



**TREAT-NMD Advisory Committee for Therapeutics (TACT)  
Terms of Reference**

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## Terms of Reference

### Aim

To provide transparent and consistent guidance and advice to the neuromuscular community, in an educational drug development, directional context, on the prioritisation and readiness of drugs and/or therapeutic targets as likely candidates for therapies for neuromuscular diseases.

### Context

The TREAT-NMD network is an EU funded network of excellence aiming to advance treatments and care for patients with neuromuscular diseases. Various network tools will accelerate clinical and, ultimately, therapy delivery. These tools include standard operating procedures for the assessment of animal models of disease, patient registries, definition of outcome measures, a trial co-ordination centre and a registry of trial sites. The network has expanded from beyond its original remit within Europe to represent patient registries and trial sites from around the world and to work with diseases beyond the original “flagship diseases” of DMD and SMA.

The pharmaceutical industry is becoming increasingly involved in identification of targets for NMD and utilising the tools of the network in planning trials and also many potential therapeutic targets are being identified by academic groups including from drugs that are already licensed for other indications. Since the majority of academic groups are unaware of the intricacies of drug development and complexities of human clinical trials, there is a pressing need to clarify the process for systematically moving these drugs forward to clinical trials in the context of a limited patient population and a potentially finite amount of money to invest in trials.

The review process will be transparent, milestone-driven and educational; aimed at helping researchers understand the overall process. TACT recommendations will facilitate human proof of concept (POC) trials, generating data that will enable subsequent development decisions and potential registration. Through its comprehensive quality recommendations, TACT may help stimulate additional funding opportunities.

### Remit of the committee

The committee will evaluate the therapeutic potential of drugs with preclinical data that suggests efficacy in a neuromuscular disease. These evaluations will help TREAT-NMD in prioritising clinical trials that will be run via the network, they will provide the background for preparing funding applications and investigational drug applications, and they will provide an unbiased appraisal to be published for the wider neuromuscular community.

Therapeutic development potential implies several things: a) not only the interpretation of data from preclinical studies; b) issues of formulation, bioavailability and toxicology; c) the likely regulatory issues; d) prospects for marketing; and e) specific issues pertaining to the practicality of performing rational and economical clinical trials, including linking the applicant with relevant services and information, for example that are already available via TREAT-NMD and other resources.

The ultimate goal is to provide information to help assess the likelihood of ultimate registration and assist in clarifying this pathway. We hope that this process would be endorsed by the major funders.

### Composition of the committee

The committee is a group run under the aegis of TREAT-NMD. However the membership of the committee will not be limited to TREAT-NMD partners but rather will be selected by the TACT Chair together with the secretariat from the pool of experts nominated, to represent the very best expertise available to address the issues pertinent to its remit (including paid consultancy as and when needed). Additional experts may be co-opted for assessment of unusual areas not within the expertise of the standing committee. The Chair of the committee will be appointed by the TREAT-NMD governing board and will serve for three years. The committee will be supported administratively and financially by a

secretariat provided by TREAT-NMD from the co-ordination office, the clinical trial co-ordination centre and those partners involved in delivery of trials. Committee members will be reimbursed for all travel expenses and will be eligible to receive an honorarium of 300 Euros for each meeting attended, with the exception of US government employees acting in official capacity.

All committee members will be asked to sign a confidential disclosure agreement and complete a declaration of all potential conflicts of interest. Committee members will be requested to update their conflict of interests before each review meeting. A short biography will be published on the TREAT-NMD website along with the members photograph.

### **Application process to TACT**

Suggestions for drugs to be appraised by the TACT will be solicited from among the network and collaborators. Applicants may include principal investigators planning a study, preclinical investigators who have promising results they wish to move to the clinical arena, a potential trial industry sponsor or a funding body seeking advice on the feasibility of a compound moving to trial. In some circumstances the TREAT-NMD network itself might approach TACT for advice about the prioritisation of drugs that may go into a funding application. All applicants will be expected to produce a dossier of information on the drug according to a set proforma. The completion of this focused application form and advice generated will become an educational tool. TACT will proactively call for nomination of drugs and approach potential principal investigators to inform them on the role of TACT.

### **Roles within the committee**

**Chair:** work with the TREAT-NMD secretariat on the following tasks: to agree on the drugs (with a predetermined maximum) to be appraised at a session, distribute review tasks ahead of the meeting, chair the meeting, oversee the preparation of the report and recommendations.

**Preclinical experts:** at least two members with expertise in the models under discussion, to be drawn from nominees which have predominantly come from the broad group who contributed to the animal models activities in TREAT-NMD and associated collaborators. Their role will be to appraise critically the preclinical data either published or unpublished on the drug under study against the defined standards for preclinical assessments of animal models. Where necessary, confidentiality agreements will be set up to protect unpublished data.

**Toxicology expert:** to advise on the current status of human exposure to the drug in question including if relevant paediatric data.

**Pharmacology expert:** to advise on the current status of pharmacokinetic and pharmacodynamic data available for the product and to make recommendations for studies needed for regulatory approval.

**Regulatory:** to advise on the likelihood of regulatory approval for entering the clinic (and potentially subsequent registration) including acceptability of endpoints.

**Clinical Trial Co-ordination Centre representation:** to advise on the protocols likely to be necessary to test the drugs in the clinic, patient numbers and likely numbers of trial sites and potential sample costings.

**Clinical representatives:** clinic leaders from different geographical areas representing major clinical networks (eg Europe and USA). To advise on the practicalities of recruitment to a particular protocol in the context of other competing demands on clinic time and commitment and other general protocol issues.

**Ethical input:** to advise on the ethical dimensions of the proposed studies.

**Patient organisation representation:** to provide the patient perspective on the proposed studies.

**TREAT-NMD secretariat:** to provide perspective on the broader TREAT NMD expectations and key issues, provide supporting data for the drugs in question, organise the experts invited to participate in the TACT meeting discussions, assist in preparation of meeting documents, minute the meeting, assist in drafting reports and developing follow up data.

**Relationships with funders:** if any funders wish to enter into a contract with TREAT-NMD to perform this work in partnership or on their behalf, then they will be represented ex-officio on the committee.

**Process and timing** (meetings to take place at least twice per year, responsive to current need in a particular disease area)

No	Task and responsible committee member	Timing
1	Application expression of interest for next meeting review identified (task of secretariat plus chair)	T-4 months
2	Completed application received (to secretariat)	T-3months
3	Call for additional preclinical data not in public domain, including unpublished data on negative results (secretariat)	T-3 months
4	Confirmation of compounds for next meeting from applications received (secretariat, core, plus chair) Confirmation of participants for next meeting from the TACT as well as additional experts as required (secretariat, core plus chair) Distribution of complete applications to meeting participants and any ad hoc external reviewers (secretariat)	T- 2.5 months
5	Feedback to all applicants to inform them if their application will be reviewed or not at the next meeting. Announce applications to be reviewed on the TREAT-NMD website and in the newsletter	T-2.5 months
6	Completion / update of conflict of interests from meeting participants (secretariat)	T-2 months
7	Meeting participants and reviewers prepare reports in their area of expertise (within 4 weeks )	T- 6 weeks
8	Expert reports circulated to all meeting participants (secretariat)	T- 2 weeks
9	Meeting convened. Review 2-3 drugs per meeting	Time 0 - Meeting
10	Integrated report/recommendations generated (responsibility rotated among the core committee)	T+4 weeks
11	Specific detailed report available to PI / applicant (secretariat)	T+6 weeks
12	General 'non-confidential' report summary available via TREAT-NMD website (responsibility rotated among the core committee)	T+2 months