EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance Impact – Update and Collaboration with Industry

9th Industry Stakeholder Platform on the Operation of EU pharmacovigilance Legislation
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PRAC Strategy for Measuring Impact of PhV Activities

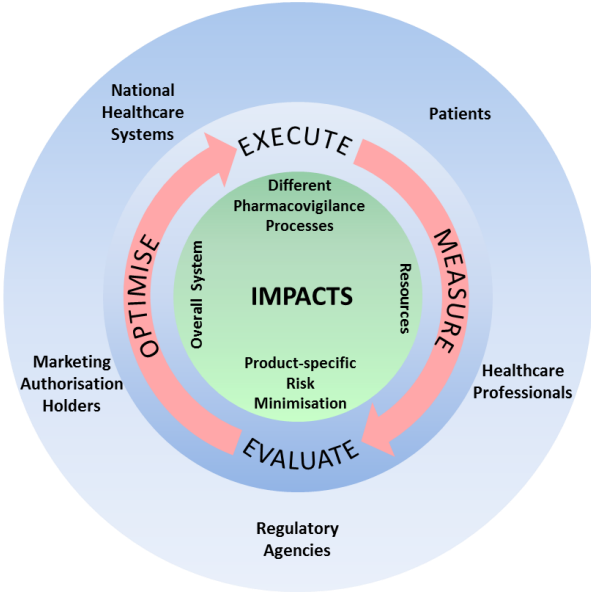
Key milestones

- Initial strategy proposal developed by EMA;
- First introduction at the *Pharmacovigilance Industry Platform*, June 2015
- Presentation and discussion with PRAC members at '*Workshop on Measurement of Pharmacovigilance Impact'*, 11 September 2015;
- Discussion at the *EMA Industry Stakeholder TC*, 14 September 2015;
- Presentation and discussion at *Informal PRAC*, Luxembourg, 28 October 2015;
- Final strategy and work plan adopted by PRAC, January 2016;
- PRAC Interest Group (IG) Impact established, January 2016;

Measuring pharmacovigilance impact: concept

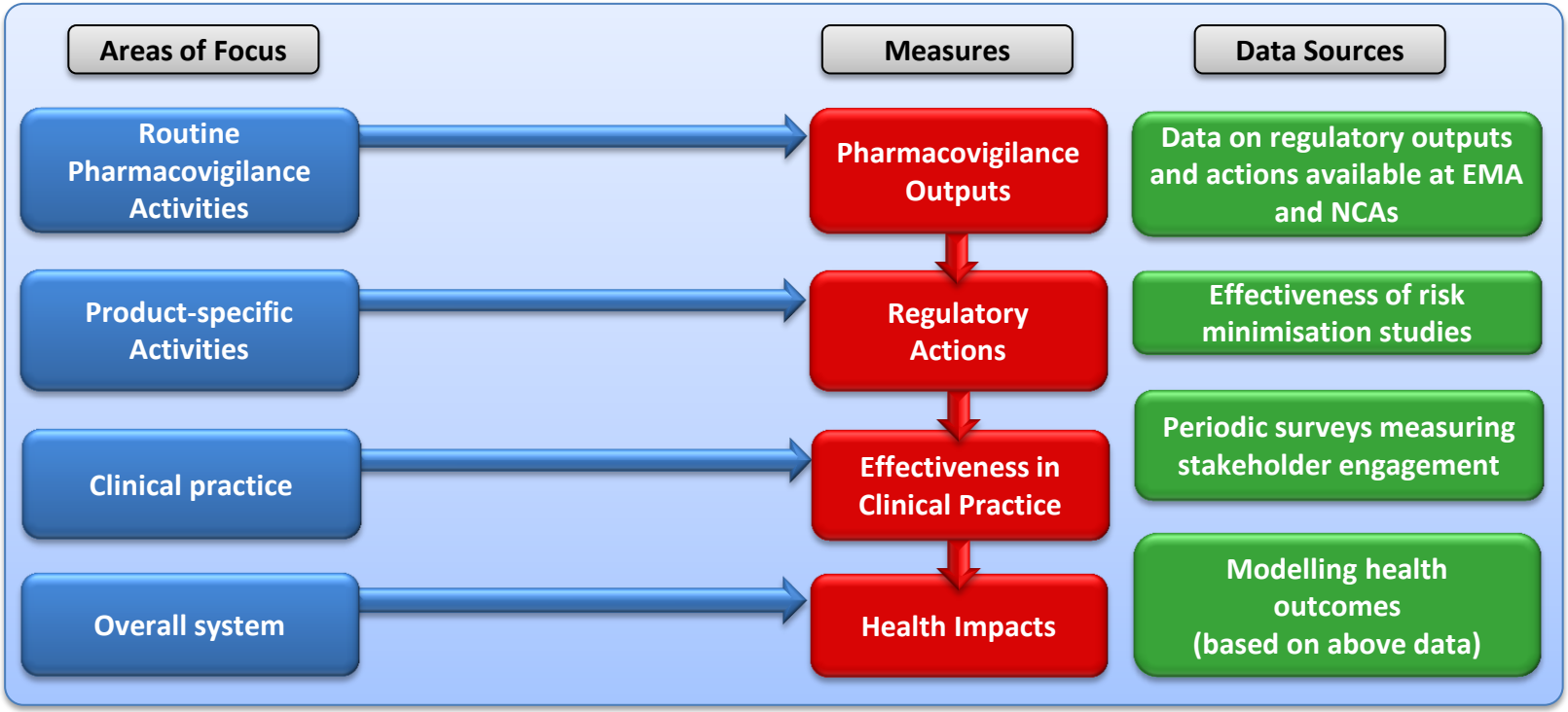
The PRAC strategy focusses on 4 key areas:

- Effectiveness of **pharmacovigilance processes** (e.g. ADR reporting, signal detection & management)
- Effectiveness of **product-specific risk minimisation** (e.g. measures following major referrals)
- Enablers of effective pharmacovigilance such as **stakeholder engagement**;
- Collaboration on **methodologies**, e.g. modelling methods for measurement of impact on health outcomes;



→ Leverage of ongoing work by regulators (NCAs + EMA), industry and academia;

How does the pharmacovigilance system generate impacts?



PRAC Strategy Impact – work plan 2016/2017

Objective	Deliverable
Establish criteria to prioritise topics for collaborative impact reseach	• Reflection paper ✓
Collection of data elements on pharmacovigilance activities and decisions (regulatory outputs)	• Annual report
Stakeholder survey (industry, patients, HCPs)	a) Conduct survey(s) b) Report on survey results
ENCePP collaboration on methodologies for impact research	a) Set up ENCePP Special Interest Group and agree mandate and work plan with ENCePP SG ✓ b) Inventory of PhV activities relevant for impact research c) Paper review of methodologies for effectiveness studies

PRAC Strategy Impact – work plan 2016/2017

Objective	Deliverable
International workshop on measuring impact of pharmacovigilance activities;	a) Launch call for expressions of interest ✓ b) (Draft) workshop programme ✓ c) Convene workshop d) Publish workshop report
Study on ADR reporting by patients/HCPs	Final study report ✓
Post-referral best evidence pilot: • assess feasibility of multi-database regulatory studies with common protocol • assess impact of referrals on drug utilisation • assess impact of CHMP Art 31 referral on regulatory communication and risk awareness	Final study report

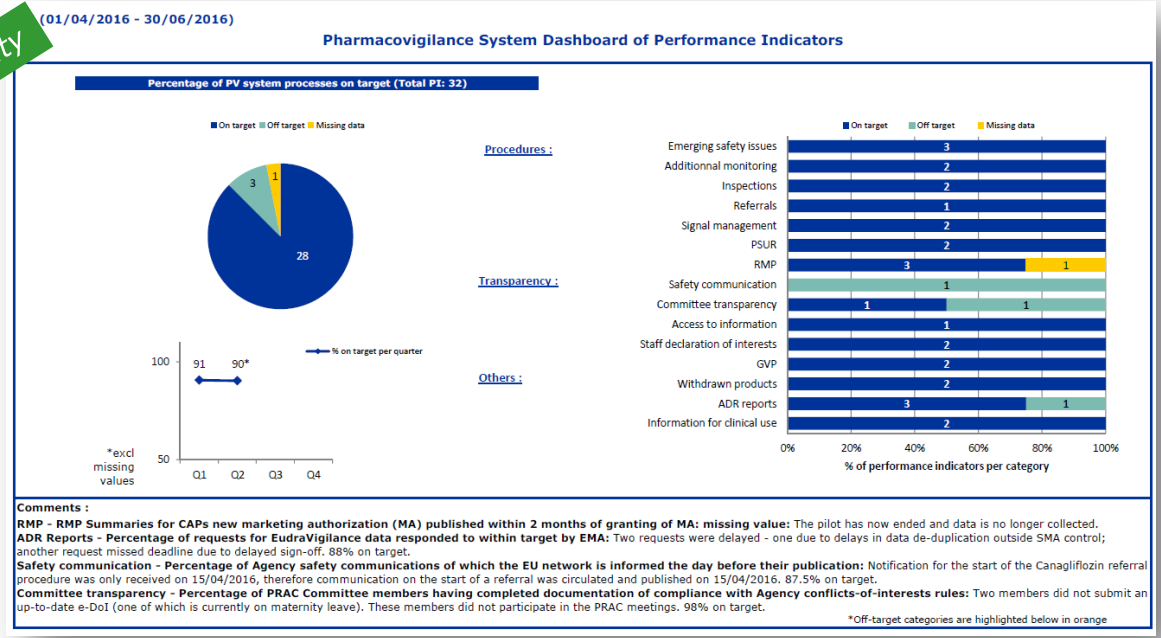
PRAC Interest Group (IG) Impact - mandate

