



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

New pharmacovigilance legislation to promote and protect public health

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An agency of the European Union





In this talk:

- Background
- Objectives
- Key measures
- Impact and risks
- EU Decision-making
- Conclusions



Background – Need To Further Strengthen Pharmacovigilance

- 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



Background

- Opportunities identified to strengthen and rationalise EU PhV to better protect public health
- Excellent public health protection and promotion requires:
 - Science
 - Law
 - Resources



Background - Making of New Legislation

- 2003: EC decision to undertake an assessment of the Community system of pharmacovigilance
- 2005 independent study results show weaknessness
- 2006 major public consultation on how to strengthen pharmacacovigilance
- 2007 Commission strategy to strengthen and rationalise pharmacovigilance:
 - Improved implementation e.g. 7th Framework Programme funding
 - Intention to strengthen legislation



Background - Making of New Legislation

- Dec 2008 – Commission makes legal proposals to the Council of Ministers and European Parliament
- Agreement on new legislation Autumn 2010
- Both **Regulation (EC) 1235/2010** and **Directive 2010/84/EC** published on 31 December 2010
- July 2012: new legislation will apply
- Some transitional provisions:
 - ADR reporting to EMA only,
 - PSUR reporting to EMA only,
 - Pharmacovigilance System Master File



Background

Much good work ongoing prior to the new legislation

e.g:

- IMI Protect – regulatory science
- EudraVigilance – key resource
- ENCePP – research capacity building
- PSUR worksharing



IMI-PROTECT EU Goal

To strengthen the monitoring of benefit-risk of medicines in Europe by developing innovative methods

to enhance early detection and assessment of adverse drug reactions from different data sources (clinical trials, spontaneous reporting and observational studies)

to enable the integration and presentation of data on benefits and risks

These methods will be tested in real-life situations.

