# EURORDIS-NORD-CORD Joint Declaration of

# 10 Key Principles for

# Rare Disease Patient Registries

1. Patient Registries should be recognised as a global priority in the field of Rare Diseases.
2. Rare Disease Patient Registries should encompass the widest geographic scope possible.
3. Rare Disease Patient Registries should be centred on a disease or group of diseases rather than a therapeutic intervention.
4. Interoperability and harmonization between Rare Disease Patient Registries should be consistently pursued.
5. A minimum set of Common Data Elements should be consistently used in all Rare Disease Patient Registries.
6. Rare Disease Patient Registries data should be linked with corresponding biobank data.
7. Rare Disease Patient Registries should include data directly reported by patients along with data reported by healthcare professionals
8. Public-Private Partnerships should be encouraged to ensure sustainability of Rare Disease Patient Registries.
9. Patients should be equally involved with other stakeholders in the governance of Rare Disease Patient Registries.
10. Rare Disease Patient Registries should serve as key instruments for building and empowering patient communities.

On behalf of an estimated 60 million people living with rare diseases in Europe and North America, the European Organisation for Rare Diseases (EURORDIS), the National Organization for Rare Disorders (NORD) and the Canadian Organization for Rare Disorders (CORD), jointly submit the following declaration on common principles regarding Rare Disease Patient Registries.

EURORDIS, NORD and CORD, along with the patients they represent in Europe and in North America, recognize that Rare Disease Patient Registries constitute key instruments for increasing knowledge on rare diseases, supporting fundamental clinical and epidemiological research, and post-marketing surveillance of orphan drugs and treatments used off-label. Furthermore, and of great importance for patients and their families, they can be instrumental in supporting health and social services planning. Rare Disease Patient Registries are powerful, cost-effective instruments to improve the overall quality of care, quality of life and survival of patients.

EURORDIS, NORD and CORD also recognize that patient involvement is a key element in the successful establishment and long-term maintenance of Rare Disease Patient Registries and many patient groups are already very active and capable in this role. On behalf of rare disease patients and their representatives in Europe and in North America, we would like to jointly put forward the following common reflections and principles regarding patient registries. These common reflections and principles may serve as a reference to all other stakeholders when shaping policies and taking actions in the field of Rare Disease Patient Registries.

A Patient Registry can be defined as an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose(s)[1]. The following principles refer to this definition.

[1] Gliklich RE, Dreyer NA, eds. Registries for Evaluating Patient Outcomes: A User's Guide. 2nd ed. Rockville, MD: Agency for Healthcare Research and Quality. September 2010. http://www.effectivehealthcare.ahrq.gov/ehc/products/74/531/Registries%202nd%20ed%20final%20to%20Eisenberg%209-15-10.pdf.

1. **Patient Registries should be recognised as a global priority in the field of Rare Diseases**.

Rare Disease Patient Registries represent a fundamental research effort upon which a number of critical activities are based. They constitute key instruments for increasing knowledge on rare diseases, by pooling data for epidemiological research, clinical research, and real-life post-marketing observational studies[2].

They broadly support health and social service planning by playing a pivotal role in healthcare organization. In particular, Centres of Expertise/Excellence and the European and International networks that connect them centralize patient data patient registries which can be used as an evidence base to shape regional, national and international health policy and standards of care.

It has also been demonstrated that Patient Registries are a major determinant for successful translational research in the field rare diseases. Where well-implemented registries and active patient organizations exist, the likelihood for developing a treatment for the disease in question is increased[3]. Furthermore, the consistent longitudinal collection of patient data facilitates the creation of standards of care and dramatically improves patient outcomes and life expectancy even in the absence of new therapies. The compelling arguments for Rare Disease Patient Registries as indispensable infrastructure tools for translating basic and clinical research into therapeutic solutions have elevated their status to a major priority for all stakeholders - a building block of any sound rare disease policy.

