



13 February 2017
EMA/69716/2017
Inspections, Human Medicines, Pharmacovigilance and Committees Division

Patient Registries Workshop, 28 October 2016

Observations and recommendations arising from the workshop

Table of content

1. Executive Summary	3
2. Background – The EMA Registry Initiative.....	5
2.1. Chronology of EMA Registry Initiative activities	5
3. Patient Registries Workshop, 28 October 2016	7
3.1. Introduction.....	7
3.2. Benefits of patient registries	8
3.2.1. Observations.....	8
3.2.1.1. Benefits for regulators	8
3.2.1.2. Benefits for Health Technology Assessment (HTA) and payers	8
3.2.1.3. Benefits for industry	9
3.2.1.4. Benefits for public health authorities	9
3.2.1.5. Benefits for clinicians and researchers	9
3.2.1.6. Benefits for patients.....	10
3.2.2. Recommendations	10
3.3. Benefits and challenges of collaborations.....	11
3.3.1. Observations.....	11
3.3.1.1. Introduction	11
3.3.1.2. Collaboration between registries	11
3.3.1.3. Collaborations between regulators and registry holders	12
3.3.1.4. Collaborations between registries and industry	12
3.3.1.5. Involvement of HTA bodies and payers	13
3.3.1.6. Involvement of patients.....	13
3.3.2. Recommendations	13
3.4. Technical challenges	14
3.4.1. Observations.....	14
3.4.1.1. Data platform.....	14
3.4.1.2. Core data elements.....	14



3.4.1.3. Data quality and completeness	15
3.4.1.4. Data analysis	16
3.4.2. Recommendations	16
3.5. Governance	17
3.5.1. Observations.....	17
3.5.1.1. General aspects.....	17
3.5.1.2. Data ownership	17
3.5.1.3. Data sharing	17
3.5.1.4. Data pooling and analysis	18
3.5.1.5. Informed consent	18
3.5.1.6. Reporting of adverse drug reactions	18
3.5.1.7. Timelines.....	18
3.5.2. Recommendations	19
3.6. Sustainability.....	19
3.6.1. Observations.....	19
3.6.2. Recommendations	20
4. Conclusions and next steps	20
Annex 1. Programme of the Patient Registries Workshop, 28th October 2016	22
Annex 2. Acronyms.....	24

1. Executive Summary

Patient registries collect information about individuals sharing health-related characteristics, for example, a particular disorder, a treatment or a procedure. While randomised controlled trials typically provide the primary evidence supporting marketing authorisations for new medicines, the patients studied may not be fully representative of everyone ultimately receiving the medicine and the trials may provide limited information about the natural history of the disorder. Information collected in patient registries is potentially of value for filling these evidence gaps in certain situations and for providing post-marketing safety and effectiveness information. Multiple stakeholders stand to benefit from using registry information in this way including patients, healthcare providers, policy makers, manufacturers and healthcare regulators.

In 2014, the EMA commenced a Registry Initiative aiming to optimise the use of registries in supporting medicines authorisations. Establishing a strategy of early engagement between marketing authorisation applicants and registry holders and a task force to support activities, a pilot phase was undertaken aiming to understand the barriers and enablers in using registries to support marketing authorisation applications and to inform the development of recommendations to optimise their use. The perspectives of multiple stakeholders including registry holders, patients, the pharmaceutical industry, health technology assessment representatives and regulators were then explored in a Registries Workshop held on the 28th October 2016. Participants described the challenges and barriers to collaboration, identified potential solutions and made recommendations to address identified limitations and to develop the next steps of the EMA Registry initiative.

This report sets out participants' observations and recommendations in five theme areas: benefits of patient registries and obstacles to be overcome, benefits and challenges of collaborations, technical considerations, governance, and sustainability.

Core recommendations in each area included the following:

Benefits of patient registries and obstacles to be overcome

- To facilitate improved stakeholder collaborations, incentives are needed for registry holders to collect data to meet needs that are not directly their own.
- Technical challenges, especially of interoperability between registries, could be overcome with standardisation of data collection, coding, and analytic procedures as well linkage of registry data to external data sources, for example prescriptions.
- Good governance procedures should be developed to safeguard transparency, accessibility of data and independence of registries and to provide clarity about legal and regulatory requirements relating to patient registries.

Benefits and challenges of collaborations

- Studies that might involve registries, including for post-marketing purposes, should be planned early in product development.
- All stakeholders, including regulators, should communicate directly with each other when a study is being planned to agree on outcomes and recognise limitations.

Technical considerations

- Regulators should provide guidance to registry holders on the core data elements and quality parameters that would be an acceptable standard for supporting regulatory decision-making.
- Data collection, quality and interoperability should be improved through use of standardised data fields, dictionaries, and coding.
- Technological advances should be exploited to increase patient participation and to improve the value of registries in clinical care by facilitating linkage with other healthcare datasets, data pooling and analyses.

Governance

- Consents obtained from patients should be clear about data sharing and access for stakeholders other than the registry holders with appropriate consents in place for levels of data sharing.
- Good governance principles should be established to guide interactions between registries, industry and regulators addressing data privacy, ownership, financial aspects, transparency, commercial-in-confidence agreements, and accessibility of data for public health purposes.

Sustainability

- Sustainability should be based on a development model, a professional management structure and the development of clear partnership with stakeholders to safeguard independence.

To help realise the recommendations, the EMA in collaboration with the Cross-Committee Task Force on Patient Registries will initiate activities including the following:

- Explore mechanisms for facilitating systematic consideration by regulators and marketing authorisation applicants of the need for registries and establish mechanisms to interact directly with registry holders at appropriate points in the authorisation process.
- Share and disseminate information through its networks on disease registries to support stakeholder collaborations.
- Recommend governance principles and standards to apply to stakeholder interactions.
- Make recommendations on core data elements and quality parameters that would be considered an acceptable standard for supporting regulatory decision-making.
- Identify methodological and technical guidance needs of registry holders in addition to that already available.
- Collaborate with patients' associations to investigate relevant patient-reported outcomes that could be collected by registries.
- Explore measures that could contribute to registry sustainability aside from those being already undertaken by individual registry holders/groups.

As next steps, the EMA is committed to develop and publish an implementation plan to support the delivery of the activities outlined above. The Cross-Committee Task Force will review and publish the Patient Registries Mandate including the new governance, together with the updated strategy and communication channels that will be used to fulfil the mission of the Patient Registry Initiative.

2. Background – The EMA Registry Initiative

The European Medicines Agency Registry Initiative is based on the recognition of the need for information across the life cycle of medicinal products in order to better understand disease characteristics and progression, to understand current clinical care and collect data on the effectiveness and safety of medicines beyond what is available from the evidence supporting the marketing authorisation. Such evidence is generally derived from randomised controlled studies, which in order to investigate efficacy, are conducted in tightly defined populations and often exclude patients in whom the medicine may be used when the product is marketed. As a result, the EMA may require the marketing authorisation applicant or holder (MAA/MAH) to provide evidence on disease outcomes, effectiveness and safety unavailable from clinical trials. There are multiple real world evidence sources of potential value, including registries, typically patient registries as defined in the EMA's [Patient Registry Initiative](#).

