

Public Consultation: the future of the TREAT-NMD Network

September 2010



Translational Research in Europe - Assessment and Treatment of Neuromuscular Diseases (TREAT-NMD)

www.treat-nmd.eu

Purpose of the Consultation

This consultation paper has been drafted to inform the neuromuscular community of the purpose and activities to date of TREAT-NMD. This paper outlines the current status of TREAT-NMD and should provide helpful information for completing the consultation questions. The current funding for TREAT-NMD from the European Commission (EC) will end in December 2011 and this consultation is designed to help TREAT-NMD define its future activities, strategy and funding sources. Through this consultation process TREAT-NMD aims to:

- Consider whether and how current and newly proposed activities might be embedded and funded in the future network
- Take this opportunity to review the priorities for the future network, and the options for governance structures, stakeholder/partner involvement and potential funding models
- Understand and take into account the views of all stakeholders, so that the next stage of TREAT-NMD can meet their needs

Responses to the consultation can be given online via the web link or by downloading the questions and emailing the completed form back to TREAT-NMD.

The consultation period will open on Friday 3rd September and responses should be submitted by the closing date of Friday 1st October 2010. If you have any queries regarding the consultation please contact Stephen Lynn (stephen.lynn@ncl.ac.uk or call +44-191-241-8697). For more detailed information about TREAT-NMD please visit: www.treat-nmd.eu

1. Executive Summary

TREAT-NMD is an international network developing the tools and resources that will accelerate therapy development and delivery for inherited neuromuscular diseases.

Its aim is to advance diagnosis and care and develop new treatments for the benefit of patients and families, working closely with scientists, healthcare professionals, the pharmaceutical industry and patient groups around the world.

TREAT-NMD provides a one-stop-shop for the private and public sector, as well as individual scientists, clinicians and patients on information, resources and tools for therapy development in the neuromuscular disease community. TREAT-NMD serves as a platform to develop these resources and tools together with other groups and organisations to support continued therapy development.

Our understanding of neuromuscular diseases is beginning to reach the point at which the network resources and tools can support therapy development and delivery for a number of different disease groups (DMD, SMA, CMD and DM1 for example). TREAT-NMD will further develop collaborative initiatives with the neuromuscular community and will disseminate the resources available to help accelerate new therapeutic approaches.

TREAT-NMD will also target new strategic partnerships by developing more awareness of its potential with the public and private sectors so that the community uses the resources and tools available and can refer new groups to TREAT-NMD.

