EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Inspections and Human Medicines Pharmacovigilance Division

Initiative for patient registries

Strategy and pilot phase

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1. Background

1.1. Problem statement

Regulators may require marketing authorisation applicants/holders (MAAs/MAHs) to establish a registry in order to measure the safety or efficacy of individual products in routine clinical practice. Various challenges with regard to registries currently exist, including a lack of sustainability and a lack of harmonised protocols and data structures. In addition, existing disease registries or other data sources established at national or international levels by physicians' associations or national agencies are not fully utilised, a situation that may lead to duplication of efforts and inefficiencies. Therefore, the need has been identified to explore opportunities to improve this situation by making better use of existing registries and facilitating the establishment and utility of new registries as a source of high-quality post-authorisation data for regulatory decision-making.

1.2. Definitions

The term registry is used in this context to indicate an organised system that uses observational methods to collect uniform data on a population defined by a particular disease, condition, or exposure, and that is followed over time. A *disease registry* includes patients based on diagnosis whereas *product registries* include patients based on the treatment they receive. Disease registries therefore gather insights in natural history and clinical aspects of diseases and allow comparison between different treatments prescribed for the same indication. The distinction between the two approaches is however imprecise as patient populations covered by registries can vary which makes it difficult to circumscribe the concept of registries to being only disease-based or product-based. Therefore, the term *patient registry* is used in this document, taking into account that the design of a registry (including the definition of the patient population and the outcomes to be measured) should be primarily based on the objectives and the planned analyses as described in a protocol.

1.3. Objective of the initiative

The main objective of the initiative for patient registries is to facilitate the use of existing patient registries and facilitating the establishment and utility of new registries if none are available or adequate, in order to collect and analyse high quality data informing regulatory decisions.

The initiative for patient registries includes two components: a strategy on registries and a pilot phase to test whether this strategy better supports MAAs/MAHs to meet regulators' (and potentially other stakeholders') needs for data and information.

2. Cross-Committee Task Force on Registries

A Cross-Committee Task Force on registries was established in late 2014. The Cross-Committee Task Force is composed of representatives of the following EMA scientific committees and working parties:

- Committee for Medicinal Products for Human Use (CHMP)
- Pharmacovigilance Risk Assessment Committee (PRAC)
- Committee for Orphan Medicinal Products (COMP)
- Committee for Advanced Products (CAT)
- Paediatric Committee (PDCO)
- Scientific Advice Working Party (SAWP)
- Patients and Consumers Working Party (PCWP)
- Healthcare Professionals Working Party (HCPWP)
- Rheumatology/Immunology Working Party (RIWP)

In addition, members of the Task Force include representatives from the European Commission, several experts from National Competent Authorities, and the work of the Task Force is supported by EMA staff. The chairperson of the Task Force is Dr. Peter Mol (SAWP).

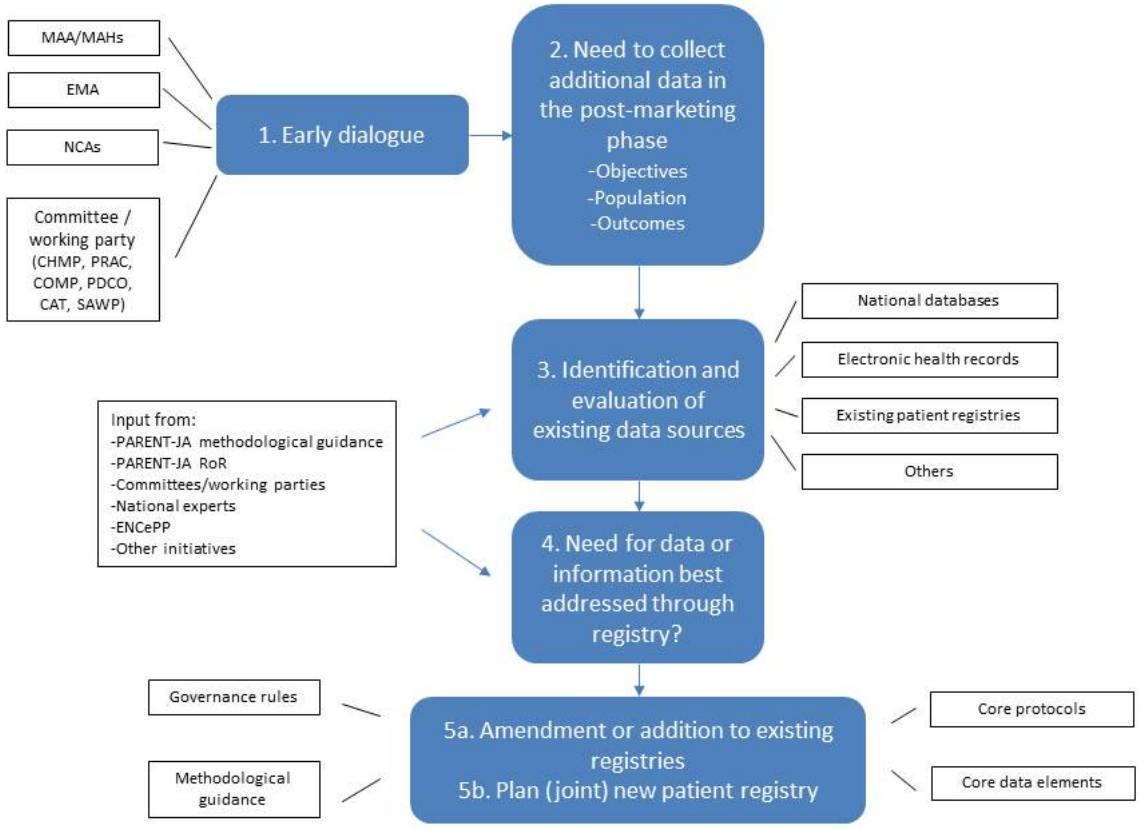
The Task Force's mandate is to support the development of the strategy outlined in this paper and to provide advice and support to EMA committees on methodological aspects of the approach – including the conduct of the pilot phase. The Cross-Committee Task Force will not have a role in assessment or decision-making on specific medicinal products.

