



## **CHARTER FOR THE TREAT-NMD PATIENT DATABASE/REGISTRY**

### **Revision history**

Revised draft by Hanns Lochmüller (July 22<sup>nd</sup>, 2007), revised by Stephen Lynn (July 23<sup>rd</sup>, 2007), sent to TREAT-NMD partners and national registries for consultation (August-October 2007), legal comments by Christopher Roy-Toole (August-October 2007). Revised version by Hanns Lochmüller (October 19<sup>th</sup>, 2007), revised by Stephen Lynn (October 23<sup>rd</sup>, 2007). Revised version by Serge Braun (December 26<sup>th</sup>, 2007), revised by Christophe Bérout (December 26<sup>th</sup>, 2007). Final version by Hanns Lochmüller (December 29<sup>th</sup>, 2007) and reviewed by Stephen Lynn (January 6<sup>th</sup>, 2008). Charter approved by the TREAT-NMD Governing Board (January 15<sup>th</sup>, 2008). Discussed at the TREAT-NMD Oversight Committee Meeting in Geneva (November 12<sup>th</sup>, 2011), revised accordingly by Karen Rafferty and Hanns Lochmüller (November 25<sup>th</sup>, 2011). Charter approved by the TGDOC (March 9<sup>th</sup>, 2012). Charter revised by Karen Rafferty (October 26<sup>th</sup>, 2012). Charter approved by the TGDOC (November 14<sup>th</sup>, 2012). Discussed at the TREAT-NMD Oversight Committee meeting in Newcastle (October 31<sup>st</sup>, 2013), revised accordingly by Agata Robertson and Jan Verschuuren (April 1<sup>st</sup>, 2014). Charter approved by TGDOC (April 16<sup>th</sup>, 2014)

### **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 where possible and to improve the standards of care. There are currently no curative treatments for most NMDs.

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 and diseases, 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 TREAT-NMD registries, patients are registered with their genetic defects and clinical status and can be contacted if their profile fits the inclusion criteria of a clinical trial or other scientific study. Moreover, the patient registries will help to answer research questions such as the prevalence of neuromuscular disorders

and support other activities such as assessing standards of diagnosis and care. The main objective of the TREAT-NMD patient registries/databases is to assess the feasibility of scientific studies or clinical trials, to facilitate the planning of appropriate clinical trials or scientific studies and to support the enrolment of patients in trials or studies, in compliance with Ethical guidelines for research involving human subjects.

## 1) Definitions

- TREAT-NMD Alliance is a network focused on ensuring the most promising new therapies reach patients as quickly as possible. TREAT-NMD will move out of the EC FP6 funded period and transition into the TREAT-NMD Alliance, remaining a non-legal entity.
- Institut National de la Santé et de la Recherche Médicale (Inserm, National Institute of Health and Medical Research) is a French biomedical and public health research institution.
- 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 or international registries refer to registries that aim to enlist the majority of patients in a given region, country or several countries.
- TREAT-NMD registries are the national or international registries that are organized under the TREAT-NMD Alliance and pledge to adhere to the Charter.
- National and international registries may join and contribute to the TREAT-NMD global database with equal rights and obligations based on compliance with the European Data Protection EC directive 95/46/EC including compliance with this Charter.
- TREAT-NMD global databases are meta-databases that compile anonymous data transferred from their corresponding TREAT-NMD registries.
- The TREAT-NMD global databases are owned by INSERM on behalf of the TREAT-NMD Alliance; as the owner, INSERM is the principal custodian of the data stored in the TREAT-NMD global databases and owner of the database infrastructure and associated Intellectual Property. Authority has been granted to TREAT-NMD Alliance to act as the international curator with all executive management rights of the TREAT-NMD global databases (under an exclusive royalty free licence). Provisions will be made to hand over ownership of the TREAT-NMD global databases to TREAT-NMD Alliance, to become effective once TREAT-NMD Alliance has been established as a legal entity. The owner of the databases shall be regarded as the maker of the global databases 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.
- The TGDOC is the TREAT-NMD Global Database Oversight Committee. Details on the structure and function are described in paragraph 5 of the charter.

- In the event that the TREAT-NMD global databases cannot be continued by TREAT-NMD Alliance, ownership of the global databases will be assumed by INSERM.
- The TGDOC is the TREAT-NMD global database oversight committee. Details on structure and function are described in paragraph 5.
- Subscription and fees refer to financial compensation provided by third parties to the TREAT-NMD global databases and to the TREAT-NMD registries for using the services of the databases including access, extraction and re-utilization of data.

## **2) Purpose of the Charter**

This Charter shall:

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

## **3) Relationship of TREAT-NMD registries with the TREAT-NMD Alliance**

- TREAT-NMD registries will transfer data for a non exclusive use to their 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 TREAT-NMD registry or they will be contacted via their physician depending on the registry involved. 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 Alliance objectives.
- TREAT-NMD 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.

