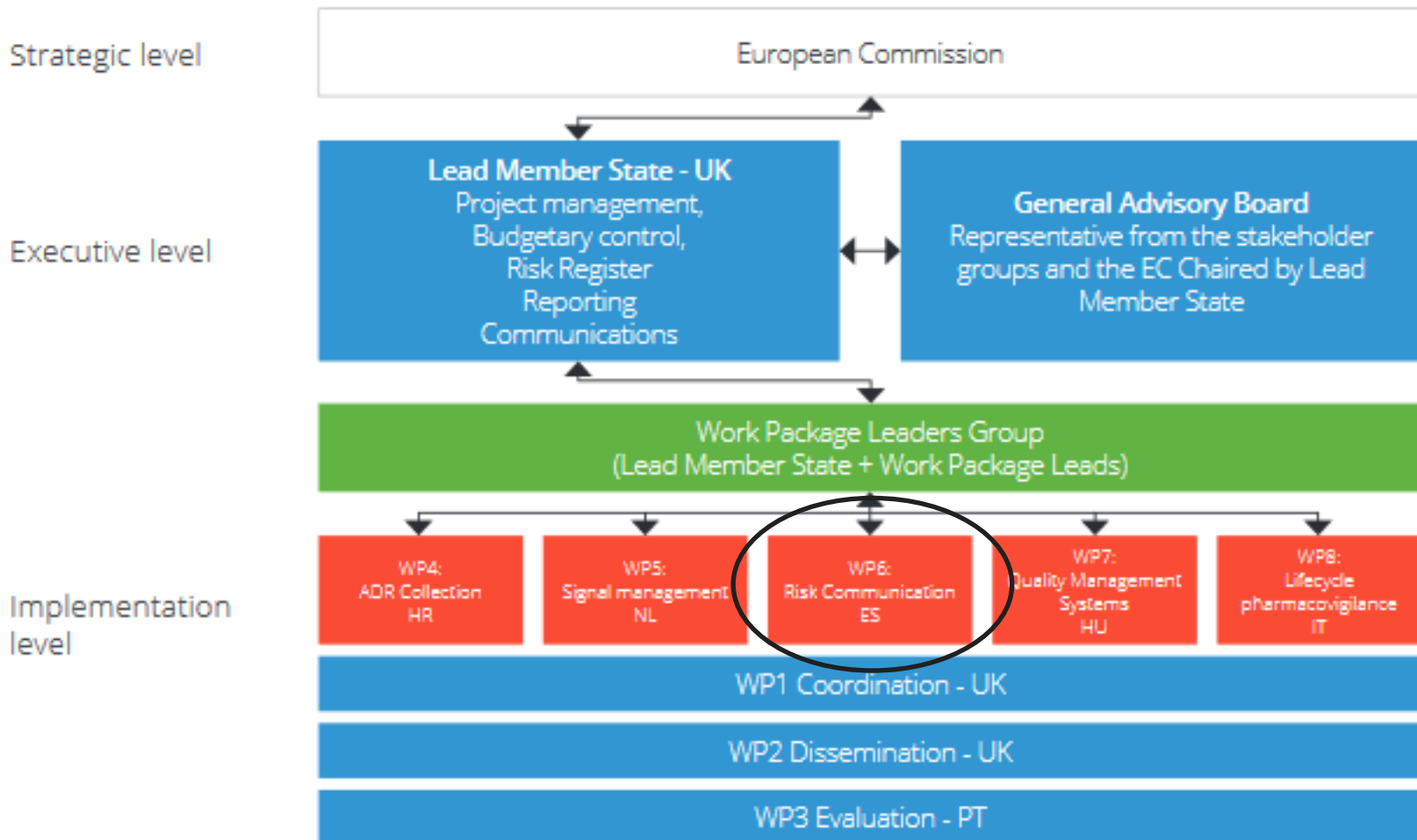


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<http://www.scopejointaction.eu/>

# SCOPE Management Structure



# Main deliverables



Practical guides



Recommendations



Training courses



Workshops



Reports



E-learning modules



EU exchange programmes for assessors



## 4. Special Populations and Product Guidance



- Develop GVP P.IV – Medicines use in older populations for release for public consultation
- Develop GVP P.III – ‘Product- or population-specific considerations: pregnancy’ for release for public consultation
- Finalise GVP special population on conduct of pharmacovigilance for medicines used by the paediatric population (PDCO lead)
- Support joint PDCO/PRAC Working Group – Joint meeting
- Finalise revision of Guideline on safety and efficacy follow up – risk management of advanced therapy medicinal products for release for public consultation (CAT lead)
- Joint work with CHMP/CMDh on PhV requirements for biosimilars



