EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Functioning of the PRAC

Sixth Stakeholders forum on the implementation of the new Pharmacovigilance legislation, November 8th 2012

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Vice Chair, Pharmacovigilance Risk Assessment Committee

Presentation Outline

- What the legislation sets out to achieve
- Legal provisions on Committees and Decision-making
- Putting the provisions into operation - establishment of the PRAC.
- First experiences of the Committee and application of the legal tools.

What the legislation sets out to achieve?

Current EU system recognised as one of the most robust in the world. However, improvements needed to ensure:

- Clarity on roles and responsibilities
- Better planning of safety monitoring
- Robust and timely decision making to take action on safety issues at EU level for nationally and centralised authorised products.
- Greater inclusion of patients and healthcare professionals.
- Duplication of effort is avoided.
- High levels of transparency

To achieve these goals

Committees and decision-making are central.

PRAC membership

Appointed by each Member State:

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

Appointed by the European Commission (public call for expressions of interest):

- 1 patient organisations[1] rep + alternate
- 1 healthcare professionals[1] rep + alternate
- 6 members to ensure relevant expertise available

[1] *Criteria for involvement in EMA activities*

Public call for expressions of interest released

Involvement of EMA Committees in drug development

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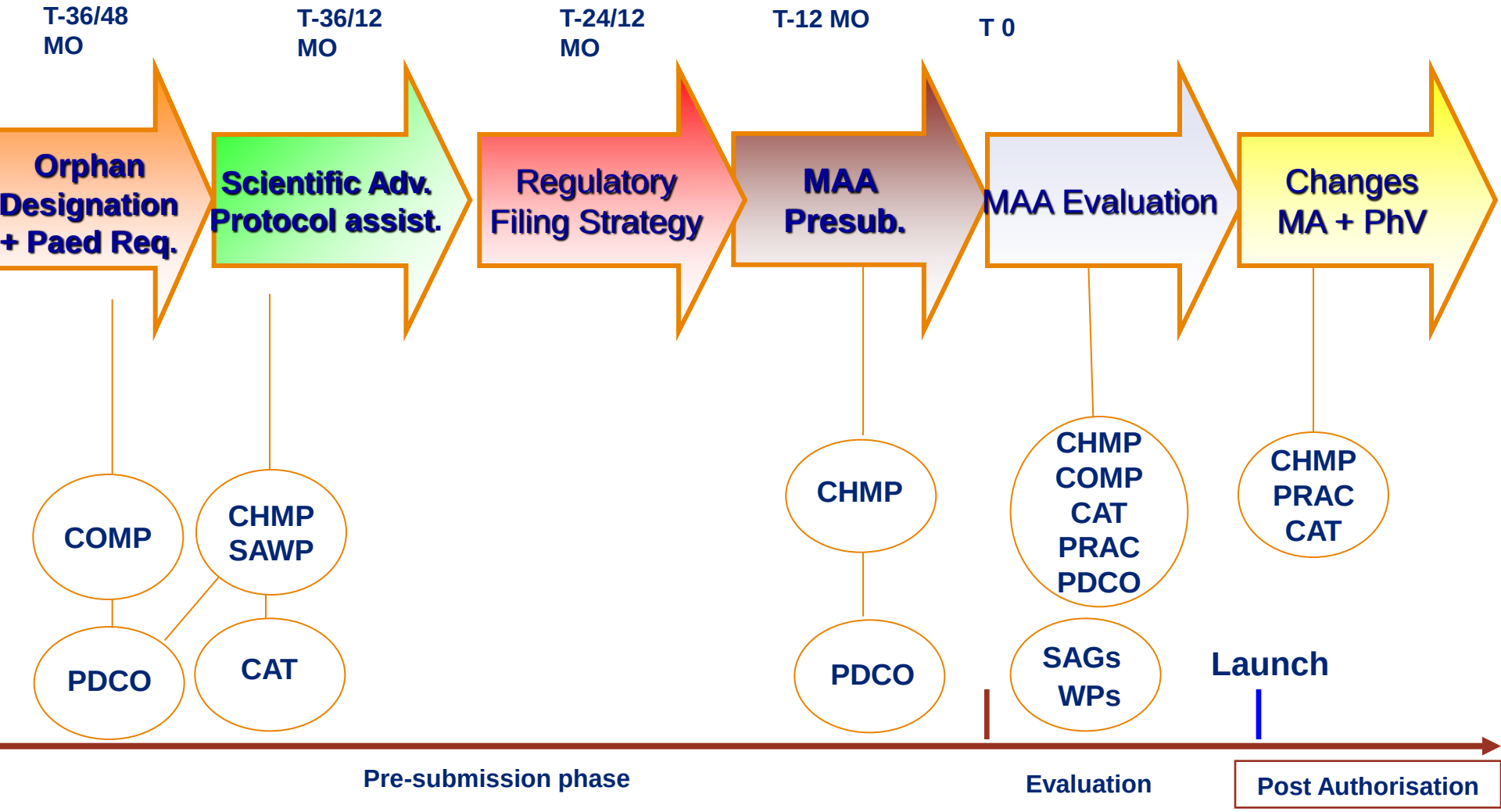