3. Components of the strategy

3.1. Main components

The key element of the strategy on registries is facilitating the use of existing patient registries within the current legal and regulatory framework for medicinal products. The strategy is a capacity-building exercise and will not interfere with the regulatory process. The main components of the collaborative approach on registries are displayed in Figure 1.

Figure 1 Proposed approach on registries.



Acronyms: MAA: marketing authorisation applicant, MAH: marketing authorisation holder, EMA: European Medicines Agency, NCA: national competent authority, PARENT JA RoR: Register of Registries developed by the PARENT Joint Action,[1] ENCePP: European Network of Centres for Pharmacovigilance and Pharmacoepidemiology[2]

The strategy proposed starts from the stage where an advice or a request has been expressed pre- or post-authorisation by a committee (CHMP, PRAC, COMP, PDCO, CAT) to a MAA/MAH of the need to collect additional data post-authorisation, or a MAA/MH has itself identified the potential need to collect data. The approach includes five steps:

1. Early dialogue with MAAs/MAHs;

[1] http://patientregistries.eu/
[2] http://www.encepp.eu

2. Definition of data collection characteristics by or with the committee or working party: objectives, population, outcomes, any hypotheses to be tested; as appropriate, input from different stakeholders may be considered;
3. Identification of existing data sources that could fulfil the objectives, and evaluation of their adequacy by MAAs/MAHs in collaboration with regulatory authorities and data source custodians;
4. Need for data or information that is best addressed through a registry;
5. a. Amendment or addition to existing registry/registries;
5. b. Definition of core components of a new registry.

The output of the process as described above would be a study protocol on the use of an existing registry, or creation of a new one, to be submitted by a MAA/MAH to the competent authority. It is however expected that a dialogue between the MAA/MAH, the competent authority and the registry custodian (and other stakeholders as appropriate) would take place to support the development of the study protocol.

This strategy recommends that a discussion on the possible need for additional data collection in the post-marketing phase should be started as early as possible. This dialogue could be initiated pre-or post-authorisation. Pre-authorisation discussions could be triggered by the PRAC/CHMP Rapporteurs, by the Applicants in the context of an ongoing evaluation procedure, or at an earlier stage through requests for Scientific Advice. Post-authorisation discussions may be triggered in the context of risk management planning for investigation of a risk or exploration of missing information, or as a follow-up of regulatory procedures in which case the PRAC will be involved in the definition of objectives and key elements of the protocol. In addition, post-authorisation studies voluntarily initiated by MAHs may be evaluated subject to Scientific Advice regarding their objectives and methods.

The identification of existing data sources that could be used will primarily be the responsibility of the MAA/MAH but within this strategy, such identification may be enhanced through dialogue with the (co-)Rapporteurs, Member States, Committees and working parties (such as the Patient & Consumers Working Party and the Health Care Professional Working Party). In cases where existing patient registries are considered potentially adequate, the possibility of collaborations or joint efforts could be explored, facilitated by standard governance principles based on an agreed code of conduct (such as the ENCePP code of conduct). EMA may facilitate initial interaction between stakeholders as part of the strategy.

Following an evaluation of existing data sources, regulators and MAAs/MAHs may agree that these data sources would not adequately fulfil the need for additional data. In such a case, a new patient registry may need to be established. Any new registry should be based on standard methodological approaches including standard core components of a protocol and core data elements, such as those developed by the PARENT-Joint Action.

In addition, the extent to which patient registries – either existing or new – might be suitable for answering health technology assessment (HTA) –related questions, when feasible and appropriate, could be explored through parallel scientific advice as well if such a need would be identified by the MAA/MAH.

4. Pilot phase

4.1. Objectives of the pilot phase

A pilot phase of the strategy has been developed to test whether this strategy better supports MAAs/MAHs to meet regulators' (and potentially other stakeholders) needs for data and information. Thereby, the pilot phase would evaluate the extent to which this approach facilitates the collection of high quality data supporting the regulatory decision-making process. For a number of diseases or products, the approach as it is outlined in Figure 1 would be applied and tested. The aim of the pilot phase is not to make decisions about the need for a registry or to accelerate the granting of a market authorisation but to test whether such a planned, collaborative approach is successful in facilitating robust data collection.

4.2. Planning

The pilot phase will be coordinated by the EMA in collaboration with the Cross-Committee Task Force on Registries. The choice of the candidate diseases/products to be included in the pilot phase will be driven by the precise objectives of the pilot phase in terms of methodological tools and approach to be tested (e.g. existing registry or need for new registry, rare or common disease, registry with combined regulatory and HTA purposes), as well as expressions of interest from MAAs/MAHs, e.g. based on preliminary discussions in a scientific advice procedure or in a committee.

The start of the pilot phase will be dependent on the timing of the regulatory procedure for the products that will participate in the pilot phase.

4.3. Evaluation

For each case study, the activities performed during the pilot phase will be evaluated against its objectives. Lessons learnt from case studies will be discussed by the Cross-Committee Task Force and lead to recommendations for facilitating the conduct of registries beyond the pilot phase.