In this presentation:

- Key pharmacovigilance improvement themes
- Highlights of PRAC work plan 2015-6
- Challenges and some approaches to solutions
PRAC activities

- 36 PRAC meetings
- Over 150 protocol reviews
- Over 600 risk management plans
- 68 safety referrals
- Over 1000 PSURs
- Over 300 signals
PRAC Improvement themes

Keeping up the PACE

Making a difference
Keeping up the PACE

Proactive & prompt public health protection

Effective decisions and systems

Accessible and open PhVig systems

Collaborative & convergent throughout lifecycle
The 2015-6 PRAC Work Plan

Comprehensive activity- focussed plans to utilise potential of all new legislative tools

Priorities include:

• Enhanced quality and consistency of PRAC benefit risk reviews
• Product lifecycle support
• Use of new tools – PAS/PAES

Focus on developing new guidance where needed – special populations

Strengthened collaboration with key stakeholders
Proactive public health protection

- Strengthening evidence and science base
- Investigating use of benefit risk decision methodologies
- Focus on Post Authorisation studies – PASS and PAES
- Signal detection methodologies
- New guidance
  - Special populations
  - Biologics and vaccines
  - Pregnancy
  - Medication errors
Vaccine vigilance

Example: Observed vs expected Rotavirus and Intussusception

MaxSPRT for Intussusception with Rotarix - 1 week risk window
(first vaccination only, assuming RR=6.8 based on Australian data)

Week

Log-likelihood ratio

100% reporting

10% reporting

25% reporting

50% reporting

75% reporting

Critical threshold

1 2 3 4 5 6 7 8 9 10

1 2 3 4 5 6 7 8 9 10

1 2 3 4 5 6 7 8 9 10

1 2 3 4 5 6 7 8 9 10
Signal management

Table 2: PRAC final recommendations regarding signals

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>N</th>
<th>Time until recommendation (days)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>SmPC update</td>
<td>51</td>
<td>81</td>
</tr>
<tr>
<td>Routine pharmacovigilance</td>
<td>33</td>
<td>60</td>
</tr>
<tr>
<td>Referral started</td>
<td>9</td>
<td>54</td>
</tr>
<tr>
<td>DHPC</td>
<td>7</td>
<td>51</td>
</tr>
<tr>
<td>RMP update</td>
<td>7</td>
<td>132</td>
</tr>
</tbody>
</table>

Pacurariu et al Drug Safety 15 Nov 2014
Disconnect between product information & clinical experience – impact on patient compliance

Review of anti-retrovirals and lipodystrophy warnings

Scientific evaluation supported risk proportionate approach to product information

Example of keeping class warnings up to date in light of clinical experience

Use of pharmacogenomics for RMMs

EU Guideline on pharmacogenomics in pharmacovigilance

finalised 27 October 2015

Guideline on key aspects for the use of pharmacogenomics in the pharmacovigilance of medicinal products

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>Draft Agreed by Pharmacogenomics Working Party</td>
<td>April 2013</td>
</tr>
<tr>
<td>Adopted by CHMP for release for consultation</td>
<td>20 December 2013</td>
</tr>
<tr>
<td>Start of public consultation</td>
<td>03 February 2014</td>
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</table>
Transformative medicines

Early access to medicines in areas of high unmet need

PRIME (Priority Medicines) medicines procedures under development

Focus on real-world real-time evaluation – adaptive pathways

ADA-SCID gene therapy
Accessible pharmacovigilance systems

Experience of engagement of health professionals and patients in referrals (safety reviews)

Introducing public hearings

Optimising safety communications

Report on experience with co-ordination of EU communications
Engaging with patients and the public

Interaction with patient and healthcare professional organisations so far ad hoc during formal European safety reviews

Rules of procedure for conduct of public hearings being finalised

First public hearings expected early next year
PRAC will be supporting work by EMA on risk communication. Focus is initially on work with healthcare professionals.
Collaborative pharmacovigilance

Working with internal and external stakeholders – building effective international collaboration

EU Joint Action project “SCOPE”

Innovative Medicines Initiative “WEB-RADR”
Strengthening pharmacovigilance collaboration:

- ADR reporting
- Signal detection
- Risk communications
- Pharmacovigilance assessment
- Quality management

Project due for completion October 2016
Development of a mobile app for
- ADR reporting
- Provision of information to users

Scientific evaluation of using social media data to identify ADRs, propose policy guidance
Effective pharmacovigilance systems

Developing strategy to strengthen evaluation of risk minimisation proposals

Developing a strategy to measure impact of pharmacovigilance

Effective decisions and systems
Removal of first-line indication in osteoporosis for HRT after WHI study showed harms

Followed by fall in incidence of breast cancer in women over 50 eg 7% in Australia

_Trends in use of hormone therapy for the menopause since 1970_
HRT and breast cancer warnings


- Number of prescriptions (millions)

Vertical dotted line indicates commencement of the period over which HRT prescriptions were expected to decline.


- Rate per 100,000 women

Vertical bars represent 95% CIs (confidence intervals are very small for women aged <50 years). Vertical dotted line indicates commencement of the period over which there was a hypothesised decrease in breast cancer incidence in women aged ≥50 years but not in women aged <50 years.
Some key challenges

Ongoing development of signal detection approaches

Optimising benefit risk assessment of “mature” products

Long term safety (biologics)

Vaccine vigilance

Medicines in pregnancy
Some approaches and solutions

Maximising use of new methodologies from collaborative research in particular PROTECT

Building capacity for PASS and PAES studies by use of European Network of Centres for Pharmacovigilance & Pharmacoepidemiology

Better use of real-world data eg registries, observed versus expected analyses

Regular strategic review and learning meetings with other EMA committees
Conclusions

Last three years have seen great progress in realising potential of EU Pharmacovigilance legislation & role of PRAC.

Experience has demonstrated areas where a strengthened, clarified or simplified approach needed.

This is the basis for developing a work plan for 2016 with a clear focus on best evidence and new methodologies.

Ongoing collaboration between all stakeholders in a European networked model essential to achieve highest standards of public health protection.