Rare Diseases Task Force

PATIENT REGISTRIES IN THE FIELD OF RARE DISEASES

Overview of the issues surrounding the establishment, management, governance and financing of academic registries

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Introduction

Patient registries and databases constitute key instruments for the development of clinical research in the field of rare diseases (RD), and the improvement of patient care and healthcare planning as well as social, economical and quality of life outcomes. They are the appropriate way to pool scarce data without bias for epidemiological and/or clinical research. They are vital to assess the feasibility of clinical trials, to facilitate the planning of appropriate clinical trials and to support the enrolment of patients and to assess the impact of new interventions.

Registries of patients treated with orphan drugs are particularly relevant as they allow the gathering of evidence on the effectiveness of the treatment and on its possible side effects, keeping in mind that marketing authorisation is usually granted at a time when evidence is still limited although already somewhat convincing.

When established, databases should be maintained and their use optimised through exchange of data between interested parties. However, the status of such databases is not well defined and most institutions have no written policies or agreements regarding this activity.

Regulations concerning registries are in early stages in most European countries and, with the multiplicity of actors and of rules at MS level, the situation is difficult to comprehend. No guidelines are available yet on best practices for exchanging and sharing data. The notion of return of benefits to research subjects/communities is fairly recent.

Databases are expensive to establish and maintain. They require the cooperation of many healthcare providers and require careful management. PR should only be established when financial resources and expertise are present to support them. Furthermore, PR systems tend to have added value if the disease in question has a good prospect for intervention, control, prevention and for research that can lead to these ends.

They are of high interest to researchers, industrial partners, healthcare professionals, patients and patient organisations, and, ultimately, for the community. It is difficult to separate research conducted by the non-profit and for-profit sectors, as researchers from both sectors are often involved in the same projects. Whilst this enables effective technology transfer, it also gives rise to concerns about conflicts of interest. There is a need to promote confidence in research based on data collections.

Patient registries have been in place for several decades in sectors such as cancer, birth defects and cardiovascular diseases. This long and broad history of data collection is the basis on which to build guidelines for registration of patients with a RD although RD patient registries have some additional features which make them specific:

- the scarcity of cases and the complexity of these diseases imposes a large geographical coverage of the data collection which implies multiple collaborations and exchanges of data, usually trans-national;

- most RD are genetic in origin and a large proportion of them may have one family member affected, which implies that it is desirable that family related cases be traceable;
- the cost of establishing and maintaining a PR is nearly equal for a common disease as it is for a RD, although budgets are more difficult to obtain for the latter.

The European Commission, in its Communication: *"Rare diseases: Europe's challenge"* emphasizes the strategic importance of PR in the field RD.

"Collaborative efforts to establish and maintain data collection should be supported, providing that these resources are accessible through agreed upon rules. Many research and public health networks financially supported by DG RTD and by DG SANCO have put in place such shared infrastructures, which have been proven to be very efficient tools in improving knowledge and organising clinical trials."

"Areas to be supported by the MS and the European Commission include: quality standards, including development of strategies and tools for periodical monitoring of the quality of databases and for database upkeep; a minimum common set of data to be collected for epidemiological and public health purposes; attention to user-friendliness, transparency and connectivity of databases; intellectual property, communication between databases/registries (genetic, more generically diagnostic, clinical, surveillance-driven, etc). Importance should be given to linking international (European) databases to national and/or regional databases, when existing."

To discuss these issues and produce recommendations from a health professional's perspective, the Rare Diseases Task Force organised a workshop on 13 March 2008 in Paris, France, to which 23 experts (see Annex 1) from 10 European countries were invited. This document was finalised as an output of this workshop where a preliminary version was presented and discussed.

The present document is based on a compilation of several previously published documents which are listed at the end of the report. An updated[1] list of patient registries in Europe in the Orphanet Report Series is also provided in Annex 2. The report and annex has been updated in June 2011 by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD).

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[1] Updated in January 2011.

Part I

Definition of Patient Registry (PR)

The WHO definition of "patient registry" is *"a file of documents containing uniform information about individual persons, collected in a systematic and comprehensive way, in order to serve a pre-determined scientific, clinical or policy purpose*[2]*"*. It does not pre-judge the amount of collected data which can be minimal or extensive, but implies continuity, as distinct from a cross-sectional survey.

The US National Committee on Vital and Health Statistics[3] defines registries as "*an organized system for the collection, storage, retrieval, analysis, and dissemination of information on individual persons who have either a particular disease, a condition (e.g., a risk factor) that predisposes (them) to the occurrence of a health-related event, or prior exposure to substances (or circumstances) known or suspected to cause adverse health effects".*

In its most simple form, a PR consists of a collection of paper cards kept inside a "shoe box" by physicians. Nowadays PR are collections of computerised data.

It is usual to distinguish between population-based registers, which refer to a geographically defined population and aim to register all cases in that population, and registers based on clinical centres or other criteria where the population coverage may not be clear. These two types of register have different uses. It may also be useful to distinguish exhaustive and non-exhaustive registers (the latter are possibly not registers by some definitions) - an exhaustive register seeks to include ALL cases which fulfil the inclusion criteria. Non-exhaustive registers (or databases) can however be very useful for finding patients for clinical research for example.

Purposes of PR in the field of RD

Monitoring prevalence and incidence

PR can be established to monitor incidence or prevalence, especially in relation to early warning of increases. Where incidence/prevalence is expected to be stable over long periods, an ad hoc study may be more cost-effective. However, for rare diseases a register and ad hoc study are often effectively the same, as a relatively long period of time is needed

[2] Brooke EM. The current and future use of registers in health information systems. Geneva: World Health Organization; 1974. Publication No. 8.

[3] Available at: Frequently Asked Questions about Medical and Public Health Registries. The National Committee on Vital and Health Statistics http://ncvhs.hhs.gov/9701138b.htm. Accessed April 2009.

to establish a precise incidence/prevalence, and to look for differences between populations if relevant.

Establishing natural history

The straightforward purpose of patient registries is to document the natural history of the disease, meaning its characteristics, management and outcomes with or without treatment. For rare diseases of genetic origin, the purpose may also be to establish a genotype-phenotype correlation. The natural history may be variable from one population group to another and usually changes over time, especially if a new therapy becomes available. The best example is the change in survival of patients with lysosomal storage diseases since the introduction of enzyme replacement therapies. Registries need to keep pace with the ever changing complexity of clinical factors in rare diseases especially in the context of increased life expectancy and ageing.

Monitoring safety: outcome surveys/post-marketing surveys

Registries have been often created in the past to monitor safety. In that context registries serve as an active surveillance system for the occurrence of unexpected or harmful events for products or interventions in general and in particular for drugs used off-label, which is the case for most drugs used by patients living with a rare disease. In the context of orphan drugs or new medical or surgical intervention, it is likely to be a necessary step as usually little is known at the time the intervention is implemented, and certainly not enough to be sure that any adverse effects have been properly assessed.

However registries to monitor safety are of limited interest for uses other than safety monitoring as they only monitor treated cases which may be a minority of cases or a skewed sample of cases. Usually they are product registries rather than disease registries. If there is more than one product from two different manufacturers for a given disease, this will lead to the establishment of two separate product registries with limited value, which will not allow the comparison of outcomes with each of the products.

Assessing clinical effectiveness

Registries can also be established to provide data for assessing the clinical effectiveness or the cost-effectiveness of new interventions in a real-world setting. This is required because the clinical studies performed to assess the clinical efficacy of new treatments are based on studies of selected patients following an “ideal protocol”, which differ from the clinical practice afterwards when the treatment is implemented in the healthcare setting. This is why more and more regulatory authorities and healthcare insurers request that a registry be implemented when an orphan drug receives a marketing authorisation. This type of registry is much more interesting than the previous type as it includes all patients, not only the treated patients. However, registries have to be designed specifically to assess cost-effectiveness in order to accomplish this purpose even if cost-effectiveness may be difficult to assess in rare diseases.

Measuring quality of care / plan services

Registries may also be established to measure the quality of care. It is usually compared to standards which have been established and which are considered as "gold standards". The IOM definition for quality of care is *"the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge"*. This type of registry is useful to identify disparities between health care outcomes and provide evidence for improving them. It is very interesting in a European context as health care systems, as well as attention given to patients with rare diseases, are very diverse. It is also useful for healthcare planning and gold standards exist only for a very limited number of rare diseases. With regard to quality of care self-reporting PR can complement reports from physicians and cover issues such as quality of life and social issues.

Performing research into aetiology

PR are also the basis for research into causes when not firmly established, providing that the potential causal factors are registered as well.

Providing an inventory of patients to re-contact for clinical research

In the field of rare diseases, a reason for establishing a patient registry is also to collect enough data on a given disease to make it visible and to motivate researchers and Industry to work on it. It seems to be an effective approach, providing that the registry is designed properly to generate useful information.

Another reason is to have an inventory of patients to re-contact for participation in epidemiological studies, clinical trials or for Health Technology Assessment to monitor real access to treatments. In that case the data needed on each patient is limited to the diagnosis and the contact details. It should be better named a "contact list" rather than a PR.

Yet another reason to make key data, such as genetic status, diagnostic criteria etc, available to research groups, is to reduce the repetitive collection of the same data thereby reducing demands on participants and their carers.

Of course most registries have the ambition to serve more than one purpose, although it is not always possible. Sticking to selected purposes requires a lot of attention in the design phase. It is common to mix up goals such as management of patients and management of data for research purpose. It is desirable for the format of data to be compatible between these two types of data registration systems to allow extraction, but the other aspects are too different to be accommodated by one system. Another common mistake is for registries to accept to collect data which they cannot successfully access, which can potentially paralyse the project.

Typology of data collections, other than registries

Registries are only one specific type of data collection. Several other types of data collection exist with their own merit and limit. They are reviewed below with reference to their particular type of use.

