EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC): Work Plan 2017

Adopted by the Committee on 23 March 2017

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1. Evaluation activities for human medicines

1.1. Pre-authorisation activities

1.1.1. Special populations and product guidances

Certain specific population groups including children, pregnant women and the elderly require specific consideration in the conduct of pharmacovigilance. This PRAC work topic channels Committee's expertise into the development of population specific guidance.

Key objectives

- Strengthen pharmacovigilance by industry and regulators through dedicated guidance on specific populations.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

- Continue to provide expert input in the development of GVP P.III – 'Product- or population-specific considerations: pregnancy' in view of its release for public consultation.
- Continue to provide expert input in the development and finalisation of GVP P. V – 'Product- or population-specific considerations: Medicines use in geriatric healthcare' in view of its release for public consultation.
- Provide expert input in the finalisation (in cooperation with PDCO) of the revision of GVP P. IV - 'Product- or population-specific considerations: Paediatric pharmacovigilance' in view of its release for public consultation.
- Support the work of the joint PDCO/PRAC working group on medicines for paediatric use: provide advice on substances/medicinal products on an ad-hoc basis.

PRAC topic leader(s): June Raine

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Dolores Montero Corominas	ES (geriatrics)
Member	Kirsti Villikka	FI (pregnancy)
Member	Jolanta Gulbinovič	LT (paediatrics)
Member	Sabine Straus	NL
Member	Ulla Wändel Liminga	SE (pregnancy)
Member	Thierry Trenque	Independent scientific expert appointed by the EC (geriatrics)
Alternate	Kirsten Myhr	Representative of healthcare professionals appointed by the EC (geriatrics and pregnancy)

1.1.2. Life-cycle approach to pharmacovigilance and risk managements

By ensuring robust, feasible and risk proportionate planning of pharmacovigilance activities including risk minimisation and further collection of data and information, the work of the PRAC supports the protection and promotion of public health. The work of PRAC also underpins innovation throughout the product lifecycle thereby and supporting the delivery of new treatments to patients, fulfilling unmet medical needs.

Key objectives

- Strengthen public health promotion and protection.
- Support innovation and the fulfilment of unmet medical needs of patients.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

- Optimise RMP content and process through finalisation of revision 2 of GVP module V on 'Risk management systems'. See also 2.5.
- Expert input into creation of common understanding on optimal PRAC input on risk management planning for high value, high uncertainty products. GVP module V on 'risk management systems': support life cycle and development through risk management planning and use of real world data. This activity should support the accelerated assessment and the PRIME scheme.
- Finalise revision 2 of GVP module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' in order to align its content with revision 2 of GVP module V on 'Risk management systems'.
- Initiate revision 3 of GVP module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' to further define and clarify the role of risk minimisation tools and address the workshop recommendations on measuring impact of pharmacovigilance activities held in December 2016.
- Revisit the outcome of the EMA workshop on risk minimisation measures held in September 2015 and the findings and recommendations from the HCPWP to identify areas of focus for the period 2017-2019. See also 2.3.1.
- Maintain and refine PRAC-SAWP interaction in scientific advice procedures on PASS protocols and in scientific advice procedures involving questions falling under the mandate of the PRAC on pharmacovigilance planning and risk mitigation[1]. See also 1.3.1.
- Based on the experience gained through the ongoing pilot on the use of effects tables in selected important benefit/risk reviews, agree on recommendation based on lessons learnt.

PRAC topic leader(s): Martin Huber

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Alternate	Valerie Strassmann	DE (scientific advice)
Alternate	Torbjorn Callreus	DK (scientific advice, GVP

[1] So called PRAC consultation in scientific advice procedures

Member/alternate/expert	Name	Member state or affiliation
		module XVI, PRIME)
Alternate	Eva Segovia	ES
Alternate	Željana Margan Koletić	HR
Member	Almath Spooner	IE
Member	Jolanta Gulbinovič	LT
Member	Sabine Straus	NL (GVP module XVI, GVP module V)
Member	Ana Sofia Diniz Martins	PT
Alternate	Márcia Sofia Sanches de Castro Lopes Silva	PT
Member	Ulla Wändel Liminga	SE (GVP module V)
Alternate	Qun-Ying Yue	SE
Member	Julie Williams	UK
Member	Brigitte Keller-Stanislawski	Independent scientific expert appointed by the EC (scientific advice)
Expert	Rafe Suvarna	UK (effects table)

