EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC): Work Plan 2018

Adopted by the Committee on 31 January 2018

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The activities outlined in the PRAC work plan for 2018 have been agreed considering the respective business priorities, as well as the Agency's relocation as a result of the UK's exit from the EU and its impact on the EMA's business continuity, and may be subject to further review and reprioritisation in accordance with the business continuity plan of the Agency.

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 objective(s)

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

Activities in 2018

PRAC activities to achieve the objectives set for this area:

- Provide expert input in the finalisation (in cooperation with PDCO) of the revision of GVP P. IV - 'Product- or population-specific considerations: Paediatric pharmacovigilance' following public consultation.
- Provide expert input in the drafting 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 drafting of GVP P.III – 'Product- or population-specific considerations: pregnancy and breastfeeding'.

PRAC topic leader(s): June Raine

Other Committee participants:

Member/alternate/expert	Name	Member State or affiliation
Member	Dolores Montero Corominas	ES
Member	Kirsti Villikka	FI
Member	Ghania Chamouni	FR
Member	Jolanta Gulbinovič	LT
Member	Sabine Straus	NL
Member	Ulla Wändel Liminga	SE
Member	Thierry Trenque	Independent scientific expert appointed by the EC
Alternate	Kirsten Myhr	Representative of healthcare professionals appointed by the EC

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 objective(s)

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

Activities in 2018

PRAC activities to achieve the objectives set for this area:

- Provide input in identifying points for improvement following the review of first RMPs submitted with the new template and implementation of revision 2 of GVP module V on 'Risk management systems'. See also 2.5.
- Provide expert input to revision 3 of GVP module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' in order 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.
- Provide input in optimising 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.

PRAC topic leader(s): Martin Huber

Other Committee participants:

Member/alternate/expert	Name	Member State or affiliation
Alternate	Valerie Strassmann	DE
Alternate	Eva Segovia	ES
Member	Ghania Chamouni	FR
Alternate	Željana Margan Koletić	HR
Member	Almath Spooner	IE
Member	Carmela Macchiarulo	IT
Member	Jolanta Gulbinovič	LT
Member	Sabine Straus	NL
Member	Ana Sofia Diniz Martins	PT
Alternate	Márcia Sofia Sanches de Castro Lopes Silva	PT
Member	Ulla Wändel Liminga	SE
Alternate	Qun-Ying Yue	SE
Member	Julie Williams	UK
Member	Hervé Le Louet	Independent scientific expert appointed by the EC
Member	Brigitte Keller-Stanislawski	Independent scientific expert appointed by the EC

1.2. Initial-evaluation activities

Not applicable

[1] So called PRAC consultation in scientific advice procedures

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 objective(s)

- 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 2018

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 and measurement of public health impact of regulatory decisions.
- In the light of the EMA landscaping of current infrastructure and data sources, contribute to the identification and utilisation of real world data to support PRAC decision making and inform the development of PRAC procedures 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 and other projects on vaccine benefit risk and consider recommendations for vaccine surveillance.
- Contribute to the EMA initiative on patient registries and the Cross-Committee task force on registries:
  - by providing input to the development of a guidance on methodological aspects and governance of patient registries based on the workshops organised for cystic fibrosis, multiple sclerosis and chimeric antigen receptor (CAR) T-cell product registries.
  - In the context of regulatory procedures, by identifying and interacting with existing disease registries to facilitate the use or development of disease-specific core data sets enabling the generation of meaningful efficacy and safety data.
  - by strengthening the role of PRAC in innovative medicines taking into account progress made in delivering registries infrastructure - planned joint work with CAT and CHMP.
- Input into the report from the HMA/EMA task force on big data.

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
Member	Carmela Macchiarulo	IT
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

See under 2.5.

1.5. Pharmacovigilance activities

1.5.1. Optimising management and utility of reported adverse reactions

In November 2017 the full functionality of EudraVigilance became operational. This allows simplified reporting and better data access and analysis.