Health system data

These are computerised hospital files where the patient diagnosis is coded using a defined nomenclature, usually the International Classification of Diseases (ICD) developed by WHO. They are clinical tools, adapted to counting patients using specific types of healthcare services. They are used by healthcare managers. They are not designed for research purposes although they may sometimes be used for research purposes. Other sources can also be used such as death certificates or health insurance data. In the field of rare diseases their use is limited as the ICD does not yet provide specific codes for more than 240 RD. This should change with the release of ICD 11, and if these systems were perfect and if ICD coding for RD were perfect, much of the data we need would be available from health system data.

Healthcare provider databases

These are defined as permanent registrations of patient information in a systematic way, carried out by healthcare providers on the basis of their referrals. It is a passive ongoing registration activity. The advantage of such a system is its low cost, as there is no cost attached to the identification of cases, as they are referred through the healthcare system. The limits of this approach include the fact that registered cases are not a true representation of the general population but rather a biased sample, usually biased towards more severe cases or cases from higher socio-economic classes. If the data collection is done properly, the data set may be of interest for some research purposes, but not suitable for epidemiologic studies, unless it can be established that all the cases are referred to the collecting centre. Observatories of cases are also called hospital registries.

Ad hoc studies

This type of data collection is targeted at offering the possibility to answer one or more specific research questions. This is one shot data gathering, which may be repeated in at another time. The data collected is in the exact format required for the anticipated analysis. The protocol of the study is designed to ensure a clear answer to the research question(s). This implies an adequate definition of the sampled population, an adequate size of the sampled population, and an adequate management of the study to minimise the number of non-responders.

The ad hoc study is the most efficient instrument for research purposes as their protocol is well adapted to the research needs (the sample is fully representative and thus the results are conclusive) and the cost of the study is much lower that any type of permanent data collection, as the study takes place during a limited period of time. Ad hoc studies are flexible instruments with protocols adapted to the most recent discoveries about a disease.

There are several types of ad hoc studies, namely clinical trials, prospective cohorts, retrospective cohorts, case-control studies, cross-sectional (prevalence) studies, etc.

Ad hoc studies can be used in combination with longer term registries to answer specific research questions

Cohorts

In the context of a registry, the data collection can be transversal (all defined patients are registered once) or longitudinal (data is collected at different points in time for the same patient). If there is a systematic follow-up protocol, the dataset is defined as a cohort. For rare disease clinical research, cohorts are highly desirable as they are usually the only way to collect enough data to allow a proper analysis, due to the very small number of cases.

Status of data collections

There are several types of data collections:

In **"anonymous" data collections** the data is originally collected without identifiers and is impossible to link to their sources. This type of data collection is adequate for incidence and prevalence studies for instance, but is less appropriate for clinical research. The advantage of this technique is to maximise data protection and to ease the collaboration between researchers.

In **"anonymised" data collections**, data is originally identified, but is then irreversibly stripped of all identifiers and are impossible to link to their sources.

In **"indirectly identifiable" data collections**, data is unidentified for research purposes, but can be linked to their sources through the use of a code. This is the most common type of data collected for clinical research.

In **"directly identifiable" data collections**, identifiers, such as a name, patient number, or clear pedigree location, are attached to the data. This is, for example, the case for hospital files. The use of this type of data is regulated by strict rules in most, if not all, countries. Rules concerning this type of data collection differ from one country to another.

It is important that the degree of anonymity of the data is made clear to patients at the time of consent as uncertainty in this area is becoming more and more of a barrier to participation.

Points to consider when planning a patient registry in the field of rare diseases

The initial steps in planning a registry should consider the following points:

- **"Articulating the purpose and the objectives of the registry"**
  A clearly defined purpose helps clarify the need for certain data, including their scope and level of details. It prevents collecting large amount of data of limited value for the targeted objectives.

- **"Determining if the data being sought has already been collected elsewhere, totally or partially"**
  Relevant data to answer the research question may exist elsewhere, for instance in clinical laboratories providing diagnostic tests. A registry for the same disease may already be in place in another country. In some situations, adding new data to an existing registry rather than setting up an entirely new registry may be more cost-effective. Orphanet maintains a database of PR in the field of RD which can be consulted online. In any case, consideration should also be given to the interoperability of registers in the same field, to allow exchange of data and availability of a common subset of data for common analysis.

- **"Deciding whether the registry is the most appropriate instrument for addressing the research question"**
  This is crucial as time and resources needed to collect and process data in a registry setting can be substantial. This question should be considered in partnership with epidemiologists who are familiar with all possible data collection types with their respective advantages and disadvantages. For instance if the primary goal is to establish the incidence and the prevalence of a rare disease, a possible approach is to perform a "capture-recapture study" using all possible sources of data to "capture" cases in a given geographical area. For this goal, it is not necessary to have a permanent registration. As a principle, PR should only be created when there is a need to collect information over a long term. When the data collection requirements are temporary, they are more efficiently handled through a research study. Once a registry is created with an administrative structure and staff, it may be difficult to terminate it even if it has served its purpose.

- "**Identifying the stakeholders to envisage a partnership with them"**
  Other stakeholders are likely to have their own interest in accessing good quality data and may be willing to share the workload and the cost. The stakeholders to systematically consider are:
  (1) the regulatory authorities, the health care providers and the payers and commissioning authorities who will wish to access data to assess the impact of interventions, especially of new drugs, new protocols;
  (2) the product manufacturers who often get a conditional market authorisation for their orphan product which obliges them to establish a post marketing follow-up, usually through a registry. Manufacturers are

also interested in accessing data on the natural history of a disease for which they have a product in development to assess the needs and the feasibility of the development;

(3) the treating physician groups, the universities or professional societies and researchers in charge of clinical research;

(4) patient organisations which rightly consider that gathering data on their disease is pivotal in motivating academic researchers and Industry to invest on their disease. Patient groups spend considerable amounts of core resources on data collection and are invaluable partners at all stages of establishing and running a registry.

- **"Defining the scope of the registry"**
  This includes the planned representativeness of the target population and the characteristics of the data to be collected. When the purpose of the registry is defined, the next step is to define the data to be collected to reach the define goal(s). The scope of the registry is defined in terms of size (targeted number of patients), setting, geographical coverage and anticipated duration. The scope is adapted to the ambition of the promoters with due consideration for feasibility. The data to be collected is defined jointly with the final users of the data, as the format of the data pre-empts its potential utility for research purposes. If the data are not appropriate or are not formatted appropriately, it will be impossible to make sense of the data and use them.

- **"Assessing the feasibility of the project and the likelihood that it will be a success"**
  Establishing a registry is an investment which requires a careful approach. A feasibility study should take into account the following elements: Commitment of all professionals at the origin of the data; accessibility of the data (physically and legally); commitment of professionals to be involved in the monitoring and the analysis of the data; anticipated availability of an appropriate tool to collect, store and analyse the data; outreach programme to educate and promote adoption and proper use; possible funding for the initial phase; and plans for funding long-term activities.

- **"Identifying possible sources of funding, including long-term funding"**
  Funding should be envisaged not only to develop the tool to collect data, as often seen, but also to monitor their quality and to analyse them and disseminate the results. Usually the budget has to be substantial and is often underestimated at the beginning, when the promoters are not used to the epidemiology field. In many cases it takes years to realise the full benefits of a PR. Therefore long term funding is crucial. It is a waste of resources to go through the developmental phase of a registry only to have it terminated because of lack of funding.

  Sources of funding are different from one country to another, usually similar to sources of funding for research activities, because most registries in the field of rare diseases are built up to serve an identified research goal. In that case, funding is likely to be limited in time, leading to a crisis at the end of the grant.

  Countries may have a specific mechanism to fund registries, usually cancer registries, birth defects registries or cardio-vascular disease registries, but the committees in charge of assessing proposals are not sensitised to the specificities of patient registries in the field of rare diseases.

Funding from the European Commission is accorded on the same grounds as national grants. Both DG Research and DG Sanco provide funding for PR in the field of RD (for DG Research, funding is only granted is the PR is a tool for research purposes), but for limited time period although the European Commission acknowledges the need for a more sustainable support.

Long-term funding challenges for rare disease PR need to be addressed by pooling non-profit and for-profit resources in the most effective way.

As a consequence a reasonable funding plan is to devise each stage of funding as having its own results, and not being just an intermediary step to a long term result or even "hope" (e.g. availability of patients for research, without knowing precisely what research). Even the pilot phase can if at all possible tackle a question of relevance, so that pilot funding serves a greater purpose than simply establishing feasibility. Each funding application needs to be able to demonstrate the feasibility of reaching one or more objectives within the funding period, regardless of whether funding thereafter continues. Funding should where possible be used to enhance sustainability for the future (e.g. the development of software may involve short terms costs, but reduce long term costs) but not completely at the expense of producing any short term useful results.

Steps to consider when developing a PR in the field of RD

Establishing a registry is a complex process which requires a range of technical and organisational skills for the process to result in an effective data system. There are eight requirements that are critical to the successful development of a new PR.

Implementation Plan

There should be an implementation plan starting with a pilot phase when procedures are carefully evaluated and refined. It is more efficient to identify and resolve problems during a pilot phase than to invest a great deal of effort and resources developing software and procedures and acquiring equipments that must be altered later. In order to maximise adoption the application must be easy to use. It is important to build self-explanatory web forms tested with the people who will use them be they patient or clinician.

Adequate registry documentation

Adequate documentation is essential for ensuring the quality and efficient operation of the registry. It should include a definition of who will operate the PR; a thorough description of the inclusion and exclusion criteria; definitions of data sources, data collection, data editing and data entry procedures; data processing procedures; hardware and software manuals; definition of analyses that will be routinely conducted; confidentiality guidelines and access rules.

Data quality

The importance of data quality and data completeness assurance measures should be highlighted as pre-requisite for ensuring meaningful analyses and outcomes. Registries are (usually) voluntary programs, and the data quality may depend on the motivation or commitment of health care professionals submitting the data.