The EMA wishes to facilitate interactions between registry co-ordinators and potential users of registry data (including industry) at an early stage of the drug development during the marketing authorisation process and post-authorisation. The Registry Initiative aims to optimise and facilitate, and thereby increase, the use of existing disease registries to create more comprehensive, flexible and sustainable resources. In addition, the initiative aims to map ongoing projects at national and international levels. Where a study is required but no suitable disease registry exists, the initiative aims to support the relevant stakeholders to create a new registry based on a standard methodological approach such as that created by the [PARENT JA](#). This includes the application of standard core data elements and standardised protocols to ensure that the new registry has wide applicability.

2.1. Chronology of EMA Registry Initiative activities

* 2014: EMA Registry strategy initiated

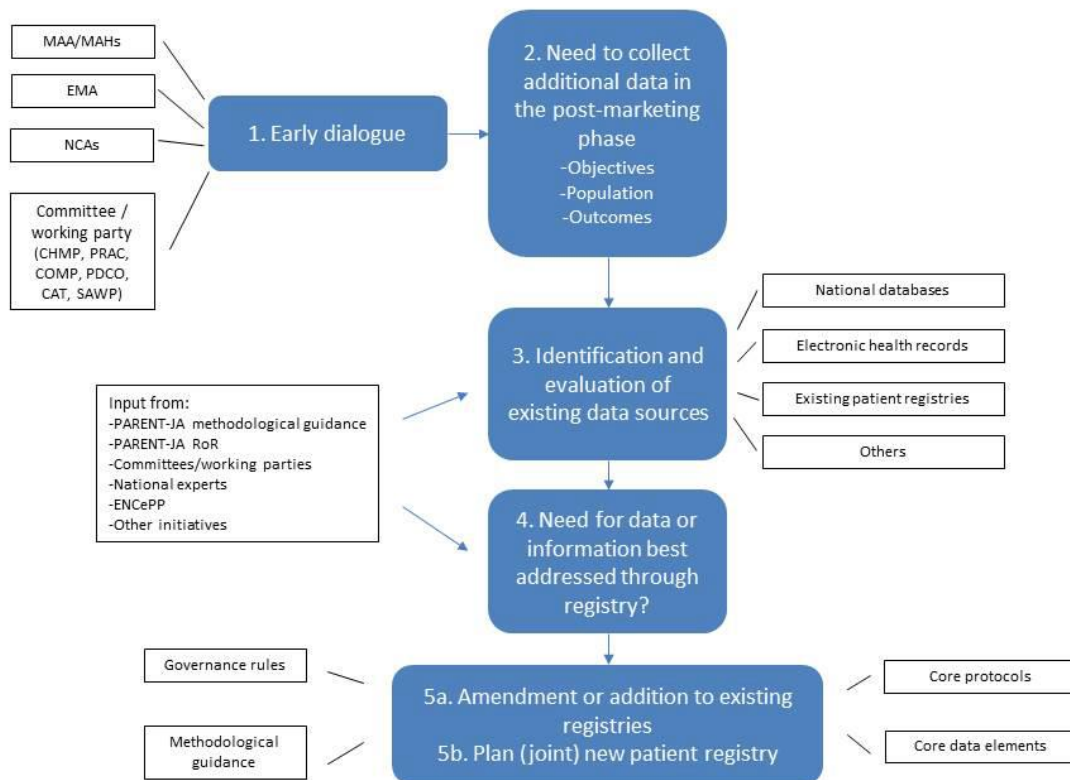
The strategy starts from the stage where an advice or a request has been expressed pre- or post-authorisation by a committee (the Committee for Medicinal Products for Human Use (CHMP), the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee for Orphan Medicinal Products (COMP), the Committee for Advanced Products (CAT), the Paediatric Committee (PDCO), or the Scientific Advice Working Party (SAWP)), 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
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. Identification of the need for data or information that is best addressed through a registry
5.
 - a. Amendment or addition to existing registry/registries
 - b. Definition of core components of a new registry.

The strategy is outlined in the [Patient Registry Initiative](#). The Figure below illustrates the strategy.

The output of the process as described above would be a study protocol based 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 holder (and other stakeholders as appropriate) would take place to support the development of the study protocol.



*** December 2014: Cross-Committee Task Force on Patient Registries established**

The Task Force’s mandate is to support the development of the registry strategy (above) 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. The work of the Task Force is supported by EMA staff.

The Task Force is chaired by Peter Mol (SAWP) and composed of representatives of the following EMA scientific committees and working parties: CHMP, PRAC, COMP, CAT, PDCO, SAWP, Patients and Consumers Working Party (PCWP), Healthcare Professionals Working Party (HCPWP) and Rheumatology/Immunology Working Party (RIWP).

The Task Force also includes representatives from the European Commission and several experts from National Competent Authorities.

***September 2015: Registry Initiative Pilot Phase commenced**

The intention of the pilot phase was 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 the Figure 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.

***Outcomes of Pilot Phase by November 2016**

A total of 17 expressions of interest or requests for information have been received so far, 8 from pharmaceutical companies and 9 from registry holders. Of the eight topics discussed with pharmaceutical companies, four concerned products under evaluation for a marketing authorisation (of which two were authorised by December 2016), two concerned products in development, one concerned a regulatory question and one concerned general aspects of interactions with existing registries. The discussions mainly addressed the following aspects:

- with pharmaceutical companies: relevance and feasibility of using existing disease registries to answer regulatory questions, issues regarding collaboration with existing registries, such as data quality and data sharing, and data elements to be included in new registries;
- with registry holders: regulatory requirements as regards data elements, data quality and processes (e.g. reporting of adverse drug reactions), and how to fulfil them in order to allow collaboration with pharmaceutical companies, and options for ensuring sustainability of the registry.

The Pilot phase is an important source of learning and knowledge about enablers and barriers to using existing registries to answer regulatory questions and to establishing new registries. This knowledge will support development of recommendations to improve the use of registries.

3. Patient Registries Workshop, 28 October 2016

3.1. Introduction

This workshop brought together multiple stakeholders including registry holders, industry, health technology assessment (HTA) representatives and regulators to discuss the challenges and barriers to collaboration and identify specific solutions.

The workshop aimed to:

- Identify the challenges faced by existing non-industry sponsored registries and industry when collaborating
- Understand the technical challenges presented by disparate datasets and find possible ways forward
- Identify concrete solutions to better facilitate cooperation, avoid duplication and facilitate timely collection of relevant data.

