

## Orphan Drug Development Guidebook

### Building Block I429

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	TREAT-NMD advisory committee for therapeutics (TACT)
References	<a href="https://treat-nmd.org/what-we-do/tact-treat-nmd-advisory-committee-for-therapeutics/tact-application-process/">https://treat-nmd.org/what-we-do/tact-treat-nmd-advisory-committee-for-therapeutics/tact-application-process/</a>  <a href="https://doi.org/10.1038/d41573-019-00199-1">https://doi.org/10.1038/d41573-019-00199-1</a>
Description	<p>Established in 2009, the TREAT-NMD Advisory Committee for Therapeutics (TACT) is a unique multi-disciplinary international group of internationally recognized academic and industry drug development experts as well as representatives of patient foundations and regulatory experts. The group meet twice a year to review and provide guidance on the translation and development path of therapeutics programs in rare neuromuscular diseases with large unmet need, such as muscular dystrophies and amyotrophic lateral sclerosis (ALS). The confidential and comprehensive review provides recommendations including go/no-go milestones, and is independent of any funding stream.</p> <p><b>TACT will:</b></p> <ul style="list-style-type: none"> <li>• Convene a bespoke panel of expert reviewers covered by full CDA and free from conflicts of interest.</li> <li>• Provide a one point in time multi-disciplinary review.</li> <li>• Meet 2 times per year (once every 6 months, in person in spring, alternating between Europe and North-America, and virtually in autumn).</li> <li>• Accept applications for therapeutics targeted to any form of rare inherited neuromuscular disease.</li> <li>• Applications are accepted from anywhere in the world.</li> <li>• Carry out reviews under a confidential disclosure agreement.</li> <li>• Review therapeutics at any stage of development (once a lead compound is identified) that are presented as having a clear perspective within the translational process with the long-term goal of an intended clinical trial and potential registration.</li> </ul>

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	<ul style="list-style-type: none"> <li>• Consider reviewing previously-reviewed programmes if they have substantially progressed or changed and if the committee felt that it could add further value.</li> <li>• Address issues of drug formulation, bioavailability and toxicology as well as possible regulatory requirements and marketing considerations.</li> <li>• Provide applicants with a comprehensive written review, including recommendations no later than 6 weeks following the meeting.</li> <li>• Publish a non-confidential summary to ensure the community receives expert feedback on the progress of the application.</li> <li>• Provide information about the projects reviewed and planned to be reviewed at TACT meetings on the TREAT-NMD website and in TREAT-NMD newsletters.</li> <li>• Include patient representatives on every review panel.</li> </ul> <p><i>TACT will not:</i></p> <ul style="list-style-type: none"> <li>• Provide on-going feedback to applicants on the development programme.</li> <li>• Respond to queries following the issue of the final report.</li> <li>• Amend or update the final report.</li> <li>• Engage with funding organisations on behalf of applicants.</li> <li>• Provide funding; TACT is not a funding organization but provides evaluation and recommendations which may facilitate development of a review into an application to a funding organization.</li> </ul> <p>If you wish to find out more about TACT you may want to view a video of a presentation given at the Faster Cures Conference in New York City, November 2012.</p> <p>For academic applicants TACT requests no contribution – they have however to cover the travel costs to the TACT meeting. For companies there is a fee based on the size of the company.</p>
Category	Development Resources Building Block
Geographical scope	International.
Availability	<p>Companies and academic researchers planning to perform clinical trials in the neuromuscular disorders can initiate a TACT review.</p> <p>Currently TACT focuses on neuromuscular disorders. However the “ACT” model could easily be implemented also for other disease groups and this is currently ongoing under the EJP-RD flag.</p>