1.2. Initial-evaluation activities

Not applicable

1.3. Post-authorisation activities

1.3.1. Information from real-world clinical use of medicines

Collection and analysis of data and information from the real-world use of medicines is important in supporting assessment and decision-making on how medicines are used, their effectiveness and their safety. Use of epidemiological approaches is key and enablers include access to electronic health and insurance records, clear governance, and collaboration across stakeholders including academia. Data and information from the real-world use of medicines is a key enabler for access to new treatments and will support the PRIME scheme and Adaptive Pathway initiatives.

Key objectives

- Strengthen the input of the network and academic research as a source of data and information in PRAC assessments.
- Improve collaboration within the network to deliver focussed results of assessment of information from clinical use.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

- Review of lessons learnt from the pilot regulatory network study involving EMA, Spain and the United Kingdom, as a source of learnings for regulatory network's support to PRAC assessment with best evidence.

- In the light of the EMA landscaping of current infrastructure and data sources, contribute to the utilisation of real world data in PRAC procedures or via scientific advice and inform the development of internal processes and future study designs. See also 1.1.2.
- Provide recommendation on maximising utility of ENCePP network for PRAC assessments. See also 1.5.3.
- Informed by input of the ADVANCE project on vaccine benefit risk, make recommendations on any need for further guidance or capacity for vaccine surveillance.
- Contribute to the EMA initiative on patient registries and the Cross-Committee task force on registries:
  - by contributing to the development of guidance for stakeholders on common methodological aspects and governance of patient registries;
  - by contributing to the development of a core data set common to all registries;
  - by contributing to the development of disease-specific core data sets, initially in the context of dedicated workshops organised in 2017 for multiple sclerosis and cystic fibrosis registries.
- Explore the ability to utilise multiple eHR databases to support PRAC decision making.

PRAC topic leader(s): Marie Louise (Marieke) De Bruin; Dolores Montero Corominas; Julie Williams

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Nikica Mirošević Skvrce	HR
Member	Almath Spooner	IE
Alternate	Nadine Petitpain	LU
Member	Roxana Stefania Stroe	RO
Member	Ulla Wändel Liminga	SE
Member	Tatiana Magalova	SK
Member	Brigitte Keller-Stanislawski	Independent scientific expert appointed by the EC
Member	Stephen Evans	Independent scientific expert appointed by the EC
Alternate	Albert van der Zeijden	Representative of patients' organisations appointed by the EC
Expert	Nils Feltelius	SE
Expert	Philip Bryan	UK
Expert	Katherine Donegan	UK

1.4. Arbitrations and referrals

Not applicable

1.5. Pharmacovigilance activities

1.5.1. Optimising management and utility of reported adverse reactions

In 2017 the results of the audit on the EudraVigilance database on the additional functionalities adopted in December 2013 will be delivered to PRAC. EU legislation requires that PRAC gives its recommendation on the independent audit report to inform a decision by the EMA Management Board on whether the functionalities have been delivered. The consequence of this decision is that 6 months after the decision, MAHs will submit suspected ADR reports to EudraVigilance only and this will be in the new ISO data format.

Key objectives

- Enhanced adverse reaction collection and management system (EudraVigilance) that delivers better health protection through simplified reporting, better quality data and better searching, analysis and tracking functionalities. Enhanced detection of new or changing safety issues allows more rapid action to protect public health.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

- Issue recommendation on the independent final audit report of EudraVigilance.
- Prepare and support the go-live of the new EudraVigilance system.
- Review relevant outputs from IMI-WEB-RADR project.
- Finalise revision 2 of GVP module VI on 'Management and reporting of adverse reactions to medicinal products' regarding the simplification of ICSRs' submission by MAHs to EudraVigilance and the implementation of ICH-E2B(R3)[2] format.
- Initiate revision 3 of GVP module VI.
- Finalise the note for clarification on collecting and reporting information on off-label use in pharmacovigilance.

PRAC topic leader(s): Jean-Michel Dogné

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Jana Mlada	CZ
Member	Martin Huber	DE
Member	Claire Ferard	FR
Member	Carmela Macchiarulo	IT
Member	Sabine Straus	NL
Member	Hervé Le Louet	Independent scientific expert appointed by the EC
Expert	Edurne Lázaro	ES

1.5.2. Signal detection and management

Key PRAC tasks include prioritisation, assessment and recommendations on safety signals.

[2] ICH guideline on clinical safety data management :data elements for transmission of ICSRs

This key public health domain has delivered important outputs during PRAC's first four-years of activity and there is an opportunity to further enhance the effectiveness and efficiency of these activities based on important regulatory science results from the PROTECT project and learnings from operation of the processes to date. Furthermore, in 2017 MAHs will have access to EudraVigilance data and the process for the resulting signal management needs to be further defined.

Key objectives

- Apply evidence-based new methodologies for signal detection.
- Improve signal management processes based on experience.
- Achieve efficient and effective industry input to signal detection and management.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

Supported by the SMART working group:

- Implement time series forecasting for the detection of UIF reporting.
- Provide expert input into the revision of the signal detection methods guidance.
- Assess new methodologies for signal detection in EudraVigilance (e.g. statistical correction of bias).
- Provide expert input to revision 1 of GVP module IX on 'Signal management'.
- Deliver an update of the user guide on electronic reaction monitoring reports to reflect the ICH-E2B(R3) format.
- Improve current methodologies in signal detection with a particular focus on paediatrics.
- Develop a guide and checklist for assessors to assess SCARs.
- Prepare for efficient handling of signals from industry and engage with stakeholders.
- Develop strategic approach with regard to signal validation activities by industry.

PRAC topic leader(s): Sabine Straus; Lennart Waldenlind

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Martin Huber	DE
Member	Carmela Macchiarulo	IT
Alternate	Amelia Cupelli	IT
Member	Jolanta Gulbinovic	LT
Member	Zane Neikena	LV
Alternate	Menno van der Elst	NL
Member	Stephen Evans	Independent scientific expert appointed by the EC
Member	Hervé Le Louet	Independent scientific expert appointed by the EC
Alternate	Qun-Ying Yue	SE
Expert	Charlotte Backman	SE

1.5.3. Measuring the impact of pharmacovigilance activities

Measuring impact allows regulators to determine what activities are successful and which are not, and therefore identifies enablers and barriers for generating positive impacts which would contribute to an effective pharmacovigilance system. Measuring impact can also inform the review of the benefits and risks of individual medicines that have been the subject of major risk minimisation efforts (e.g. post referral procedure).

Key objectives

- Improve pharmacovigilance through feedback on impact of regulatory actions.
- Strengthen targeted product assessment through measuring the impact of regulatory actions taken.
- Achieve a better understanding of stakeholder views.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

Supported by the PRAC IG:

- Revise the PRAC impact strategy and work plan based on the recommendations of the workshop on impact of pharmacovigilance activities held in 2016.
- Review and act on the outcomes of case studies evaluating public health impacts of regulatory actions.
- Review the criteria for prioritising collaborative impact reseach.
- Provide expert advice on the research questions for impact studies.
- Contribute to establish robust methodologies for measuring health impacts of regulatory actions in collaboration with ENCePP. See also 1.3.1.
- Consider the revision of GVP module VIII on 'Post-authorisation safety studies' and GVP module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' to facilitate impact evaluation.
- Engage with patient communities and healthcare professional bodies to support impact research. See also 2.3.1.

PRAC topic leader(s): Marie Louise (Marieke) De Bruin; Dolores Montero Corominas; Sabine Straus; Almath Spooner; June Raine

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Alternate	Laurence de Fays	BE
Member	Martin Huber	DE
Alternate	Valerie Strassmann	DE
Alternate	Torbjorn Callreus	DK
Member	Maia Uusküla	EE
Member	Nikica Mirošević Skvrce	HR
Member	Carmela Macchiarulo	IT
Alternate	Amelia Cupelli	IT
Member	Ana Sofia Diniz Martins	PT

Member/alternate/expert	Name	Member state or affiliation
Alternate	Márcia Sofia Sanches de Castro Lopes Silva	PT
Member	Tatiana Magalova	SK
Member	Julie Williams	UK
Expert	Ingebjørg Buajordet	NO
Expert	Karl-Mikael Kälkner	SE

1.6. Other specialised areas and activities

1.6.1. Regulatory science

Certain medicinal product types bring specific issues that necessitate additional focus. This PRAC work topic channels Committee's expertise into the development and maintenance of product-type- and patient population- specific guidance. In addition, the PRAC supports initiatives and activities in the domain of regulatory science strategies.

