Clinical Trials Programs at NIAMS

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NIH Institute Homes for Neuromuscular Diseases

MH - malignant hyperthermia
CNM - centronuclear myopathies
MChan - muscle channelopathies, non-dystrophic myotonias, periodic paralyses
IM - inflammatory myopathies, DM, PM, IBM

MD - DBMD, DM, FSHD, CMD, LGMD, OPMD, EDMD and others

NIH Institute Homes for Neuromuscular Diseases

NINDS

CMT, ALS, MG, PN

SMA

Mchan, MH, CNM, IM

NIAMS

MD

Pompe

NHLBI
Clinical Research and Clinical Trials at NIH

- NIH as a whole has been reviewing the process of scientific management and oversight of clinical trials

Premise and Reproducibility

Trial design and Implementation

Time to Publication
Revision NIH Definition for Clinical Trials

• In January of 2015, revised NIH definition of clinical trials took effect
  – A research study in which one or more human subjects are prospectively assigned to one or more interventions to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes

• Why the new definition?
  – So that clinical trials can be identified and adequately monitored for:
    ▪ Safety
    ▪ Recruitment / inclusion
    ▪ Reporting / publication

• What does this mean for researchers?
  – Many NIH ICs have revised policies on how clinical trials are accepted and reviewed
NIAMS Clinical Trial Policies

• NIAMS does not accept clinical trials received through parent announcements (NOT-AR-14-021)
  – Investigator-initiated applications submitted to NIAMS must be submitted to one of the NIAMS program announcements with special review (PAR) specifically designed for clinical trials

• Why?
  – Increase the rigor, timeliness, and impact of trials supported
  – Review by NIAMS standing study section (AMSC)
    ▪ Members include clinical trialists, statisticians, physician-scientists
    ▪ Consistency of advice
    ▪ Note: Panel includes reviewers with expertise across entire NIAMS mission

• Are similar policies in place across the entire NIH? Varies by institute.
  – NINDS also requires all clinical trials be submitted to specific PAR reviewed within NINDS
NIAMS Clinical Trial Opportunities

- Clinical Trial Implementation (U01) PAR-15-165
- Clinical Trial Planning (U34) PAR-15-166
- Exploratory Clinical Trials (R21) PAR-14-192
- Clinical Observational Studies (R01) PAR-15-115

http://www.niams.nih.gov/Funding/Clinical_Research/clinical_main.asp
Clinical Observational Studies in Musculoskeletal, Rheumatic, and Skin Diseases

• **R01** (PAR-15-115)

• **Goal: To obtain data necessary for designing clinical trials**
  – Address significant obstacles or questions in the design of clinical trials
    ▪ Determine appropriate outcome measures
    ▪ Disease progression
    ▪ Study recruitment strategies
    ▪ Standard of care data to be used as control in future trial
    ▪ Support biomarker development and validation (but not discovery)
      - Relate biochemical or imaging biomarker with established surrogate markers

• **No interventions**

• Most responsive applications will have clear connection enhancing future clinical trials
  – Other natural history /observational studies may be best served by parent R01 (CSR review)
Exploratory (Pilot) Clinical Trial Grants

- **R21** (PAR-14-192)

- **Goal:** Facilitate short-term interventional studies to obtain data needed to launch future clinical trials

  - First-in-human studies
  - Safety / tolerability / dosing
  - Testing new formulation or delivery of intervention
  - Trials aimed at prevention, delayed or halted progression
  - Feasibility studies focused on novel, cost-effective, or alternative designs

- Other opportunities to consider: NCATS BrIDGs and TRND; NINDS Blueprint Neurotherapeutics
Clinical Trial Planning Cooperative Agreement Grants

- **U34 (PAR-15-166)**

- **Goal:** Facilitate design of studies and completion of administrative activities prior to implementation phase

- **NIAMS requires all clinical trial implementation awards (U01) first go through a U34 planning phase**
  - Exceptions can be made if preparatory work is sufficiently far along
  - Contact NIAMS PO