2. Current Management and Governance Structure of TREAT-NMD

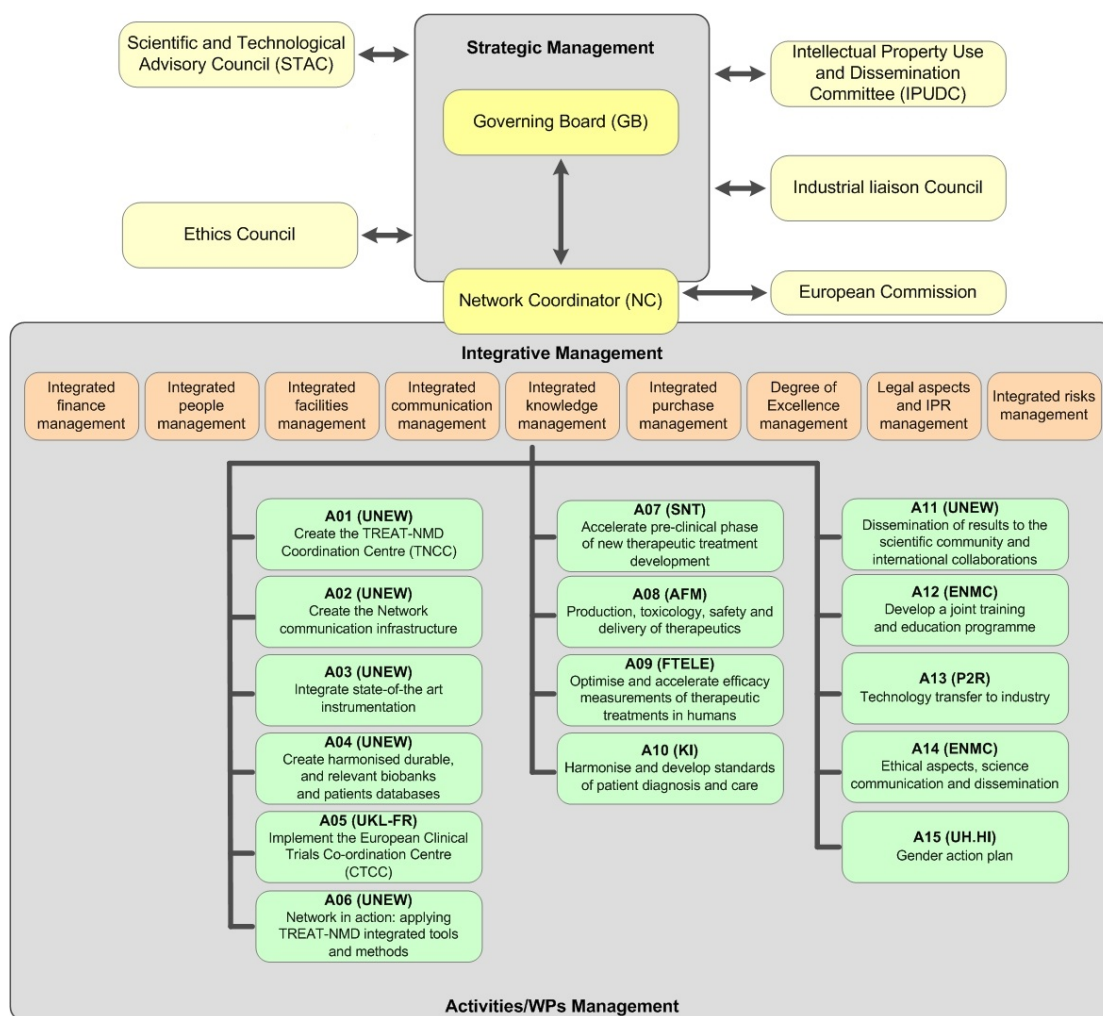
As an EC-funded 'Network of Excellence' through Framework Programme 6 (FP6) and in accordance with our contract with the EC, TREAT-NMD is currently managed by a central Coordination Office based at Newcastle University, under the coordination of Professor Kate Bushby and Professor Volker Straub. They are supported by a coordination and project management team led by Dr Stephen Lynn, who is responsible for the current management, administrative and financial activities in relation to the EC funding provided through FP6. The Project Coordinators are also responsible for ensuring the TREAT-NMD Network achieves all its deliverables as laid out in the contract with the EC. In addition to this coordination role TREAT-NMD is also managed by a Governing Board made up of representatives from each partner in the TREAT-NMD consortium who not only deliver the aims and objectives of the current Network but also oversee its strategic direction and governance.

The Governing Board is supported by advisory councils and committees made up of partners and external experts (these include Scientific and Technological, Industrial Liaison, Intellectual Property and Use, and Project Ethics). The Scientific and Technological Advisory Council (STAC) meets in person on an annual basis to review the progress of the TREAT-NMD Network and to offer recommendations to the TREAT-NMD Governing Board on activities related to the objectives of the Network. The current members of the STAC include:

- Marianne de Visser (University of Amsterdam) – STAC Chairperson
- Ségolène Aymé (Orphanet)
- Kenneth Fischbeck (NIH/NINDS)
- Roland Foisner (Medical University Vienna)
- Pat Furlong (Parent Project Muscular Dystrophy)
- Krzysztof Jagla (INSERM/MYORES)
- Christophe Marcelle (MYORES)
- John Porter (NIH/NINDS)
- Boris Šuštaršič (EAMDA)

In addition the progress of the TREAT-NMD Network is reviewed on an annual basis by an external reviewer appointed by the EC, who reports on whether the project has fully achieved its objectives and technical goals for the period and makes recommendations to the EC.

The following diagram illustrates the current management structure and organisation of the network activities and workpackages (WPs) and the partners responsible for their oversight as defined in the original funding application to the EC in 2006.