Key objectives

- Strengthen pharmacovigilance by industry and regulators through dedicated guidance on specific product types and specific patient populations (e.g. genetic).

Activities in 2017

- Provide expert input (under the lead of CAT) in the revision of the 'Guideline on safety and efficacy follow-up – Risk Management of advanced therapy medicinal products' for release for public consultation and for finalisation as well as provide expert input in the RMP guidance template for ATMPs.
- Review the use of pharmacogenomics in PRAC regulatory procedures – referrals, signal evaluation, and risk management plans in order to evaluate progress in implementing the guideline on pharmacogenomics in pharmacovigilance.
- Strengthen collaboration with the PgWP via regular interactions (twice a year).
- Contribute and provide expert advice in pharmacovigilance objectives of EMA SciRS.

PRAC topic leader(s): June Raine

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Julie Williams	UK (ATMP)
Alternate	Qun-Ying Yue	SE (Pharmacogenomics)
Member	Brigitte Keller-Stanislawski	Independent scientific expert appointed by the EC (ATMP)
Member	Marie Louise (Marieke) De Bruin	Independent scientific expert appointed by the EC (regulatory science strategy)

2. Horizontal activities and other areas

2.1. Committees and working parties

Not applicable

2.2. Inspections and compliance

The PRAC plays an important role in the implementation of the human pharmacovigilance legislation in the domain of inspections and compliance to strengthen links between pharmacovigilance assessment, pharmacovigilance inspection and compliance-related aspects.

Key objectives

- Strengthening the links between assessment, compliance and pharmacovigilance inspections.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

- Advise on optimisation of procedures of non-compliance follow up.
- Support training on pharmacovigilance inspection.
- Provide expert input in revision 2 of GVP module II on 'Pharmacovigilance system master file'.
- Provide input in the drafting of the 'Union guidance on pre-authorisation pharmacovigilance inspections and routine pharmacovigilance inspection follow up'.
- Support the work of the PhV IWG–PRAC subgroup and contribute to the revision of the 'template from assessors to inspectors' and 'template for inspectors to assessors' for sharing inspection information.

PRAC topic leader(s): Julie Williams

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Maia Uusküla	EE
Alternate	Kimmo Jaakkola	FI
Alternate	Željana Margan Koletić	HR
Member	Julia Pallos	HU

2.3. Partners and stakeholders

2.3.1. Engage patients and healthcare professionals, communication with stakeholders

The engagement of patients and healthcare professionals is important for effective pharmacovigilance. Patients and healthcare professionals can be involved throughout the process from risk management planning, through reporting of suspected adverse drug

reactions, managing safety signals, assessments and decision e.g. through PSURs and referrals and on benefit risk communications. For PRAC, key engagement has included membership of the committee, patients' and healthcare professionals' reporting, involvement in ad-hoc expert groups and scientific advisory groups.

Key objectives

- Improve engagement of patients and healthcare professionals through availability of public hearings.
- Strengthen communication tools and coordination of safety information.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

- Hold first public hearing to high standard of engagement of patients and healthcare professionals.
- Provide expert input in revision 1 of GVP module XV on 'Safety communcation' post-public consultation.
- Strengthen collaboration with the PCWP and HCPWP via regular interactions. See also 1.1.2.
- Support EMA activities on personalised medicines, in particular by contributing to the PCWP/HCPWP workshop on the role of patients, consumers and healthcare professionals and following up on the workshop's outcome. See also 1.5.3.

PRAC topic leader(s): Albert van der Zeijden

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Dolores Montero Corominas	ES
Alternate	Caroline Laborde	FR
Member	Julia Pallos	HU
Member	Almath Spooner	IE
Alternate	Amelia Cupelli	IT
Member	Sabine Straus	NL
Member	Marco Greco	Representative of patients' organisations appointed by the EC
Member	Raymond Anderson	Representative of healthcare professionals appointed by the EC
Alternate	Kirsten Myhr	Representative of healthcare professionals appointed by the EC

2.4. Data-management support

Not applicable

2.5. Process improvements

The PRAC has an important role in continuous improvement of its processes. Key processes

through PRAC include risk management plans, post-authorisation study protocols and results, signal management, referrals, periodic safety update reports including single assessment procedures and variations. Observations from running these processes combined with feedback from stakeholders and outputs from the SCOPE project provide opportunities for such improvements.