This document provides a synopsis of the observations made during the workshop based on the presentations delivered (see agenda in Annex 1). Based on the subsequent panel discussions, it gives recommendations intended to address the limitations identified and develop the next steps of the EMA Registry initiatives. The topics discussed during the workshop are divided into five main themes:

1. Benefits of patient registries
2. Benefits and challenges of collaborations
3. Technical aspects
4. Governance

5. Sustainability.

The presentations will be published on the EMA website together with the final version of this document (video-recordings are already available).

3.2. Benefits of patient registries

3.2.1. Observations

Patient registries have a utility for many stakeholders. They often represent a unique source of evidence supporting the authorisation of medicinal products and their availability to patients.

3.2.1.1. Benefits for regulators

Registries provide evidence that is relevant to the life-cycle assessment of medicinal products from basic research to the evaluation of their effectiveness and safety in clinical practice. More specifically, they may:

- provide robust data on disease epidemiology, patients' characteristics and current standard of care,
- represent a source population for the conduct of randomised clinical trials, and enrich data by contributing with linked data on specific outcomes,
- facilitate pragmatic trials and post-authorisation studies,
- provide information on drug utilisation related to defined patient groups, and
- provide for the follow-up of small patient populations.

On the other hand, regulators can also support registries. They may

- highlight important scientific questions that registries should be able to answer to support patient access to new medicines,
- create understanding among registries for regulatory needs, including MAH obligations,
- support quality improvement,
- facilitate multinational collaboration between registries, and
- provide common guidelines on the data elements needed and on quality.

3.2.1.2. Benefits for Health Technology Assessment (HTA) and payers

Incorporating data from clinical practice into the drug development process is also a growing interest from HTA bodies and payers since reimbursement decisions can benefit from methods which are able to estimate and predict relative effectiveness of treatments at the time of product launch. A concrete example of where registries can provide clinical practice data is to support the building of predictive models that incorporate data from both RCTs and registries to bridge the efficacy-effectiveness gap, i.e. to generalise results observed in RCTs to a real-world setting. Collecting relevant HTA data in early development and planning post-authorisation data collection, facilitated as needed by an early dialogue with industry, may therefore support rapid relative effectiveness assessment and decision-making on drug pricing and reimbursement. In this context, the EUnetHTA project has issued guidelines for the definition of the research questions and the choice of data sources and methodology that will support the generation of post-launch evidence by registries. A workstream of the EUnetHTA Joint Action 3 has issued several documents:

- Criteria to select and prioritise health technologies for additional evidence generation
- A position paper on the definition of the research questions
- A position paper on the choice of data sources and methodology that will support the generation of post-launch evidence.

A workstream of the EUnetHTA Joint Action 3 will focus more specifically on the use of registries as a source of evidence for post-launch evidence generation, including the development of standard tools for registries. For medicinal products, these actions are planned to be done in cooperation with EMA.

3.2.1.3. Benefits for industry

Data needed by regulators, HTA bodies and payers for decision-making may be part of routine development programmes established by pharmaceutical companies or can be specifically requested as post-authorisation commitments or obligations. The usefulness of patient registries for industry therefore is at least partly driven by the needs of regulators, HTA bodies and payers. At an early stage in drug development, patient registries may provide a characterisation of the target population according to co-morbidities, medication use, complications and safety concerns, data on disease epidemiology in terms of prevalence, incidence and natural outcomes, and a measure of the baseline risks associated with standards of care. In the context of clinical trials, patient registries may allow the capture of patients with similar demographic and clinical characteristics to the clinical programme under study (i.e., disease severity, age group, median/mean follow-up time, comorbidities) and provide a comparator sub-cohort for the exposed cohorts. Such an approach (as used in the UK Biologics registry) may allow a valid characterisation of the safety and efficacy of the drug under study. Through post-authorisation follow-up, safety data (including those required to be collected in the risk management plan) and effectiveness outcomes can also be collected, provided adequate information is available.

3.2.1.4. Benefits for public health authorities

For public health authorities, establishing patient registries may allow an assessment of outcomes of therapies and their determinants, effectiveness and safety of new interventions, changes induced by new therapeutic guidelines and continuous improvement in clinical practice. For example, the UK Renal Registry collects an extensive dataset (including demographics, data on the renal disease, co-morbidities, treatments, laboratory results and patient-reported outcomes) on all renal replacement therapy (RRT) patients in the UK (7,000 incident and 50,000 prevalent patients/ year). Laboratory and medication data are collected in real time and fed back to patients and clinicians (with the patient's consent). Data can be linked to primary care data and hospital episode statistics and have recently started to be used in clinical trials. Similarly in the Belgian Healthdata.be project, data capture from primary sources of health care and registries permits maximum re-use of such data. Linkage with previously collected data and timely feedback within a single reporting environment aims to reduce the administrative burden and increase quality of care and quality of research. The longitudinal structured clinical data of the Swedish Multiple Sclerosis (MS) registry is a tool to understand important aspects of the disease such as disease course, prognostic factors (including genetics) and heterogeneity, to validate biomarkers and results of magnetic resonance imaging, to understand the potential of personalised medicine and the importance of lifestyle factors, to address the long-term safety and effectiveness of disease modifying therapies, and to improve the design of healthcare services.

3.2.1.5. Benefits for clinicians and researchers

Many patient registries were originally established by clinicians and researchers to measure the use, effects and safety of medications.

For example, the European Society for Blood and Marrow Transplantation (EBMT) registry enables the monitoring of the impact of novel drugs and clinical care and the comparison of interventions through both clinical trials and non-interventional prospective studies. In the area of rare diseases, the RD-Connect project provides an example of an integrated platform which connects databases, registries and biobanks and uses clinical bioinformatics for research in which complete clinical profiles are combined with -omics data. The Pharmachild registry for patients with juvenile idiopathic arthritis (JIA) has been built in such a way that it provides a research and clinical service to the paediatric rheumatology community through immediate feed-back via the system, allowing its use to support routine clinical care and decision-making on patient management based on quantitative data.

3.2.1.6. Benefits for patients

Patients are at the heart of registries and should be the first beneficiaries of the outputs of the data collected throughout the life cycle of a product. Like other registries established by or with patients' associations, the International Niemann-Pick Disease Registry (INDPR), is owned by an international patient association, integrates clinical and patient-reported data with the purpose of understanding the natural history and impact of the disease, providing a single universal resource on the disease (i.e. avoiding multiple registries) and providing independent support for post marketing surveillance.

3.2.2. Recommendations

These examples of patient registries demonstrate their capacity to provide data throughout the life-cycle of medicinal products from drug development to the post marketing phase. Duplication of effort to collect data within disease areas should be avoided and different stakeholder needs should be assessed at an early stage and addressed in the registry design.

For example, reimbursement authorities may need registry data to inform decisions about reimbursement and evaluate outcomes of reimbursement decisions. Thus in this multi-stakeholder environment with limited resources, establishing in a structured way data sources which can provide the wide range of data needed by different stakeholders should become the norm rather than the exception.