2. **Rare Disease Patient Registries should encompass the widest geographic scope possible.**

Due to the low individual prevalence and the scarcity of information related to each rare disease, collaboration and maximum use of limited resources is particularly meaningful for rare diseases. This is especially true for very rare diseases where no single

[2] EURORDIS Position on Rare Disease Research. http://www.eurordis.org/publication/eurordis-position-rd-research
[3] Orphanet. Report on Rare Disease Research, Its Determinants in Europe and the Way Forward, May 2011. http://asso.orpha.net/RDPlatform/upload/file/RDPlatform_final_report.pdf

institution, and in many cases no single country, has a sufficient number of patients to conduct fundamental, clinical and translational research. In fact, geographic dispersion of patients continues to make recruitment for clinical trials difficult, often aggravated by the dearth of scientific and medical knowledge and relevant endpoints for study designs. The International Rare Diseases Research Consortium (IRDiRC)[4], launched in April 2011, fosters international collaboration in research on RD. Canada, Europe and the United States have fully committed to this endeavour agreeing on the principle that maximizing scarce resources and coordinating research efforts are key elements for success in the rare disease field. IRDiRC advocates that the worldwide sharing of information, data and samples gathered by robust and harmonised Rare Disease Patient Registries will boost research at all levels and ultimately favor therapy development.

3. **Rare Disease Patient Registries should be centred on a disease or group of disease rather than a therapeutic intervention.**

Treatment-specific registries, frequently funded by industry, are required by regulators to monitor the effectiveness and side-effects of treatments approved under exceptional circumstances. However, because treatment-specific registries must be re-created for each product, limitations in their completeness, quality, and cost-effectiveness have been demonstrated. Consensus is growing around the opinion that disease-centric patient registries provide a more comprehensive and collaborative approach to rare disease patient data collection by aligning stakeholder efforts, avoiding fragmentation of patient populations and dissipation of resources, and ultimately addressing regulatory and payer requirements with greater accuracy.

4. **Interoperability and harmonization between Rare Disease Patient Registries should be consistently pursued.**

Centres of Expertise/Excellence and the international networks that connect them play a pivotal role in capturing data of patients treated at their facilities and centralizing them in Rare Disease Patient Registries. Nevertheless, no uniform, accepted standards

[4] International Rare Disease Research Consortium. http://ec.europa.eu/research/health/medical-research/rare-diseases/irdirc_en.html

currently govern the collection, organization, or availability of data collected by Rare Disease Patient Registries which may even vary within the same disease group or health system. Moreover, registry custodians frequently hold proprietary views on their data or face legal limitations on data-sharing as a result of patient consent restrictions and privacy protection or conflicting national legislations. These data-sharing barriers create a compelling argument for developing globally accepted definitions, classifications, ontologies[5,6], data standards and favourable and congruent policies and resources facilitating data sharing and pooling. Ideally, standard operating procedures and common resources or platforms for centralizing new or existing registries should be developed.

## 5. A minimum set of Common Data Elements should be consistently used in all Rare Disease Patient Registries.

A pillar for the systematic, coordinated approach to Rare Disease Patient Registries would be the definition of minimum set of Common Data Elements (CDEs) and corresponding validated standards and ontologies globally endorsed by all stakeholders. The consistent use of CDEs would facilitate the standardization of data (ensuring that data are defined and entered in the same way, use the same standards, and the same vocabularies), harmonization (allowing data to be more easily exchanged and compared), and interoperability (enabling common strategies for quality assurance and data security). Lastly, the definition of CDEs will allow greater opportunities for meta-analysis across diseases providing evidence for public health and social planning. The NIH Office of Rare Disease Research[7] and EPIRARE[8] are currently establishing such CDEs for North America and Europe.

[5] Disease ontology refers to a consistent, reusable and sustainable set of descriptions that defines human disease terms, phenotypic/genotypic characteristics and related medical vocabulary. Common disease ontologies are needed to ensure both shared understanding between people and interoperability between information systems about diseases. Common ontologies are particularly important for rare diseases as exiting vocabulary (disease definition, diagnosis, phenotype/genotype) describing many of them is still incomplete and inconsistent.