In addition, test results may not be comparable due to differences in test methods and equipment, as well as some methods of evaluation which are not-standardised between institutions. These may influence the analyses of the data and hence the outcomes.

In view of this, the realistic expectations from the database should be established, and the careful quality monitoring and quality improvement, as well as motivation of the health care professionals performing the data entry, have to be implemented. In addition, the voluntary and observational nature of registries necessitate that analyses and reports be undertaken with the appropriate consideration of potential cohort biases, confounders and incomplete data sets, using standard epidemiologic methodology.

Flexibility

Given the constant progress in scientific research, ensuring "flexibility" of the data base for research questions is critical to be able to respond to the research needs. For example, the minimum data elements may need to be subject to regular change and adaptation.

Technology

The data base has to be user-friendly and easy-to-use. The newer technologies are better, but usually more expensive. It is important to note that the change in a technology (for example implementation of a newer and a better software platform to capture the data) might have (considerable) financial and staffing implications.

Determination of data elements

One should be realistic when defining the data to be collected, bearing in mind the resources available and likely compliance of collectors as well as potential value for research. The definition of data elements should conform to professional standards and to International nomenclature when they exist. Coding in non standard format makes the merging of information with other PR virtually impossible.

Ways to pool data and connect databases

Interconnecting data bases may have some limitations which need to be taken into consideration, and of which the most important are:

1. Legal considerations relating to data privacy and data protection. For example, for processing of data for a combined analysis, in order to export the data from 1 database, new protocols (including these combined analysis) have to be established, and all enrolled patients have to be re-consented;

2. Technological barriers, such as differences in software, may preclude processing of data for a combined analysis, or limit possibilities for comparisons.

The type of software to be selected should be adapted to the specificities of the diseases and of the data collection organisation. The possibilities include:

(1) An off line system:

A unique central database stores all the data.

This is a very secure and inexpensive system. When collected at distance, data can be sent by post, by fax, by e-mail, although these systems have their limitations in terms of security. This is a less costly approach as non commercial soft wares for managing a unique database are available and can be easily customised after a short training.

As many local databases as there are entry points for data collection store their own data.

The data is transferred from time to time to a central registry (EUROCAT model). This model is a bit more costly as there is a need for software at each point of data collection, but is still a relatively low cost approach.

(2) An online system:

All data collectors have the right to electronically submit data to the distant database either by physicians or patients.

This solution can require high costs in terms of initial development and maintenance of the online system, raising many legal and security issues when the data are collected in one country and stored in another.

Both models have pros and cons depending on the data to be collected, the number of places where data are collected in one or more countries, and the choices of the different partners.

Whatever system is used, it should be possible for the provider of the data to be able to see easily what data they have provided, correct it if necessary, and produce local data reports.

It is recommended that Member States and/or the European Commission facilitate a centralised mainframe for data collection, storage and analysis, to allow long term maintenance and reduced costs.

Data access policy

The ability to access information in an efficient, flexible and timely fashion is a key element to the success of a PR. However PR store highly personal and sensitive information. Therefore the confidentiality of the information must be guaranteed. Allowing access to PR data without breaching confidentiality requires thought and planning. Establishing a policy for data access is a crucial task to guarantee the protection of confidential data and maximise the use of data by all stakeholders.

Framework for disseminating data and findings

It is necessary to define the routine data products and reports that will be needed to fulfil the goals of the registry. In addition the data should be used as much as possible to maximise output. The value of a PR is limited by the extent to which the data are analysed and results disseminated to relevant audiences. Nowadays the availability of data products and reports on a website is required.

Part II

Ethical and legal issues

Serious ethical concerns have led to legal requirements for using health information for research purposes. The creation and use of PR for research purpose constitute "research involving human subjects". Legal requirements exist on regional, national and European level, but are not always the same. Many PR have difficulties consolidating this information and fulfilling the various obligations. These legal requirements may influence the selection of data elements and the way verification can be organised, as well as affecting the subsequent use of data for secondary research purposes.

The purpose of the PR, the status of its developer and the extent to which registry data are identifiable largely determine applicable regulatory requirements.

Ethical concerns about the conduct of biomedical research and the use of health information in the past has led to a call for the establishment of a code of conduct for the various third parties who usually have a contact in this process: the patient organisations, the academic researchers, the policy makers and the Industry.

Consent requirement

The ethical principle of respect for persons supports the practice of obtaining individuals' consent to the use of their health information for research purposes. This includes consent to registry creation by the compilation of patient data, consent to the initial research purpose and uses of registry data, and consent to subsequent use of data by the PR developer or others, for the same purpose or other research purposes.

Individuals (children and parents included) should be informed with respect to the type of research that will or might be carried out, the arrangements for access to or sharing of stored information, and the duration of storage.

The consent process should also include instructions about the way to withdraw at any time. Conflicts of interest may result in undue influence on patients and compromise voluntary

participation. Consent should be given freely, free from pressure or persuasion, based on information provided by trained staff. If consent is withdrawn, the data is no longer usable.

When data is collected for research use, an ethics review committee will oversee the process and will be required to assess and ensure that benefits of the goals of research outweigh the risks of participation.

Information and consent should be obtained in writing and specific protections should be provided for vulnerable subjects and vulnerable populations, based on the general principle of acting in their best interest.

If the data collection is undertaken by a group from a different country, regulations from both the country of origin of the data and of the country where the data is stored should be respected in order to maximise the protection of the rights of the investigated group of patients.

The applicable regulations are different depending on the model of registration chosen:

- The **first model** is to register contact data, demographic and diagnosis data or exposure data, and to re-contact the registered individuals every time that a research study is initiated, to invite them to participate. This is the best model in terms of respect for persons, as individuals will have the opportunity to participate or not in any new study. This requires keeping track of people's movements or of patient deaths: most legal frameworks require that all persons registered revalidate their data annually.
- The **second model** is to register all needed data for an identified research purpose and to provide access to the dataset to a permanent, well-identified group of researchers. No disclosures of data will occur and all research activities have the same scientific purpose.
- The **third model** is to register data for an initial specific purpose with the clear intention to provide access to third parties and to subsequently use the data for other not yet identified purposes. This is the most complicated model, requiring a lot of attention in terms of protection of data privacy and respect for persons.

In the case of existing data collections, investigators should be required to re-contact subjects to obtain consent for new studies. If it is impossible or impractical to gain consent, an appropriate ethics review board must give its consent for the further use of the data.

Previously collected anonymous data, irreversibly anonymised, may be used for purposes other than those originally intended.

The decision to strip datasets of identifiers irreversibly requires careful consideration. The benefit of having unlinked anonymised data is to ensure absolute confidentiality thereby allowing further use of the data. However, retaining identifiers, though requiring further consent from the subject, permits more effective biomedical research and the possibility of re-contacting the subject.

Anonymised data are useful in allowing information sharing for research purposes with minimum risk. Anonymisation techniques should be standardized to ensure their robustness.

Patient organisations (or patients, when no organisation exists) should be involved in the elaboration of the consent form and the consent form process in order to ensure the best understanding of the information provided.

Protection of patient privacy

As a principle, research use of identifiable patient information is subject to legal requirements. The identifiability can be direct or indirect. Especially in the field of RD, a patient with a specific diagnosis, located in a defined place may be easily identified as being the only one. It is recommended to consult with the appropriate national authorities in charge of data protection to ensure compliance with requested standards.

Transparency, oversight and ownership

Transparency

Transparency contributes to public and professional confidence in the scientific integrity and validity of registry, and promotes inquiries from other interested parties. Registry developers achieve transparency by making the PR objectives, governance, eligibility criteria, sampling and recruitment strategies, general operating protocol, sources of data and of funding, available to anyone. Creating a website describing all these elements is one way to achieve transparency.

Security

Good security is essential for legal, ethical and operational considerations. It should not be underestimated. Security is easier to maintain on a dedicated server, but that also requires a backup strategy and an intrusion detection system on the server itself to avoid hackers.

Oversight

The independence of a PR depends more on its governance and the funding conditions than on the origin of the funding. Possible governing structures can vary widely depending on the project. The PR developer can be the sole decision-maker, but usually there is a governing board including all stakeholders: the data providers, the patient organisation(s), the funding agency, the professionals running the PR (clinical researchers, statisticians, information technology specialists). It is also desirable to appoint an independent advisory board to provide oversight of registry operations, particularly regarding the scientific independence.

The governing structure has to control that provision is specified to ensure continued care of the database under any circumstances.

Ownership

The concept of ownership does not fit health information comfortably as it fails to acknowledge individual patient privacy interests in health information. Alternatively, the legal concept of custody is useful. Custodians have legal rights and responsibilities, among which to preserve privacy and dignity of individual patients. Custody is also transferable from one custodian to another, which is particularly relevant for PR which are long-term projects.

Agreements about ownership of data and access to data should be determined by multi-party contracts and not regulated by legislation. Practices should be based on the following principles:

- The subject should always be considered as a primary controller of its data and information directly derived from it. Once the information has been processed, it becomes research data (i.e. data) unless there is agreed private ownership. The processor and/or principle investigator of data should be considered as the guardian of the data. As such, it is up to this person to take all the appropriate steps to protect the data, its storage, use and access. It follows that the researcher holds ultimate intellectual property with due consideration for benefit sharing data.
- Ownership of data implies an actual or potential financial return. A protocol including the donation of data by the subject to the researcher eliminates the subjects expectation of an individual compensation, but no the possibility of commercialisation by the researcher through traditional intellectual property rules.
- Use of collections by third parties should be allowed providing that there is no transfer of ownership and that the use is in agreement with the present guidelines.

PR can also receive Copyright protection as they satisfy the statutory definition of a compilation.

Finally, careful attention to the ethical considerations related to the design and operation of a PR, as well as the applicable legal requirements, contributes to the success of a PR and ensures the realisation of its social and scientific benefits. A quality procedure should be implemented to ensure the compliance to the present guidelines.

