

Procedural document: Data collection and registration of research projects in Orphanet

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I. INTRODUCTION

1. Purpose/objectives

Orphanet offers, amongst a range of expert resources on rare diseases, a catalogue of research projects aiming to help:

- Researchers working in the field of rare diseases to establish collaborations.
- Patients and general public to retrieve information on ongoing research projects for a particular disease.
- Experts to get visibility and the ability to analyse the evolution of the field.

This document aims to explain the workflow and set of criteria for the selection, registration and update of research projects for rare diseases for the Orphanet database.

2. Disclaimer

- This procedural document is part of the OrphaNetWork Direct Grant (831390) which has received funding from the European Union's Health Programme (2014-2020).
- The content of this procedural document represents the views of the author only and is his/her sole responsibility; it cannot be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

3. Range of application

The present procedure applies to all the research projects (monocentric and multicentric) registered in Orphanet. The registration and update of the research projects is performed by the Orphanet national teams (ONT) having signed a Network Agreement and a Data Transfer Agreement (DTA) with the Orphanet Coordinating Team (OCT).

4. References

- [Orphanet Standard Operating Procedures](#)

5. Definitions

Coordinator of multicentric research project: An investigator assigned the responsibility for the coordination of investigators at different centres participating in a multicentric research project. He/she should sign the protocol along with the funding body.

Data transfer agreement (DTA): Contract between the providing and recipient institutions that governs the legal obligations and restrictions, as well as compliance with applicable laws and regulations, related to the transfer of such data between the parties.

European Reference Network (ERN): A virtual network involving healthcare providers across Europe, aiming to facilitate discussion on complex or rare diseases and conditions that require highly specialised treatment, and concentrated knowledge and resources.

Funding body: The organization that funds the project.

Information scientist (IS): A member of the Orphanet team with a scientific and/or medical background in charge of collecting, producing and updating information provided in the Orphanet database.

IRDiRC: International Rare Diseases Research Consortium – Consortium that unites national and international governmental and non-profit funding bodies, companies (including pharmaceutical and biotech enterprises), umbrella patient advocacy organizations, and scientific researchers to promote international collaboration and advance rare diseases research worldwide.

Multicentric research projects: A collaborative research project conducted by more than one research institution.

Orphadata (<http://www.orphadata.org>): A platform developed by Orphanet to provide the scientific community with comprehensive, high-quality and freely accessible datasets related to rare diseases and orphan drugs, in a reusable format.

Orphanet coordinating team (OCT): Based at the French National Institute of Health and Medical Research (INSERM-US14, Paris, France), the coordinating team is responsible for the coordination of the Orphanet Network, the production of the Orphanet database, the elaboration of procedures and trainings, and the coordination of quality control activities, enabling the production of the knowledge base and the catalogue of expert resources by the Orphanet national teams. The coordinating team is in charge of producing the Orphanet nomenclature in English.

Orphanet national teams (ONT): An Orphanet team based in one of the member countries of the Orphanet Network as per the Orphanet Network Agreement, and responsible for the collection of data on national expert resources. Some of the national teams are also in charge of the translation of the Orphanet nomenclature into one of the

languages of translation of the database (German, Italian, Spanish, Portuguese, Polish, Czech and Dutch).

Orphanet national validator (ONV): Professional designated to assess at the national level the appropriateness to enter a specific expert resource in the Orphanet database. It can be the national coordinator, a member of the national advisory board or of the Health Authorities.

Orphanet network: ONTs contributing to the Orphanet Database in the frame of the signed Network Agreement and DTAs.

Orphanet online registration service: Service allowing the professionals to register and/or update their activities related to rare diseases in the Orphanet database.

Principal investigator (PI) of a research project: The individual who assumes full responsibility for a research project¹.

Rare disorder (RD): A disorder that affects less than five in 10,000 persons in Europe, as defined by the European Regulation on orphan medicinal products (Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products). For the US, the Orphan Drug Act (ODA) in 21 CFR 316 defines a “rare disease or condition” to include any disease or condition that affects fewer than 200,000 persons in the United States.

National Advisory Board (NAB): A consultative group for the ONT. Its members can be nominated by the appropriate legitimate institutions (learned societies, national authorities, etc.), which are defined at country level. National Advisory Board members contribute with their expertise to Orphanet at country level and validate any database content concerning resources listed for the country in question as well as translation of the Rare Disease Nomenclature and of the Encyclopaedia in national language if relevant.

Rare disease research project: According to Orphanet inclusion criteria, an ongoing and unpublished research project explicitly focusing on a rare disease or a group of rare diseases and funded by a funding body with a scientific committee or the regular funding of a research institution.