Current TREAT-NMD Project Partners (and Governing Board members)

- **Newcastle University, UK (UNEW: Kate Bushby and Volker Straub – Project Coordinators)**
- Institut National de la Santé et de la Recherche Médicale, France (INSERM: Christophe Beroud)
- Leiden University Medical Center, The Netherlands (LUMC: Annemieke Aartsma-Rus)
- European Neuromuscular Centre, The Netherlands (ENMC: Katelijne Senden)
- Association Française contre les Myopathies and Institut de Myologie, France (AFM : Serge Braun)
- Biozentrum, University of Basel, Switzerland (UNIBASEL: Markus Ruegg)
- European Organisation for Rare Diseases, France (EURORDIS: Fabrizia Bignami)
- Karolinska Institute, Sweden (KI: Thomas Sejersen)
- King's College London, UK (KCLSM: Michael Rose)
- Santhera Pharmaceuticals (Switzerland) LTD Liab.Co. (SNT: Thomas Meier)
- Helsingin yliopisto, Finland (UH.HI: Carina Wallgren-Petterssen)
- Medical Research Council, UK (MRC: Kay Davies)
- Fondazione Telethon, Italy (FTELE: Anna Ambrosini)
- Université Catholique de Louvain, Belgium (UCL: Peter van den Bergh)
- Universitat Autònoma de Barcelona, Spain (UAB: Miguel Chillon)
- GenoSafe SAS, France (GENOSAFE: Muriel Audit)
- ACIES/P2R, France (P2R: Maud Seguy)
- National Institute of Environmental Health, Hungary (NIEH: Veronika Karcagi)
- Genethon, France (GENETHON: Philippe Moullier)

- University College London, UK (UCLON: Francesco Muntoni)
- University of Freiburg, Germany (UKL-FR: Rudolf Korinthenberg)
- Ludwig Maximilians University, Munich, Germany (LMU: Maggie Walter)

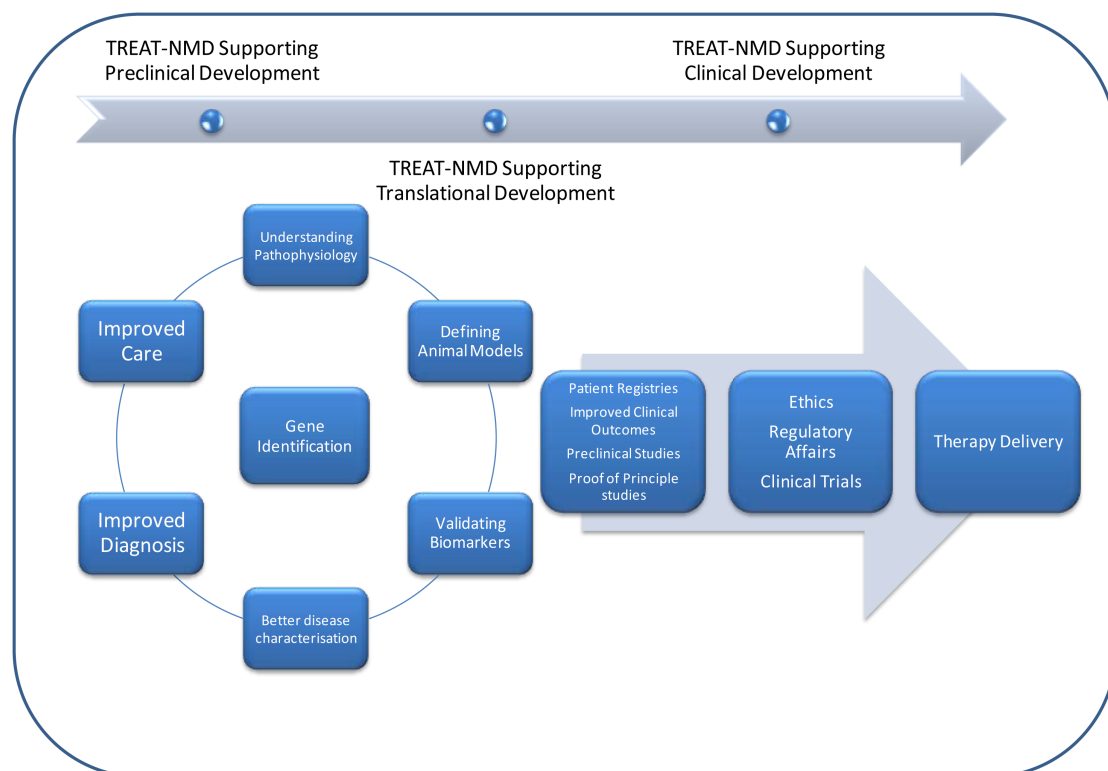
It is proposed that the future network could consist of an Executive team that would oversee working groups responsible for key activities and resources. These working groups would, for example, address issues such as registries, outcome measures, standards of care, training and education, and communication. The Executive team would be advised and monitored by the TREAT-NMD board that includes representatives from financial investors and key advisors. The precise governance structure will be developed with input from the public consultation and in discussions with partners, patient organisations and potential future funders.