Key objective(s)

- 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 2018

PRAC activities to achieve the objectives set for this area:

- Provide expert input to the initiation of revision 3 of GVP module VI on 'Management and reporting of adverse reactions to medicinal products', taking into account outputs of the IMI-WEB-RADR project.
- Finalise the note for clarification on collecting and reporting information on off-label use in pharmacovigilance aiming at providing an overall guidance to MAHs on the collection and reporting of information on off-label use as ICSRs and in PSURs depending whether or not the off-label use of the medicinal product is considered to raise a safety concern and is included in the RMP as an important potential risk. This is conducted in line with

revision 2 of GVP module V on 'Risk management systems' and revision 2 of GVP module VI on 'Management and adverse reactions to medicinal products' finalised in 2017.

- Monitor the operations of the new EudraVigilance system functionalities and the experience gained as regards the impacted business processes.
- Agree on the EudraVigilance operational plan.
- Contribute to the data collection of Member States' experience and perspective in the EMA's and Member States' report to the European Commission on the use of the additional monitoring.

PRAC topic leader(s): Jean-Michel Dogné

Other Committee participants:

Member/alternate/expert	Name	Member State or affiliation
Member	Martin Huber	DE
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. This key public health domain has delivered important outputs during PRAC's first five-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, as of end of 2017 MAHs have access to EudraVigilance data and the new processes for managing MAHs' communication of signals raised from EudraVigilance will require an oversight.

Key objective(s)

- 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 2018

PRAC activities to achieve the objectives set for this area:

Supported by the SMART working group:

- Review operation of the signal reporting pilot by MAHs based on the new EudraVigilance functionality.
- Provide expert advice in the following areas: detection of UIF reporting, statistical correction of bias, and methodologies in signal detection with a particular focus on paediatrics.
- Update the guide and checklist for assessors to assess SCARs agreed in 2017 in light of the experience gained.

- Initiate a review of the risk of drug-induced hepatotoxicity in order to improve its management, based on work conducted by different delegations and PRAC independent experts.

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 (SMART)
Member	Hervé Le Louet	Independent scientific expert appointed by the
Expert	Charlotte Backman	SE

1.5.3. Measuring the impact of pharmacovigilance activities

Systematically measuring patient-relevant health outcomes of major regulatory interventions (e.g. post referral procedures) and key pharmacovigilance processes is shifting the focus of pharmacovigilance to those activities and regulatory tools that make a difference in daily healthcare.

Key objective(s)

- 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 2018

PRAC activities to achieve the objectives set for this area:

Supported by the PRAC IG:

- Establish a process for prioritising collaborative impact research topics based on agreed criteria.
- Provide expert advice on research questions for impact studies conducted by the EU regulatory network. See also 1.3.1.
- Provide expert input into the:
  - Conduct of independent collaborative impact studies of key regulatory actions.
  - Conduct of targeted studies of key pharmacovigilance processes (e.g. PASS).
  - Development of guidance on methodologies for measuring impact of pharmacovigilance activities.
  - Exploration of models for multi-stakeholder collaboration and sharing of impact relevant information.

- Establish a process for systematic consultation of patient and healthcare providers regarding the effectiveness of risk minimisation measures. See also 2.3.1.

PRAC topic leader(s): Valerie Strassmann; 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
Member	Maia Uusküla	EE
Member	Ghania Chamouni	FR
Member	Nikica Mirošević Skvrce	HR
Member	Almath Spooner	IE
Member	Carmela Macchiarulo	IT
Alternate	Amelia Cupelli	IT
Member	Zane Neikena	LV
Member	David Benee Olsen	NO
Member	Ana Sofia Diniz Martins	PT
Alternate	Márcia Sofia Sanches de Castro Lopes Silva	PT
Member	Julie Williams	UK
Member	Marieke De Bruin	Independent scientific expert
Expert	Francoise Willaume	BE
Expert	Simone Bergner	DE
Expert	Wiebke Seemann	DE
Expert	Silvia Duarte	PT
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 need further risk assessment. 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 objective(s)

- Strengthen pharmacovigilance by industry and regulators through dedicated guidance.