Type of research project: A category attributed by Orphanet to characterize the purpose of a research project. For more information please refer to the annex I of this document (definition of research projects types).

¹ <https://orra.rutgers.edu/researchroles>

6. Filing and updates

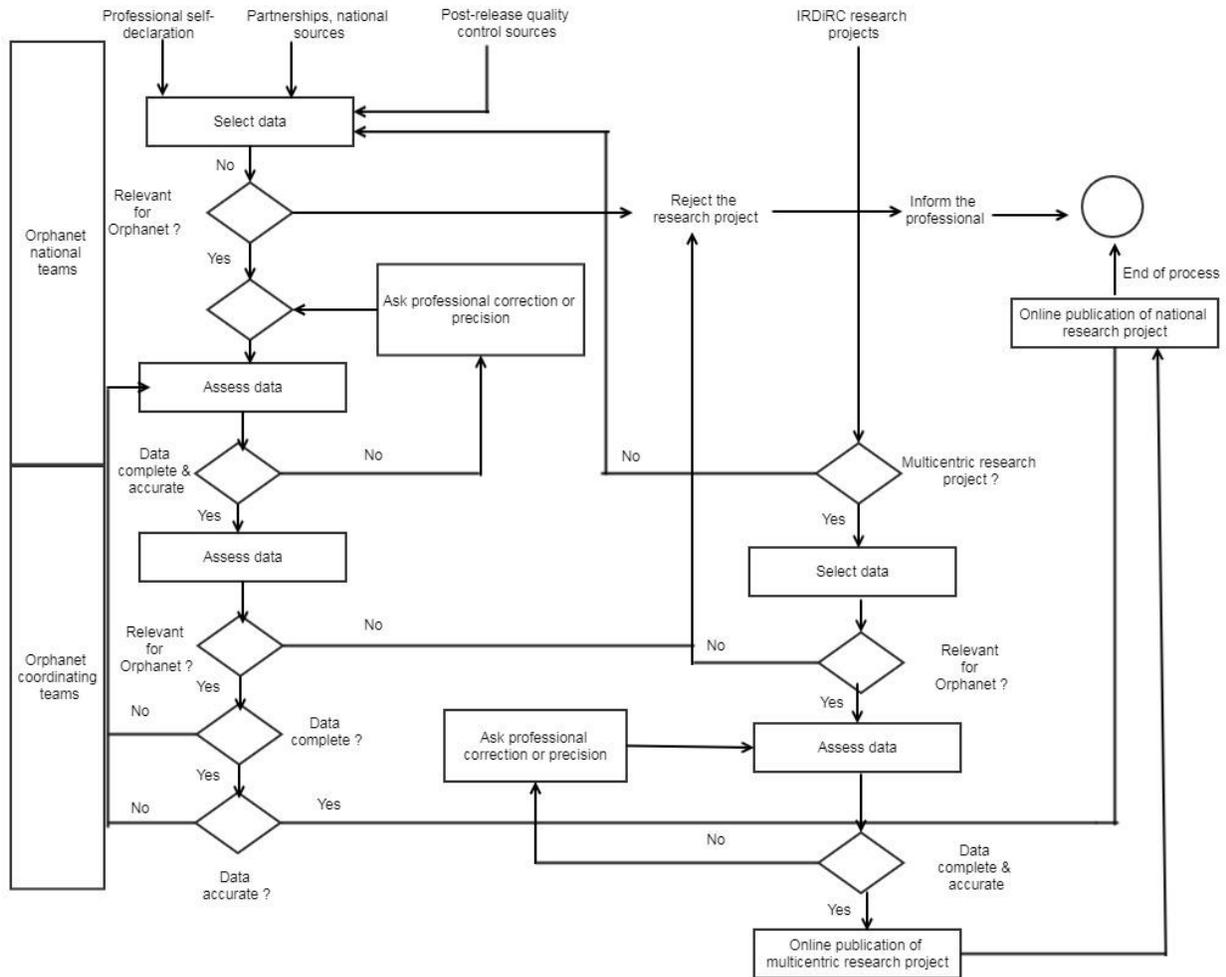
This document is updated by the coordinating team as often as necessary and at least once a year. The most up-to-date version is available on the Orphanet website:

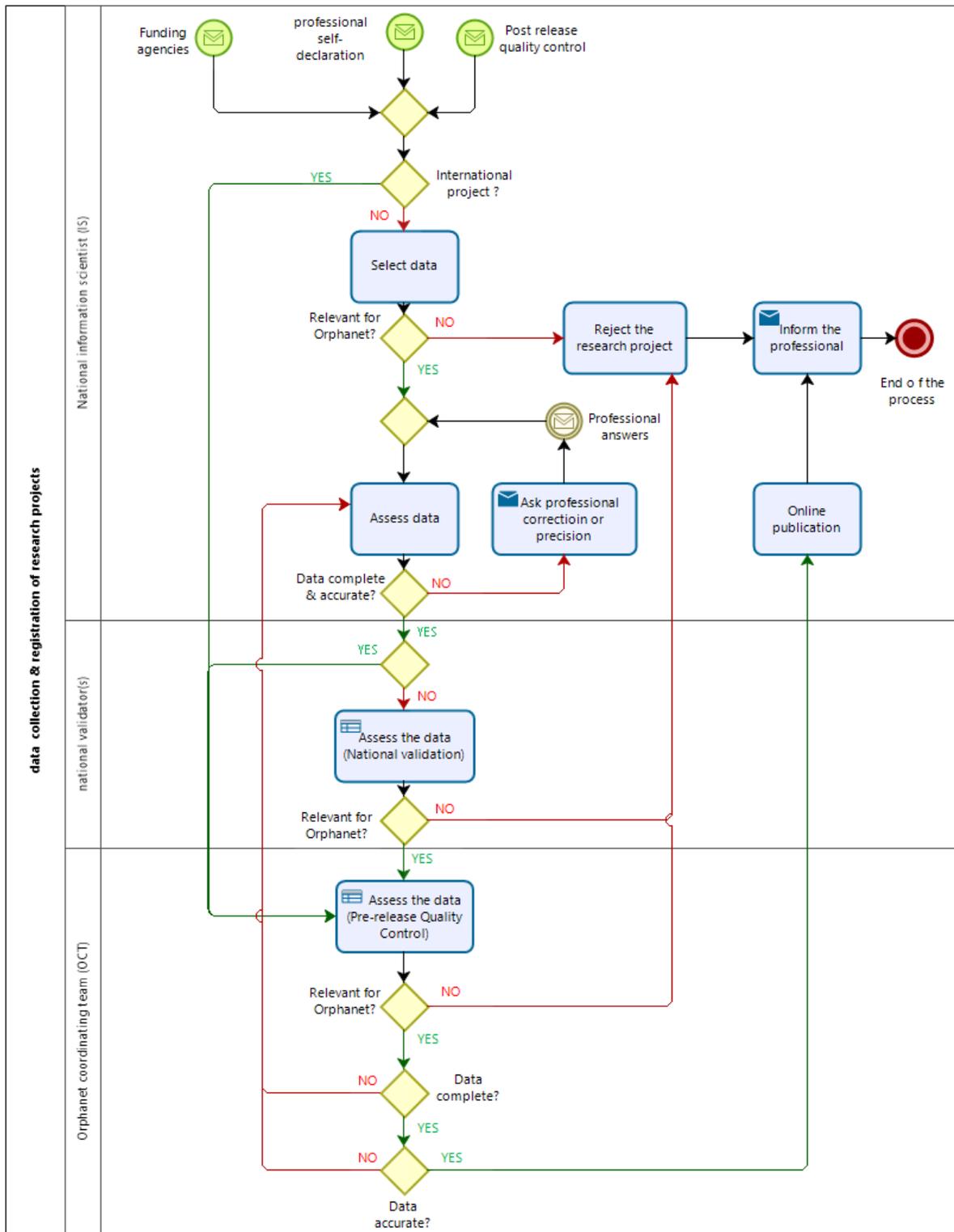
https://www.orpha.net/orphacom/cahiers/docs/GB/eproc_Research_Projects_R2_R&D_RP_EP_04.pdf.

II. METHODOLOGY

1. Flowchart

The general process for research projects data collection, registration, validation is presented below:





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2. Description

The process of registration / update of monocentric or multicentric research projects starts with:

- Professionals declaring their activity through the Orphanet online registration service or in any form (e-mail, phone calls, etc.).
- An exchange of data through a partnership with a source of data (i.e. national authorities, funding agencies, IRDiRC members, etc.).
- A post-release quality control task focused on research projects or multicentric research projects.

An annual update campaign is organized and launched by the Orphanet coordinating team where all professionals registered in the database are invited to review and update their activities. Orphanet national teams are responsible to follow up the professional's feedback.

2.1. Sources of information

National teams are in charge of identifying the sources of information for research projects in their country³, and are advised to establish partnerships with their national funding agencies to obtain lists of funded projects and be as exhaustive as possible.