[6] Rath A, Olry A, Dhombres F, Brandt MM, Urbero B, Ayme S (2012) Representation of rare diseases in health information systems: The orphanet approach to serve a wide range of end users. Hum Mutat 33:803-8. http://onlinelibrary.wiley.com/doi/10.1002/humu.22078/pdf

[7] NIH Office of Rare Disease Research. Common Data Elements. http://www.grdr.info/files/ORDR_CDE_10_2_2012.xls

[8] European Platform for Rare Disease Registries (EPIRARE). http://www.epirare.eu/

6. **Rare Disease Patient Registries data should be linked with corresponding biobank data.**

Biobanks are collections of human biomaterials and represent an essential tool for fundamental and translational research. The high value of biological samples only increases when coupled with well-documented, associated data housed in a patient registry. The development of a system that assigns a unique global identifier to each patient is recommended to facilitate data linkage and avoid duplicate entries and waste of precious biomaterial. Engagement of patients and patient organizations is instrumental for the development of networks between registries and biobanks.

7. **Rare Disease Patient Registries should include data directly reported by patients *along* with data reported by healthcare professionals.**

Many patient organizations in Europe and North America are actively and successfully collecting clinical and non-clinical patient data. Most stakeholders in the rare disease community recognized that patients and their caregivers are best placed to report on their health-related quality of life, satisfaction with and utility of care and treatment. Much progress has been made in creating regulatory standards[9,10] to validate this type of data reported by patients and caregivers, which are also of significant benefit to patients' management of their own outcomes.

Out of necessity, patient groups further proceeded to collect data beyond perceived outcomes and collect post-marketing treatment outcomes, off-label drug use outcomes and even natural history data. By complementing clinician-reported data in Rare Disease Patient Registries, patients can contribute to improving their robustness, comprehensiveness and quality. Continued creation of easily accessible and validated standards, platforms and scientific guidance to ensure the high quality collection of patient entered clinical data should be encouraged and guaranteed.

[9] US Food and Drug Administration.
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf
[10] European Medicines Agency.
http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500003637

**8. Public-private partnerships should be encouraged to ensure sustainability of Rare Disease Patient Registries.**

In context of the current economic climate, the need for the optimal sharing of resources is an imperative. Different scenarios are being proposed to provide financial sustainability to registries and their networks, and the most promising rely on the collaboration amongst all the stakeholders[11,12]. This collaborative approach has been recognized as a requirement to: avoid duplication of efforts and take advantage of economies of scale; foster improved quality and robustness of data collected; to unify patient data especially for diseases where several treatments exist, and best sustain registries as long-term endeavours. With both governments and private groups showing interest in patient registries, public-private partnerships are a promising collaborative scheme. Patient groups can be instrumental facilitators of public-private partnerships driving the common goals of all stakeholders through a patient-centred approach and assuring optimal efficiency and transparency. Regulatory bodies can strongly encourage such collaboration in this pre-competitive space. The nature of potential public-private partnerships, the issues to consider when establishing such a partnership, and best practices enhancing the success of such efforts should be investigated in a prompt and transparent manner.

**9. Patients should be equally involved with other stakeholders in the governance of Rare Disease Patient Registries.**

Patient involvement is a key element in the successful establishment of registries and many patient groups are already very active in this role. Patients should be involved at all levels of development, management and maintenance in order to best represent patient needs, increase awareness among all stakeholders of the existence of the registry and, ultimately, improving the quality and quantity of data collected through a patient-centred approach. Patient groups are willing and able to be involved in initiating the establishment of registries; defining content and purposes of the registries; resolving

[11] NIH/FDA Workshop on Natural History Studies of Rare Diseases.
https://events-support.com/events/Natural_History_Studies
[12] EUCERD Workshop of Public-Private Partnerships for RD Registries.

ethical and legal issues; authorising access and utilisation of data; creating partnerships with health professionals and industry representatives; contributing to the selection of data items collected (in particular on the impact of the disease on their daily life); helping to recruit patients for participation into the registry; preparing specific information for patients to be registered prior to their consent; motivating health professionals to input data, and directly entering data. This essential role of the patients should be reflected in the governance of the registry.

**10. Rare Disease Patient Registries should serve as key instruments to build and empower patient communities.**

Registries can be instrumental in building patient communities around a disease, a cluster of diseases or even common clinical features or common underlying causes. Registries thus become the aggregation point around which an organised patient community can be built where none exists. The creation of a patient registry can facilitate the congregation of patients and their families as they engage directly into the development of the very databases in which their data will be entered. Registries thus become the medical home for patients scattered internationally and empower patients with data available to share with health care professionals, clinical researchers and drug developers.