Activities in 2018

- 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' following public consultation for finalisation of the guideline.
- Review the use of pharmacogenomics in PRAC regulatory procedures (e.g. referrals, signal evaluation, and risk management plans) in order to evaluate progress in implementing the guideline on pharmacogenomics in pharmacovigilance.

- Contribute and provide expert advice regarding pharmacovigilance aspects in support of the development of EMA's regulatory science strategy.
- Support a review of the current guidance on pharmacovigilance and risk management for medicinal products for human use reviewed by EMA that are intended exclusively for markets outside of the EU[2].

PRAC topic leader(s): June Raine

Other Committee participants:

Member/alternate/expert	Name	Member State or affiliation
Member	Julie Williams	UK
Member	Sabine Straus	NL
Member	Ulla Wändel Liminga	SE
Alternate	Qun-Ying Yue	SE
Member	Brigitte Keller-Stanislawski	Independent scientific expert appointed by the EC
Member	Marie Louise (Marieke) De Bruin	Independent scientific expert appointed by the EC

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 objective(s)

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

Activities in 2018

PRAC activities to achieve the objectives set for this area:

- Advise on optimisation of procedures of non-compliance follow up.
- Provide expert input in the drafting of the 'Union guidance on pre-authorisation pharmacovigilance inspections and routine pharmacovigilance inspection follow up'.
- Support a pilot phase on the use of the 'template from assessors to inspectors' and 'template for inspectors to assessors' for sharing inspection information.

[2] Article 58 of Regulation (EC) No 726/2004 allows the CHMP to give opinions, in co-operation with the WHO on medicinal products for human use that are intended exclusively for markets outside of the EU

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 objective(s)

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

Activities in 2018

PRAC activities to achieve the objectives set for this area:

- Review the impact and value of the first PRAC public hearing.
- Support early engagement of HCPs and patients in risk minimisation through guidance. See also 1.5.3.
- Provide expert input on activities related to better communicating concepts and pharmacovigilance activities to the general public (e.g. use of infographics).
- Review and improve communications outputs of PRAC meetings: review the current content of the monthly PRAC highlights with a focus on how to communicate on signal management.

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/alternate/expert	Name	Member State or affiliation
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 objective(s)

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

Activities in 2018

PRAC activities to achieve the objectives set for this area:

- Consolidate assessors' and industry's feedback from PSUR roadmap exercise in preparation of revision 2 of GVP module VII on 'Periodic safety update report'.
- Review and support the implementation of improvements proposed by the GPAG as per its work plan 2018, namely on criteria to set the periodicity of PSUSA procedures; on scoping the PSUSA and EURD scientific grouping exercise; and on an estimation of workload related to PSUSA procedures.
- Implement and operate the new RMP template and implementation of revision 2 of GVP module V on 'Risk management systems'. See also 1.1.2.
- Monitor the adherence to the principles of the 'Best Practice Guide on using PRAC plenary time efficiently and effectively' dedicated to the improvement of the functioning of the Committee and regularly measure quantitative and qualitative goals defined in the BPG. This activity is supported by the 'PRAC working group on efficiency and effectiveness for PRAC plenary meetings'.
- Provide expert advice on optimal role of PRAC for safety related variations.
- Provide input in the development of points to consider to better support Member States in preparing a potential safety referral, in the context of the referral roadmap initiative on

sharing experience, optimising the preparation and conduct of safety referral procedures. See also 1.4.

- Adopt a training plan as part of the EU Operation of Pharmacovigilance Training curriculum and oversee training 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
Member	Maia Uusküla	EE
Member	Dolores Montero Corominas	ES
Member	Ghania Chamouni	FR
Member	Almath Spooner	IE
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

BPG: Best Practice Guide

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Products for Human Use

EC: European Commission

eHR: Electronic health records

EMA: European Medicines Agency ('Agency')

ENCePP: European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

EU: European Union

EURD: European Union Reference Dates

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

HMA: Heads of Medicines Agencies

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

ICSR: Individual Case Safety Report

IMI: Innovative Medicines Initiative

ISO: International Organization for Standardization

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

WHO: World Health Organisation