## 5. Partners and stakeholders



Operate tool of public hearings in the context of safety referrals

Increase transparency

Empower EU citizens

Improve the public's understanding

Add value

First public hearing will  
be held later in 2017

## 6. Inspections and Compliance



Strengthening links between assessors and inspectors

Advise on procedures of non-compliance

Support training on pharmacovigilance inspection

Inspectors to work on revision of PSMF – and involvement of PRAC



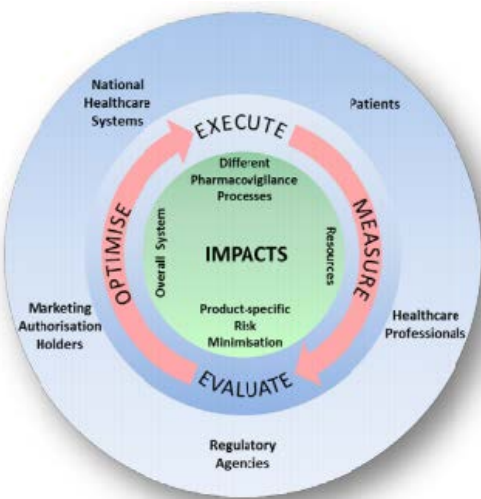
# 7. Measuring the Impact of Pharmacovigilance Activities



Pharmacovigilance legislation provides the basis for collaboration between EMA and EU NCAs to continuously develop PhV systems capable of achieving high standards of public health protection for all MPs, and **monitor the outcomes of RMMs** [Article 107h DIR 2001/83/EC].

EU Regulatory Network and stakeholders - role in collecting data and information on regulatory measures

- to ensure they are effective and efficient [Article 28a REG (EC) 726/2004]
- to continuously drive process improvement [Article 28e REG (EC) 726/2004]



# PRAC Strategy for measuring PhV impact

## Four key areas

- Effectiveness of PhV processes (e.g. ADR reporting, signal detection & management, PAS)
- Effectiveness of product-specific risk minimisation (e.g. measures following major referrals)
- Stakeholder engagement
- Collaboration on methodologies



# 2017 Key objectives and activities

- Apply prioritisation criteria for studies on impact to key public health decisions (referrals and signals)
- Contribute to methods of measuring impact of pharmacovigilance liaising with ENCePP Special Interest Group
- Review overall strategy in light of the recommendations of Impact workshop





## 8. Cross Committee Collaboration



Press release

28/04/2017

**EMA and heads of national competent authorities discuss consequences of Brexit**

Based on the general principles, EMA, its scientific committees and working parties, together with the NCAs, will now assess the different options for workload distribution.

Establish task force (CAT/CHMP/SAWP/PRAC/EMA & Heads of Agencies)

Design and analyse distribution scenarios

Agendas and minutes

Press Releases

**BREXIT**



- Notice to marketing authorisation holders of national authorised medicinal products for human use (May 2017)



## 8. International collaborations



Sharing PhV assessments supports international collaborations in best interests of global public health

PRAC ARs available under Art 58, confidentiality agreements and/or on request

PRAC advice - clarification on reporting of ADRs for donated medicines



27 April 2015  
EMA/102873/2015  
Inspections and Human Medicines Pharmacovigilance Division

Reporting requirements of marketing authorisation holders in the EU regarding suspected adverse reactions occurring with medicinal products they donate outside the EU to public health programmes against neglected tropical diseases

# Article 58 medicines for use outside EU

## Article 58 procedure

### What is Article 58?

- > EMA assessment of quality, safety and efficacy of a medicine or vaccine intended for use only outside the EU;
- > Evaluation carried out in collaboration with WHO and relevant non-EU regulatory authorities;
- > Licensing decision taken by non-EU regulators in countries where the medicine or vaccine will be used;
- > Same standards and procedures as for medicines marketed in the EU.

### Outcomes 2005–2016

Umbipro: umbilical cord infection treatment;  
Mosquirix: malaria vaccine;  
Pyramax: malaria treatment;  
Hemoprostol: post-partum haemorrhage treatment;  
Alluvia, Lamivudine ViiV, Lamivudine/ Zidovudine ViiV: HIV treatments;  
Hexaxim, Tritanrix HB: combination vaccines against childhood diseases.

### Which medicines are eligible?

Vaccines or medicines used to prevent or treat public health priority diseases:

- > Vaccines used in the WHO Expanded Programme on Immunization;
- > Medicines for protection against diseases, such as HIV/AIDS, malaria and tuberculosis;
- > Medicines for maternal and newborn healthcare.

### What is the process?

- Company requests eligibility for Article 58
- Company submits application for scientific review to EMA
- Scientific assessment carried out in collaboration with WHO and non-EU regulators

EMA adopts scientific opinion

### After the opinion

- > WHO may include the medicine or vaccine in public health recommendations;
- > Companies can use EMA's opinion to support marketing authorisation applications to regulators in non-EU countries;
- > Companies are required to implement risk management plans and follow-up measures;
- > EMA can perform a benefit-risk review at any time if new safety information becomes available.

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Organization



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# What contexts for sharing PhV assessments?



Regular bilateral  
pharmacovigilance  
teleconferences



Bilateral confidentiality  
agreements with FDA, Health  
Canada & Japan PMDA



Health  
Canada



## Provision of ADR data to WHO UMC

- Article 28c(1), 2<sup>nd</sup> paragraph of Regulation (EC) No 726/2004 as amended in 2010 states that:
- *"The Agency shall make available promptly all suspected adverse reaction reports occurring in the Union to the World Health Organization".*



- Starts after centralisation of industry reporting – later in 2017



# Conclusions

Commitment to sustained pursuit of rigorous science, risk proportionate decision making and relevance to public health

Stand ready to support a collaborative cross Agency, cross Committee response to guarantee continuity of public health protection for EU citizens

PRAC Groups being established to feed into cross functional Taskforce





Thank  
you

#### CONTATTI

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