EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update on PRAC Impact Strategy (Rev. 2) and impact research projects

17th Industry Stakeholder Platform – Operation of EU Pharmacovigilance

7 November 2022

Presented by Thomas Goedecke
Pharmacovigilance Office | Human Medicines Division

In this presentation

- PRAC Impact Strategy Rev.2
  - Activities and achievements
  - Scope of Rev. 2
- Impact research projects

PRAC Impact Strategy

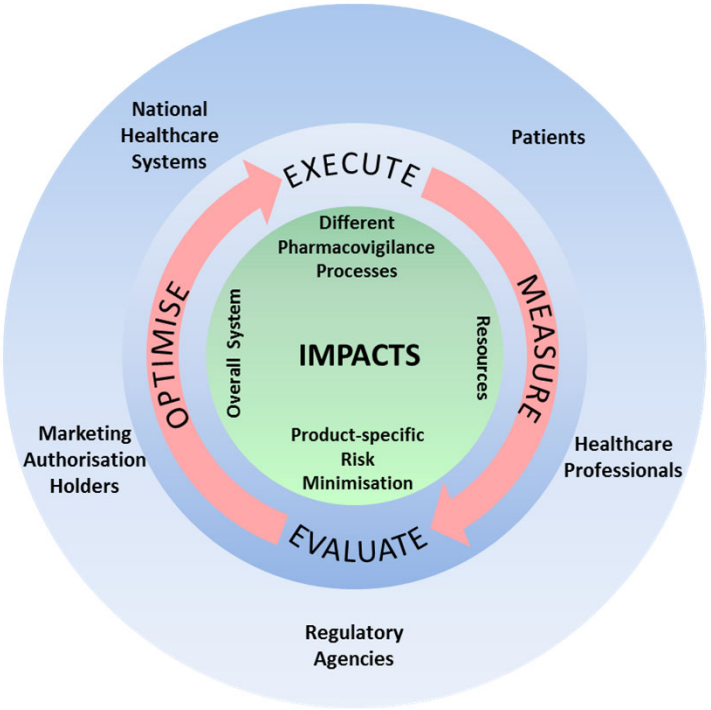
Launched in 2016 with focus on:

I. Effectiveness of risk minimisation activities;

II. Effectiveness of specific pharmacovigilance processes;

III. Enablers of effective pharmacovigilance and stakeholder engagement;

IV. Identification and development of analytical methods;

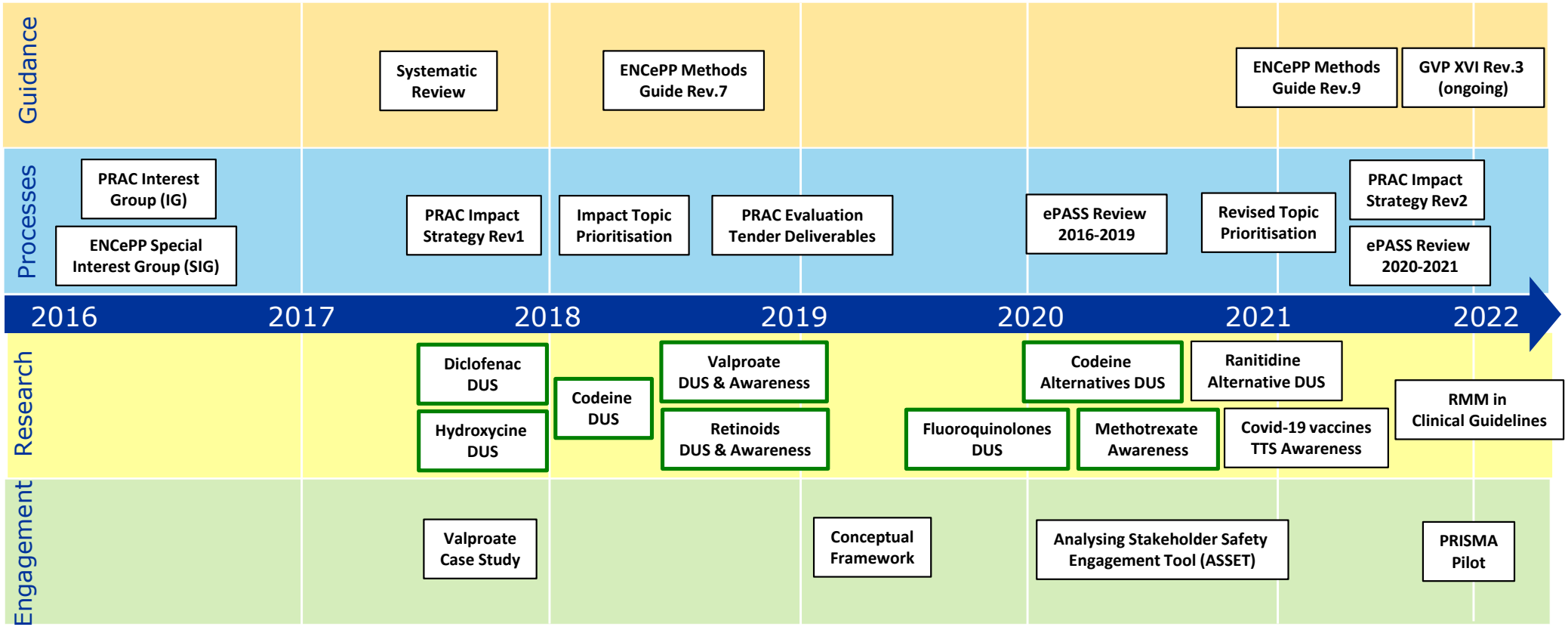


Main activity areas:

- ✓ **Conduct of impact research**
- ✓ **Pharmacovigilance processes**
- ✓ **Patient and HCP engagement on RMM**
- ✓ **Guidance and training on methods**

PRAC Strategy on Measuring the Impact of Pharmacovigilance Activities (Rev 2)

Activities over time



Achievements

Conduct of impact research

- Diclofenac DUS
- Hydroxyzine DUS
- Valproate Awareness/DUS
- Retinoids Awareness/DUS
- Fluroquinolones DUS
- Ranitidine DUS
- Methotrexate Awareness
- Covid-19 vaccines TTS Awareness
- RMM implementation in clinical guidelines (qual.)

- Codeine DUS (EMRN collaborative study)
- Alternatives to Codeine DUS (EMRN collaborative study)

Patient and HCP engagement on RMM

- Conceptual framework for engaging patients and HCPs in regulatory pharmacovigilance
- Valproate public hearing case study
- Analysing Stakeholder Safety Engagement Tool (ASSET) for engaging patients and HCPs in RMM
- PRAC Risk Minimisation Alliance (PRISMA) pilot

Pharmacovigilance processes

- PRAC Interest Group (IG) Impact monthly meetings
- Prioritisation of impact research topics (monthly)
- PRAC evaluation of deliverables of commissioned impact studies under FWC
- Revision 1 and 2 of PRAC Impact Strategy
- Review of PASS evaluating RMM effectiveness assessed by PRAC 2016-2021, including qualitative analysis

Guidance and training on methods

- ENCePP SIG Impact guidance on impact research methods
- ENCePP Methods Guide - Revision 7 and Revision 9
- GVP Module XVI Revision 3 on RMM effectiveness evaluation (XVI.B.5 and Addendum II)

- DIA Information Day on Measuring Impact of PhV 2017
- DIA Information Day on Risk Minimisation Measures 2021
- PRAC Assessors Training on impact research methods 2021
- PRAC Assessors Training on impact research methods 2022

PRAC Impact Strategy - Scope of Revision 2, 2022

- **Guidance on impact research** (i.e. principles, objectives and conceptual approach to RMM effectiveness evaluation) and methodologies for impact research (aligned with GVP XVI Rev.3 and new Addendum II on methods);
- **Learnings** from commissioned and collaborative/in-house impact research since launch of the strategy (8 drug utilisation studies, 4 survey studies, 1 qualitative study);
- **Frameworks** for conduct of regulatory impact research added (EMA framework contract, EMRN collaborative research, EMA in-house studies, DARWIN-EU from 2023/2024);
- Activities to **enhance patient and HCP engagement** for informing and evaluating RMM effectiveness and RMM implementation in healthcare:
  - Analysis of stakeholder input to valproate public hearing* and PRAC points-to-consider
  - PRAC Risk Minimisation Alliance (PRISMA)

*Drug Safety (2021) 44:193–209 doi.org/10.1007/s40264-020-01005-3

PRAC Risk Minimisation Alliance (PRISMA)