- Prioritise design, methods and choice of outcomes for **studies measuring the effectiveness of risk minimisation** measures at EU and Member State level;
- Establish **criteria for the prioritisation of PRAC regulatory decisions** for collaborative impact studies;
- Assess the feasibility of **multi-database regulatory impact studies** by means of a common core protocol;
- Collaborate with ENCePP Special Interest Group (SIG) on Impact on **methodological aspects** of studies;
- **Composition:** 14 PRAC members with expertise and experience in impact research chaired by Marieke De Bruin, University of Copenhagen, DK

PRAC IG Impact deliverables – routine data collection

- Seven activity areas relevant for impact research identified where information is readily available or could be generated in terms of procedure or work load counts (**activity indicators**):
  - ADR reporting
  - PASS protocols
  - PASS results
  - Signals
  - Referrals
  - Renewals
  - Additional risk minimisation

Ongoing activity

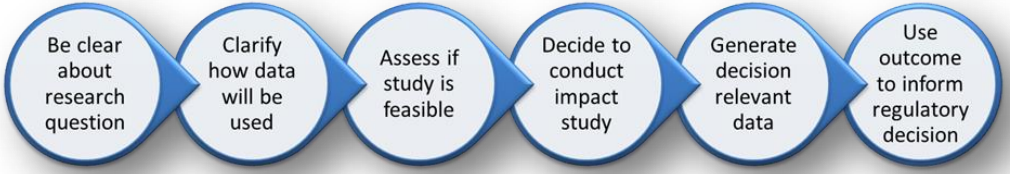


PRAC IG Impact deliverables – prioritisation criteria (I)

- Reflection paper on criteria to prioritise collaborative impact research adopted Sep'16;

completed

- Criteria are based on **key considerations**:



- Prioritisation of safety topics is based on:
  - **I. Public health importance of the regulatory action**
  - **II. Potential impact on clinical practice**
  - **III. Delivery of decision relevant data**
- Pilot testing and practical implementation started;
- For review in Q2/2017;

Criteria	Explanation	High/ Yes	Low/ No	Not clear
Public health importance of the regulatory action				
1. Nature and severity of the risk in the affected population;	*How serious are the consequences for the patient? How is the risk perceived by the general public in terms of intensity (mild, moderate, severe)?*	□	□	□
2. Magnitude of the risk (absolute and relative) in the population where the product is used;	*How big is the risk in the treated, compared to the untreated population? How big is the population using the product in the EU taking into account exposure data from several Member States where the product is marketed, and if available recommendations in national clinical guidelines.*	□	□	□
3. Amount of public concern, e.g. due to risk in vulnerable populations, public debate, disagreement within the scientific community etc.;	*Are affected populations perceived as particularly vulnerable (children, pregnant women, elderly people)? Has the safety concern been subject to public debate in the media? Is there conflicting evidence about the safety concern in the scientific literature?*	□	□	□
Potential impact on clinical practice				
4. Extent of the regulatory intervention;	*Is the regulatory action expected to lead to changes in patient and/or HCP behaviour, to change the way the product is used in clinical practice or to changes in clinical guidelines? Regulatory interventions may include label changes e.g. addition of adverse reaction(s), warnings and/or contraindications to SmPC, additional risk minimisation measures, restriction of the indication, suspension or revocation.*	□	□	□
Delivery of decision relevant data				
5. Regulatory action is amenable to research generating impact relevant data?	*Are there any measurable effects of the regulatory intervention which allow to assess if the intended outcome (e.g. lower risk incidence) has been delivered in clinical practice or did any unintended consequences occur?*	□	□	□
6. Suitable data sources and methodologies are available in several Member States to allow generalisability of results?	*Are suitable data sources available and accessible for impact research or can they be generated within reasonable time frames? Do these data sources allow for generalisability of the results across different healthcare systems for the whole EU?*	□	□	□
7. Does the study fill gaps in knowledge and understanding of the safety issue?	*Are there clearly defined knowledge gaps about the risk to patients under real world conditions, about the effectiveness of risk minimisation measures or how the product is used in practice which could be answered by collaborative impact research?*	□	□	□
8. Does the study add to the evidence beyond the studies conducted by MAH(s)?	*Are there any other ongoing or planned studies from MAH(s) which provide evidence on the impact of the regulatory action in question? Are MAH(s) in the position to conduct such a study e.g. as joint study?*	□	□	□
Topic prioritised for impact research: □ **Yes** □ **No**		**Comment:**		