New Pharmacovigilance Risk Assessment Committee PRAC

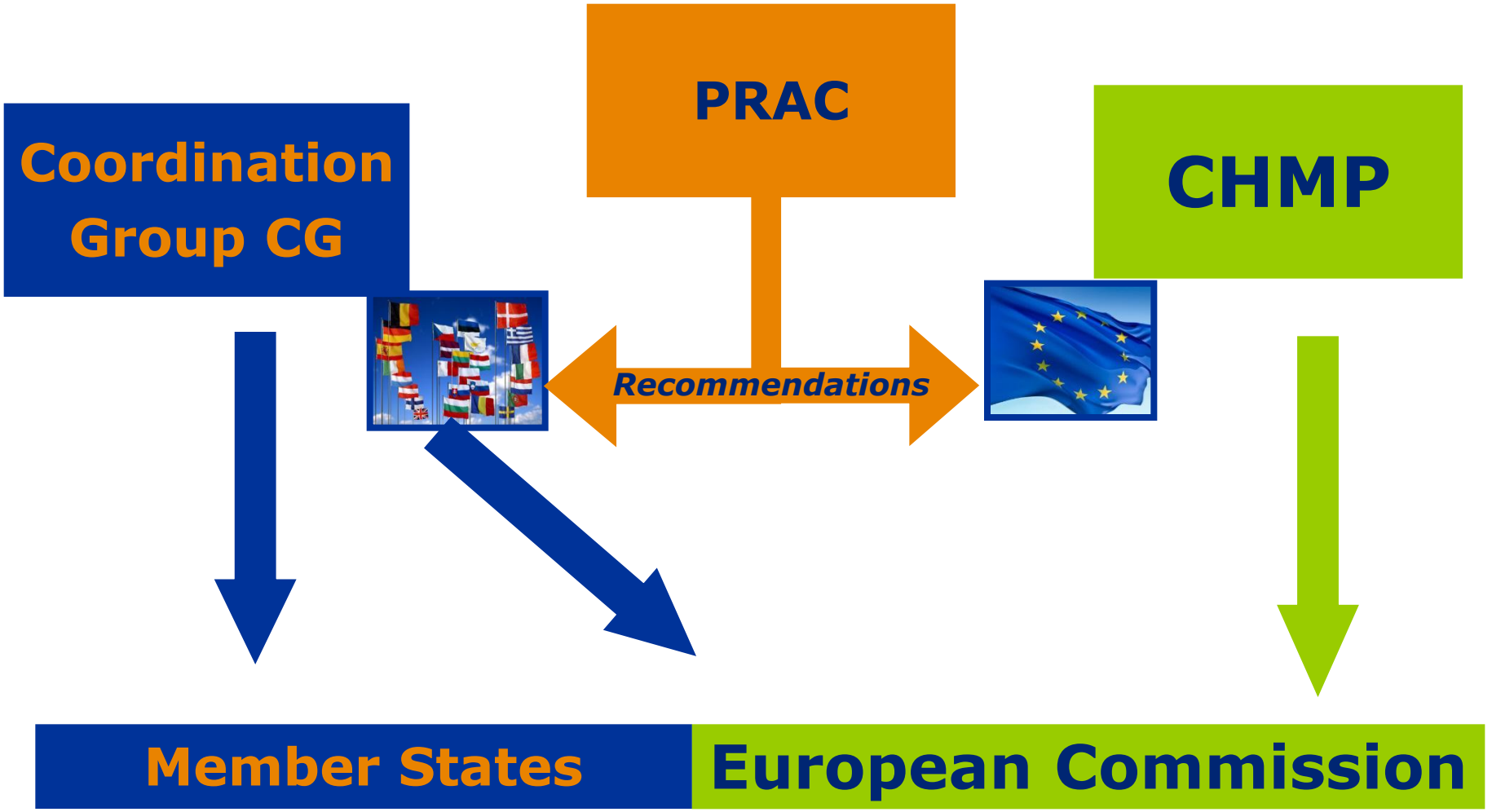
REGULATION (EU) No 1235/2010 the Mandate shall cover…

