



Best Practice Guidelines for the Development and Use of the ENRAH Registry

The "ENRAH for SME" Project

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- e. information on Human Biological Material (HBM) in AHC
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- g. a protocol database for clinical trials and other forms of research related to AHC
- h. a results database for clinical trials and other forms of research related to AHC
- i. an information centre on scientific, ethical, legal, and other forms of documents related to AHC research and patient care

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GLOSSARY

Clinical Data

Any information collected by a doctor or healthcare professional in the course of providing normal healthcare to a patient. Clinical data here includes all patient information collected for healthcare purposes by doctors or other healthcare professionals, including data related to a patient's family.

Health Research Data/Clinical Trial Data

Any information collected by a researcher or research organization in the course of carrying out a medicinal or other health intervention research project, including a clinical trial.

Human Biological Materials (HBMs)

Tissues or bodily substances collected from a person for the purposes of healthcare or research.

Research Data

Any information obtained by an investigator for the purposes of clinical or genetic research

Network/ Research Network

A consortium of individuals or/and organizations that make substantial contributions to the ENRAH Registry, are committed to the responsible sharing of the Registry, are engaged in the custodianship of the Registry.

Reference Center

A Member of the Network responsible for collecting clinical data for the Registry in a specific country or location.



INTRODUCTION

The European Network for Research in Alternating Hemiplegia in Childhood (ENRAH) is a European-wide networking project, initially funded by the European Commission Research Program FP6 from April 2005 till June 2007. It has been established by patient organizations and researchers seeking improved therapeutic, diagnostic, and prophylactic interventions for Alternating Hemiplegia in Childhood (AHC). The project seeks to build a European patient, science, and medical registry that acts as a portal for developing health research into AHC that includes SMEs and other sponsors. The primary purpose of the ENRAH Registry is to provide access to information and communication related to AHC for patients, families, patient groups, researchers, and sponsors of research, including SMEs. It is a tool for sharing information, ideas, and science in AHC that forms a platform for discussion and a place to meet for those interested in AHC.

The objective of this Guideline is to provide an ethical and scientific standard for the development and use of the ENRAH Registry. The Guideline is intended to be of value to, and assist, patients, researchers, clinicians from the ENRAH Reference Centres, ethics committees, sponsors and funders of health research, and regulatory authorities. The principles established in this Guideline are based on a broad consideration of research networks using patient registries as a primary instrument for promoting the development of new health interventions.

This first draft of the Guideline was developed with consideration of the current and arising ethical issues in the project and is based on the previous *ENRAH Report* (2005) and *ENRAH Survey* (2006) on ethical issues in the project. The *Report* identified the ethical challenges in the project and found that these are large and constant, and there is a need for a procedural approach in order to consistently address them within the framework of the ENRAH values. This was followed by a *Survey* addressing the ethical issues. This *Survey* was a major step forward in the project that allowed the collective interests and concerns of the members of the project to be drawn together.

The key stakeholders, including patients, will be further involved and consulted at all stages of this Guideline development as well as in its dissemination and implementation to achieve a patient-centered multidisciplinary Guideline. Additionally, the Guideline will be externally reviewed by experts prior to its publication.

1. ETHICAL AND SCIENTIFIC PRINCIPLES

In establishing the project's design, the project partners agreed on a set of values (Annex I, chapter 9): to ensure

- 1) the promotion and protection of the dignity, basic freedoms, privacy and confidentiality, and rights of all project participants, particularly the patients and their families;
- 2) the **confidentiality and security** of all data and biological materials maintained by ENRAH or its members in their collection, storage, transfer, and access; and



3) the **high quality** of data entered into and maintained in the ENRAH Registry.

The commitment to, and promotion of, these values provides a general framework for ENRAH's engagements and activities.

2. METHODOLOGY

The ethical and Good Clinical Practice (GCP) issues have been divided into the following **categories**:

- Clinical Data
- Human Biological Materials
- Data from Clinical Trials on Medicines and Other Health Interventions
- Research Data

3. OPERATIONAL PRINCIPLES FOR THE ENRAH REGISTRY

3.1. Data and HBMs should be collected at the Reference Centers with the informed, free and documented consent of the patient and/or his/her legal representative. The patient's assent should be sought, as appropriate and to the extent possible, in all cases where consent is provided by a legal representative.

3.2. An explicit consent for including patient information in the ENRAH Registry should be sought and documented.

3.3. Data and HBMs should be collected, stored, and transferred in compliance with the protocol(s) that has received prior independent ethics committee approval/favorable opinion and in accordance with European and national legislation and regulation.

3.4. Each individual involved in data and HBMs collection, storage, and/or transfer should be qualified by education, training, and experience to perform his or her respective task(s).

3.5. Clinical data should be collected following a protocol established by the ENRAH Executive Committee following advice from an ENRAH Working Party.

3.6. HBMs from patients assigned to the Registry should be collected at the Reference Centers for defined purposes.

3.7. All collected data and HBMs should be recorded, handled, and stored in a way that shows respect for the persons from whom the data and HBM come, provides for confidentiality, and allows for future accurate reporting, interpretation, and verification.



3.8. The confidentiality of records and HBMs that could identify subjects should be protected during all steps of their handling, respecting the privacy and confidentiality in accordance European ethical and regulatory requirement(s).