In case of establishing a partnership, national teams must inform the coordinating team, as some types of partnerships require the signature of a data transfer agreement (DTA).

The main sources of information are:

- Professionals declaring a research project through the Orphanet online registration service.
- IRDiRC: projects funded by [IRDiRC members](#) including those operating in the countries outside of the Orphanet network.
- Partnerships with national authorities/national agencies funding research.
- Research projects conducted by members of European Research Networks (ERN).

2.2 Data selection

Orphanet teams are responsible for data selection of national research projects (ONT) and of international multicentric research projects (OCT) (including those funded by members of IRDiRC).

The data selection is based on the following inclusion and exclusion criteria:

³ This list should be displayed on the national Orphanet website of each country.

a) Inclusion criteria:

In order to be registered in Orphanet, a research project should meet all the following criteria.

The project must:

- Be ongoing at the time of registration.
- NOT have final results published in a peer-reviewed journal at the time of registration.
- Have an explicit focus on a rare disease or on a group of rare diseases.
- Be funded by a funding body (public or private, for profit or not-for-profit) with a scientific committee performing a competitive selection of research projects, or issued from the regular national research funding scheme.

b) Exclusion criteria:

Orphanet does not register a research project if it is a:

- Study on general aspects of a common disease which has rare forms (i.e. Parkinson disease, Alzheimer disease, breast cancer).
- Study that is too fundamental and/or could one day be applicable in the field of rare diseases but without explicit focus on rare diseases (i.e. listing rare diseases just as examples).
- Study already published.

2.3 Data assessment

If the research project complies with the Orphanet inclusion criteria listed above, the national IS analyses the information to check that the mandatory dataset (cf. below) is provided and that it is coherent, and eventually introduces the necessary corrections before submitting to national and international pre-release quality control.

In case of inconsistency or missing information, the IS contacts the professional in order to clarify or obtain the information needed.

a) Mandatory dataset for a research project

- Official title in local language and in English.
- Website of the research project or a summary description of it.
- Start and end dates of the research project.
- The disease(s), gene(s) and/or drug(s) the project is focused on.
- The type of research project representing the research project's objective (please refer to annex I for more information on the types).
- Name and contact details (email address and phone number) of the principal investigator (PI).

- Name and contact details of the funding body(ies).
- If the research project is funded by a member of IRDiRC at the time the study starts.

b) Mandatory dataset for a multicentric research project

In addition of the dataset cited above, Orphanet also collects the geographical coverage of the project for multicentric research projects.

2.4 Pre-release national validation

A validation process at the national level is mandatory for research projects exclusively when they are not received from an official source (i.e. national agency/funding body). It is performed by the national coordinator of the given country and/or an expert appointed by him/her. During this step the national validator focuses on the relevance of the project for Orphanet and the name of the principal investigator of the research project.

2.5 Pre-release quality control (PrRQC)

Once the candidate research project passed the first assessment and eventually the national validation steps, the OCT performs a pre-release quality control to assess the relevance and correctness of the data collected by the national teams. This quality control is mainly focused on the disease(s) linked, the type of research project, as well as on the coherence of the whole dataset.

In case some information is missing or needs correction, the form is sent back to the national teams for correction.

2.6 Data publication

Once all the quality control steps have been completed, the data are accessible on the Orphanet website and can be retrieved from [Orphadata](#) after signature of a Data Transfer Agreement (DTA) or a service contract.

Once published, the ONT are in charge of informing the professional(s) that the research project has been published.

2.7 Post-release validation

The post-release quality control for research project includes the quality control projects, which are organized by the coordinating team on a regular basis to check the completeness and consistency of the data.

III. ANNEX

Annex I: Definition of the types of research projects

Animal model creation/study: Research project which the ultimate goal is to create an animal model of a disease (transgenic, knock-in, knock-out models), which will be further used to better understand the physiopathology or the genetics of the disease, to test treatments in pre-clinical studies, etc., and/or to perform functional or physiological studies on animals.

Biomarker development: Research project designed to identify disease biomarkers. Biomarkers are indicators for the assessment of disease risk, early detection of disease, therapeutic prognosis, and response to treatment as well as disease recurrence.

Biotechnology innovation: Project that focuses on the use of living organisms or other biological systems in the manufacture of drugs or other products. This category can be used when the project aims to develop antibodies, oligonucleotides, or recombinant proteins among other products issued from biotechnology.

Biorepositories development/creation: Study that focuses on the development and/or creation of biorepositories. It does not apply to the outcomes of an already existing biorepository or biobank.

CRISPR-Cas9 study: Project designed to apply the CRISPR-Cas9 technique, a genome editing tool that enables to edit parts of the genome by cutting out, replacing or adding parts to the DNA sequence, to the development of therapies for a disease.