A number of obstacles restricting the ability of existing registries to meet several stakeholders' needs were highlighted during the workshop and should be addressed in the future. They are summarised below and further described in the following sections of this document:

- **Challenges of collaborations:** Better collaborations between registry holders, pharmaceutical companies and regulatory/reimbursement authorities require incentives for registry holders to collect data to meet needs that are not directly their own;
- **Technical challenges:** Standardised protocols with clear objectives and endpoints, standards for data completeness, quality, analytic procedures and reporting, more harmonised data structure and coding and the possibility of linking registry data to external data sources;
- **Governance:** Procedures that safeguard transparency, accessibility of data and independence of registries, better adaptability to accommodate future changes in needs, more clarity about legal and regulatory requirements (such as for the reporting of adverse events and adverse reactions) and timeliness for providing data;
- **Sustainability:** long term sustainability of patient registries.

3.3. Benefits and challenges of collaborations

3.3.1. Observations

3.3.1.1. Introduction

Registries are costly and can take years to establish and grow. It is therefore essential that effective collaborations are put in place between all parties involved in the creation and maintenance of patient registries to avoid duplication of efforts as noted above and to facilitate effective use of the data collected. Research conducted by the Patient Registries Initiative (PARENT Joint Action) has shown that cross-border re-use of registry data may serve many purposes, including drug regulation, public health (for example, surveillance, alerts, identification of best and cost-effective practices, bioterrorism threats), research (risk factor studies, genetic research, clinical and therapeutic research), and health technology assessment. However, it has also found that data exchange or aggregation across organisations, regions and countries for secondary purposes is often difficult to perform for reasons that include lack of collaborations with resulting inability to aggregate data, limited data access for research purposes, insufficient data dissemination, differences in modes of data collection, content, semantics and quality of data, and unstable funding.

Examples of multi-stakeholders collaborations presented during the workshop show that good collaborations may be successful and result in effective data integration. The RD-Connect project on rare diseases has established an integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research. An essential component of this work is interaction with the rare disease community to facilitate patient input and patient access to data. The TREAT-NMD registry in the neuro-muscular field has been built as a collaboration between academia, patient organisations and industry. It aims to link all existing registries to a centralised global registry and now includes more than 14,000 patients from 40 countries. The International Niemann-Pick Disease registry (INPDR) has been successful in collaborations with patients and their families, clinicians, researchers, pharmaceutical companies, regulators, HTA bodies and funders. In the field of multiple sclerosis, the Swedish registry is part of a rich research infrastructure allowing linkage of data from health insurance, the national patient registry, the pharmacy database, Statistics Sweden, health-related public registries, laboratory data, genomic data, life-style and exposures data. Interactions between different partners involved in registries are further described below.

3.3.1.2. Collaborations between registries

Wherever possible in collaborations between registries, pooling of raw or aggregated data is preferable to increase the study population size for statistical analyses or detection of rare events. For example the Big Multiple Sclerosis Data network includes registries from several countries and offers them an opportunity to collaborate on research based on pooled data. It acts as a multiplier for MS research for the member registries and external partners and provides an opportunity to obtain industry sponsorship and apply for EU funding. This collaboration is supported by a strong governance organisation involving representatives of each registry. In the field of cancer, the European Network of Cancer Registries (ENCR) promotes collaborations between population-based cancer registries, with coordinating activities and mapping of priorities for research topics. The European Bone Marrow Transplantation (EBMT) registry provides a number of services to registry users, including monitoring quality control of daily clinical care, a scientific and educational program and market surveillance in collaboration with health authorities. Benchmarking of clinical outcomes for every transplant program is being explored with a view to providing this service in the future.

Non-interventional studies have been performed based on scientific interest or regulators' requests to companies.

3.3.1.3. Collaborations between regulators and registry holders

As explained above, registries can support regulators and regulators can support registries. However the usual process currently is for regulators to request registry data from pharmaceutical companies who then liaise with registry holders; there is therefore limited direct interaction between regulators and academia/registry holders. The workshop highlighted that in many countries and at the European level, more direct interactions would facilitate an improved understanding of the regulatory requirements and regulators' need for data. As different legal regulations may exist in different countries, and such regulations may change, it is difficult for registry holders to keep up-to-date with changing requirements.

Hence, there is a need to expand the direct dialogue between regulators and registries, not only through general guidance but also on a case by case basis. Guidance would be needed to agree on a common terminology, to agree on standards for data quality, analytic procedures and reporting that meet regulatory needs, and to develop procedures that safeguard transparency, accessibility of data and independence of registries.

More specifically, the following proposals for interactions were presented by workshop participants:

- to exploit existing procedures at the European Medicines Agency, such as the Innovation Task Force, the EMA Qualification (possibly joint with FDA) or the parallel EMA/HTA Scientific Advice
- to organise an EMA audit of a registry proposed to be used by a pharmaceutical company, or to establish a certification procedure to establish that the registry is suitable
- to provide guidance on acceptance criteria for studies to be conducted by a pharmaceutical company based on registry data.

3.3.1.4. Collaborations between registries and industry

Registry data are potentially very useful to industry and the experience shared during the workshop across different treatment areas highlighted the enablers and barriers for successful collaborations between industry and registries. Where several registries are involved, using a common protocol, statistical plan and endpoints and applying transparent governance principles (see section "Governance") would be useful to generate interpretable data on a large population across several countries. Numerous barriers exist however: compliance to quality standards varies between registries, there are differences in methods and data adequacy, quality and completeness which make it difficult to pool data for rare events across registries. In addition, the timelines for a registry to agree to participate in a study, to obtain informed consent if needed and to extract and analyse the data may be too long to allow a pharmaceutical company to fulfill its regulatory obligations if it has approached the registry holders after obtaining marketing authorisation.

For collaborations between registries and industry (and possibly with other stakeholders as well), data sharing will depend on the consents that have been obtained from patients. Sharing of anonymous data with regulators is often allowed depending on the study protocol. However, there may be limitations in what data can be shared with private commercial companies especially if another private company funded the original data collection and put restrictions on the use of the data. In general, purely academic registries are less restrictive as the academic institution may "own" the dataset and have the ability to make the final decision on how and with whom data are shared.

In some registries, the possibility of re-using data has been embedded in the design of the registry. For example, in Belgium the Heathdata.be services (re-use of existing registry data or new data collection) have been made available for pharmacovigilance, pharmacotherapeutic and pharmaco-economic studies (e.g. reimbursement negotiations), which facilitates re-use of source data by all involved registries, regulators and industry. In the Pharmachild registry, direct data transfer to companies for regulatory purposes is possible.