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

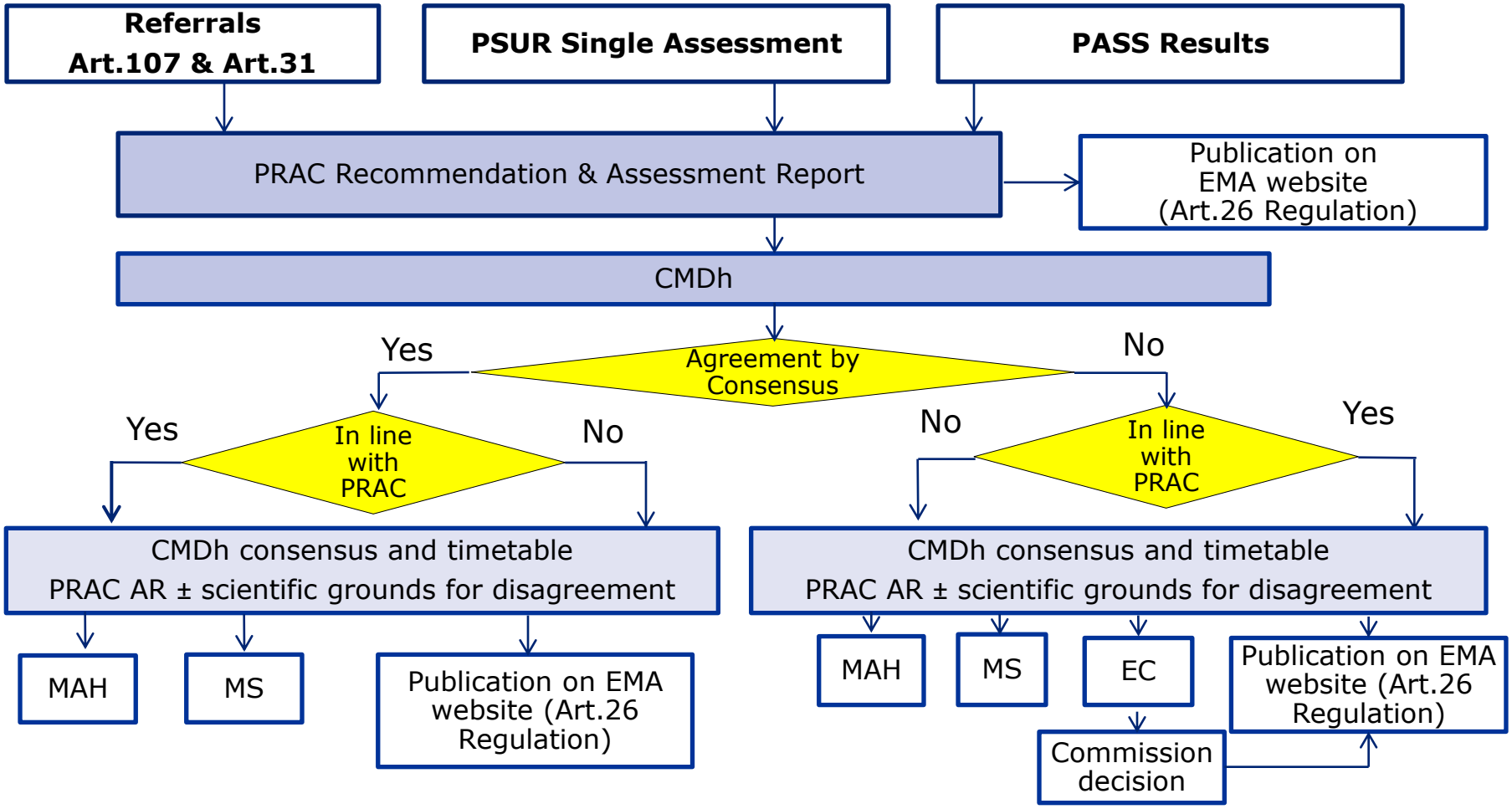
Establishment of the PRAC

- Document "Countdown to July 2012: the Establishment and Functioning of the PRAC" – Status Report 28 June 2012, was published on EMA website
- Document summarises the outcome of the discussions within the EU Regulatory Network on topics including
  - PRAC mandate and tasks
  - PRAC outputs
  - PRAC Rapporteur appointment principles
  - Transparency and communication
  - PRAC-CHMP-CMD(h) interaction