Key objectives

- Continuously improve processes involving the PRAC.
- Increase the efficiency of PRAC plenary discussion.
- Strengthen the quality of PRAC recommendations.

Activities in 2017

PRAC activities to achieve the objectives set for this area:

- Continue to provide expert input into the review of content and process for PSURs/PSUSA and support its implementation (based on the roadmap for PSURs adopted by PRAC in 2015).
- Initiate revision 2 of GVP module VII on 'Periodic safety update report'.
- Support better guidance for assessors with the view to facilitate publication of PSUR assessment reports/summary.
- Support the work of the GPAG.
- Implement and operate the new format of GVP module V on 'Risk management systems'. See also 1.1.2.
- Continue to review quarterly workload and performance measures, making recommendations where appropriate.
- Support the established PRAC working group on efficiency and effectiveness for PRAC plenary meetings[3]: including quarterly measurement of quantitative and qualitative goals defined in the 'Best Practice Guide on on using PRAC plenary time efficiently and effectively' adopted in 2016.
- Provide expert advice on optimal role of PRAC for safety related variations.
- Advise on the implementation and maintenance of SCOPE output, embed/train and maintain in PRAC-related work.
- Adopt a training curriculum on operation of pharmacovigilance in the EU as part of the EU NTC activities.

PRAC topic leader(s): Martin Huber; Menno van der Elst

Other Committee participants:

Member/alternate/expert	Name	Member state or affiliation
Member	Jan Neuhauser	AT
Alternate	Marianne Lunzer	AT
Member	Maia Uusküla	EE

[3] Previously known as PRAC virtual group on making recommendations on efficiency and effectiveness improvements for PRAC plenary meetings

Member/alternate/expert	Name	Member state or affiliation
Member	Dolores Montero Corominas	ES
Member	Almath Spooner	IE
Member	Carmela Macchiarulo	IT
Alternate	Amelia Cupelli	IT
Member	Jolanta Gulbinovič	LT
Member	Ana Sofia Diniz Martins	PT
Alternate	Márcia Sofia Sanches de Castro Lopes Silva	PT
Member	Ulla Wändel Liminga	SE
Member	Tatiana Magalova	SK
Member	Julie Williams	UK
Member	Hervé Le Louet	Independent scientific expert appointed by the EC
Alternate	Albert van der Zeijden	Representative of patients' organisations appointed by the EC
Expert	Charlotte Backman	SE

3. List of acronyms and abbreviations

ADR: Adverse Drug Reaction

ADVANCE: Accelerated Development of Vaccine benefit-risk Collaboration in Europe

ATMP: Advanced Therapy Medicinal Product

CAT: Committee for Advanced Therapies

eHR: Electronic health records

EMA: European Medicines Agency

EC: European Commission

ENCePP: European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

EU: European Union

EU NTC: European Network Training Centre

GPAG: Granularity and Periodicity Advisory Group

GVP: Good Pharmacovigilance Practice

HCP: Healthcare Professional

HCPWP: Working Party with Healthcare Professionals' Organisations

ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

IMI: Innovative Medicines Initiative

ISO: International Organization for Standardization

ICSR: Individual Case Safety Report

MAH: Marketing Authorisation Holder

PASS: Post-Authorisation Safety Study

PCWP: Working Party with Patients' and Consumers' Organisations

PDCO: Paediatric Committee

PgWP: Pharmacogenomics Working Party

PhV IWG: Pharmacovigilance Inspectors Working Group

PRAC: Pharmacovigilance Risk Assessment Committee

PRAC IG: PRAC Interested Group on Impact

PRIME: Priority Medicines

PROTECT: Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

PSUR: Periodic Safety Update Report

PSUSA: PSUR Single Assessment

RADR: Recognising Adverse Drug Reactions

RMP: Risk Management Plan

SCARs: Serious Cutaneous Adverse Reactions

SciRS: Scientific Committees Regulatory Science Strategy

SCOPE: Strengthening Collaborations for Operating Pharmacovigilance in Europe

SMART: Signal Management Review Technical

UIF: Unexpected Increase in Frequency