3.3.1.5. Involvement of HTA bodies and payers

The European network of health technology assessment (EUnetHTA) is a Joint Action including 80 partners representing national, regional and non-for-profit agencies that produce or contribute to HTA. The EUnetHTA Joint Action³ was established to increase the joint HTA work at EU level and to ensure its uptake at national level. One activity of EUnetHTA focuses on the collection of relevant observational data for HTA purposes, notably using registries. Beyond collaborations between HTA bodies, it aims to interact with all relevant players and stakeholders, including the EMA and registry holders. A procedure for such interactions is the scientific advice/early dialogue involving regulators and HTAs.

3.3.1.6. Involvement of patients

The International Niemann-Pick Disease Registry (INPDR) was presented as a successful example of a registry run by patient associations, including 11 partners in 7 EU countries. Such collaboration provides a single universal resource on the disease thereby avoiding multiple registries while also providing a fully independent support for post marketing surveillance, and data to increase the understanding of the natural history and impact of the disease.

The examples of the Swedish MS Registry and of the Pharmachild registries demonstrate the usefulness of involving patients to collect and measure outcomes.

3.3.2. Recommendations

The workshop clearly illustrated the importance of collaboration to increase the success of registries and enable the best use of the collected data. Most stakeholders are prepared to collaborate, recognising the benefits for all concerned but a number of barriers exist. Several recommendations arose from the discussions.

- Currently MAAs/MAHs are the primary route of communication between registry holders and regulators when registry-based regulatory studies are being discussed. As a general principle, all stakeholders, including regulators, should communicate directly with each other when a study is being planned to agree on outcomes and recognise limitations. More specifically, there is a need to registry holders and regulators to communicate directly so that there is clear information about what information is sought and what are the available data.
- Concrete solutions to better facilitate interactions should be identified. Duplication of interactions should be avoided through partnerships between academia, industries, patients' representatives and regulators. More transparency is required to know what data are needed and what data are being collected.
- Among governance considerations, there is a need for consents obtained from patients to be clear about data sharing and data access for stakeholders other than the registry holders; for data sharing, there has to be clarity on the level permitted with appropriate consents in place, for example, aggregated anonymised data versus individual patient data.

- Regulators should play a role in facilitating the application of rules of engagement, creating a platform on how to work within the regulator/industry/academia triangle and foster collaboration between different stakeholders.
- The involvement and feedback of patients is essential. There is a need to find ways to motivate patients to participate in the registries. Technical tools may be introduced to allow patients, and their families/carers, if appropriate to provide patient-reported outcomes, enter personal data, view their medical records and have access to aggregated statistics. Such registries could thus support empowerment of patients.
- Registry holders recommend that guidance should be issued by the regulators so that in further development of registries compliant with such guidance, there is reassurance that the data would be appropriate from a regulatory perspective.
- Available registries should be explored early in clinical development, around the time Phase II studies are initiated. Especially, in areas of orphan disease and diseases where definite clinical outcome data may be hard to acquire (slowly progressive diseases). In this way, clarity on what outcomes are routinely collected may be available earlier, studying the natural disease progression, providing the possibility to validate surrogates, but also understanding limitations in what data may be available.

3.4. Technical challenges

3.4.1. Observations

3.4.1.1. Data platform

Depending on the scope, objectives and date of their creation, data platforms underpinning registries exist at various levels of sophistication. Several examples were presented in the workshop, which demonstrate several common features:

- 1) Existing infrastructures may be used to avoid duplication of efforts, such as in the RD-Connect project, which aims to link all relevant registries (including biobank databases, phenotypic databases, registries with clinical data, genomic and other omics data) to a centralised global registry that serves as a repository for reprocessing, storing and analysing data on rare diseases.
- 2) Accurate, structured, coded and standardised manually-entered data may be kept at the local level in local registries, such as in the Healthdata.be project and the EBMT registry.
- 3) Centralised data services may include a data submission portal, open-source harmonised data cleaning software, data-visualisation tools and provision of statistics such as incidence or mortality.
- 4) A web platform with user-friendly online analysis interface, such those built by the Swedish MS Registry and the Pharmachild project, may provide tools for decision support and standardised web information to families.

3.4.1.2. Core data elements

It was noted during the workshop that 56 (53.8%) population-based cancer registries which participated in the 2015 ENCR-JRC call for data collect some basic information related to drug or other treatments and only 10 (18%) of the cancer registries collect detailed information on prescribed treatments, with the source of information for such data being most often clinical records (54%), notification by clinicians (20%) or both (13%). The failure to collect routine data on treatments may arise from a lack of an agreed process for treatment data collection and coding. Other examples show

that many registries do not collect enough information to identify precisely the medications prescribed and therefore do not allow pharmacotherapeutic, pharmaco-economic, and pharmacovigilance investigations, or that registries collect different sets of data elements with different coding systems based on their specific objectives. These examples illustrate the need to have agreement on the collection of a minimal set of data elements in a standardised format within specific disease areas. For example, all national registries that are part of the TREAT-NMD Global Registries collect, as a minimum, a standardised disease-specific core dataset based on trial inclusion criteria to help recruitment into clinical trials. The UK Renal Registry collects core data on demographics, renal disease, co-morbidities, treatments and laboratory results to allow monitoring of the use, effects and safety of medications. In the Big Multiple Sclerosis Data registry, core data items are similar in all participating registries to allow analysis of pooled data. In line with these registries, the Parkinson's Disease group of registry holders had to overcome obstacles of different data elements and formats and now has an agreed common set of data elements collected by all affiliated registries. Agreeing a mandatory minimum data subset has also been recommended by the UK National Institute for Health and Care Excellence (NICE) as a point to consider when setting up a registry for evidence generation for new treatments.

Common core data elements collected across all registries for the same disease would therefore facilitate inter-operability of registries and joint analyses, with the objective that all registries should potentially be linkable. Evolving nomenclatures for categories of disease, medicinal products and biological data, as well as their increasing complexity, would need to be overcome. Defining common core data elements would also require common rules to harmonise data collection and coding. This may however conflict with governance principles established by some registries.

A specific challenge with linking core data elements relates to the use of a unique identifier for every concerned individual. This challenge was illustrated in the RD-Connect project where the platform cannot store personally identifiable information for privacy reasons but where it should ideally be possible to link different data items (e.g. biosample, natural history data, exome sequence) coming from the same patient. Assigning a unique identifier centrally would be a simple solution but would require a central point (e.g. clinician) knowing the link between the patient and the identifier for all datasets and require appropriate patient consents. An alternative solution is to generate a unique identifier from personally identifiable information, but this solution requires consensus on a set of personal information sufficient for generating the unique identifier, which may be hard to do retrospectively if this information is not available. In the interim, RD-Connect will establish an identification system for European rare disease projects contributing data to RD-Connect..

3.4.1.3. Data quality and completeness

Most registries have recognised that data quality and completeness may be very variable across different investigators or local registries and there is a need to understand the available data and their quality. In addition, existing patient registries often collect data only once a year with variable completeness of data extraction (in some cases only the most recent data or a summary are extracted), which does not meet the needs of secondary users where, for example, continuous data collection, all available data or baseline data before medication use are needed.

In order to address data quality issues, the most of registries have introduced audit and quality assurance processes for benchmarking, validating (at entry or retrospectively) and improving data quality and completeness. In the case of re-use of the data, many registry holders are nevertheless faced with the question of whether quality control is the responsibility of the local investigator or should be controlled at a central level. In one study, designed for regulatory use, data from several rheumatoid arthritis registries was requested by a pharmaceutical company. Endpoint alignment

across databases was required, thus data re-use was not possible. This, coupled with time constraints, led to data validation challenges.

The EBMT registry illustrates how procedures may be put in place for quality management at different levels:

- Benchmarking of clinical outcome is required in international standards for hematopoietic cellular therapy for transplant programs seeking accreditation"
- Definitions of all items are developed before being placed in the data collection forms in such a way to ensure that the same items in different collection forms are equivalent;
- Data managers receive education and training on clinical knowledge and use of the software;
- The database has internal quality controls to ensure the accuracy and internal consistency of what is entered in the database at the point of entry, and data quality reports can be run by users at any point to check for missing or unusual data; periodic queries on missing or incorrect data and follow up are requested;
- Continuous support is provided through a helpdesk.

Participants to the workshop suggested that regulators could support quality improvement in different ways, though inspections or certification of registries, by performing validation studies or by agreeing in collaboration with registry holders on standards for data quality, analytic procedures and reporting that meet regulatory needs.

3.4.1.4. Data analysis

Several examples of analytical methods to optimise use of registry data were presented. In the field of health technology assessment, predictive models that incorporate data from both RCTs and registries are developed to bridge the efficacy-effectiveness gap, and generalise results observed in RCTs to a real-world setting. In the UK Renal Registry, work is done with experts in causal modelling and novel statistics to better analyse the data and learn about strengths and weaknesses of novel statistics.

3.4.2. Recommendations

One of the main recommendations arising from the workshop is that regulators should provide registry holders with guidance to help them make informed choices as regards core data elements (optimal elements from a regulatory perspective) and quality parameters that would be considered an acceptable standard for supporting regulatory decision-making. A definition of basic criteria with respect to core data should accompany quality standards for such data and how they would be assured. To facilitate this, regulators also need to better understand what data are collected in registries and their quality and limitations. Marketing authorisation applicants and holders would also welcome such guidance. It is however acknowledged that, while a core data set is desirable, additional data might be required for specific studies and defined on a study by study basis.

The technical challenges presented by disparate datasets should be addressed. There is a need to provide rules to standardise data fields, data dictionaries and coding systems to improve data collection, quality and interoperability. In addition, where data from several datasets are combined, it is necessary to characterise the registry populations to understand endpoints, co-morbidities and safety concerns.

It is recommended to decrease data collection paper forms and exploit current technology. User-friendly web-based platforms, use of mobile devices and user-friendly apps for providing feed-back information could increase participation of health care professionals, patients and families /parents.

Technology may also facilitate the use of structured data (e.g. common endpoint definition and coding), data linkage, data pooling and data analyses.

3.5. Governance

3.5.1. Observations

3.5.1.1. General aspects

Nearly every registry has its own governance model generally determined by its main source of funding, which impacts on its policy for collaborations with other stakeholders, including data ownership and data sharing. For example, the Swedish Multiple Sclerosis register receives public funding and its governance is based on a political consensus with commitment and voluntary participation of doctors and patients. Many registries (such as the EBMT registry) have also been established for clinical evaluation and academic research purposes. Although procedures have been put in place to provide data for commercial purposes, e.g. to support registration, there is limited flexibility for commercial access or commercial data ownership and individual patient level data can rarely be provided. On the other hand, the UK Biologics register is funded with grants from pharmaceutical companies to the British Society for Rheumatology (BSR) which subcontracted the University of Manchester to run the register and perform the primary data analyses. As a consequence, an industry-funded study is approved by the BSR where there is no objection from other participating marketing authorisation holders. The details of such approvals and what data may or may not be shared with other industry partners may also be influenced by this funding model. As a general principle, however, many patient registries will participate in research only if they can preserve their scientific independence, maintain control of the management of registry data and provide aggregated data to the contractor. This principle may conflict with policies and research standards in place within pharmaceutical companies in terms of data quality and data access to which their suppliers have to adhere, especially where the study (and use of a specific registry) has been imposed as a legal obligation by a regulatory authority. Assurance of data quality is often a point of friction as data entry by clinicians or patients is generally voluntary (unless there is a system for automated data extraction like in the UK Renal Registry) and compliance is variable across centres. Clear regulatory guidance would be useful to address such conflicting priorities.

3.5.1.2. Data ownership

It is a general principle that ownership of the data lies within the registry, such as in the EBMT and the Pharmachild registries. In the International Niemann-Pick Disease Registry (INPDR), an operational charter established patient ownership (with professional management) but allows universal access of data via requests to the Scientific Advisory Board. In the UK Biologics register, the dataset holder is the British Society for Rheumatology, an independent third party from the pharmaceutical companies and The University of Manchester, although it receives funding from pharmaceutical companies.

3.5.1.3. Data sharing

An important example of registries connected by a network is that of the ENCR - European Network of Cancer Registries, supported by the European Commission whose services developed an ad-hoc platform to facilitate harmonized data collection, as well as dissemination of aggregated indicators on cancer burden in Europe (incidence, mortality and survival). Others, like Pharmachild, have been designed to allow direct data transfer to companies for regulatory purposes following approval.

In the context of rare diseases, the benefits of data sharing are multiple, including reducing duplication of efforts and costs, facilitating validation of results, enabling engagement with experts and the patient community and overcoming the “rare disease problem” in terms of cohort size, powering trials and finding confirmatory cases. But barriers to data sharing are also numerous: privacy protection issues (“Do I have the patient’s permission?”), lack of infrastructure (“I want to share data but where do I put it?”), lack of standards, lack of interoperability, lack of incentives, academic culture of protecting research results, and from an industry perspective concerns over intellectual property and competition (sharing own data) and concerns over data quality and regulatory compliance when re-using data from academia.

3.5.1.4. Data pooling and analysis

Organising operational and scientific support (i.e., programming and statistics) is an important component of good governance. At EBMT, a final phase of the service provided to non-interventional studies includes data file preparation, statistical analysis, reports, publication, filing and storage of data.

3.5.1.5. Informed consent

Informed consent and data protection is a concern for all registries where individual patient data are collected and stored. Of note, the UK Renal Registry has been granted a legal basis to collect data without individual patient consent by the Secretary of State for Health and the Health Research Authority under Section 251 of the NHS Act. Permission is granted separately for national audit and research. In EBMT, a unique identifier is assigned to each individual in order to allow patient mobility and avoid double registration. In the Healthdata.be project, a Trusted Third Party has been contracted for encryption and pseudonymisation.