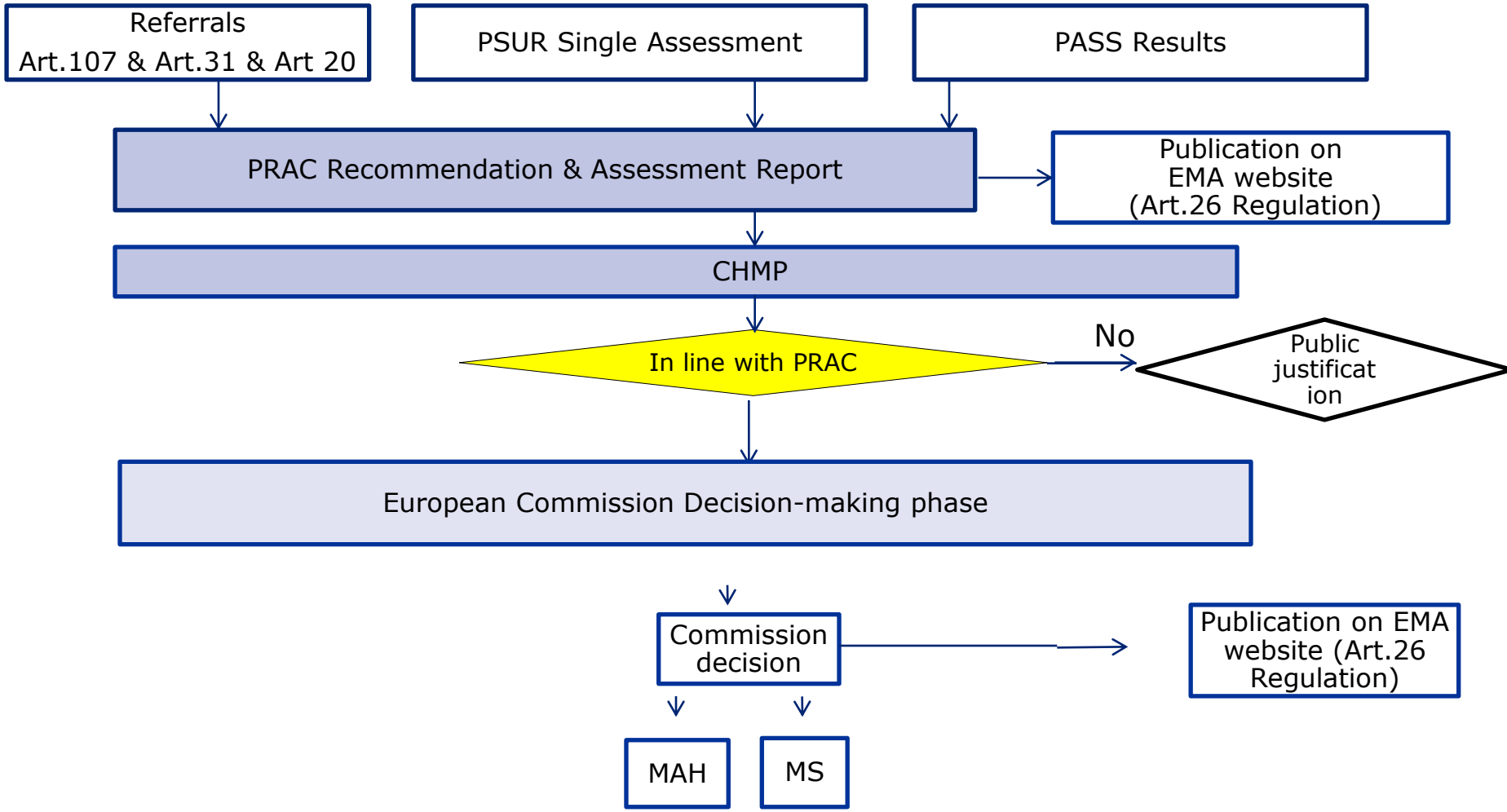
PRAC and the other Groups/Committees



PRAC Output with formal decision-making phase – NAPs only

