



CHARTER FOR TREAT-NMD PATIENT DATABASE/REGISTRY

Revision history

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Preamble

Inherited neuromuscular diseases (NMD) form a large group of diseases, each of which is individually rare (prevalence < 5/10,000). They are present in all populations and affect both children and adults. Most NMDs result in chronic long-term disability that poses a significant healthcare burden for society. Death may result from cardiac and respiratory muscle involvement. The goal of existing management is to minimise the impact of complications such as joint or spinal deformity and improve cardiac and respiratory function as there are currently no curative treatments for any NMD.

Scientific advancement recently has led to substantial changes on how to approach the treatment of NMD. New therapeutic strategies are being developed, and for some of these treatments, there are plans for large, multi-centred studies already in place. Several new therapeutic strategies for NMD aim to target specific genetic defects. Once planning for a clinical trial starts, it is very important that patients are identified and contacted within a short period of time. In national and pan-European databases/registries initiated by TREAT-NMD for Duchenne Muscular Dystrophy, Spinal Muscular Atrophy and other muscular dystrophies, patients will be registered with their genetic defects and clinical status and can be contacted if their profile fits the inclusion criteria of a clinical trial. Moreover, the patient registries will help to answer research questions such as the prevalence of neuromuscular disorders in Europe and support other activities such as assessing standards of diagnosis and care. The main objective of the TREAT-NMD patient registries/databases for Duchenne Muscular Dystrophy and Spinal Muscular Atrophy is to assess the feasibility of clinical trials, to facilitate the planning of appropriate clinical trials and to support the enrolment of patients in clinical trials, in compliance with Ethical guidelines for research involving human subjects.

1) Definitions

- TREAT-NMD (Translational Research in Europe for the Assessment and Treatment of Neuromuscular Diseases) is a network of excellence funded by the European Commission under contract 036825. Partners relates to institutions and organizations as defined in the EC contract.
- Patient registries and databases are structured as searchable data collections of individuals with a shared characteristic such as a disease or a gene defect.
- National registry refers to a registry that aims to enlist the majority of patients in a given region, country or several countries.
- TREAT-NMD national registries are the national registries that are organized under the TREAT-NMD network and pledge to adhere to the charter.
- National registries that belong to countries which are not part of TREAT-NMD may join and contribute to the TREAT-NMD global database with equal rights and obligations as TREAT-NMD national registries based on compliance with the European Data Protection EC directive 95/46/EG and signed contracts with TREAT-NMD including the compliance with the charter
- The TREAT-NMD global database is a meta-database that compiles data transferred from the national registries.
- The TREAT-NMD global database is owned by the INSERM U827 group of Montpellier, partner of TREAT-NMD, on behalf of TREAT-NMD. Provisions will be made to hand over ownership of the TREAT-NMD global database to TREAT-NMD, to become effective once TREAT-NMD has been established as a legal entity. The owner of the database shall be regarded as the maker of the global database as defined in the DIRECTIVE 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases
- In the event that the TREAT-NMD global database cannot be continued by TREAT-NMD, ownership of the global database will be assumed by the INSERM U827 group of Montpellier.
- Subscription and fees refer to financial compensation provided by third parties to the TREAT-NMD global database and to the national registries for using the services of the database including access, extraction and re-utilization of data.

2) Purpose of charter

This charter shall:

- Regulate the relationship of national registries with the TREAT-NMD global database, shall define the basic requirements for national registries to become and remain a TREAT-NMD registry, and shall define the relationship of the TREAT-NMD global database with third parties (such as industrial and academic partners aiming to use the database for research or clinical trials).
- Be an integral part of agreements and contracts between TREAT-NMD network and institutions/associations in charge of national registries, and between TREAT-NMD and third parties (such as industrial and academic partners aiming to use the database for research or clinical trials).
- Be made publicly available on the TREAT-NMD website.

3) Relationship of national registries with TREAT-NMD

- National registries will transfer data for a non exclusive use to the TREAT-NMD global database. Transferred data will be reversibly encrypted and will include a standardized and harmonized set of core items. Mutations will be annotated according to the guidelines of the Human Genome Variation Society (<http://www.hgvs.org/>). The TREAT-NMD global database will not hold identifiable patient data and shall not have direct access to patients. Patients eligible for a study will be contacted through the appropriate national registry and via their physicians. A document on the standardized and harmonized items to be transferred is attached to the charter (enclosure).
- The TREAT-NMD global database stores, processes, and uses the data for defined purposes according to the TREAT-NMD objectives as described in contract 036825 with the European Commission.
- National registries collect and process data according to European and national laws and best practices (in particular, accuracy and minimisation of data; informed consent concerning use of the data for research; right of the patients to withdraw) and update data at least every 12 months.
- National registries remain owner, maker or author of the data included in the national databases and are free to grant access, re-utilization or permit extraction or grant any right in accordance to this ownership.
- National registries will return benefits to patients (information on what data are transferred to TREAT-NMD; information on trials/research projects recruiting via national registries; information on other TREAT-NMD activities; information on results with direct relevance to patients or any other way to return benefit in accordance with the ethical principal of benefit sharing).
- National registries will refer inquiries by third parties (for example for accessing data for multi-centre studies) to the TREAT-NMD database. The mandatory and exclusive point of entry for data access by third parties related to multinational clinical trials is the TREAT-NMD global database. This principle does not apply to inquiries that are related to a single national registry only.
- Financial compensation by third parties for services of the TREAT-NMD global database will be shared between TREAT-NMD and national registries, in proportion to the data utilised by such third parties. This compensation will also take into account the effort incurred including the degree of data curation. TREAT-NMD will negotiate on behalf of the national registries with third parties. A fee structure for such services will be developed by the TREAT-NMD global database oversight committee and approved by the TREAT-NMD Governing Board and national registries, and will be reviewed on a regular basis.
- A contract shall be established between the owner of the global database and a third party on the basis of the negotiation established by the oversight committee and following the principles, which come from the present charter.