3. Strategies, Support and Implementation

TREAT-NMD wants to serve as a platform for all stakeholders in the neuromuscular field to deliver on our joint objectives. TREAT-NMD is NOT a patient organisation and will NOT seek funds from the public directly. TREAT-NMD does NOT seek to fund basic research or clinical trials, and is NOT tied to one particular industrial partner.

TREAT-NMD can support the aims of other organisations to implement translational research and delivery of therapies and care for patients worldwide. This will directly benefit patients with neuromuscular diseases internationally by:

1. Providing a strong and united voice for the translational agenda for these rare diseases with industry, governments and other funders
2. Actively working to promote and implement best practice standards of diagnosis and care
3. Accelerating therapy delivery through support for preclinical and clinical therapy development (see below)



3.1 Fundraising Strategy

It is forecasted that initial funding will be required for the future network before the end of the current EC-funded project (December 2011) to ensure that staff and personnel are retained and recruited. The EC will be consulted to discuss help with bridge-funding as was recommended by the Commission report on sustaining Networks of Excellence. However, it is unclear whether further funding from the EC will be available before 2012. The award of EC grants to partners in the network has already begun, with projects such as NMD-Chip, BIO-NMD and CARE-NMD utilising the communication infrastructure developed for the TREAT-NMD Network. The funding model to sustain the network activities could combine both direct and indirect grant income with subscriptions and consultancy agreements as well as fees for particular services.

4. What is the future perspective for the TREAT-NMD Network?

TREAT-NMD is currently funded with €10 million for 5 years by the EC as a Network of Excellence (2007-2011). The rules of a Network of Excellence preclude renewal but endorse the establishment of a durable organisation after the period of EC funding. The Network wants to continue to support the efforts of the neuromuscular disease community in achieving their shared goals. The future network structure will co-ordinate, develop and implement the enduring resources of the network in preclinical and clinical therapy development and delivery after 2011.

5. Current Activities and Resources of TREAT-NMD

5.1 Preclinical resources

Evaluation of animal models for NMD and SOPs for their analysis

There are numerous animal models and strains used in research and comparing data between these models is difficult and is confounded by the multitude of experimental protocols and readout parameters. TREAT-NMD partners Santhera and Markus Ruegg (University of Basel) recognised this barrier and through close collaboration with the Wellstone Centre in Washington and the international research community has so far identified the most appropriate animal models for Duchenne muscular dystrophy and the experimental protocols to best assess and analyse data from these models and work is ongoing in SMA. Through unification of experimental protocols and publication of standard operating procedures (SOPs) this is an important step that will allow data comparability across research laboratories around the world.

To ensure their relevance to the field the SOPs will be extended in scope and in terms of disease models, reviewed and updated on a regular basis to respond to the needs of the research community <http://www.treat-nmd.eu/research/preclinical/animalmodels/>.

TREAT-NMD Advisory Committee for Therapeutics (TACT)

This committee includes internationally renowned experts and patient representatives covering preclinical data analysis, clinical development, as well as ethical and regulatory requirements and commercial considerations. The aim of TACT is to provide objective, transparent and consistent guidance to the neuromuscular community, in an educational and advisory context, on the readiness of drugs and/or therapeutic targets for clinical trials in neuromuscular diseases. This evaluation will also be helpful for preparing funding applications and investigational drug applications, and will serve as an unbiased appraisal for the wider neuromuscular community.

TACT will act as a resource for the community in understanding in detail the challenges facing specific molecules on the threshold of translation into the clinical arena (www.treat-nmd.eu/tact)

Biobanking

The improvement of supranational biobanks is a major goal within TREAT-NMD. The idea of a supranational biobank is to provide a network of biobanking facilities that will encourage the storage of biomaterials from patients and help scientists to obtain more easily the specific material they need for their experiments in neuromuscular diseases. For new treatments to make their way into clinical practice for patients affected with neuromuscular disorders, it is essential that access to biomaterials is facilitated.