Databases & Registries development/creation: Study that focuses on the development and/or creation of database & registry as the outcome of the study. It does not apply to the outcomes of an already existing database or registry.

Diagnostic tool/protocol development: Research project specifically designed for the development/optimisation of a specific tool (reagent, antibody, DNA probes, genomic or proteomic arrays, etc.) or protocol that will serve for the diagnosis of a disease.

Drug repurposing: Project that focuses on studying the possibility that a certain drug already approved to be used for a certain disease is also safe and effective for treating other diseases.

Epidemiological study: Statistical study on human populations, which attempts to link human health effects to a specified exposure, or to evaluate disease prevalence and/or incidence.

Gene expression profile: Research project designed to perform the analysis of the expression pattern of a gene or a group of genes, at the RNA or protein level, in a particular tissue or developmental stage to assign biological relevance to genes involved in rare diseases.

Gene search: Research project designed to identify the gene(s) involved in a disease, including causative and susceptibility genes.

Genotype-phenotype correlation: Research project designed to analyse the correlation between a genotype (DNA sequence) and a phenotype (physical trait, abnormality or pattern of abnormalities) when the causative gene of a disease has already been identified.

Health economics study: Research project designed to understand issues related to efficiency, effectiveness, value and behaviour in the production and consumption of health and healthcare, including cost/utility, cost/effectiveness and cost/benefit studies. It can include studies of the determinants of behaviours in an economic context, such as willingness to pay for a service or attitude towards a service or a technology.

Health sociology study: Research project using sociology and sociological research methods to understand health and illness, including quality of life studies, as well as equity, social justice, social policy and social work.

Human physiopathology study: Research project designed to better understand the disturbance of normal mechanical, physical, and/or biochemical functions caused by a disease by using clinical data or samples.

In vitro functional study: Research project designed to assess the functional consequences of rare gene variants associated with human diseases.

Induced pluripotent stem cells (iPS) creation/study: Study that focuses on the creation of induced pluripotent stem cells (adult cells that have been genetically reprogrammed to an embryonic stem cell-like state by being forced to express genes and factors important for maintaining the defining properties of embryonic stem cells) and/or their use as disease models as an alternative to animal models and/or their use to study drug safety pharmacology and discovery.

Medical device development: Research project intended to develop a medical instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software developed by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes.

Mutation search: Research project that designed to identify new mutation(s) in gene(s) involved in a rare disease.

Natural history study: Study following a cohort of patients with a specific disease over a period of time and collecting health information in order to understand how the disease develops. This is a specific type of observational clinical study.

Observational clinical study: Clinical research project designed to study the course of a disease, or the relationship between exposures and outcomes, in which the investigator makes no intervention, but observes and assesses the effects of an intervention or exposure. Types of observational studies are case series studies, cross-sectional studies, case-control studies, cohorts and database studies.

Ontology/bioinformatics study: Project that focuses on a computer-based approach to study a hypothesis in order to obtain meaning from biological data and/or to create a computable representation of knowledge.

Outcomes measures development (patient-centered or PCOMs and patient-reported or PROMs): Study focusing on developing measures of the status of a patient's health condition assessed by a healthcare professional or a carer or directly by the patient itself (patient-reported outcome measures – PROMs) after going through a specific therapy.

Pre-clinical research project: Research project aiming at developing a therapy and its proof of concept in an in vitro setting and/or in animal model in order to gather evidence justifying for a clinical trial. Depending on the therapeutic approach, they can be assigned to one of the following categories:

- Pre-clinical drug development/drug delivery:** aimed to develop a chemical/synthetic substance.

- Pre-clinical gene therapy:** aimed to deliver nucleic acids either in cells or tissues in order to correct a genetic defect.

- Pre-clinical cell therapy:** aimed to deliver cells in a tissue.

- Pre-clinical vaccine therapy:** aimed to develop an inactivated or attenuated organic compound or a virus that will stimulate the immune system to produce antibodies against infections or tumour cells.

- Pre-clinical biotherapy:** aimed to deliver drugs or other products using living organisms or other biological systems in their process of fabrication.

- Pre-clinical medical device:** aimed to use a medical instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including software.

Public health study / Health services research / Health policy study: Research project designed to generate generalizable knowledge on disease prevention or control and health promotion through improved health policies and practices.

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

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D_RP_EP_04.pdf](https://www.orpha.net/orphacom/cahiers/docs/GB/Data_collection_and_registration_of_research_projects_R2_R-D_RP_EP_04.pdf)