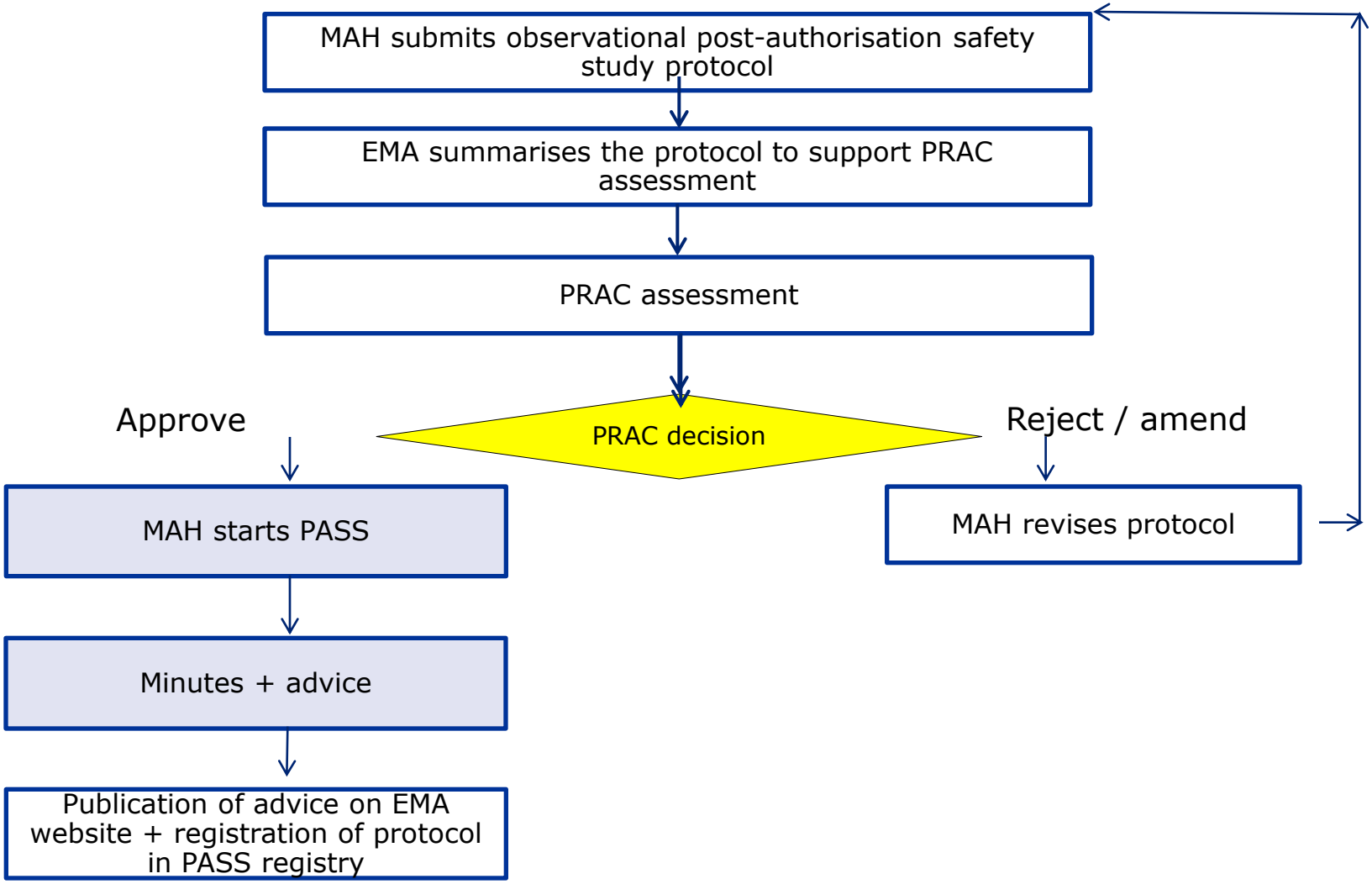


PRAC Output with formal decision-making phase –includes one or more CAP

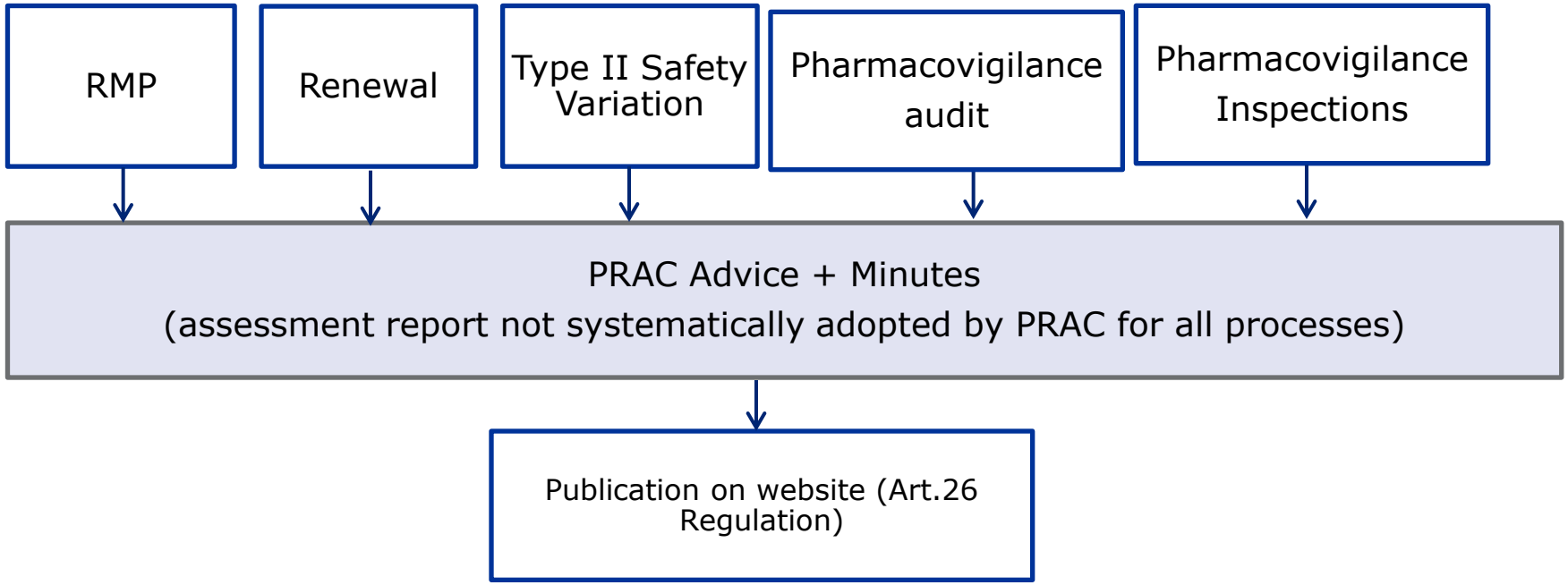