<table>
<thead>
<tr>
<th>Planning Activity</th>
<th>Status</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study protocol</td>
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<tr>
<td>Budget proposal for U01 application</td>
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<tr>
<td>Identification and qualifications of clinical trial sites, pharmacies and laboratories</td>
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<td>Investigator Brochure (IRB) or equivalent</td>
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<td>MOOP</td>
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<td>Data and safety monitoring plan</td>
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<tr>
<td>Finalize plans to obtain intervention related products (drugs, placebo, device)</td>
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<tr>
<td>Develop Clinical Trial Agreement (CTA) and/or Cooperative Research and Development Agreement (CRADA)</td>
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<td>Develop template informed consent (and assent form, if applicable)</td>
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<tr>
<td>Develop case report forms</td>
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<td>Program database</td>
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<tr>
<td>Establish data collection system for primary and/or remote sites</td>
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<td>Submit/obtain approval for IND/IDE</td>
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<td>Develop and plan materials for training and site initiation</td>
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<tr>
<td>Initiate IRB approval/request applicable waivers (e.g., HIPAA)</td>
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<tr>
<td>Documentation of adequate co-funding, if applicable and necessary for completion of the trial</td>
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http://www.niams.nih.gov/Funding/Clinical_Research/clinical_milestone_checklist.asp
Clinical Trial Implementation Cooperative Agreement Grants

- **U01** (PAR-15-165)

- **Goal:** Support clinical trial implementation phase

- Activities that would fall under this FOA:
  - Enrollment of subjects
  - Data collection, analysis and oversight
  - Preparation of final study report and other post-enrollment activities

- **Note:** Preceding U34 planning grant required unless waiver granted

- Pre-submission consultation with NIAMS Program Officer is strongly encouraged prior to submitting an application
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Mechanism</th>
<th>Budget Caps (Direct Cost)</th>
<th>Review</th>
<th>Special Considerations</th>
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</thead>
<tbody>
<tr>
<td>Clinical Observational</td>
<td>R01</td>
<td>$450K** over 3 years</td>
<td>NIAMS (AMSC)</td>
<td>How will this inform / enhance subsequent trials?</td>
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<tr>
<td>Pilot / Exploratory</td>
<td>R21</td>
<td>$400K** over 3 years</td>
<td>NIAMS (AMSC)</td>
<td>How will this inform / enhance subsequent trials?</td>
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<tr>
<td>Planning</td>
<td>U34</td>
<td>$250K per year for up to 2 years</td>
<td>NIAMS (AMSC)</td>
<td>Required for U01 unless waiver granted</td>
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<tr>
<td>Implementation</td>
<td>U01</td>
<td>No budget cap^^, up to 5 years</td>
<td>NIAMS (AMSC)</td>
<td>Requires prior U34 unless waiver granted</td>
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</table>

** excludes consortium F&A

^^ Applications requesting ≥ $500K in direct costs in any year (excluding consortium F&A) requires approval prior to submission (10 weeks prior)
Request for Information – Feedback on NIAMS Clinical Trial Programs

• Ways the current NIAMS suite of clinical trials Funding Opportunity Announcements can be improved
  – Goal: adequately provide opportunities for all types of clinical trials

• Types of funding support that are necessary for the different stages of clinical trial implementation
  – Conceptualization → full implementation

• Ways the NIAMS can optimize the early review of a future clinical trial concept
  – Benefits that might result from having the NIAMS review a clinical trial concept at an early stage

• Other areas relevant to optimizing NIAMS clinical trials support

• See NOT-AR-15-019
  – Responses due by October 15, 2015
  – Email to NIAMSclinicaltrials@mail.nih.gov
Look Forward to Working with You

• Pre-application discussion or letter of intent always welcome

• For scientific/programmatic questions
  Tom Cheever, Ph.D.
  Program Director
  thomas.cheever@nih.gov

• Clinical trial policy questions
  Shahnaz Khan, MPH
  Clinical Coordinator
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  Anna Nicholson, MSHS
  Clinical Coordinator
  nicholsona@mail.nih.gov

• Helpful Links
  – NIAMS Clinical Research Funding Info Page
    ▪ Policies, FOAs, FAQs, more
    ▪ http://www.niams.nih.gov/Funding/Clinical_Research/clinical_main.asp