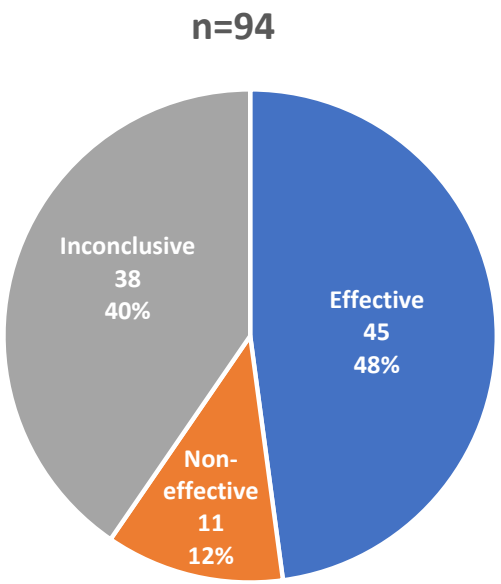
- **New pilot** with monthly meetings to **enhance PRAC engagement with patients and HCPs** on RMM for selected products;
- Based on **concept of knowledge exchange** and review of past stakeholder engagement events RMM options are discussed early in the regulatory procedure from **different stakeholder perspectives**;
- Participants include PRAC members/alternates including patient & consumer and HCP representatives, Rapporteurs and (co)-chairs, and representatives of EMA's General Practitioners' Forum;

→ Aim is to create **knowledge base for RMM across products** with focus on **barriers and enablers of RMM implementation** in healthcare

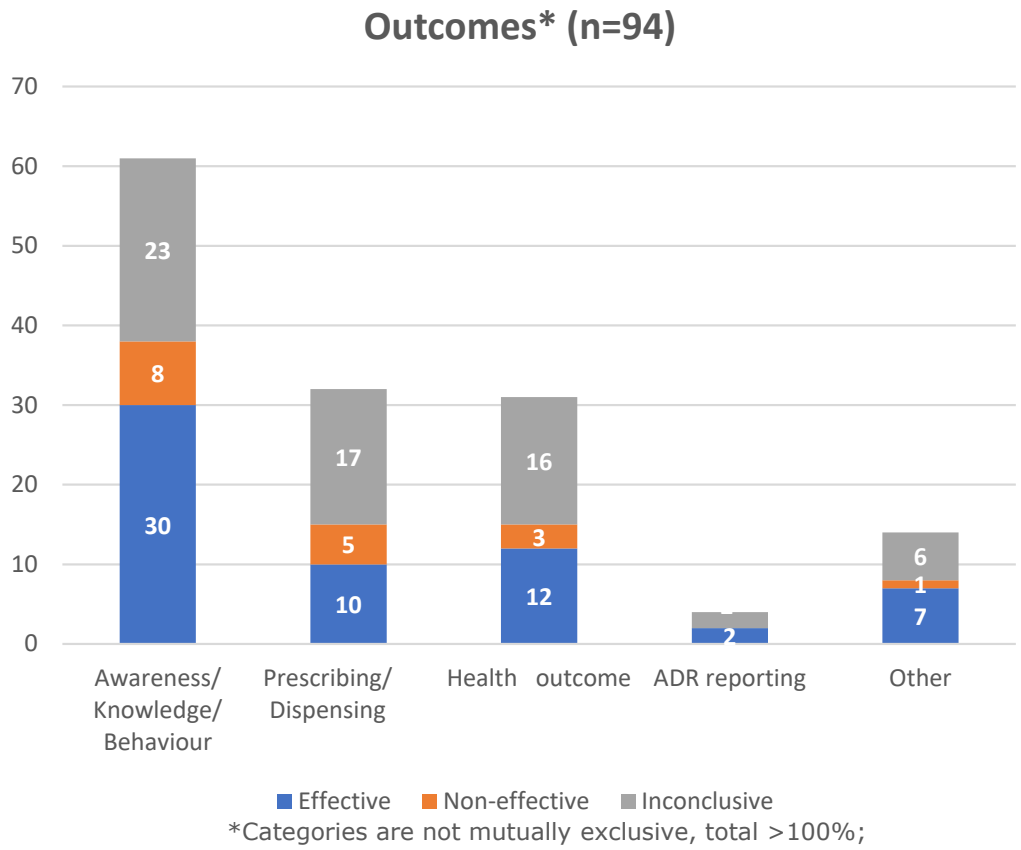
PRAC Impact Strategy - Scope of Revision 2, 2022