PRAC Output without formal decision-making phase:

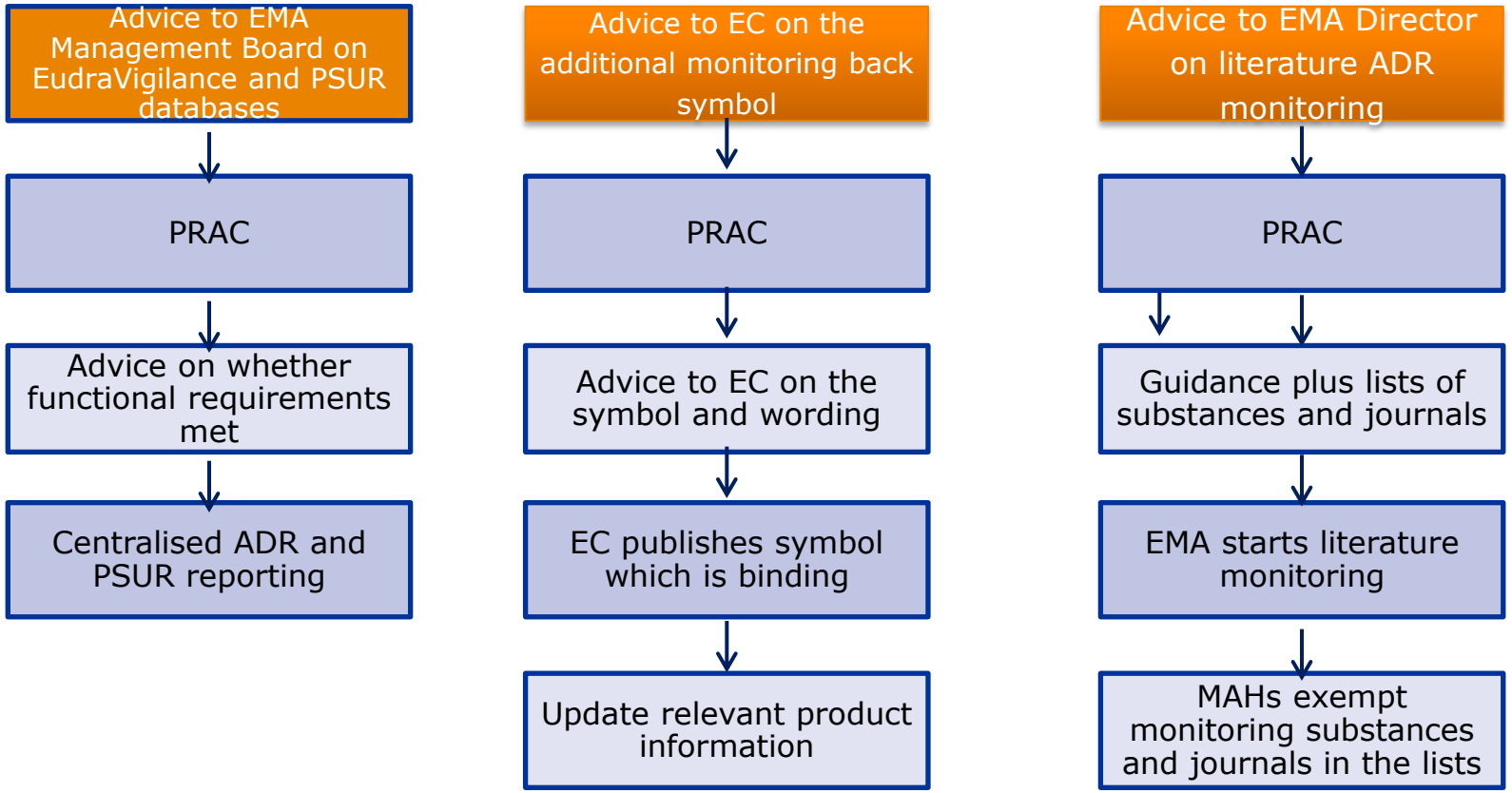
Directly applicable output (PASS protocol)