3.5.1.6. Reporting of adverse drug reactions

Timely reporting and follow-up as necessary of adverse reactions is a requirement described in the Good Pharmacovigilance Practices (Module VI) for marketing authorisation holders in case of post-authorisation studies based on primary data collection. This requirement cannot be fulfilled if the post-authorisation study is based on a registry where only de-identified drug data can be provided to a pharmaceutical company (such as in the UK Biologics registry). Moreover, there is no legal obligation to force investigators to report adverse drug reactions or to track patients. In some registries, such as EBMT and Pharmachild, processes have been put in place to inform investigators about the spontaneous reporting of adverse events/adverse reactions, but there is no standardised procedure across registries. In some cases, this is due to a lack of knowledge about reporting requirements.

3.5.1.7. Timelines

The utility of registries for regulatory purposes is contingent on timelines as existing product registries often collect data quarterly or once in a year, and sometimes this concerns only the most recent data or aggregated data.

In addition to the issue of the frequency of data extraction, a considerable amount of time may be needed between the first discussions and the initiation of the study. In EBMT, it has been estimated that the start-up phase of a study may take up to one year as it requires many different steps: feasibility analysis, writing of study proposal including statistical plan, legal considerations, including ethic committee and contract procedure per country and site, data ownership and publication rights, data base creation, infrastructure implementation, centre identification, ethic approval for centres and budget calculation for the recruitment phase. In the UK Biologics register, the total lead-up time (from

idea to contract) has been measured for one study at 17 months, the total time for analysis at 4 months, and the time for the final report preparation and approval at 2 months. These activities relied heavily on existing registry infrastructure, data preparation and staffing. In the UK Renal Registry, laboratory and medication data are extracted daily for multiple purposes including PatientView, but the rest of the data set is extracted quarterly and the time to publication has been estimated at 11-23 months.

3.5.2. Recommendations

Successful collaboration between registries and industry (or other stakeholders) is possible but experience shows it is contingent on agreement on data ownership and sharing, timelines, established protocols and statistical analysis plans, consideration of methodological differences between data sources, due consideration to adequate sample size, and provision of operational and scientific support (i.e. for programming and statistical analyses). It is therefore recommended to identify/define and disseminate good governance principles of interactions between registries, stakeholders and industry that would address such aspects as well as data privacy, data ownership and financial aspects. Guidance issued by ENCePP, the PARENT Joint Action, STROBE and other projects such as ADVANCE in the field of vaccines can be used as a starting point.

Procedures need to be developed and implemented by registries in order to safeguard core principles such as transparency, accessibility of data for public health purposes and independence. It is emphasised that for registry holders working with pharmaceutical companies in the pre/post-approval context may be a valuable exercise in generating a better understanding of their own data in relation to other datasets.

A key aspect of governance is the good understanding of the legal or regulatory context and requirements of different stakeholders. Guidance or clarification documents may be needed from regulators, for example in the area of reporting of adverse events/adverse drug reactions.

Agreement on principles of data sharing applicable to all registry-based studies is needed. In some cases, commercial confidentiality agreements have prevented registries reporting full information on adverse events and some MAAs/MAHs felt this was inappropriate given their legal responsibility. Collaboration on data-sharing methods and achieving interoperability between data sets would be helpful. Stakeholders should actively collaborate on data-sharing and interoperability between registries.

Roles and responsibilities in data analysis, interpretation and publication should also be agreed. For examples, pooling of aggregated results from different data sources should only be considered if possible from scientific and data protection perspectives.

The FAIR principles for data management and stewardship should be considered (the data should be findable, accessible, inter-operable and re-usable) and funding should be allocated to this activity.

Guidance on the implementation of the new General Data Protection Regulation, and its consequences for running registries should be developed.

3.6. Sustainability

3.6.1. Observations

Sustainability of a patient registry is an issue faced by most registries following the initial phase of funding for their creation. Sustainable funding may be needed to directly fund core registry features, such as a professional management, an IT platform and the infrastructure, to maintain core definitions

and core datasets, to adapt the registry to changes in legal requirements, to hire new staff for specific studies (especially where strict timelines need to be met) and to provide funding to local centres as necessary.

Different sources of funding, sometimes temporary or transitional, often co-exist. Special cases are the UK Renal Registry, which receives funding through a NHS capitation fee, and the UK Biologics register, which receives funding through a grant from pharmaceutical companies to the British Society for Rheumatology, which is the dataset IP holder. In the International Niemann-Pick Disease registry (INDPR), funding was initially established based on unrestricted grant funding support from pharmaceutical companies, partner contributions and research grant with applications. In a second stage, the registry aimed to become self-financing with contracts negotiated for data access. In the RD-Connect project, several solutions to ensure sustainability of the platform and tools needed to be identified. They included embedding the registry within existing infrastructures with sustainable funding, applying for future EU funding, developing RD-Connect 'services' into future funding applications which require genomic data deposition, storage or analysis, to request a fee for access to service (industry only), to set up partnership with private companies or through licensing and to seek support from patient organisations.

In the INDPR, sustainability has been addressed from the start by design, the aim being to build a registry that is adaptable to future changes in needs, to involve stakeholders from the start and to carefully define and agree strategic outcomes.

3.6.2. Recommendations

Experience from successful registries in ensuring sustainability should be considered. Registry holders need to engage with public agencies and define/clarify the role of industry in the long-term as opposed to short-term funding support.

Sustainability should be based on a development strategy, a professional management structure and the development of clear partnership with stakeholders to safeguard independence.

4. Conclusions and next steps

From the observations made during the workshop and during the pilot phase so far, there is clearly a need for a set of recommendations to be agreed between stakeholders on the use of registries to support drug regulation and evaluation. The topics identified during the workshop are listed in the previous sections of this document. They concern use of patient registries during a medicinal product life-cycle, collaborations between stakeholders, technical aspects such as common core data elements, core elements of common study protocol to address registry limitations, data quality, governance principles and sustainability.

Taking into consideration the stakeholders' expressed wish for regulator guidance and endorsement of registries as sources of information to support decision-making, the EMA recognises it may contribute to facilitate the use of registries in assisting decision-making and informing medicines monitoring. It is keen to investigate with other regulators and stakeholders options to overcome barriers to maximising use of technologies, build on the experience of solutions, advance governance, interoperability, simplification of technology and data integration.

The following activities will be initiated by the EMA in collaboration with the Cross-Committee Task Force on Patient Registries, the regulatory network and other relevant stakeholders:

1. Facilitate sharing and dissemination of information on disease registries to support collaborations - options for this purpose will be explored, including collaboration with the European Network of

Centres of Pharmacoepidemiology and Pharmacovigilance (ENCePP) and the addition of registries into the ENCePP Resources database.