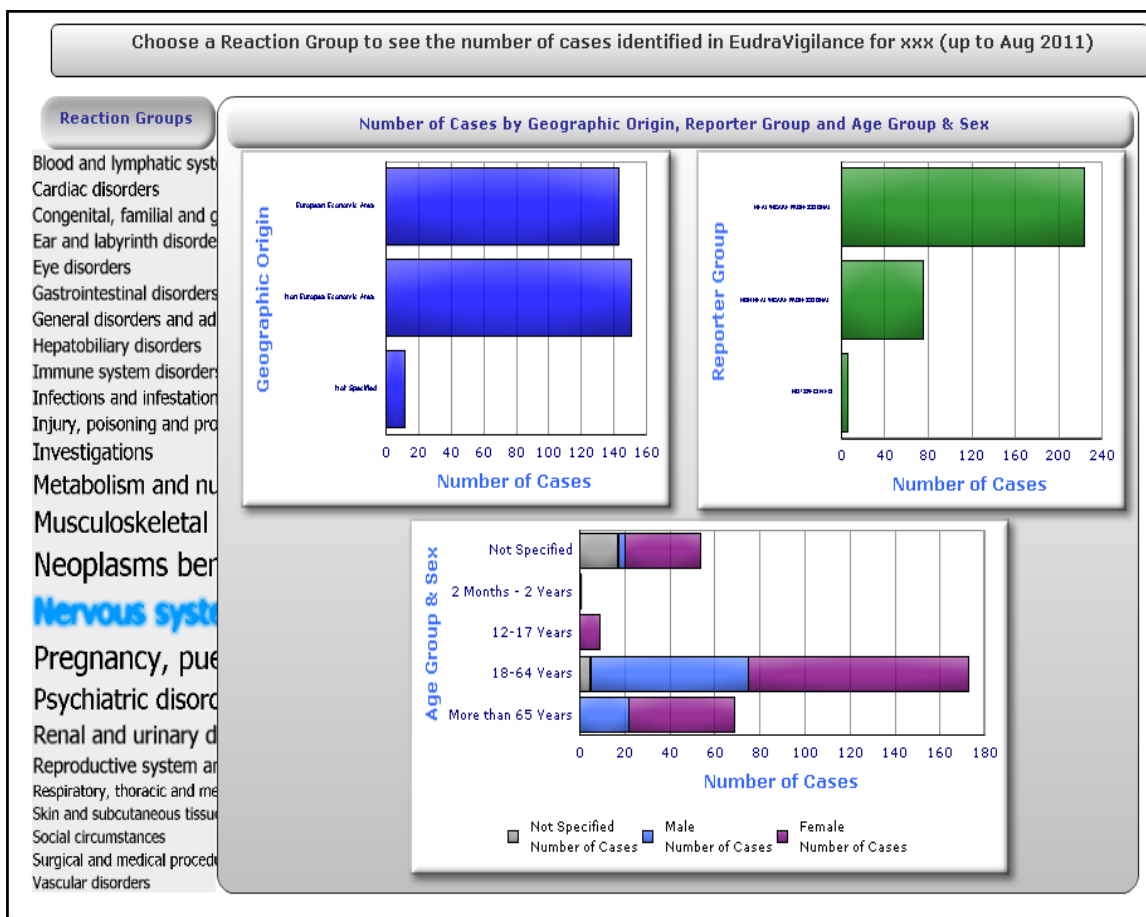


EudraVigilance – Current Status

- EudraVigilance Data-Processing Network
 - Facilitates secure electronic reporting of Individual Case Safety Reports (ICSRs) between the EU Regulatory Network, the Agency, MAHs and Sponsors
 - 4.300 organisations (NCAs, MAHs, Sponsors) registered
 - 8.114 users registered
 - 11.5 million transactions during 2010
 - An average of 62.500 ICSRs are reported on a monthly basis to EudraVigilance
 - Total ICSRs now amounts to 4.1 million ICSRs



EudraVigilance Access Policy Implementation



Dashboard - Example 3

View for a selected Reaction Group

The user can select the Reaction Group to see the number of cases by:

- Geographic Origin
- Reporter Group (HCP/Non HCP)
- Age Group & Sex



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New legislation



Why? High Level Objectives

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

- Clear roles and responsibilities / robust and rapid EU decision-making
- Engage patients and healthcare professionals (involve + empower)
- Science based
- Integrate benefit and risk
- Risk based/proportionate
- Increased proactivity/planning
- Reduced duplication/redundancy - Strengthen the EU Network
- Increase transparency and provide better information on medicines



What? - Scope of Changes

- Coordination / lists of medicines
- Authorisation requirements
- Risk Management Plans
- Post-Authorisation Studies (Safety and Efficacy)
- Effectiveness of risk minimisation
- Adverse Drug Reactions reporting
- Signal detection
- Periodic Safety Update Reports
- Scientific Committees / decision-making
- Transparency and communication
- Coordination of inspections
- Pharmacovigilance Audits
- Fees charged and payments for assessments / services



Impact

Biggest change to the legal framework for human medicines since 1995



Implementation – key risks

- For EMA: the lack of **human and financial** resources is the biggest risk to the implementation and operation of the new legislation → Scenario planning and prioritisation exercise ongoing
- Commission bridging budget 2012? **Critical for success**
- Commission proposal in 2012 for a fee regulation revision (effective 2014?) **Critical for success**
- For all Stakeholders: lack of involvement (i.e. information, consultation) in the implementation
- For all Stakeholders: manage expectations



Focus on EU decision-making



PRAC membership

Appointed by each Member State:



- 1 member + alternate
- 27 + EEA countries non voting members

Appointed by EC following a public call for expressions of interest:



- 1 patient organisations¹ rep + alternate
- 1 healthcare professionals¹ rep + alternate
- 6 members to ensure relevant expertise available

¹ *Criteria for involvement in EMA activities*

Public call for expressions of interest released (deadline 1st Dec)



PRAC membership – key points

- **Members appointed** for 3-year term, which may be prolonged once and thereafter renewed
- **Delegation** 'A Member State may delegate its tasks in the Pharmacovigilance Risk Assessment Committee to another Member State. Each Member State may represent no more than one other Member State.'