TREAT-NMD will improve the availability and the exchange of biomaterial among scientists, in collaboration with the already existing EuroBioBank network established by Eurordis (www.eurobiobank.org)

Preclinical forum

Partners in TREAT-NMD have initiated a series of forums to facilitate and encourage multidisciplinary collaboration, not only between partners but with the wider scientific community. These forums are currently exploring areas such as antisense oligonucleotide research, and can assist in developing future funding applications by creating the links between scientists and clinicians to bring forward new ideas and innovations. This has already led to new projects, such as NMD-Chip (<http://www.nmd-chip.eu/>) and BIO-NMD (<http://www.bio-nmd.eu/>), which are funded through FP7.

TREAT-NMD will foster idea generation and exchange of views amongst stakeholders facilitating further harmonisation of the field.

5.2 Maintenance, development and implementation of network associated clinical resources

Clinical trial support and advice

The expertise within TREAT-NMD can help clinical investigators and industry with all aspects of trial planning from protocol development, trial management, and data monitoring. An extensive regulatory affairs database created by Rudolf Korinthenberg and the team at the University of Freiburg on behalf of TREAT-NMD is an important resource for planning multi-national studies and contains the appropriate regulations and guidelines of the various national authorities (www.treat-nmd.eu/regulatoryaffairs).

TREAT-NMD will support and advise sponsor-initiated clinical trials from industry and clinical investigators.

Patient registries

In collaboration with clinicians and patient advocacy groups across the world, TREAT-NMD has helped create over 30 national patient registries across Europe and beyond (such as Japan, Australia, South America and the US) and containing the information needed to establish whether a particular patient might be eligible for a trial, together with the means of contacting them. In establishing these national registries this also attracted significant funding from other national and international organisations to support their development. Christophe Beroud and his team at the University of Montpellier has established the global registries for patients with DMD, SMA and FKRP associated muscular dystrophies and are already running and accepting enquiries, with registries for other conditions in preparation. Over 40 countries on all continents are involved in the global patient registries for DMD and SMA. The global registries comply with all EU and national data protection legislation and have full ethical approval as well as a defined oversight and governance structure. The information they contain makes them valuable tools and resources when identifying and recruiting patients for clinical studies. To date the registries have provided data for seven industry and one academic feasibility studies.

TREAT-NMD will deliver the global registry programme, supporting quality control and training for best practice and acting as a resource for industry at the level of trial feasibility, recruitment and long term monitoring. (<http://www.treat-nmd.eu/patients/patient-registries/global-registries/>)

Care and Trial Sites Registry

The TREAT-NMD Care and Trial Sites Registry (CTSR; www.treat-nmd.eu/ctsr) is a growing database of currently over 200 clinical sites and medical centres set up by the TREAT-NMD Clinical Trial Coordination Centre (CTCC) at the University of Freiburg to provide a valuable and accurate source of information regarding the experience, facilities, equipment and personnel of sites worldwide caring for neuromuscular patients.

The CTSR will be a source of sites for clinical trials, both by supplying feasibility information and also by raising standards through training and education. Sites will also act as a resource for dissemination and implementation of standards of care and standardised operating procedures.

Standards of diagnosis and care

TREAT-NMD works with leading specialists and organisations worldwide, such as the ICC and CDC, as well as patient groups to create international consensus on care and management for patients suffering from neuromuscular diseases. TREAT-NMD has a team led by Thomas Sejersen (Karolinska Institute) dedicated to working on this issue and the TREAT-NMD website (www.treat-nmd.eu) hosts user-friendly versions of a range of documents relating to patient care. This has created a platform for other projects focusing on the further development and implementation of care standards, such as CARE-NMD (www.care-nmd.eu).

TREAT-NMD will foster the updated delivery of standards of care for different neuromuscular diseases as well as co-ordinating efforts in dissemination and implementation of standards of care

Outcome measures

The Registry of Outcome Measures (ROM; www.researchrom.com) is an on-line database that provides TREAT-NMD partners and the wider NMD research community with information about existing outcome measures. The ROM was established by Michael Rose (King's College London) and is a convenient first stop for important baseline information about existing outcome measures with clear directions to key points of contact and comprehensive sources of information. This and other efforts on consensus building on the use of and training in outcome measures will inform natural history studies and trial developments as well as feeding into regulatory discussions.

TREAT-NMD will work with the community and regulators to help develop and validate appropriate outcome measures for future clinical studies.

Meetings and workshops

TREAT-NMD recognises that generating innovation and support for these initiatives is crucial in order to advance the neuromuscular field. Through organising meetings and workshops we can communicate opportunities to potential partners and support applications for funding to ensure new initiatives are properly supported and implemented.