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Annex 1: Participants at the workshop 13 March 2008

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Other contributors to the report in addition to workshop participants

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Annex 2: List of rare disease registries in Europe

Orphanet Report Series on Disease Registries in Europe (January 2011)
http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf

Orphanet Report Series

Rare Diseases collection

January 2011

Disease Registries in Europe

www.orpha.net

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Institut national de la santé et de la recherche médicale

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HEALTH-F2-2008-201230

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Methodology

Patient registries and databases constitute key instruments to develop clinical research in the field of rare diseases (RD), to improve patient care and healthcare planning. They are the only way to pool data in order to achieve a sufficient sample size for epidemiological and/or clinical research. They are vital to assess the feasibility of clinical trials, to facilitate the planning of appropriate clinical trials and to support the enrolment of patients.

Registries of patients treated with orphan drugs are particularly relevant as they allow the gathering of evidence on the effectiveness of the treatment and on its possible side effects, keeping in mind that marketing authorisation is usually granted at a time when evidence is still limited although already somewhat convincing.

This report gather the information collected by Orphanet so far, regarding systematic collections of data for a specific disease or a group of diseases.

The concept of coverage (regional, national, european or international) that is associated with patient registries reflects the area of collection of a single physical database, to which several clinical entities are contributing.

The notion of networks corresponds to the relationship existing between several databases (or patient registries), whether a coordinating database exists or not.

Cancer registries are listed only if they belong to the network RARECARE or focus on a rare form of cancer.

American registries are listed only if they cover the European area and focus on a rare disease uncollected in Europe.

For any questions or comments, please contact us: *contact.orphanet@inserm.fr*

Summary

1- Distribution of registries by country

COUNTRY	REGIONAL	NATIONAL	EUROPEAN	GLOBAL	NOT DEFINED	TOTAL
AT - Austria	1	12	2	0	0	15
BE - Belgium	2	16	1	1	0	20
BG - Bulgaria	0	4	0	0	0	4
CH - Switzerland	1	5	1	2	0	9
CY - Cyprus	0	1	0	0	0	1
CZ - Czech Republic	0	4	0	0	0	4
DE - Germany	4	57	20	5	0	86
DK - Denmark	1	3	0	0	0	4
EE - Estonia	0	2	0	0	0	2
ES - Spain	4	25	3	0	0	32
FI - Finland	0	5	0	0	0	5
FR - France	17	92	11	1	1	122
GR - Greece	0	2	0	0	0	2
HR - Croatia	0	1	0	0	0	1
HU - Hungary	0	3	0	0	0	3
IE - Ireland	4	6	0	0	0	10
IL - Israel	0	2	0	0	0	2
IS - Iceland	0	2	0	0	0	2
IT - Italy	9	35	2	5	0	51
LT - Lithuania	0	1	0	0	0	1
LU - Luxembourg	0	1	0	0	0	1
LV - Latvia	0	1	0	0	0	1
MK - Republic of Macedonia	0	1	0	0	0	1
MT - Malta	0	1	0	0	0	1
NL - Netherlands	1	6	3	5	0	15
NO - Norway	0	3	1	0	0	4
PL - Poland	3	6	0	0	0	9
PT - Portugal	1	8	0	0	0	9
RO - Romania	0	2	0	0	0	2
RS - Serbia	0	4	0	0	0	4
SE - Sweden	0	15	0	3	0	18
SI - Slovenia	0	2	0	0	0	2
SK - Slovakia	0	2	0	0	0	2
TR - Turkey	0	4	0	0	0	4
UA - Ukraine	0	1	0	0	0	1
UK - United Kingdom	13	38	6	1	0	58
US - United States of America	0	0	0	6	0	6
TOTAL	61	373	50	29	1	514

2- Distribution of registries by coverage

COVERAGE	NUMBER OF REGISTRIES
REGIONAL	61
NATIONAL	373
EUROPEAN	50
GLOBAL	29
NOT DEFINED	1
TOTAL	514

3- Distribution of registries by institution

INSTITUTION	NUMBER OF REGISTRIES
ACADEMIC	490
PATIENT ORGANISATION	8
PRIVATE COMPANY	16
TOTAL	514

4- Network registries

NETWORKS	NUMBER OF NETWORKS
TOTAL	9

Distribution of registries by country

AT - AUSTRIA (15 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Austrian acromegaly registry	National	Academia
Austrian alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
Austrian brain tumor registry	National	Academia
Austrian cancer registry - contributes to the RARECARE project	National	Academia
Austrian chronic myeloid leukemia registry	National	Academia
Austrian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Austrian Haemophilia Registry	National	Academia
Austrian Huntington disease registry	National	Academia
Austrian myeloma registry	National	Academia
Austrian registry for inborn errors of metabolism	National	Academia
Austrian severe chronic neutropenia patient registry - contributes to the SCN international registry (SCNIR)	National	Academia
EMSA-SG: central patient registry of the European multiple system atrophy network	European	Academia
ENRAH: European alternating hemiplegia and rare epilepsies registry in childhood	European	Academia
MDS: Austrian myelodysplastic syndromes patient registry	National	Academia
Styrian registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia

BE - BELGIUM (20 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
ACROBEL: the Belgian registry on acromegaly, epidemiology and quality of care	National	Academia
Antwerpen registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Belgian alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
Belgian cystic fibrosis patient registry (BMR-RBM) - contributes to the EUROCARE CF and the ECFS registries	National	Academia
Belgian familial adenomatous polyposis registry	National	Academia
Belgian Neuromuscular Disease Registry	National	Academia
Belgian patient database for Wilson disease - contributes to the EuroWilson registry	National	Academia
Belgian patient registry for Duchenne and Becker muscular dystrophy - part of the TREAT-NMD network	National	Academia

Belgian patient registry for rare bleeding disorders - contributes to the RBDD international registry	National	Academia
Belgian registry of primary immunodeficiencies - contributes to the ESID European registry	National	Academia
Belgian rituximab therapy registry for immune anemia and thrombocytopenia	National	Academia
Belgian severe chronic neutropenia patient registry - contributes to the SCN international registry (SCNIR)	National	Academia
Belgian sickle cell anemia registry	National	Academia
Belgian systemic sclerosis cohort	National	Academia
ENRAH: Belgian contribution to European registry for alternating hemiplegia in childhood	National	Academia
EUNEFRON: registry of the European network for the study of orphan nephropathies	European	Academia
EURECHINOREG: Belgian contribution to the European registry of human alveolar echinococcosis	National	Academia
Hainault and Namur registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
LCH: Belgian Langerhans cell histiocytosis registry	National	Academia
Pediatric granulomatous arthritis international registry	Global	Academia

BG - BULGARIA (4 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Bulgarian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Bulgarian registry of patients with thalassaemia	National	Academia
Duchenne and Becker muscular dystrophy and spinal muscular atrophy patient registries in Bulgaria - part of the TREAT-NMD network	National	Academia
The Bulgarian genetic registry of monogenic disorders	National	Academia

CH - SWITZERLAND (9 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
BH4: international patient registry of tetrahydrobiopterin deficiency	Global	Academia
Duchenne and Becker muscular dystrophy and spinal muscular dystrophy patient registries in Switzerland - contributes to the TREAT-NMD network	National	Academia
PFAPA Registry: Periodic fever aphtous stomatitis, pharyngitis and adenopathy patient registry	European	Academia
PNH Registry: Paroxysmal Nocturnal Hemoglobinuria registry	Global	Industry
SIOLD: Swiss registry for Interstitial and Orphan Lung Diseases	National	Academia

Swiss alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
Swiss cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Swiss registry of biliary atresia - contributes to the EBAR registry	National	Academia
Vaud registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia

CY - CYPRUS (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Cyprian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

CZ - CZECH REPUBLIC (4 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Czech cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Czech severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
Duchenne and Becker muscular dystrophy patient registry in the Czech Republic and Slovakia - contributes to the TREAT-NMD network	National	Academia
Spinal muscular atrophy patient registry in the Czech Republic - part of the TREAT-NMD network	National	Academia

DE - GERMANY (86 registries)		
DE-ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
AID-NET : Clinical Registry and Biobank (DNA/RNA/serum) for autoinflammatory syndromes (children)	National	Academia
Ataxia-Telangiectasia patient registry - contributes to the ESID Database	National	Academia
Central Cutaneous Lymphoma Registry	National	Academia
Centre Saxony-Anhalt registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
CMMR: Central Malignant Melanoma Registry in germany	National	Academia
CompERA-XL: International, prospective registry for the documentation of first-line and maintenance therapy in patients with pulmonary hypertension	European	Academia
Conn Registry: German registry of primary aldosteronism	National	Academia
CPT-SIOP-Registry : International Registry for Choroid Plexus Tumors	Global	Academia
CURE-Net : National registry for congenital uro-rectal malformations	National	Academia