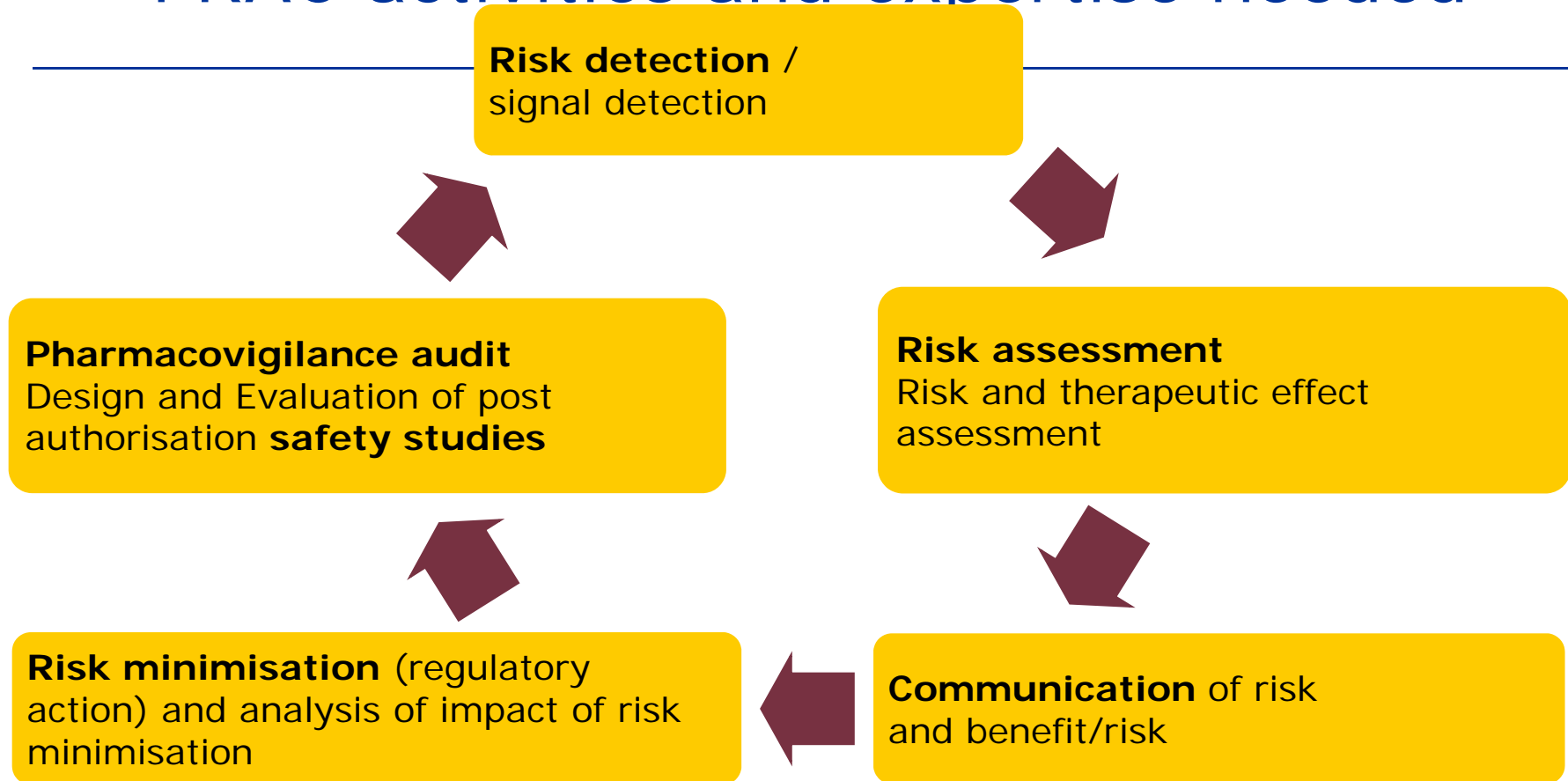
New Pharmacovigilance Risk Assessment Committee PRAC

REGULATION (EU) No 1235/2010 the Mandate shall cover...