2. In collaboration with regulatory authorities and EUnetHTA, explore options to interact directly with and to support registry holders in specific situations, e.g. through Scientific Advice, Qualification process, the Innovation Task Force, or specific meetings with registry holders per treatment areas. The output from such meetings would be agreement on common core data elements that registries in a disease area would collect and on methodological aspects and quality assurance / validation.
3. Build on other initiatives (such as the ENCePP code of conduct and the ADVANCE good practice guide) and recommend principles and standards to apply to interactions between the stakeholders on governance aspects including cross-border collaborations, data sharing and acceptable commercial-in-confidence agreements between MAHs and registry holders for studies being conducted. Registry holders could self-assess their registries and studies undertaken against these principles and standards and make the information / evidence of adherence available on their websites.
4. Identify the need for additional methodological and technical guidance in addition to that already available (e.g. from PARENT JA and AHRQ) on interoperability, data standardisation, coding systems, data linkage, registry design, use of comparator groups or safety monitoring. A survey of registry holders could be performed about awareness, usefulness and implementation of current guidance and missing guidance.
5. Reflecting back on the pilot phase and the need for early interactions between pharmaceutical companies and registry holders, mechanisms facilitating systematic consideration of the need of registries by committees will be explored.
6. In collaboration with patients' associations, investigate relevant patient-reported outcomes that could be collected by registries.
7. Explore measures that could contribute to registry sustainability aside from those being already undertaken by individual registry holders/groups.

The report of the registry workshop is published on the EMA website, together with the presentations and video recordings.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000658.jsp

A companion position statement on the use of registries to support drug regulation and evaluation will be published in the peer-reviewed literature.

Annex 1. Programme of the Patient Registries workshop, 28th October 2016

Session 1: Setting the scene - Challenges and Opportunities for Collaboration

- *Challenges and Opportunities for Collaboration, the European Society for Blood and Marrow Transplantation (EBMT).* Jürgen Kuball, Head of Department, Hematology, University Medical Centre, Utrecht, The Netherlands.
- *Ensuring sustainability.* Jim Green, President of the International Niemann-Pick Disease Registry, UK
- *Product versus disease registry – what drives the choice?* Jonathan Appleby, Chief Scientific Officer, Rare Diseases Gene Therapy, GlaxoSmithKline, UK
- *The Health Technology Assessment perspective.* François Meyer, Director, International Affairs, Haute Autorité de la Santé, France and EUnetHTA
- *A Regulator's perspective.* Nils Feltelius, Member of the Rheumatology-Immunology Working Party (RIWP), Senior Expert and Clinical Assessor, Medical Products Agency, Sweden.
- *Questions and panel discussion.* Panel Moderators: Sabine Straus, Pharmacovigilance and Risk Management Committee (PRAC) member, staff member at the Medicines Evaluation Board, The Netherlands and Associate Professor at the Erasmus Medical Centre, Department of Medical Informatics, Rotterdam; Peter Mol, Vice-Chair, Scientific Advice Working Party (SAWP), Principal Clinical Assessor, Medicines Evaluation Board, The Netherlands.

Session 2: Success factors for international collaborations,

- *Standardisation of cancer registries data collection and validation at European level.* Carmen Martos, Joint Research Centre (JRC), ISPRA, Italy.
- *The Pharmachild project: the PRINTO pharmacovigilance registry.* Nicola Ruperto, Pharmachild project, Genoa, Italy.
- *Case Study: Challenges of comparator groups and the role of disease registries in medicines development.* Jamie Geier, Senior Director of Epidemiology, Pfizer Inc., USA, and Kimme Hyrich, Principal Investigator of BSRBR-RA registry, Professor of Epidemiology, University of Manchester, UK.
- *Questions and panel discussion.* Panel Moderators: Tomas Salmonson, Chair, Committee for Medicinal Products for Human Use (CHMP), Senior Scientific Advisor, Medical Products Agency, Sweden; Jan Span, Member of the Cross-Committee Task Force on Registries and Senior Clinical Assessor, Medicines Evaluation Board, The Netherlands

Session 3: Possible solutions

- *Is the answer active data extraction from hospital records?* Fergus Caskey – Medical Director, UK Renal Registry.
- *Integration of data across multiple data sources.* Jan Hillert, Group Leader, Neurogenetics, Multiple Sclerosis, Karolinska Institute, Sweden; Metka Zaletel, PARENT Joint Action, Head of Health Data Centre, National Institute of Public Health, Slovenia ; Johan van Bussel, Head of healthdata.be, Scientific Institute of Public Health, Brussels, Belgium.

- *Designing integrated platforms for rare diseases research.* Emma Heslop, Project Manager, RD CONNECT, UK.
- *Questions and panel discussion.* Panel Moderators: Martin Van Der Graaff, Secretary Scientific Advisory Board, Sector Healthcare, **National Healthcare Institute, The Netherlands**; June Raine Chair, Pharmacovigilance and Risk Assessment Committee (PRAC), Director of Vigilance and Risk Management of Medicines Division, MHRA, UK

Annex 2. Acronyms

ADVANCE	Accelerated development of vaccine benefit-risk collaboration in Europe
BEUC	Bureau Européen des Unions de Consommateurs
BPWP	Blood Products Working Party
BSRBR-RA	The British Society for Rheumatology – Rheumatoid Arthritis
BWP	Biologics Working Party
CAT	Committee for Advanced Therapy
CMDh	Co-ordination Group for Mutual Recognition and Decentralised Products – Human
CHMP	Committee for Medicinal Products for Human Use
COMP	Committee for Orphan Medicinal Products
EATG	European Aids Treatment Group
EBMT	European Society for Blood and Marrow Transplantation
ECFS	European Cystic Fibrosis Society
ECPC	European Cancer Patient Coalition
E-IMD	European Registries and Network for Intoxication type of metabolic diseases
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance.
ENCR	European Network of Cancer Registries
ESC	European Society of Cardiology
ESID	European Society for Immunodeficiencies
EUnetHTA	European Network for Health Technology Assessment
EUHASS	EUHASS European Haemophilia Safety Surveillance
FDA	Food and Drugs Administration
GSK	GlaxoSmithKline
HCPWP	Healthcare Professionals Working Party
HTA	Health Technology Assessment
IBD	Inflammatory Bowel Disease
INPDR	International Niemann-Pick Disease
JIA	Juvenile Idiopathic Arthritis
JRC	Joint Research Centre

MAA	Marketing Authorisation Applicants
MAH	Marketing Authorisation Holders
NICE	National Institute for Health and care Excellence
PARENT - JA	Cross Border Patient Registries Initiative – Joint Action
PCWP	Patients and Consumers Working Party
PDCO	Paediatric Committee
PRAC	Pharmacovigilance Risk Management Committee
PRINTO	Paediatric Rheumatology International Trials Organisation
RCTs	Randomized Control Trials
RIWP	Rheumatology/Immunology Working Party
RTT	Renal Replacement Therapy
SAWP	Scientific Advice Working Party