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EMA/153279/2016
Pharmacovigilance Risk Assessment Committee

PRAC criteria to prioritise impact research (Rev.1)

Background

To facilitate implementation of the PRAC Strategy on Measuring the Impact of Pharmacovigilance Activities[1] ('PRAC Impact Strategy') criteria for prioritisation of impact research topics have been established.

Scope

Impact research conducted under the remit of the PRAC Impact Strategy focusses on regulatory actions of major patient and public health importance, considering the nature, severity and seriousness of the risk, the magnitude of population exposure and the amount of public concern. Outcomes of risk minimisation measures (RMM) are monitored to evaluate the effectiveness of routine and additional RMM for specific medicinal products.

Objectives

The objectives for setting criteria to prioritise impact research are:

1. Guidance on the identification and selection of safety topics discussed at PRAC which require the generation of data to monitor outcomes of regulatory actions beyond the data submitted by marketing authorisation holders.
2. Informing the implementation of a selection process for PRAC topics eligible for impact research.

Criteria to prioritise topics for impact research

The decision on initiating an impact study addressing the objectives outlined above should be based on a clear understanding of the research question (i.e. which information about a safety concern is required), on a clear understanding of how the data generated by the study will be used (i.e. does the study reduce uncertainty, will provide answers to relevant questions), clear understanding of the feasibility of the study and generalisability of the study outcome for informed regulatory decision-making (Fig.1).

[1]EMA/590673/2020 Rev.2

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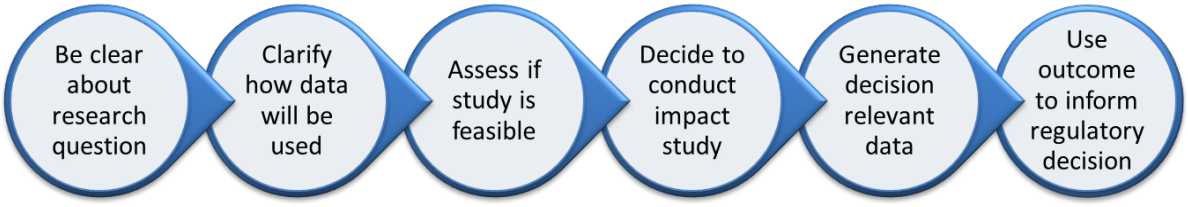
Figure 1: Key considerations for initiating impact studies.



The prioritisation of PRAC safety topics for impact research should consider the following three **key aspects**:

I. Public health impact of the regulatory action

- Nature and severity of the risk in the affected population.
- Magnitude of the risk (absolute and relative) in the population where the product is used, considering the size of the affected population across Member States and product use in the context of clinical guidelines.
- Amount of public concern, for example due to risk in vulnerable populations (i.e. children, adolescents, elderly, pregnant women), public debate on the regulatory decision or disagreement within the scientific community.
- Extent of the regulatory action (e.g. from label changes such as adding adverse reactions, warnings, or contraindications to additional risk minimisation measures, restricting the indication, suspension or revocation).

II. Delivery of decision relevant data

- Is the nature of the regulatory action amenable to research that will ultimately generate decision relevant data?
- Are suitable data sources and methodologies available in several Member States to allow for generalisability of results across different healthcare systems?
- Does the study fill gaps in knowledge and understanding of RMM effectiveness in a broader clinical context?
- Are MAH-sponsored RMM effectiveness studies requested and does the impact study provide evidence beyond the objectives addressed by MAH's planned or ongoing RMM effectiveness studies?

III. Regulatory follow-up

- Which further regulatory action may be warranted based on the generated data?
- Are there alternative causes (e.g. changes in clinical guidelines, reimbursement policies, events impacting healthcare) to be considered for interpreting impact study results?

Practical application

The PRAC Interest Group (IG) Impact has established a process[2] for prioritisation and regulatory follow-up of impact research, and to agree the research question and study objectives of impact research including methodological aspects in collaboration with the PRAC (Co-)Rapporteur and EMA.

[2] Process for PRAC prioritisation and regulatory follow-up of impact research (EMA/359640/2023 Rev.2.1)

Checklist for prioritisation of impact research topics

Criteria	Explanation	High/ Yes	Low/ No	Not clear	Comment
Public health importance of the regulatory action					
1. Nature and severity of the risk in target 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 target population	*How big is the risk in the treated, compared to the untreated population? What is the exposure in Member States where the product is marketed?*	☐	☐	☐	
3. Amount of public concern	*Are affected populations particularly vulnerable (children, adolescents, pregnant women, elderly people)? Is there public debate in the media? Is there disagreement about the safety concern in the scientific community?*	☐	☐	☐	
4. Extent of the regulatory intervention	*Is the regulatory intervention expected to lead to changes in patient and/or HCP behaviour or the way the product is used in clinical practice?*	☐	☐	☐	
Delivery of decision relevant data					
5. Regulatory action is amenable to research generating impact relevant data?	*Are there measurable effects of the regulatory intervention to evaluate if the RMM intended outcomes have been achieved in clinical practice or are there concerns of any unintended outcomes (e.g. switching, spill-over)?*	☐	☐	☐	
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 RMM effectiveness?	*Are there clearly defined knowledge gaps about RMM effectiveness or how the product is used in practice which could be answered by impact research?*	☐	☐	☐	
8. Does the study complement the evidence from MAH-sponsored RMM effectiveness studies?	*Are there ongoing or planned RMM effectiveness studies which provide evidence on the impact of the regulatory action? Are MAH(s) in the position to conduct a Joint study?*	☐	☐	☐	
Regulatory follow-up					
9. Which further regulatory action(s) may be warranted?	*Is there room for further regulatory action and which results are expected to lead to which types of regulatory action?*	☐	☐	☐	
10. Are there alternative causes to be considered for interpreting results?	*Are there alternative causes (e.g. changes to clinical guidelines, reimbursement policies) that could influence the measured outcomes?*	☐	☐	☐	
Topic prioritised for impact research: ☐ **Yes** ☐ **No**		**Comment:**			