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 activities and expertise needed





Identified PRAC Activities (1/2)

Activity	Involvement
Risk Management Systems	Agreement on RMPs + monitoring their effectiveness
Periodic Safety Update Reports PSURs	List of harmonised submission frequencies and substances, assessment + recommendation
Eudravigilance + Periodic Safety Update Reports repository	Functional specifications, any substantial changes
Medicines subject to additional monitoring	Addition to/removal from list, extension of timeframe, symbol
Signal Detection	Initial analysis + prioritisation assessment + recommendations

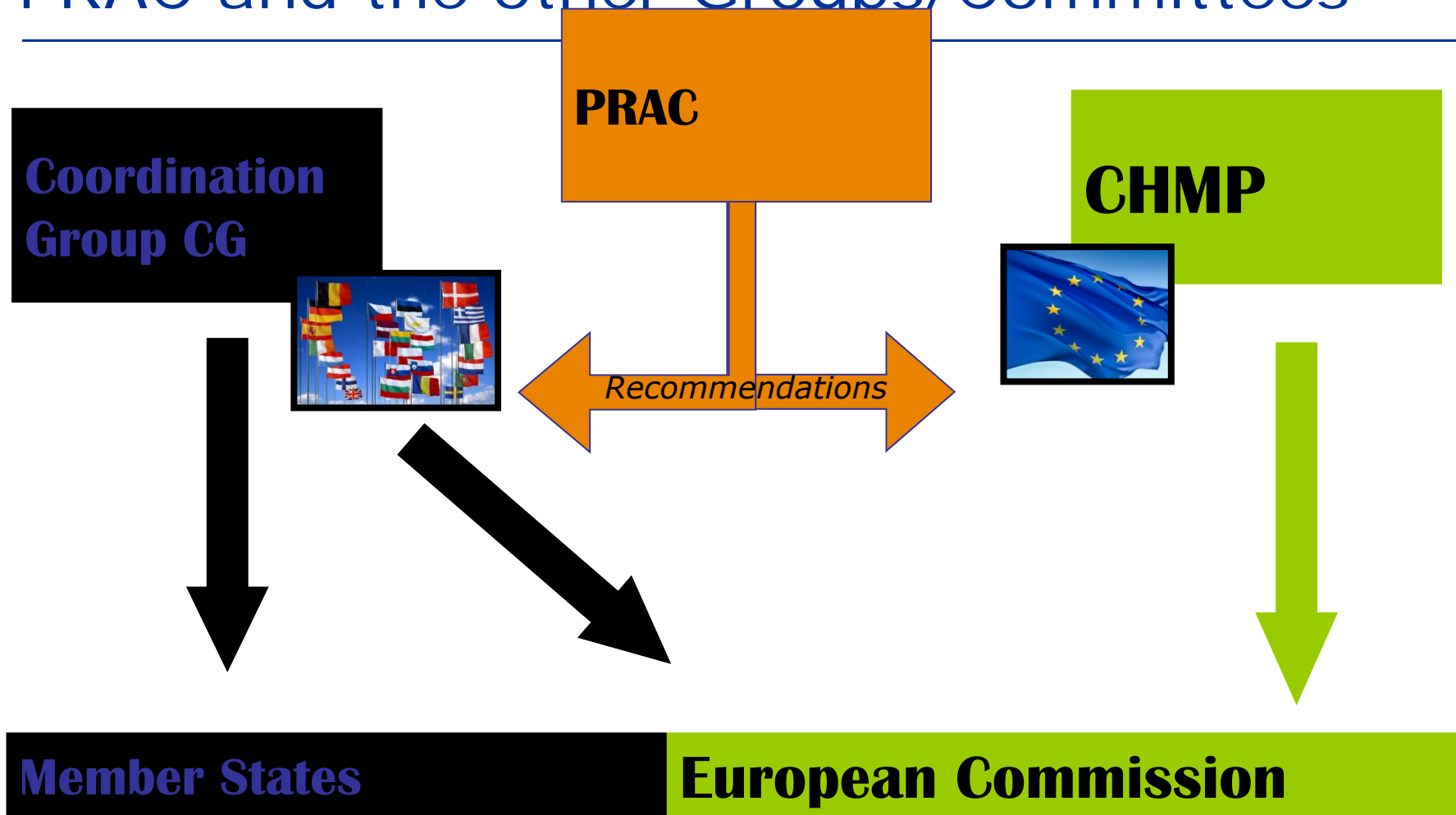


Identified PRAC Activities (2/2)

Activity	Involvement
Urgent Safety Procedures for the EU	Assessment, public hearings, recommendations
Post Authorisation Safety Studies	Consultations on requests (pre and post MA), assessment of protocols (incl. amendments) + recommendations, assessment of results + recommendations
Literature Adverse Drug Reactions monitoring	Consultation on list of active substances and medical literature subject to monitoring?
Safety announcements	Advice