CWS-SoTiSaR: A registry for soft tissue sarcoma and other soft tissue tumours in children, adolescents, and young adults	European	Academia
DÖSAK tumor registry for documentation of tumors of the face and jaws in germany, austria and switzerland	European	Academia
Duchenne and Becker muscular dystrophy and spinal muscular atrophy patient registries in Austria and Germany - part of the TREAT-NMD network	National	Academia
EBAR: European Biliary Atresia Registry	European	Academia
EHDN: European Huntington's disease registry	European	Academia
EHDN: neuroacanthocytosis patient registry	Global	Academia
EKRS: Saarland Cancer Registry - contributes to the RARECARE Project	Regional	Academia
ENETS: European Neuroendocrine Tumour Registry	European	Academia
EPICURE-bank: European Epilepsy Brain Bank	European	Academia
ESID: European registry of primary immunodeficiencies	Global	Academia
EU-RHAB: European Rhabdoid Registry	European	Academia
EURIPFREG: European idiopathic pulmonary fibrosis registry	European	Academia
EURIPIDES: European Registry for ICD and CRT devices in pediatrics and adults with congenital heart disease	European	Academia
EUROFA: European Friedreich Ataxia Registry	European	Academia
European Alport registry	European	Academia
EUROSCA-R: European patient registry on spinocerebellar ataxias	European	Academia
EUTOS: European chronic myeloid leukemia patient registry (collaboration between the European LeukemiaNet and Novartis Europe)	European	Academia
GeNeMove: German database for wilson disease	National	Academia
German acromegaly registry	National	Academia
German adrenal tumors registry	National	Academia
German AID (Autoinflammatory disorders) registry -subproject AID-NET	National	Academia
German alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
German childhood cancer registry (Partner of ACCIS: Automated Childhood Cancer Information System)	National	Academia
German cystic fibrosis registry - contributes to the EUROCARE CF registry	National	Academia
German Epilepsy Registry	National	Academia
German Fanconi anemia registry	National	Academia
German gastrointestinal stromal tumor registry	National	Academia
German Haemophilia Registry (DHR)	National	Academia
German mucopolysaccharidosis patient registry	National	Academia
German multiple endocrine neoplasia type 1 (MEN 1) registry	National	Academia
German national case collection of familial pancreatic cancer	National	Academia
German paroxysmal nocturnal hemoglobinuria registry	National	Academia

German pituitary tumors registry	National	Academia
German registry for congenital heart defects - part of the competence network for congenital heart defects	National	Academia
German registry for congenital thrombocytopenia	National	Academia
German registry for Morbus Adamantiades-Behçet e.V.	National	Academia
German registry for papulosis atrophicans maligna	National	Academia
German registry for patients with pulmonary hypertension	National	Academia
German registry of congenital dyserythropoietic anemias (CDA)	National	Academia
German severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
German vasculitis registry	National	Academia
GMALL-registry and biobank: registry for adult patients with acute lymphoblastic leukemia or related diseases	National	Academia
GOLD.net : Registry and biobank for Diffus Parenchymal Lung Disease	National	Academia
HepNet: German hepatocellular carcinoma (HCC) registry	National	Academia
International pheochromocytoma and paraganglioma registry	Global	Academia
INVM (Isolated Noncompaction of Ventricular Myocardium) registry	National	Academia
KINDLERNET: Central patient registry Kindler syndrome	European	Academia
LCH: German Langerhans cell histiocystosis registry	National	Academia
Lupus nephritis registry (established by the german paediatric nephrology association)	National	Academia
Mainz registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
MAISTHRO-Registry : multicentric thrombophilia registry (MAIn-ISar-THROmbose-Register)	National	Academia
MDS: German myelodysplastic syndromes patient registry	National	Academia
MEFOPA: registry for patients with rare Mendelian forms of Parkinson's Disease	European	Academia
National FKRP-patient registry germany - part of the TREAT-NMD network	National	Academia
National nephrogenic systemic fibrosis registry	National	Academia
National PSHN registry (german society for paediatric nephrology GPN)	National	Academia
National registry for Blackfan-Diamond disease	National	Academia
NCL-Registry: International neuronal ceroid lipofuscinoses patient registry	European	Academia
NET-Registry: German neuroendocrine gastrointestinal tumors	National	Academia
Neuromyelitis optica patient registry	National	Academia
NIRK: national central registry for ichthyoses and related keratinization disorders	National	Academia
NIRK: patient registry for autosomal recessive congenital ichthyosis	National	Academia
NKR: German registry for adrenocortical carcinoma	National	Academia

Patient registry for primary hyperoxaluria	National	Academia
Patient registry of the German Network for Systemic Scleroderma	National	Academia
PID-NET: National registry of primary immunodeficiencies	National	Academia
PODONET: Registry for Steroid-Resistant Nephrotic Syndrome (SRNS) patients	European	Academia
RAMEDIS : Rare Metabolic Diseases Database	National	Academia
RegiSCAR: European registry of severe cutaneous adverse reactions (SCAR) to drugs and collection of biological samples	European	Academia
Registry for children with congenital limb malformations	National	Academia
Registry for congenital melanocytic nevi and neurocutaneous melanocytosis	National	Academia
Registry for Merkel Cell Carcinoma	National	Academia
Registry for patients with mitochondrial diseases (mitoREGISTER) - subproject of mitoNET	National	Academia
Registry for Patients with WT1 Mutation Associated Diseases	National	Academia
RetDis Database (blood or DNA samples and associated clinical descriptions of patients and families with inherited eye diseases)	European	Academia
STER: FVII deficiency treatment international registry	Global	Academia
Von Hippel-Lindau registry	Regional	Academia

DK - DENMARK (4 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Danish cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Danish malignant hyperthermia registry - contributes to the European Malignant Hyperthermia Group (EMHG)	National	Academia
Funen county registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Mendelian cytogenetics network online database	National	Academia

EE - ESTONIA (2 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Estonian cancer registry - contributes to the RARECARE project	National	Academia
Estonian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

ES - SPAIN (32 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Asturias registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Barcelona birth defects registry - contributes to the EUROCAT network	Regional	Academia
Budd-Chiari syndrome (BCS) and hepatic vascular diseases registry	National	Academia
ERCUSYN: European registry on Cushing's syndrome	European	Academia
EUGINDAT-PIADATABASE: European primary inherited aminoacidurias database	European	Academia
GIRMOGEN_PRO Database: mental retardation with genetics etiology registry in Spain	National	Academia
MOLDIAG-PACA: patient registry of pancreatic cancer	European	Academia
REA: Acromegaly Spanish registry	National	Academia
RECOMINA: patient registry of microscopic colitis and study of the environmental risk factors	National	Academia
REDIP: Spanish registry of primary immunodeficiencies - contributes to the ESID European registry	National	Academia
Registry for rare disorders in Extremadura (Spain)	Regional	Academia
Registry of congenital anomalies of the Basque Country (Spain) - contributes to the EUROCAT network	Regional	Academia
REHAP: Spanish Registry of Pulmonary Arterial Hypertension	National	Academia
RETEGEP: Spanish Registry of Gastroenteropancreatic Endocrine Tumors	National	Academia
Spanish alpha-1 antitrypsin deficiency registry (REDAAT) - contributes to the Alpha One International Registry (AIR)	National	Academia
Spanish cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Spanish Familial Adenomatous Polyposis Registry	National	Academia
Spanish Gaucher's disease registry	National	Academia
Spanish Overgrowth Syndrome Registry	National	Academia
Spanish patient registry for spinal muscular atrophy - part of the TREAT-NMD network	National	Academia
Spanish patient registry of hereditary angioedema	National	Academia
Spanish patient registry of hereditary retinal dystrophy	National	Academia
Spanish patient registry of myelodysplasic syndromes	National	Academia
Spanish patient registry of rare diseases: multiple endocrine neoplasia, acromegaly and enteropancreatic endocrine tumors.	National	Academia
Spanish patient registry of transmissible spongiform encephalopathies	National	Academia
Spanish registry of Duchenne muscular dystrophy - part of the TREAT-NMD network	National	Academia
Spanish registry of metabolic hereditary diseases	National	Academia
Spanish registry of patients with fragile X syndrome	National	Academia

Spanish registry of POEMS syndrome patients (Osteosclerotic myeloma)	National	Academia
Spanish Registry of Rare Diseases	National	Academia
Spanish registry of renal hereditary diseases	National	Academia
Spanish severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia

FI - FINLAND (5 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Duchenne and Becker muscular dystrophy and spinal muscular dystrophy patient registries in Finland - contributes to the TREAT-NMD network	National	Patient organisation
Finnish cancer registry - contributes to the RARECARE project	National	Patient organisation
Finnish patient registry on Fabry disease	National	Academia
Finnish registry of congenital anomalies - contributes to the EUROCAT network	National	Academia
The Finnish registry of visual impairment	National	Academia

FR - FRANCE (122 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Aquitaine registry of mesothelioma	Regional	Academia
Auvergne registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Bas-Rhin registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Basse Normandie registry of hematological malignancies	Regional	Academia
BLAU registry: French pediatric granulomatous arthritis registry	National	Academia
Breast and other gynecological cancers registry of Côte-d'Or	Regional	Academia
CEREDIH: French primary immunodeficiencies registry	National	Academia
CoF-AT study: a French cohort on ataxia-telangiectasia	National	Academia
Cohort of patients affected by Marfan or related syndrome	National	Academia
Cohort of patients with hereditary dystrophies of retina	Not defined	Academia
Côte d'Or registry of hematological malignancies	Regional	Academia
Cystadane post marketing registry of patient with homocystinuria	European	Industry
D[4]/Phenodent: French registry of patients affected by rare odontologic diseases	National	Academia
Duchenne and Becker muscular dystrophy patient registry in France - part of the TREAT-NMD network	National	Academia
EDMUS - NOMADMUS: French cohort and biobank of Devic's neuromyelitis optica and related neurological disorders	National	Academia
EDMUS: European Database for Multiple Sclerosis and other related diseases	European	Academia