3.9. Data in the ENRAH Registry should be handled according to the rules established by the ENRAH Executive Committee as well as respecting the rules of the provider while maintaining an efficient ENRAH Network work flow.

3.10 Systems for data quality need to be implemented and followed according to Standard Operating Procedures established by the ENRAH Executive Committee.

3.11. Patients and their families should be kept informed by providing validated information on the results from the studies utilizing the Registry.

3.12. Patients and their families should also be able to obtain information on the use of their clinical data in research projects making use of the Registry.

4. ROLES AND RESPONSIBILITIES IN THE USE OF THE ENRAH REGISTRY

4.1. Patients

4.1.1. Patients and their families should be fully informed of the use of their data and HBMs at the time of entering their data and HBMs into the Registry,

4.1.2. Patients and their families should be kept informed on the current use of their data and HBMs stored or maintained by the Registry.

4.1.3. Patients and their families should be involved in the process establishing the data parameters of the Registry.

4.1.4. Patients and their families should be involved in validating the information provided to patients and researchers, and in reviewing the disease treatments recommendations.

4.2. Reference Centers and clinicians

4.2.1. A Reference Center and its respective clinicians should be involved in the process establishing the data parameters of the Registry.

4.2.2. A Reference Center should ensure that all persons engaged in data collection and handling are adequately informed regarding the ENRAH protocol for data collection and management as well as the associated duties and functions.



- 4.2.3. A Reference Center should receive ethical review approval prior commencing the collection of data or HBMs for entry into the Registry.
- 4.2.4. A Reference Center should be able to verify that each subject, or his/her legal representative, has consented in writing for the use of his/her data and/or HBM in the Registry.
- 4.2.5. A Reference Center should ensure the accuracy, completeness, legibility, and timeliness of the collected data. Data entered into the Registry derived from other sources should be consistent with the source documents or the discrepancies explained.
- 4.2.6. A Reference Center should ensure that the patient records from which data are entered are stored for at least five years after the data is entered into the Registry.
- 4.2.7. A Reference Centre should share, as appropriate, the collected clinical data with the Registry.
- 4.2.8. A Reference Centre should share information in the Registry only with parties who have received an authorization from the Executive Committee.
- 4.2.9. In case of a patient withdrawing data from the Registry, a Reference Centre should inquire as to the reason(s), when possible, while fully respecting the patient's rights.
- 4.2.10. A Reference Centre should ensure consistency in labeling data and HBMs for the transfer and exchange of such data and HBMs.
- 4.2.11. A Reference Centre should have the liberty to decide on the use, transfer, and exchange of its collection of patient HBMs.
- 4.2.12. A Reference Centre should provide a reference in the Registry regarding the availability of data and HBMs from its AHC patients.
- 4.2.13. A Reference Centre should inform the Network in case of sharing of HBMs entered into the Registry.
- 4.2.14. A Reference Centre should share the research data from the use of data and HBMs entered into the Registry.



4.3. Researchers utilizing the Registry and related HBMs

- 4.3.1. Researchers utilizing the Registry and related HBMs should be involved in establishing the data parameters of the Registry.
- 4.3.2. Researchers utilizing data and HBMs entered into the Registry should publish the results of their research on the Registry in a timely fashion.
- 4.3.3. Researchers utilizing data and HBMs entered into the Registry are invited to share their research data (including clinical trial data) through the Registry.
- 4.3.4. Researchers utilizing data and HBMs entered into the Registry should be engaged in the development of research proposals and studies related to the disease treatment.

4.4. Web Registry Provider

- 4.4.1. A Web Registry Platform Provider should be a certified party (by the regulatory bodies in its country of residence).
- 4.4.2. A Web Registry Platform Provider should ensure the confidentiality and integrity of data and HBMs entered into the Registry, adhering to the technical specifications provided by the Executive Committee.
- 4.4.3. A Web Registry Platform Provider should provide an adequate training to the members of the Network.

4.5. Ethics Committees

- 4.5.1. An Ethics Committee should promote and safeguard the dignity, rights, safety, and well-being of all persons whose data or HBMs are entered into the Registry.
- 4.5.2. An Ethics Committee should obtain the following documents: a description of the Registry and its intended uses, the questionnaire used for data collection, the information sheets for patients and their legal representatives; the assent and informed consent forms for patients and their legal representatives.
- 4.5.3. An Ethics Committee should review a proposed application within a reasonable time and document its views in writing, clearly identifying the documents reviewed and the dates for the approval/ favorable opinion and/or modifications required prior to its approval/favorable opinion, or, disapproval / negative opinion; and /or termination/suspension of any prior approval/favorable opinion.



4.6. The Network

- 4.6.1. The Network should promote and facilitate the timely and proper use of the data and HBMs entered into the Registry.
- 4.6.2. The Network should promote and facilitate the timely publishing of results from the use of the Registry.
- 4.6.3. The Network should ensure the further maintenance, development, and use of the Registry.



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Appendix II: Custodianship

The Registry is considered a public good housed under the custodianship of the ENRAH. ENRAH discourages the ownership of data and HBMs entered into the Registry, as well as any results arising from research making use of the Registry. ENRAH promotes the registry as a tool for sharing information and knowledge related to AHC for the benefits of the patients and their families.