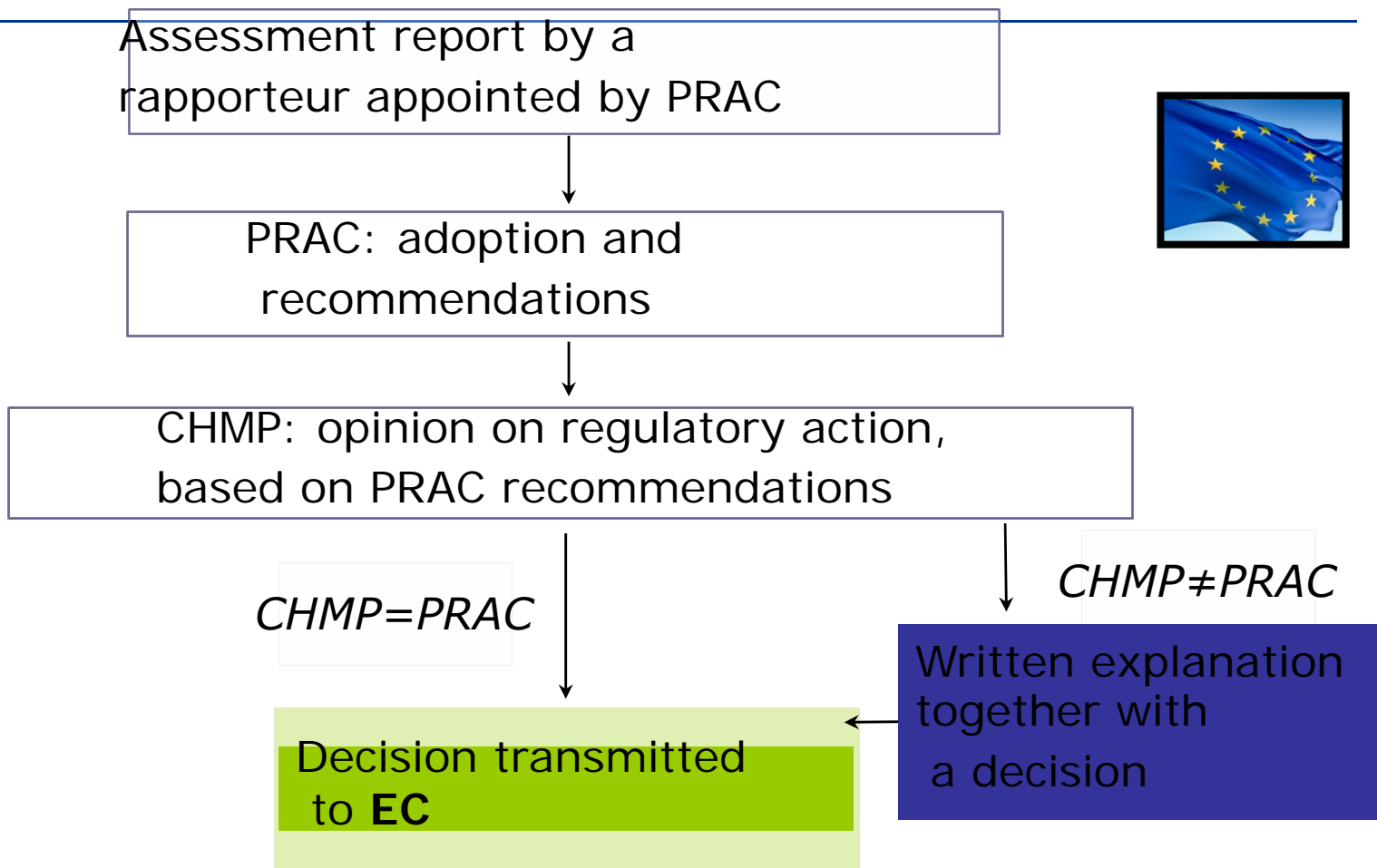
PRAC and the other Groups/Committees





Role of PRAC in decision-making process

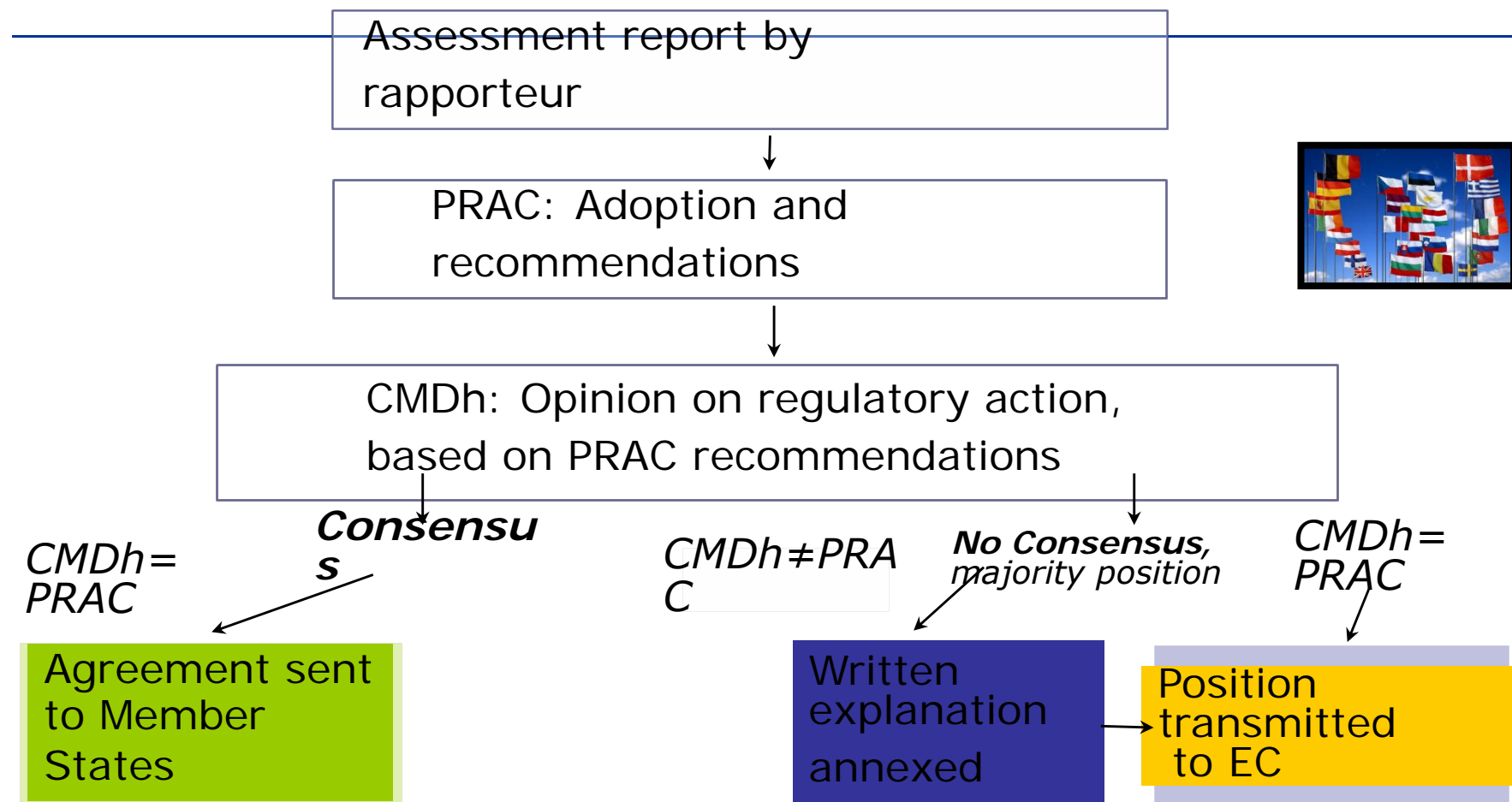
When at least one centrally authorised medicine is involved





Role of PRAC in decision-making process

Only nationally authorised medicine are involved





PRAC and Transparency



**Agenda &
Minutes**

Assessments

Decisions

**Opinions
Agreements
Positions**

Recommendations

Available
to the public



Article 57(2), second subparagraph of Regulation (EC) No. 1235/2010 – Legal requirements

Article 57(2), second subparagraph of Regulation (EC) No. 1235/2010 requires:

- **The Agency** to publish the format for the electronic submission of information on medicinal products for human use by 2 July 2011
- **The marketing-authorisation holders** to submit information to the Agency electronically on all medicinal products for human use authorised or registered in the European Union by 2 July 2012, using this format
- **The marketing-authorisation holders** to inform the Agency of any new or varied marketing authorisations granted in the EU as of 2 July 2012, using this format



Article 57(2), second subparagraph of Regulation (EC) No. 726/2004 – Benefits

This information will help the Agency to:

- Create a list of all medicines authorised and registered in the EU, including medicines authorised centrally via the Agency and medicines authorised by regulatory authorities in EU Member States

This information will help the Agency and Stakeholders to:

- Identify medicines (including biologics/biosimilars) accurately, especially medicines included in reports of suspected adverse reactions
- Coordinate the regulation and safety-monitoring of medicines across the EU
- Facilitate the international harmonisation activities (ICH E2B and M5)



In 2012 – watch out for:

- Coordination / lists of medicines – industry submits data
- Authorisation requirements – RMP, PSMF
- Risk Management Plans – new format
- Post-Authorisation Studies – new requirements from 2012
- Effectiveness of risk minimisation – new guidance
- Adverse Drug Reactions reporting – non-serious to some MSs, EMA only for some MS
- Signal detection - – new guidance and processes
- Periodic Safety Update Reports – new format and content
- Scientific Committees / decision-making – From July 2012
- Transparency and communication – agendas and minutes and recommendations



P.S. - Making of New Legislation

- But..... now Commission has made new proposals for further (more minor changes) as part of the information to patients legal proposals currently discussed at Council and European Parliament.
Scope:
 - Compulsory EU referrals (much less discretion for Member States)
 - Compulsory notification of product withdrawals (and reasons) – may then trigger referrals
 - Minor changes to the 'additional monitoring' rules

MSs have agreed to prioritise these pharmacovigilance proposals



Conclusions

- **Excellent pharmacovigilance requires:**
 - Science
 - Law
 - Resources
- **New law: prioritisation /planning critical + collaboration,**
For better health protection and promotion