EHN - EURO-HISTIO-NET: European registry of Langerhans Cell Histiocytosis	European	Academia
ENET Registry: European Neuro-Endocrine Tumors Group	National	Academia
EPI-EPNET: European hepatic and erythropoietic porphyrias registry	European	Academia
EPIMAD: registry of chronic inflammatory intestine diseases in North-West	Regional	Academia
Escort-Hu: European sickle cell disease cohort- hydroxyurea	European	Industry
Establishment of children and adolescents cohort in Behcet disease in France	National	Academia
EURECHINOREG: European registry of alveolar echinococcosis	European	Academia
European prospective registry of children born to mothers affected by the antiphospholipids syndrome	European	Academia
EUROTRAPS: European patient registry on TRAPS syndrome	European	Academia
FranceCoag: French prospective cohort of patients affected with haemophilia or severe form of other hereditary hemorrhagic diseases except platelet disorders	National	Academia
French acromegaly registry	National	Academia
French addictive acute intoxications cohort	National	Academia
French amyotrophic lateral sclerosis patient registry	National	Academia
French atypical sarcoïdosis clinical forms registry	National	Academia
French auto-immunity and Rituximab (AIR) registry: prospective study of patients treated with Rituximab	National	Academia
French bradykinic idiopathic angioneurotic edema and oestrogen-sensitive registry	National	Academia
French central hypoventilation syndrome registry - will contribute to the European CHS registry	National	Academia
French certified patient registry for Langerhans cell histiocytosis and biological collection	National	Academia
French certified registry of glycogen storage disease type 2	National	Academia
French certified registry of patients affected by Gaucher disease	National	Academia
French certified registry of patients affected by thalassemia	National	Academia
French cohort creation in retinitis pigmentosa	National	Academia
French cohort for auto-inflammatory diseases	National	Academia
French cohort in genetic microcephalies	National	Academia
French cohort in primary ciliary dyskinesia	National	Academia
French cohort of acquired autoimmune haemolytic anemia	National	Academia
French cohort of Castleman's disease	National	Academia
French cohort of common variable immunodeficiency with hypogammaglobulinemia in adults (CVID)	National	Academia
French cohort of focal dystonia famillies	National	Academia
French cohort of idiopathic pulmonary fibrosis	National	Academia
French cohort of inflammatory bowel disease (IBD)	National	Academia
French cohort of rare diabetes (monogenic forms and syndromic forms)	National	Academia
French cohort of rhombencephalosynapsis	National	Academia

French cohort of Usher syndrome	National	Academia
French Cohorts in Sneddon syndrome and suspected Sneddon syndrome livedo	National	Academia
French constitutive hematologic diseases registry	National	Academia
French cystic fibrosis cohort	National	Academia
French cystic fibrosis patient registry	National	Patient organisation
French cystinosis registry	National	Academia
French epidemiological registry of esophageal atresia	National	Academia
French familial cardiac malformations registry	National	Academia
French observatory of biliary atresia	National	Academia
French observatory of gastric linitis plastica	National	Academia
French observatory of primary biliary cirrhosis	National	Academia
French observatory of primitive sclerosing cholangitis	National	Academia
French patient registry affected by genetic deafness in France	National	Academia
French Patient registry in chorioretinopathy, birdshot type	National	Academia
French pediatric registry of rituximab treated patients affected by severe systemic diseases - contributes to the French AIR registry	National	Academia
French prospective cohort of childhood care for autoimmune haemolytic anemia and Evans syndrome	National	Academia
French prospective follow-up cohort of child affected by autoimmune haemolytic anemia (AHAI), Evans syndrome and thrombocytopenic autoimmune purpura (ATP)	National	Academia
French registry for capillary leak syndromes	National	Academia
French registry for macrophagic myofasciitis	National	Academia
French registry for right arrythmogenic ventricular dysplasia (ARVC/D)	National	Academia
French registry of autosomal recessive polycystic kidney disease	National	Academia
French registry of cases of spontaneous periodic hypothermia	National	Academia
French registry of child handicap and perinatal observatory	National	Academia
French registry of child hematological malignancies	National	Academia
French registry of child hemolytic uremic syndrome	National	Academia
French registry of children solid tumors	National	Academia
French registry of corticosteroid-sensitive aseptic abscess	National	Academia
French registry of familial and premature prostate cancers (before 50 years)	National	Academia
French registry of generalized resistance to thyroid hormone	National	Academia
French registry of hereditary dyslipidemia in children: familial combined dyslipidemias	National	Academia
French registry of Iron overload genetic rare diseases, non-related to the HFE gene	National	Academia
French registry of Kabuki syndrome	National	Academia

French registry of Marshall's syndrome with periodic fever	National	Academia
French registry of neuromuscular diseases from reference centres	National	Academia
French registry of patients affect by Leber amaurosis and retinitis pigmentosa to assess the clinical trial in gene therapy	National	Academia
French registry of pregnant women carriers of anti-SSA antibodies	National	Academia
French registry of rare genetic metabolism disorders of steroids - contributing to the international RGSDC registry	National	Academia
French registry of rare hypersomnias	National	Academia
French registry of rare pulmonary hypertension (HTAP)	National	Academia
French registry of tetrahydrobiopterin deficiencies	National	Academia
French severe chronic neutropenia certified patient registry - contributes to the SCN international registry (SCNIR)	National	Academia
French sickle cell anemia registry	National	Academia
French Still disease patient registry	National	Academia
French Williams syndrome cohort	National	Academia
FROG: FRench Observatory on Gaucher disease	National	Industry
GENEPSO: French epidemiological cohort of BRCA systemic mutations carriers	National	Academia
Gironde registry of hematological malignancies	Regional	Academia
GMF: French registry of myelodysplastic syndromes and leukemia chemo- and radio-induced	National	Academia
GTE: French registry of endocrine tumors	National	Academia
Idiopathic pulmonary fibrosis: Cohort studies for evaluation of pronostic factors, therapeutic evaluation	National	Academia
INFEVERS: European registry of mutations involved in familial mediterranean fever (FMF) and hereditary autoinflammatory disorders	European	Academia
International FKRP (Fukutin-Related Protein) defects registry - part of TREAT-NMD network	Global	Academia
ITINERAIR-HTAP: French cohort of adult with pulmonary arterial hypertension	National	Industry
ITINERAIR-pediatrie: French cohort of children with pulmonary arterial hypertension	National	Industry
ITINERAIR-scleroderma: French pulmonary arterial hypertension screening cohort of patients with scleroderma	National	Industry
LEA: children and adolescents with acute leukemia : propective cohort in France	National	Academia
Left ventricular noncompaction French registry	National	Academia
Mesothelioma cohort in Seine Saint-Denis and Val de Marne	Regional	Academia
Myotonic dystrophy patient registry in France - part of the TREAT-NMD network	National	Academia
Paris registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
PHA1-NET: PseudoHypoAldosteronism type 1 cohort	National	Academia
Primary central nervous system tumors registry of Gironde	Regional	Academia

Regional registry of thyroid cancers in Rhône-Alpes	Regional	Academia
Registry and pronostic cohort of cutaneous lymphomas in Aquitaine	Regional	Academia
Registry for digestive cancers in Burgundy	Regional	Academia
Registry of digestive tumors in Calvados (province of France)	Regional	Academia
Registry of observed trichinellosis cases in France yearly	National	Academia
Registry of the network studying thrombotic microangiopathies	National	Academia
Rhône-Alpes registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Rhône-Alpes registry of systemic mastocytosis	Regional	Academia
SYRENE: Rett syndrome network - French database of clinical and genetic aspects of Rett syndrome	National	Academia
VALID: cohort creation on Budd-Chiari syndrome, hepatic venooclusive disease, hepatoportal sclerosis and portal vein thrombosis	European	Academia
Vedrop registry of chronic cholestasis patient with vitamin E deficiency	European	Industry

GR - GREECE (2 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Greek cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Greek severe chronic neutropenia patient registry - contributes to the SCN international registry (SCNIR)	National	Academia

HR - CROATIA (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Croatian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

HU - HUNGARY (3 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Duchenne and Becker muscular dystrophy and spinal muscular dystrophy patient registries in Hungary - contributes to the TREAT-NMD network	National	Academia
Hungarian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Hungarian severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia

IE - IRELAND (9 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
CFRI: The Cystic Fibrosis Registry of Ireland - contributes to the EUROCARE CF registry	National	Academia
Dublin registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Galway registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Irish myelodysplastic syndromes specific registry	National	Academia
Irish registry for Bernard-Soulier syndrome	National	Academia
Irish registry of amyotrophic lateral sclerosis and motor neurone disease	National	Academia
Irish registry of Hurler syndrome	National	Academia
Irish severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
South East of Ireland registry of congenital anomalies - part of BINOCAR and EUROCAT network	Regional	Academia
South of Ireland registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia

IL - ISRAEL (2 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Israeli cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Israelian severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia

IS - ICELAND (2 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Icelander cancer registry - contributes to the RARECARE project	National	Patient organisation
Icelander cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

IT - ITALY (51 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Arrhythmogenic right ventricular cardiomyopathy/ dysplasia: clinical registry and database, evaluation of therapies, DNA banking	National	Academia
Campania registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Duchenne and Becker muscular dystrophy and spinal muscular dystrophy patient registries in Italy - contributes to the TREAT-NMD network	National	Academia

Emilia Romagna registry of congenital anomalies (IMER) - contributes to the EUROCAT registry	Regional	Academia
EUROFEVER: European registry for autoinflammatory diseases	Global	Academia
European registry of congenital dyserythropoietic anemia	European	Academia
FMF: Italian registry for familial mediterranean fever in the young	National	Academia
Friedreich's ataxia Italian patient registry	National	Academia
GLATIT: Glanzmann thrombasthenia Italian registry	National	Academia
HAE-registry: European hereditary angioedema patient registry	European	Academia
IBAHC: Italian registry for alternating hemiplegia of childhood	National	Academia
International registry of bone fragility fractures in the young	Global	Academia
International Registry of Rare Bleeding Disorders (RBDD)	Global	Academia
International registry of recurrent and familial hemolytic uremic syndrome / thrombotic thrombocytopenic purpura	Global	Academia
International registry on thrombotic thrombocytopenic purpura (TTP)	Global	Academia
Italian alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
Italian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Italian genetic movement disorders registry	National	Academia
Italian Li-Fraumeni syndrome registry	National	Academia
Italian neuroblastoma registry	National	Academia
Italian registry for cri du chat syndrome (monosomy 5p)	National	Academia
Italian registry for hereditary multiple exostoses	National	Academia
Italian registry for MYH9-related thrombocytopenia	National	Academia
Italian registry of adult patients affected by familial mediterranean fever	National	Academia
Italian registry of congenital nephrotic syndromes	National	Academia
Italian registry of Creutzfeldt-Jakob disease and correlated syndromes	National	Academia
Italian registry of diffuse infiltrative pneumopathies	National	Academia
Italian registry of hemophilia centre (AICE)	National	Academia
Italian registry of hypertrophic cardiomyopathy in Anderson-Fabry disease	National	Academia
Italian registry of Legionellosis	National	Academia
Italian registry of maturity onset diabetes of the young (MODY)	National	Academia
Italian registry of muscle channel-diseases	National	Academia
Italian registry of myotonic dystrophies	National	Academia
Italian registry of patients and families affected by Pseudoxanthoma Elasticum	National	Academia
Italian registry of skeletal dysplasia	National	Academia
Italian retinoblastoma registry	National	Academia