Focussed training and education

TREAT-NMD is developing a neuromyology curriculum to help educate the next generation of myologists to ensure the current excellence in the field continues. The development of the curriculum is lead by Mary Reilly (University College London) and the ENMC in close collaboration with national and international neurology, paediatric neurology and myology societies. In addition, TREAT-NMD is able to offer specialised training courses in key areas, such as standards of care and diagnosis, as well as for preclinical scientists. This training programme can also be extended to include planning and conduct of clinical studies that can

be offered via the Clinical Trial Coordination Centre (CTCC) based in Freiburg, Germany. Focussed training for physiotherapists and other trial study staff can be delivered on outcome measures and standards of care.

Systematic reviews

TREAT-NMD recognises the need for access to the best evidence for treatment and diagnosis of neuromuscular diseases through systematic reviews and, where possible, meta-analyses of randomised controlled trials and high quality diagnostic studies. It supports the efforts of the international Cochrane neuromuscular disease group, led by Richard Hughes, to establish and maintain continuously updated systematic reviews for neuromuscular diseases. These reviews are published electronically and readily, often freely, available internationally in the Cochrane Library. Abstracts and lay summaries are freely available to all. Key reviews are advertised with podcasts and press releases. To facilitate access, overviews of reviews for each individual disease will be developed and published. These reviews are needed for development of standards of care.

Appendix

Summary of major milestones reached by TREAT-NMD partners and collaborators

1. Standards of Care for SMA developed and disseminated (in collaboration with the ICC and patient organisations)
 - a. Publication and dissemination of a family guide based on the care recommendations
 - b. Family guide translated and currently available in 12 languages
2. Standards of Care for DMD developed and disseminated (in collaboration with the CDC and patient organisations)
 - a. Publication and dissemination of a family guide based on the care recommendations
 - b. Family guide translated and currently available in 4 languages with another 18 translations currently in progress
3. Global Patient Registries for DMD, SMA, FKRP and DM1 available (in collaboration with national registries)
 - a. Over 40 countries on all continents involved in the DMD and SMA global registries
 - b. Currently over 10,000 DMD patients and over 2,000 SMA patients are registered
 - c. Registries have attracted investment from multiple organisations and governments for research and care
 - d. The global registries have defined best-practice standards for oversight and governance via the Registry Charter and Oversight Committee
 - e. Provided feasibility data for industry and academic-sponsored clinical trials
4. Care and Trial Site Registry available with details of major centres worldwide
 - a. Provided feasibility data on potential sites for industry-sponsored clinical trials
5. Standard operating procedures (SOPs) for assessing animal models for DMD and SMA published (in collaboration with the wider academic community)
6. Established the TREAT-NMD Advisory Committee for Therapeutics (TACT)
 - a. Independent body of experts to advise and educate new therapy developments
7. Registry of Outcome Measures (ROM)
 - a. Freely available online registry of information on over 100 outcome measures designed for use in clinical studies
8. TREAT-NMD web site and biweekly newsletter
 - a. Central source of information available for wide ranging audience (industry, patients, academics and clinicians)
9. Meetings with Regulatory bodies (EMA/FDA) in partnership with patient organisations
 - a. Appropriate outcome measures for trials in SMA
 - b. Requirements for antisense oligonucleotide therapies in DMD
10. Training workshops
 - a. Annual ICH-GCP and clinical trial design training workshops offered
 - b. Clinical training and education workshops offered across Eastern Europe
11. Academic Workshops
 - a. Support and organised academic-led workshops in collaboration with ENMC and workshop sponsors; these include
 - i. CMD Outcome Measures workshop
 - ii. DMD Diagnostic guidelines workshop
 - iii. DMD Outcome Measures workshop
 - iv. Antisense oligonucleotide therapies for DMD workshop
 - v. High-throughput Screening strategies workshop

- vi. Patient Registries for Myotonic Dystrophy workshop
- 12. Address and offer advice on ethical issues regarding neuromuscular diseases
 - a. Article on stem cell tourism – hope versus hype
 - b. Clinical trials and therapeutic misconception
- 13. TREAT-NMD Membership
- 14. TREAT-NMD/NIH Conference in Brussels, November 2009
 - a. Wide-ranging programme addressing the barriers to translational medicine
 - b. Follow-up conference planned for November 2011 in Geneva