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	<p>TACT is available to both Industry (for a contribution towards meeting costs) or academic researchers (no contribution requested). TACT is a not for profit organization and reviewers receive only a small honorarium for their time.</p>
<p>Scope of use</p>	<p>TACT will provide an assessment and advice that involves all aspects of drug development. It will encourage early phase developers to already start thinking about requirements for later phases (e.g. upscaling manufacturing). It will provide all developers with information to set clear go/no-go criteria and with information to design their trials better. It reduces the risk of sub-optimal trials and/or taking drugs into clinical trials without sufficient preclinical data.</p> <p>So far 22TACT meetings have been held reviewing 82applications. About 2/3 applications are from industry and 1/3 from academia. Applications have covered multiple neuromuscular disorders, such as Duchenne muscular dystrophy, spinal muscular atrophy, myotubular myopathy, FSHD and Pompe disease.</p> <p>TACT has received applications in both early (first in man) and later (phase 2/3) clinical trials for academia, small/medium sized enterprizes and big pharma. The aim of TACT is to provide a multi-disciplinary assessment of a therapeutic approach, to help define clear go/no go decision points and to help optimize clinical trials.</p>
<p>Stakeholders</p>	<p>TACT consists of a core group (around 10) with expertise in preclinical experiments, clinical trials, toxicology, outcome measures and regulatory issues. In addition, there are a number of extended members (around 80) who can provide additional expertise for specific neuromuscular disorders or for different aspects of therapy development including the patient perspective. A typical review panel is made up of 12-18 experts depending on the requirements of each application.</p> <p>The core and extended committee can be seen here: <a href="https://treat-nmd.org/what-we-do/tact-treat-nmd-advisory-committee-for-therapeutics/tact-committee-members/">https://treat-nmd.org/what-we-do/tact-treat-nmd-advisory-committee-for-therapeutics/tact-committee-members/</a>. The TACT Secretariat is based at Newcastle University and supports the running, logistics and administration of TACT.</p> <p>TACT is and has been supported by generous funding from patient organisations including: CNMC (via DoD grant), PPMD, Cure Duchenne, MDUK, MDA, Joining Jack, Duchenne UK, Duchenne Ireland, Myotubular Trust, Duchenne Now, Duchenne Children’s Trust, SMA Europe</p>

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Enablers/ Requirements	<p>Interested companies/researchers contact the TACT coordinator located at the TREAT-NMD Secretariat (<a href="mailto:Laura.Robertson@treat-nmd.com">Laura Robertson (Laura Robertson &lt;laura.robertson@treat-nmd.com&gt;)</a>) to discuss the eligibility and timing of the TACT review. When eligible, the applicant needs to fill out the ‘TACT review form’, thus providing the TACT review committee with the requested information for assessment. In addition, they can provide additional information (publications, posters, manuscripts etc).</p> <p>The information is then reviewed by committee members (selected as needed for each application’s panel). They provide feedback (both strengths and limitations) and address specific questions from the applicant based on their individual expertise and collected by the TACT coordinator. One experienced TACT expert is assigned the role of ‘Lead reviewer’ and he/she collates the comments to be shared with the panel. During the TACT face-to-face meeting, the Lead briefly introduces the application, and chairs further discussion by the committee. The applicant then joins the committee meeting to facilitate clarification and further discussion about the application. Finally, the TACT committee discusses further in light of the face-to-face meeting. Subsequently, the Lead writes the TACT report, which is then distributed amongst the committee members for input. The final report is shared with the applicant as a confidential document which is for their own use. The applicant may choose to share this with others but TACT will not do so.</p>
Output	<p>TACT helps to provide independent, expert advice and go/no-go decisions which may be used to prioritize which drugs should be taken into clinical trials. TACT helps to ensure that trials are well planned and data is robust – it helps to ensure more optimal clinical trials.</p> <p>The applicants will be provided with a <b>confidential comprehensive TACT report</b> that includes a multidisciplinary assessment from the TACT reviewers (with input on preclinical data, clinical data (if available), clinical trial design, manufacturing, safety, regulatory and patient perspective). Furthermore, a <b>brief non-confidential summary</b> will be provided on the TREAT-NMD website (this is done in collaboration with the applicant to avoid that any confidential information becomes public).</p>
Best time to apply and time window	<p>In order to submit a TACT application, applicants need to have at least identified a lead compound. However, applications can also be reviewed during later clinical phases of a development program, before the initiation of a clinical trial.</p> <p>Pre-application at least 3 months in advance of a TACT meeting (dates</p>

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	<p>published on the TACT website). Full application submitted at least 8 weeks in advance of a TACT meeting.</p> <p>Applicant requested to attend the face-to-face meeting for up to half a day.</p> <p>TACT confidential report provided to applicant within 6 weeks of the face-to-face meeting.</p> <p>Non-confidential report for the TACT website agreed within 2 weeks of the full report being issued.</p>
Expert tips	<p>Contact the TACT coordinator early when considering to apply for a review so the best timing can be discussed</p> <p><b>PROs:</b></p> <ul style="list-style-type: none"> <li>• Multidisciplinary approach</li> <li>• Constructive approach (the aim is to make things better through advice from world experts and optimize therapy development)</li> <li>• One stop shop for companies needing scientific advise</li> </ul> <p><b>CONS:</b></p> <ul style="list-style-type: none"> <li>• At the moment only applicable for the neuromuscular disorder field</li> </ul>