Italian severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
North-east Italy registry of neurofibromatosis	Regional	Academia
North-East of Italy registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Regional registry for neuromuscular disorders	Regional	Academia
Registry of inherited bleeding disorders in Emilia-Romagna region	Regional	Academia
Registry of pregnant patients affected by essential thrombocythemia	National	Academia
RIAF: Fanconi's anemia Italian registry	National	Academia
RIAT: Ataxia teleangiectasia Italian registry	National	Academia
RICH: Italian registry of infants with congenital hypothyroidism	National	Academia
RIMM: Italian registry for myelofibrosis with myeloid metaplasia	National	Academia
RISMD: Italian myelodysplastic syndromes registry	National	Academia
Sicilian registry of congenital anomalies (ISMAC) - contributes to the EUROCAT network	Regional	Academia
Tuscany registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
Venetian registry of rare diseases	Regional	Academia
V-RIAT: variant Ataxia telangiectasia Italian registry	National	Academia

LT - LITHUANIA (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Lithuanian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

LU - LUXEMBOURG (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Luxembourgers cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

LV - LATVIA (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Latvian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

MK - REPUBLIC OF MACEDONIA (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Macedonian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

MT - MALTA (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Maltese cancer registry - contributes to the RARECARE project	National	Academia

NL - NETHERLANDS (15 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
CONCOR: Dutch registry of patients with a congenital heart malformation	National	Academia
Duchenne and Becker muscular dystrophy patient registry in the Netherlands - part of the TREAT-NMD network	National	Academia
Dutch alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
Dutch cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Dutch severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
ECARUCA: cytogenetic and clinical database on rare chromosomal disorders	European	Academia
EPCOT: European prospective cohort on thrombophilia	European	Academia
Nephrotic syndrome registry	Global	Academia
North Netherlands registry of congenital anomalies - contributes to the EUROCAT network	Regional	Academia
PAN research: Prospective amyotrophic lateral sclerosis (ALS) study Netherlands	National	Academia
The intenational Pompe registry	Global	Industry
The International Collaborative Gaucher Group (ICGG) Gaucher registry	Global	Industry
The international Fabry registry	Global	Industry
The international Mps I registry	Global	Industry
X-ALD: X-linked adrenoleukodystrophy database	European	Academia

NO - NORWAY (4 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
EURADRENAL: European patient registry on autoimmune Addison's disease (sera, DNA and RNA)	European	Academia
Norwegian cancer registry - contributes to the RARECARE project	National	Academia

Norwegian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Norwegian severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia

PL - POLAND (9 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Cracow cancer registry - contributes to the RARECARE project	Regional	Academia
Duchenne and Becker muscular dystrophy and spinal muscular dystrophy patient registries in Poland - contributes to the TREAT-NMD network	National	Academia
Kielce cancer registry - contributes to the RARECARE project	Regional	Academia
Polish cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Polish registry of primary immunodeficiencies - contributes to the ESID European registry	National	Academia
Polish severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
Polish Silver-Russell syndrome patient registry	National	Academia
PRCM: Polish registry of congenital malformations - contributes to the EUROCAT network	National	Academia
Warsaw cancer registry - contributes to the RARECARE project	Regional	Academia

PT - PORTUGAL (9 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
Duchenne and Becker muscular dystrophy patient registry in Portugal - contributes to the TREAT-NMD network	National	Academia
Portugues centre for study and registry of congenital anomalies (CERAC) - contributes to the EUROCAT network	National	Academia
Portuguese cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Portuguese Fabry registry	National	Academia
Portuguese registry of biliary atresia - contributes to the EBAR registry	National	Academia
Portuguese registry of primary immunodeficiency diseases (REPORID)	National	Academia
Portuguese Rett syndrome registry	National	Academia
Portuguese severe chronic neutropenia patient registry - contributes to the SCN international registry (SCNIR)	National	Academia
Southern Portugal cancer registry - contributes to the RARECARE project	Regional	Academia

RO - ROMANIA (2 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Romanian biliary atresia registry	National	Academia
Romanian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

RS - SERBIA (4 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Serbian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Serbian registry of hemophilia and von Willebrand disease patients	National	Academia
Serbian registry of patients with rare bleeding disorders - contributes to the RBDD international registry	National	Academia
Serbian severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia

SE - SWEDEN (18 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
FOS : Fabry Outcome Survey	Global	Industry
HOS : Hunter Outcome Survey	Global	Industry
IOS : Icatibant Outcome Survey for hereditory angioedema	Global	Industry
National registry on bronchopulmonary dysplasia	National	Academia
SPAHR: Swedish Pulmonary Arterial Hypertension Registry	National	Academia
SWEDCON: Swedish Registry of Congenital Heart Disease	National	Academia
Swedish Acute Lymphoblastic Leukemia Registry	National	Academia
Swedish Acute Myelogenous Leukemia Registry	National	Academia
Swedish alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
Swedish Childhood Cancer Registry	National	Academia
Swedish Chronic Myeloid Leukemia Registry	National	Academia
Swedish cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Swedish database on Usher syndrome	National	Academia
Swedish Multiple Myeloma Registry	National	Academia
Swedish Polyposis Registry	National	Academia
Swedish Registry for Familial Amyloid Polyneuropathy	National	Academia
Swedish severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
SWEDROP: Swedish Registry for Retinopathy of Prematurity	National	Academia

SI - SLOVENIA (2 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Slovenian cancer registry - contributes to the RARECARE project	National	Academia
Slovenian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

SK - SLOVAKIA (2 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Slovakian cancer registry - contributes to the RARECARE project	National	Academia
Slovakian cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia

TR - TURKEY (4 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Database setup for the visualisation and examination of oral ulcers in Behcet disease patients	National	Academia
Duchenne and Becker muscular dystrophy and spinal muscular dystrophy patient registries in Turkey - contributes to the TREAT-NMD network	National	Academia
Turkish cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Academia
Turkish severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia

UA - UKRAINE (1 registry)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
Spinal muscular atrophy patient registry in Ukraine - part of the TREAT-NMD network	National	Academia

UK - UNITED KINGDOM (58 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	INSTITUTION
AOMIC: adult onset myositis immunogenetic collaboration	National	Academia
BPOLD: British Paediatric Orphan Lung Disease Registry	National	Academia
CARIS - Welsh registry of congenital anomalies - part of BINOCAR and EUROCAT network	Regional	Academia
CAROBB - congenital anomalies registry for Oxfordshire, Berkshire & Buckinghamshire - part of the BINOCAR and EUROCAT network	Regional	Academia

CRANE: database of patients with cleft lip and/or cleft palate in England and Wales	National	Academia
Duchenne and Becker muscular dystrophy patient registry in United Kingdom and Ireland - part of the TREAT-NMD network	National	Patient organisation
EBV associated NK/T cell diseases registry	National	Academia
EHDN: registry of juvenile Huntington's disease	Global	Academia
EMSYCAR - East Midlands & South Yorkshire congenital anomalies registry - part of BINOCAR and EUROCAT network	Regional	Academia
English alpha-1 antitrypsin deficiency registry - contributes to the Alpha One International Registry (AIR)	National	Academia
English and Irish Fanconi anemia registry	National	Academia
English central hypoventilation syndrome registry - will contribute to the European CHS	National	Academia
English cystic fibrosis database	National	Academia
English cystic fibrosis patient registry - contributes to the EUROCARE CF and ECFS registries	National	Academia
English cystinosis registry	National	Academia
English dyskeratosis congenita registry	National	Academia
English Gaucher registry	National	Academia
English hereditary angioedema patient registry - part of the HAE European registry	National	Academia
English hyperoxaluria registry	National	Academia
English juvenile dermatomyositis registry and repository	National	Academia
English mucopolysaccharidosis registry	National	Patient organisation
English phenylketonuria registry	National	Academia
English registry for lymphangioleiomyomatosis	National	Academia
English registry of biliary atresia - contributes to the EBAR registry	National	Academia
English registry of primary immunodeficiencies - contributes to the ESID European registry	National	Academia
English registry of syndromes with abnormal vertebral segmentation	National	Academia
English registry of Wolf-Hirschhorn syndrome	National	Academia
English severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Academia
EUHASS: European haemophilia safety surveillance - pharmacovigilance program monitoring the safety of treatments for people with inherited bleeding disorders in Europe	European	Academia
EUMDS: European Registry for Myelodysplastic Syndromes - part of EuroLeukemiaNet (ELN)	European	Academia
EURODSD: European disorders of sexual development registry	European	Academia
EUROPAC: the European registry of hereditary pancreatitis and familial pancreatic cancer	European	Academia
European Prader-Willi syndrome database	European	Academia

EUROWILSON: European clinical database for Wilson disease	European	Academia
Glasgow registry of congenital anomalies - part of BINOCAR and EUROCAT network	Regional	Academia
LCH: English Langerhans cell histiocytosis registry	National	Academia
Merseyside and Cheshire registry of congenital anomalies -part of BINOCAR and EUROCAT network	Regional	Academia
Myotonic dystrophy patient registry in United Kingdom - part of the TREAT-NMD network	National	Academia
National Congenital Anomaly System (NCAS) - part of BINOCAR and EUROCAT network	Regional	Academia
NDSCR - National Down syndrome cytogenetic registry - part of BINOCAR and EUROCAT network	National	Academia
NHD: the national haemophilia database	National	Academia
NHR: National Haemoglobinopathy Registry	National	Academia
NorCAS - Northern registry of congenital anomalies - part of BINOCAR and EUROCAT network	Regional	Academia
Regional spinocerebellar ataxia registry	Regional	Academia
SCAR - Scottish registry of congenital anomalies - part of BINOCAR and EUROCAT network	Regional	Academia
Spinal muscular atrophy patient registry in United Kingdom and Ireland - part of the TREAT-NMD network	National	Academia
Spinocerebellar ataxia type 1 registry	National	Academia
SWCAR - South West congenital anomalies registry - part of BINOCAR and EUROCAT network	Regional	Academia
The regional paediatric cardiology database	Regional	Academia
UK Paediatric ITP (Immune Thrombocytopenic Purpura) Registry	National	Academia
UK renal rare disease registry	National	Academia
UKAITPR: United Kingdom adult idiopathic thrombocytopenic purpura registry	National	Academia
UKCCCR: English familial ovarian cancer patient registry	National	Academia
UKESR: United Kingdom Evans Syndrome Registry	National	Academia
UKFITPR: United Kingdom familial idiopathic thrombocytopenic purpura (ITP) Registry	National	Academia
United Kingdom neuromyelitis optica registry	National	Academia
WANDA - Wessex registry of antenatally detected anomalies - part of BINOCAR and EUROCAT network	Regional	Academia
West Midlands registry of congenital anomalies - part of BINOCAR and EUROCAT network	Regional	Academia

US - UNITED STATES (6 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COVERAGE**	**INSTITUTION**
CMDIR: congenital muscular dystrophy international registry	Global	Academia
International Friedreich Ataxia Research Alliance (FARA) registry	Global	Patient organisation
International Morquio A registry	Global	Patient organisation
International Rare Genetic Steroid Disorders Consortium (RGSDC) registry	Global	Academia
International registry for primary hyperoxaluria	Global	Academia
THAOS: transthyretin amyloidosis outcomes survey	Global	Industry

European registries

EUROPEAN REGISTRIES (50 registries)		
ENGLISH LABEL OF THE ACTIVITY	COORDINATION	INSTITUTION
EMSA-SG: central patient registry of the European multiple system atrophy network	AT	Academia
ENRAH: European alternating hemiplegia and rare epilepsies registry in childhood	AT	Academia
EUNEFRON: registry of the European network for the study of orphan nephropathies	BE	Academia
PFAPA Registry: Periodic fever aphtous stomatitis, pharyngitis and adenopathy patient registry	CH	Academia
CompERA-XL: International, prospective registry for the documentation of first-line and maintenance therapy in patients with pulmonary hypertension	DE	Academia
CWS-SoTiSaR: A registry for soft tissue sarcoma and other soft tissue tumours in children, adolescents, and young adults	DE	Academia
DÖSAK tumor registry for documentation of tumors of the face and jaws in germany, austria and switzerland	DE	Academia
EBAR: European Biliary Atresia Registry	DE	Academia
EHDN: European Huntington's disease registry	DE	Academia
ENETS: European Neuroendocrine Tumour Registry	DE	Academia
EPICURE-bank: European Epilepsy Brain Bank	DE	Academia
EU-RHAB: European Rhabdoid Registry	DE	Academia
EURIPFREG: European idiopathic pulmonary fibrosis registry	DE	Academia
EURIPIDES: European Registry for ICD and CRT devices in pediatrics and adults with congenital heart disease	DE	Academia
EUROFA: European Friedreich Ataxia Registry	DE	Academia
European Alport registry	DE	Academia
EUROSCA-R: European patient registry on spinocerebellar ataxias	DE	Academia
EUTOS: European chronic myeloid leukemia patient registry (collaboration between the European LeukemiaNet and Novartis Europe)	DE	Academia
KINDLERNET: Central patient registry Kindler syndrome	DE	Academia
MEFOPA: registry for patients with rare Mendelian forms of Parkinson's Disease	DE	Academia
NCL-Registry: International neuronal ceroid lipofuscinoses patient registry	DE	Academia
PODONET: Registry for Steroid-Resistant Nephrotic Syndrome (SRNS) patients	DE	Academia
RegiSCAR: European registry of severe cutaneous adverse reactions (SCAR) to drugs and collection of biological samples	DE	Academia

RetDis Database (blood or DNA samples and associated clinical descriptions of patients and families with inherited eye diseases)	DE	Academia
ERCUSYN: European registry on Cushing's syndrome	ES	Academia
EUGINDAT-PIADATABASE: European primary inherited aminoacidurias database	ES	Academia
MOLDIAG-PACA: patient registry of pancreatic cancer	ES	Academia
Cystadane post marketing registry of patient with homocystinuria	FR	Industry
EHN - EURO-HISTIO-NET: European registry of Langerhans Cell Histiocytosis	FR	Academia
EPI-EPNET: European hepatic and erythropoietic porphyrias registry	FR	Academia
Escort-Hu: European sickle cell disease cohort- hydroxyurea	FR	Industry
EU-CHS: European central hypoventilation syndrome registry	FR	Academia
EURECHINOREG: European registry of alveolar echinococcosis	FR	Academia
European prospective registry of children born to mothers affected by the antiphospholipids syndrome	FR	Academia
EUROTRAPS: European patient registry on TRAPS syndrome	FR	Academia
INFEVERS: European registry of mutations involved in familial mediterranean fever (FMF) and hereditary autoinflammatory disorders	FR	Academia
VALID: cohort creation on Budd-Chiari syndrome, hepatic venooclusive disease, hepatoportal sclerosis and portal vein thrombosis	FR	Academia
Vedrop registry of chronic cholestasis patient with vitamin E deficiency	FR	Industry
EUHASS: European haemophilia safety surveillance - pharmacovigilance program monitoring the safety of treatments for people with inherited bleeding disorders in Europe	GB	Academia
EUMDS: European Registry for Myelodysplastic Syndromes - part of EuroLeukemiaNet (ELN)	GB (+ IT)	Academia
EURODSD: European disorders of sexual development registry	GB	Academia
EUROPAC: the European registry of hereditary pancreatitis and familial pancreatic cancer	GB	Academia
European Prader-Willi syndrome database	GB	Academia
EUROWILSON: European clinical database for Wilson disease	GB	Academia
European registry of congenital dyserythropoietic anemia	IT	Academia
HAE-registry: European hereditary angioedema patient registry	IT	Academia
ECARUCA: cytogenetic and clinical database on rare chromosomal disorders	NL	Academia
EPCOT: European prospective cohort on thrombophilia	NL	Academia
X-ALD: X-linked adrenoleukodystrophy database	NL	Academia
EURADRENAL: European patient registry on autoimmune Addison's disease (sera, DNA and RNA)	NO	Academia
EURADRENAL: European patient registry and biobank on autoimmune Addison's disease	NO	Academic

International registries

INTERNATIONAL REGISTRIES (29 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COORDINATION**	**INSTITUTION**
Pediatric granulomatous arthritis international registry	BE	Academia
BH4: international patient registry of tetrahydrobiopterin deficiency	CH	Academia
PNH Registry: Paroxysmal Nocturnal Hemoglobinuria registry	CH	Industry
CPT-SIOP-Registry : International Registry for Choroid Plexus Tumors	DE	Academia
EHDN: neuroacanthocytosis patient registry	DE	Academia
ESID: European registry of primary immunodeficiencies	DE	Academia
International pheochromocytoma and paraganglioma registry	DE	Academia
STER: FVII deficiency treatment international registry	DE	Academia
International FKRP (Fukutin-Related Protein) defects registry - part of TREAT-NMD network	FR	Academia
EHDN: registry of juvenile Huntington's disease	GB	Academia
EUROFEVER: European registry for autoinflammatory diseases	IT	Academia
International registry of bone fragility fractures in the young	IT	Academia
International Registry of Rare Bleeding Disorders (RBDD)	IT	Academia
International registry of recurrent and familial hemolytic uremic syndrome / thrombotic thrombocytopenic purpura	IT	Academia
International registry on thrombotic thrombocytopenic purpura (TTP)	IT	Academia
Nephrotic syndrome registry	NL	Academia
The intenational Pompe registry	NL	Industry
The International Collaborative Gaucher Group (ICGG) Gaucher registry	NL	Industry
The international Fabry registry	NL	Industry
The international Mps I registry	NL	Industry
FOS : Fabry Outcome Survey	SE	Industry
HOS : Hunter Outcome Survey	SE	Industry
IOS : Icatibant Outcome Survey for hereditory angioedema	SE	Industry
CMDIR: congenital muscular dystrophy international registry	US	Academia
International Friedreich Ataxia Research Alliance (FARA) registry	US	Patient organisation
International Morquio A registry	US	Patient organisation
International Rare Genetic Steroid Disorders Consortium (RGSDC) registry	US	Academia
International registry for primary hyperoxaluria	US	Academia
THAOS: transthyretin amyloidosis outcomes survey	US	Industry

Network registries

NETWORK REGISTRIES (9 registries)		
ENGLISH LABEL OF THE ACTIVITY	**COORDINATION**	**COVERAGE**
SCNIR: severe chronic neutropenia international registry	DE	Global
EU-CHS: European central hypoventilation syndrome registry	FR	European
HAE-registry: European hereditary angioedema patient registry	IT	European
RARECARE: surveillance of rare cancers in Europe	IT	European
PAAIR: Patient's Association and Alpha-1 International Registry network	NL	Global
BINOCAR: British Isles network of congenital anomaly registries	UK	National
ECFS: European Cystic Fibrosis Society patient registry	UK	European
EUROCAT: European surveillance of congenital anomalies	UK	European
TREAT-NMD: Accelerating Treatments for Neuromuscular Diseases (registries)	UK	European

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