- Ongoing **review of PASS evaluating RMM effectiveness** assessed by PRAC *(EUPAS45978)* with the objective to describe study designs, analytical methods and measures for RMM effectiveness, to determine proportion of successful RMMs and how success was defined, and to compare effective RMMs with non-effective RMMs:
  - → Initial review of 2016-2019 data showed 43% (31/72) of PASS were inconclusive;
  - → 80% (33/41) of PASS where conclusion could be drawn assessed RMM as effective;
  - → Follow-up research into factors associated with (in)conclusive PASS/(in)effective RMM on expanded data set (2016-2021) is under way;

Review of effectiveness PASS assessed by PRAC 2016-2021



Adapted from Gardarsdottir H, Hoekman J, Scheffers J. Review of studies evaluating the effectiveness of risk minimization measures assessed by PRAC, University of Utrecht (2021) (EUPAS45978)



*Categories are not mutually exclusive, total >100%;

Revised process for impact research

- **Simplified prioritisation process** with focus on regulatory action(s) that warrant regulatory communication (e.g. DHPC, PRAC Highlights, EMA news item or other regulatory communication);
- Clarification of **PRAC Rapporteur role** for EMA commissioned impact research (i.e. PRAC Rapporteur(s)' contribution to technical specification for tender, evaluation of research contract deliverables and assessment of results in context of regulatory procedures);
- **Regulatory follow-up on impact research**, closing the cycle from PRAC request to evaluation of impact study results, informing **PRAC regulatory decision-making** on RMM effectiveness → after evaluation of final study report PRAC Rapporteur(s) identify relevant **ongoing or upcoming regulatory procedures** where the results are included in the assessment;

Overview of research projects

NEW

EMA website lists ongoing and completed impact studies under Research Projects:

Home ▸ How we work ▸ About us ▸ Big Data ▸ Research Projects

- Study title
- Objectives
- Timelines
- Link to Deliverables via EUPAS® Register (protocol, study results, publication)
- Contractor/Framework

Same information linked to ▸ **PRAC Impact Strategy**

Examples https://www.ema.europa.eu/en/about-us/how-we-work/big-data#research-projects-section

Diclofenac prescribing and use in patients with cardiovascular risks

Project title	Impact of EU label changes for systemic diclofenac products: post-referral prescribing trends
Objectives	This study aims to determine: • How medicines containing diclofenac are prescribed before and after the Article 31 referral • Prescriber compliance with product information warnings about cardiovascular risk factors • Prescriber compliance with the product information recommendation to avoid diclofenac in patients with certain cardiovascular diseases • Drug use and prescribing patterns for alternative treatments in patients who previously used diclofenac It was commissioned under the PRAC strategy on measuring the impact of pharmacovigilance activities, which includes the effectiveness of product specific risk-minimisation.
Timelines	• Start of project: September 2017 • First deliverables: November 2017 • Final delivery: March 2019
Deliverables	For more information on protocol and study results, please visit EU PAS Register. The study registration number is EUPAS24089.
Contractor	University of Dundee

Methotrexate awareness and adherence to measures avoiding dosing errors

Project title	Impact of EU label changes for medicinal products containing methotrexate for weekly administration: risk awareness and adherence
Objectives	This study aims to determine the extent of awareness and knowledge among: • Prescribers, of the risk of methotrexate dosing errors and adherence to risk minimisation measures following the Article 31 referral • Pharmacists, of the patient card and outer packaging reminder • Patients, of the risk minimisation measures to avoid incorrect administration schedules It was commissioned under the PRAC strategy on measuring the impact of pharmacovigilance activities, which includes the effectiveness of product specific risk-minimisation.
Timelines	• Start of project: May 2021 • First deliverables: June 2021 • Final delivery: November 2022
Deliverables	For more information on protocol and study results, please visit EU PAS Register. The study registration number is EUPAS44827.
Contractor	IQVIA Ltd

Outlook

- PRAC Impact Strategy has **shifted the focus of pharmacovigilance** towards activities and regulatory tools that are most relevant to patients & consumers and HCPs, and that make a difference in daily healthcare

  → we moved on from developing concepts and guidance to measuring impact of major regulatory actions and reviewing related processes in pharmacovigilance

- Over the next two years activities will focus on
  - Establishing a process for **enhanced patient and HCP engagement** in RMM development and implementation in clinical practice;
  - **Lessons learnt** exercise of past-experience with RMM effectiveness studies (industry-sponsored and EMRN/commissioned research);
  - Preparing for running impact research projects through **DARWIN EU** in addition to FWC;

Thank you for your attention

Further information

Thomas Goedecke thomas.goedecke@ema.europa.eu
European Medicines Agency
Send a question via our website www.ema.europa.eu/contact

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