- TREAT-NMD registries remain owner, maker or author of the data included in their databases and are free to grant access, re-utilization or permit extraction or grant any right in accordance to this ownership.
- TREAT-NMD registries will return benefits to patients (information on what data are transferred to the TREAT-NMD global database; information on trials/research projects recruiting via the registries; information on other TREAT-NMD Alliance 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).
- TREAT-NMD registries will refer inquiries by third parties (for example for accessing data for multicentre studies in several countries where TREAT-NMD registries are operational) to the TREAT-NMD global database. The TREAT-NMD registries strongly support the use of the TREAT-NMD global database as a single point of entry for data access by third parties related to multinational clinical trials and studies. This principle does not apply to inquiries that are related to a single national or international TREAT-NMD registry only.
- Financial compensation by third parties for services of the TREAT-NMD global databases will be shared between TREAT-NMD Alliance and TREAT-NMD 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 Alliance will negotiate on behalf of the TREAT-NMD registries with third parties. A fee structure for such services will be developed by the TREAT-NMD global database oversight committee (TGDOC) and approved by the TREAT-NMD Executive Board and TREAT-NMD registries, and will be reviewed on a regular basis.
- A contract shall be established between the owner of the global databases and a third party on the basis of the negotiation established by the TGDOC and following the principles which come from the present Charter.
- The TREAT-NMD website displays information about the activities of the TREAT-NMD global databases and informs patients and the public about TREAT-NMD registries that contribute to the TREAT-NMD global databases.
- TREAT-NMD registries may display the TREAT-NMD logo and name on their websites and publications; TREAT-NMD Alliance may display the logo and name of TREAT-NMD registries on the TREAT-NMD Alliance website.
- National or international registries that sign and adhere to the Charter, and contribute to a TREAT-NMD global database, have a seat and voting rights on the TGDOC.

#### **4) Relationship of third parties with the TREAT-NMD global databases and 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 TGDOC.

- A contract will be signed between the owner of the global database and the third party.
- Services for non-industrial and academic institutions shall be provided free of charge. Any research publications derived from these services must acknowledge support by the TREAT-NMD Alliance and by the TREAT-NMD 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 with the third party by the TGDOC. Reimbursement shall be given in the form of service subscriptions (inquiries of the third party into the TREAT-NMD global database for a limited period of time) or as a service fee (contacting a given subset of patients eligible for a trial or scientific study through the TREAT-NMD global database).
- A statement of the cost of service subscription and service fees shall be established and revised annually by the TGDOC.
- 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 EMA.
- 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 Databases Oversight Committee (TGDOC)**

- The TGDOC is the governing structure of the TREAT-NMD global database on behalf of the TREAT-NMD Alliance and all associated TREAT-NMD registries.
- The TGDOC is composed of representatives of the TREAT-NMD Alliance (Clinical Trial Coordination Centre; Care and Trial Site Registry, Ethics Council), patient organizations, and TREAT-NMD registries curators.
- The TGDOC will have a current chair, chair-elect and past chair; with the chair being elected annually. The term of the chair can be extended for an additional year by a two thirds vote of the TGDOC members. If the current chair is re-elected for an additional 1 year term of office the vice chair will then serve a 2 year term of office. Industry shall not be represented in the committee.
- All members of the TGDOC must disclose financial interests and update the disclosure statements on an annual basis.
- All members of the TGDOC will be required to sign confidentiality agreements when they join the TGDOC or they will not be allowed to review any third party documents.
- The TGDOC will meet in person at least once per year, and by teleconference or by e-communication upon request.

- The TGDOC will report to the TREAT-NMD Executive Committee and to the TREAT-NMD registries annually.
- The TGDOC reviews inquiries of third parties into the TREAT-NMD global databases. The TGDOC will come to a decision within 14 calendar days upon receipt of the inquiry, after negotiation for financial compensation have been completed, and will report the decision in writing to the third party and the owner of the global database. The inquiry will be sent by email to all TGDOC members. A minimum of two thirds of the TGDOC must vote and of those votes two thirds must be in favour for the vote to stand. If a decision cannot be reached, the inquiry shall be rejected. In the case of a rejection, the TGDOC may report the reason for rejection to the third party and set a time frame for reconsideration.
- Until TREAT-NMD Alliance is established as a legal entity, the TGDOC shall report to the owner of a global database the decision to give access to the global database. A contract will be signed, as mentioned supra (3) between the owner of a global database and the third party.

## **6) Validity of the Charter**

- The TGDOC shall ratify the Charter and its enclosures after discussion with the TREAT-NMD Executive Committee and taking advice from any necessary TREAT-NMD Alliance advisory committees (e.g. Project Ethics Council).
- The Charter shall be reviewed on an annual basis. The Charter can be subject to change by the TGDOC 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 global databases and registries:**

- 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