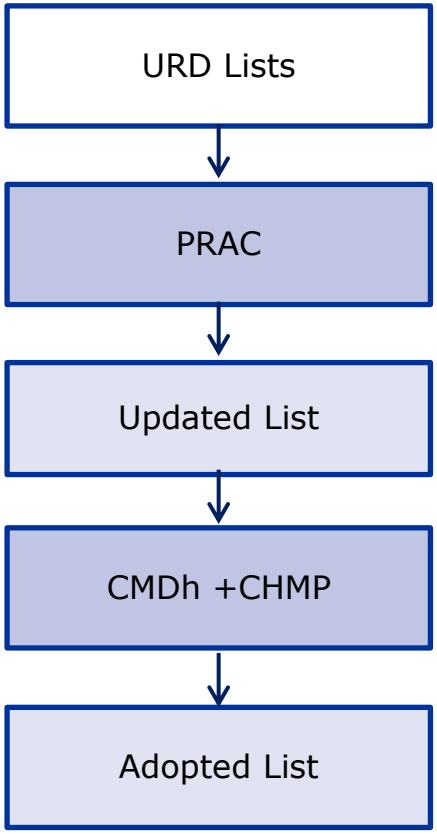
PRAC Output without formal decision-making phase: output = advice

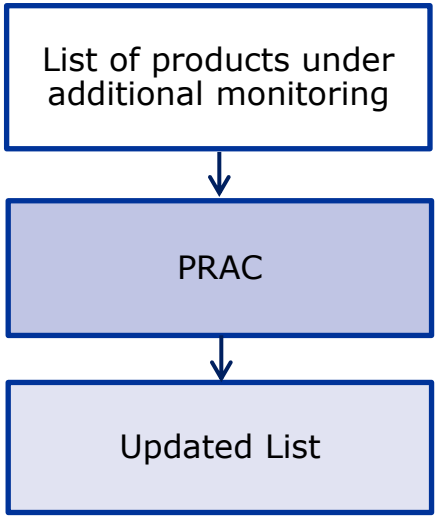


Other PRAC advice (no step through CHMP or CMDh)



Lists


URD Lists
PRAC
Updated List
CMDh +CHMP
Adopted List


List of products under additional monitoring
PRAC
Updated List

PRAC Rapporteur Appointment and Responsibilities for CAPs

- PRAC Rapporteur should be appointed from a different MS compared to the CHMP Rapporteur/Co-Rapporteur, whenever possible
- PRAC Rapporteur is the lead expert on safety/risk management for specific medicines/active substances
- PRAC Rapporteur is involved throughout the lifecycle of a product
- PRAC Rapporteur provides the lead assessment for procedures where CHMP should rely on the PRAC recommendation
- Role of CHMP Rapporteur and Co-Rapporteur will change

Collection and assessment of key information on medicines

1. Risk Management Plans:

– Establishment and operation of the new procedure since July 2012. New format compulsory from Jan 2013.

- Experience has just started – the PRAC will systematically give advice on RMPs submitted according to routine procedures pre- and post-authorisation but can also recommend updates according to discussed signals and referrals.

- PRAC focus will be on the scientific questions relevant to post authorisation benefit-risk monitoring and ensuring effective risk minimisation.

Collection and assessment of key information on medicines

2. Periodic Safety Update Reports:

– Operation of new procedures related to PSURs for CAPs started July 8 2012 –> scope is benefit-risk evaluation and legally binding outcome.

- First PSUR assessments will be on the PRAC Agenda end of November.

– Development and publication of harmonised birthdates to support PSUR submission - published 1 October 2012 and will be reviewed monthly.

Collection and assessment of key information on medicines

3. Post-Authorisation Safety and Efficacy Studies

– Implementation of the PASS procedure for protocols approval and results management for CAPs Started July 2012 – first protocol at October PRAC.

- PRAC will promote early dialogue with stakeholders to maximise best use of resources when protocols are requested.

- Joint PASS –processes are being refined but PRAC is committed to using the available legal tools to strengthen public health protection in the best interests of EU citizens.

– Consultation on PAES Commission consultation awaited

Supporting collection and understanding of information

1. Additional Monitoring

- Work ongoing to develop and publish the list of medicines with additional monitoring status.
- PRAC agreed by consensus a recommendation for the black symbol at its October meeting - first additional monitoring list will be timed for when Commission adopts the symbol based on the PRAC recommendation (? March 2013)

Prioritisation and initial analysis of signals

1. Signal Management by PRAC:

- Data Monitoring in EudraVigilance and signal detection from other sources (signal – includes new information on a previously known risk).
- Start of signal management through the PRAC - multiple signals prioritised September - November PRAC meetings.
- For signals, the PRAC prioritises according to the available information, strength of evidence and public health context.
- Where appropriate, signals escalated to a formal EU safety referral.
- Transparency with publication of agendas and minutes.
- PRAC will deliver according to timelines as reported in the minutes.

Regulatory action to safeguard public health

- **Decision making**

PRAC has been taking decisions by consensus although majority vote is an option.

- **Strengthening referral procedures:**

➢ New referral procedure in operation – first referral under the new legislation launched in October.

➢ New levels of transparency are already evident.

Establishment and functioning of the PRAC - Inaugural Meeting

- Held on 19-20 July 2012 in Brussels
- First, information was provided on aspects such as the new legal provisions, the key interactions between PRAC-CHMP-CMD(h), transparency, conflicts of interests, the Rapporteur appointment process, the PhVWP legacy, the EURD list, signal management, additional monitoring and black symbol
- Rules of Procedure adopted by majority – ongoing review at EMA Management Board particularly regarding the possibility of Rapporteurship for Commission Appointed Members.

Functioning of the PRAC - September

- Main focus was on
  - Election of Chair and Vice-Chair
  - **Signals assessment and prioritisation (n=13)**
    - 11 new signals detected from EU spontaneous reporting systems
    - 1 new signal detected from other sources and 1 signal follow-up
  - Risk Management Plans pre-authorisation (n=1)
  - Pharmacovigilance inspections (n=2)
  - **Organisational, regulatory and methodological matters**
    - EURD list: was adopted by the PRAC
    - List of substances subject to signal management worksharing: was adopted by the PRAC for submission to CMD(h) to appoint lead MSs
    - Selection of the symbol for products subject to additional monitoring: trend vote in view of final discussion in October

Functioning of the PRAC - October

- Signal recommendations x 14
- **1st referral started**
- **1st safety variation advice**
- **1st PASS protocol decision**
- **1st renewal advice**
- **Black symbol** selected for recommendation to the EC (input received from representative of Patient and Consumer Working Party.)
- RMP advice x 3
- Inspection advice x 3
- Updated EURD list endorsed

Functioning of the PRAC - November

Agenda is growing....

- Signal recommendations x 12
- RMP advice x 11
- Second safety referral started
- Inspection related issues x 4
- Renewals of the marketing authorisation x 2
- Safety related variations x 3
- Other requests – DUS protocol, proposal for a joint PASS.

Conclusion

- Establishment of the PRAC is a key milestone in the application of the new Pharmacovigilance Legislation.
- PRAC Chair and Members are committed to ensuring that the new tools are used in a way that best serves EU citizens.
- Mandate and processes are important.
- Importance of collaboration across Committees is recognised.
- Public health objectives and the importance of robust scientific decision making will drive the work of the PRAC.
- An emphasis on proportionality and ensuring best use of available resources and expertise will inform ways of working.
- PRAC is committed to transparency and stakeholder engagement.

Questions?

List of PRAC deliverables (and legal refs)

CAPs and NAPs

Urgent union procedure (Dir Art 107(j))

Article 31 procedure (Dir Art 31)

Article 20 procedure (Reg Art 20)

PSUR single assessment (Dir Art 107(e) + Reg Art 28(5))

PASS protocol (Dir Art 107(m - o) + Reg Art 28b(1))

PASS results (Dir Art 107(p - q) + Reg Art 28b(1))

Signals (Dir Art 107(h) + Reg Art 28a(2))

PSUR reference dates (Dir Art 107(c)

List of products under additional monitoring (Reg Art 23(2) and (4))

For cause phv inspections (Dir Art 111(8) + Reg Art 56(1) and 57(i))

List of PRAC deliverables

CAPs

RMPs and outcome of risk minimisation (Reg Art 5(2) and 28a(1))

PSURs for for single CAPs (Reg Art 28(3))

Renewals, annual reassessment, safety type II variations (Reg Art 5(2) and 56(1)(aa))

Non-CAPs

- PSUR single assessment (Dir Art 107(e))
- RMPs, outcome of risk minimisation, renewals, safety type II variations (Reg Art 56(1) and 27(1) and Dir Art 107(h)1)
- Member States safety announcements (Dir Art 106(a)(3))

List of deliverables

Other PRAC tasks

Functionalities of the EudraVigilance database (Reg Art 24(2) and 25(a))

Black symbol (Reg Art 23(5))

Literature ADR monitoring (Reg Art 27)