PRAC IG Impact deliverables – prioritisation criteria (II)

Applied to safety topics under the following **PRAC agenda items**:

- **Urgent EU referral procedures** for safety reasons: for finalisation
- **Other EU referral procedures** for safety reasons: for finalisation
- **Signals assessment and prioritisation** - Signals follow-up and prioritisation where PRAC recommends **changes to Product Information and/or RMP** including:
  - New contraindication(s),
  - New warning(s),
  - Restriction of the indication or
  - Additional risk minimisation measures
- After pilot: **PSURs** resulting in variation, suspension or revocation

To be reviewed after the pilot

ENCePP SIG Impact – collaboration on methods

ENCePP Special Interest Group (SIG) Impact established with the mandate to:

- **Provide recommendations** (e.g. in form of guidance documents or publications in peer-reviewed journals) to PRAC IG Impact.
- **Develop methods for modelling health outcomes** of pharmacovigilance activities based on epidemiological parameters (e.g. population attributable risk, prevalence of exposure, behavioural changes, switching therapies etc.) and identification of **relevant data sources**.
- **Composition:** 30 ENCePP Centres representatives with expertise in methodologies for impact research, chaired by Agnes Kant, Netherlands Pharmacovigilance Centre Lareb, NL

ENCePP SIG Impact – deliverables 2016/2017

Deliverables
1. **Inventory** of pharmacovigilance activities to be taken into account for impact measurement, including a description why these activities have been chosen;
2. **Paper**: review of methodologies of studies measuring the effectiveness of risk minimisation measures included in the EU PAS Register (only those with published protocol and results), including an inventory of data sources and a discussion of methodological limitations and gaps;
3. **Discussion** and agreement of inventory report (1) and review paper (2), including a proposal for work streams to develop deliverable 4.
4. **Paper:** modelling the results of effectiveness studies to predict effects of pharmacovigilance activities. This review should also include selected examples from scientific literature;

Workshop: Measuring impact of PhV Activities, 5-6 Dec'16

- Call for EoI to participate closes 30 Sep'16 (>140 pre-registrations so far);
- Workshop included on EMA events calender;
- Draft programme published:
  - **Session 1** - Importance of measuring the impact of pharmacovigilance
  - **Session 2** - Approaches for measuring impact of pharmacovigilance and regulatory decisions
  - **Session 3** - Parallel breakout sessions:
    - 3.1 Enablers and barriers to measuring impact – patient and HCP engagement.
    - 3.2 From regulatory outputs to health outcomes.
    - 3.3 Measures of impact of pharmacovigilance processes.
  - **Session 4** - Reports from breakout sessions: gaps and observations.
  - **Session 5** - Way forward and next steps

Opportunities for collaboration with industry

- Re-activation of 'EMA Industry Stakeholder Group on Impact';
- Establish mechanism to inform on impact relevant initiatives (e.g. IMI project, surveys etc.)
- Where would industry see added value in surveys with a view to process improvements (e.g. periodic surveys on impact relevant processes)?
- Collaboration on methods of measuring impact of pharmacovigilance activities and for effectiveness studies following the workshop in December 2016;
- **Workshop:** invitation to **submit topics/questions** for discussion in **interactive breakout sessions** 3.1, 3.2 and 3.3 (pharmacovigilance.impact@ema.europa.eu)

Thank you for your attention

Further information

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