- The TREAT-NMD website displays information about the activities of the TREAT-NMD global database and informs patients and the public about national registries that contribute to the TREAT-NMD global database.
- National registries may display the TREAT-NMD logo and name on their websites and publications; TREAT-NMD may display the logo and name of national registries on the TREAT-NMD website.
- National registries that sign and adhere to the charter, and contribute to the TREAT-NMD global database, have a seat and voting rights on the TREAT-NMD global database oversight committee.

4) Relationship of third parties with the TREAT-NMD databases and national registries

- The TREAT-NMD global database will grant access to encrypted data to third parties under the following conditions: Third parties provide appropriate ethics approval (Institutional review board); the study is not in conflict with TREAT-NMD goals and is approved by the TREAT-NMD global database oversight committee.
- A contract will be signed between the owner of the global database and the third party.
- Services for non-industrial TREAT-NMD partners and academic institutions shall be provided free of charge. Any research publications derived from these services must acknowledge support by TREAT-NMD and by the national registries that contributed to the research.
- Services of the TREAT-NMD global database for commercial third parties shall be reimbursed. The reimbursement shall be negotiated by the TREAT-NMD global database oversight committee with the third party. Reimbursement shall be given in form of service subscriptions (inquiries of the third party into the TREAT-NMD database for a limited period of time) and as a service fee (contacting a given subset of patients eligible for a trial through the national registry).
- A statement of the cost of service subscription and service fees shall be established and revised annually by the Oversight committee.
- Third parties will not be given direct access to patients or identifiable data.
- All parties agree that data derived from the TREAT-NMD global database may be used for registering medicinal products through the FDA and EMEA.
- All parties agree with the ethical principle of benefit sharing, which requires that benefits resulting from any scientific research and its applications should be shared especially with the persons and groups that have taken part in the research.
- The parties signing this charter must not be held liable by each other for actions covered under this charter.

5) TREAT-NMD Global Database Oversight Committee

- The TREAT-NMD Global Database Oversight Committee (GDOC) is the governing structure of the TREAT-NMD global database on behalf of TREAT-NMD and national registries.
- The TREAT-NMD GDOC is composed by representatives of the TREAT-NMD network (Leader of the work package on patient registries; Clinical Trial Coordination Centre; Ethics Council; and partner organizations), patient organizations, and national registries. It is chaired by the TREAT-NMD activity leader on databases. Industry partners of TREAT-NMD shall not be represented in the committee.
- All members of the TREAT-NMD GDOC must disclose financial interests and update the disclosure statements on an annual basis. All members of the TREAT-NMD GDOC will be required to sign confidentiality agreements if a third party requests them prior to having access to the inquiry of the third party.
- The TREAT-NMD GDOC will meet in person, by teleconference or by e-communication at least once per year, and upon request.
- The TREAT-NMD GDOC will report to the TREAT-NMD Governing Board and to the national registries annually.
- The TREAT-NMD GDOC reviews inquiries of third parties into the TREAT-NMD global database. The committee will come to a decision within 14 calendar days upon receipt of the inquiry and will report the decision in writing to the third party, the owner of the global database and the TREAT-NMD Governing Board as per the approval process agreed by the GDOC. If a decision cannot be reached, the inquiry shall be rejected. In the case of a rejection, the GDOC may report the reason for rejection to the third party and set a time frame for re-consideration.
- Until TREAT-NMD will be established as a legal entity, the TREAT-NMD GDOC shall report to the owner of the global database the decision to give access to the global database. A contract will be signed, as mentioned *supra* (3) between the owner of the global database and the third party.

6) Validity of the charter

- This charter shall be in effect after ratification by the TREAT-NMD Governing Board and after discussion with TREAT-NMD partners and advice from TREAT-NMD advisory committees (Ethics, Industry Liaison, Intellectual Property Rights and Use).
- The ratification by the TREAT-NMD Governing Board on the Charter and its enclosures shall be identified as such on the notice of meeting of the Governing Board, in accordance with the §4.1 of the Consortium Agreement.
- The charter shall be valid for an unlimited time. The charter can be subject to change by the TREAT-NMD Governing Board at any time without prior notification.

7) Ethical and legal principles

Recall of the ethical guidelines endorsed by the TREAT-NMD Network

World Medical Association, *Declaration of Helsinki* (June 1964, amended in Tokyo in 2004) Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (CIOMS 2002)

HUGO (Human genome organization), *Statement on benefit sharing* (April 2000)

UNESCO *International Declaration on Human Genetic Data* (16 October 2003)

UNESCO *Universal Declaration on Bioethics and Human Rights* (19 October 2005)

Recall of some of the binding laws applicable to the activities of the TREAT-NMD databases:

Council of Europe, Convention N° 108 for the Protection of Individuals with regard to Automatic Processing of Personal Data

Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data

Directive 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases