Summary of the First Meeting of the Steering Committee for a Multidisciplinary International Project on Developing New Criteria for the Idiopathic Inflammatory Myopathies and their Major Subgroups

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This document summarizes a meeting of the following individuals, which was held on Tuesday October 26, 2004 from 8:00 AM to 5:00 PM at the National Institutes of Health, 9000 Rockville Pike, Building 31, Room B1C02, Bethesda, Maryland, USA. The purpose of the meeting was to begin to define approaches to develop new criteria for the idiopathic inflammatory myopathies and their major subgroups.

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1. Introduction– Ingrid Lundberg summarized the developments that led to the current meeting emphasizing the growing split among different specialities in terms of how the idiopathic inflammatory myopathies and their major subgroups are viewed and defined and how this could lead to great difficulties in future meta-analyses and attempts to correlate findings from one trial or study to another. She also described current interest by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) to support these efforts to develop criteria that would be recognised by these and possibly other groups.

2. Matthew Liang reviewed experience from previous work on development or revision of criteria in other disorders and the various methodologies that have been used (see PDF file named Appendix, Criteria for Rheumatic Diseases). He emphasized a number of lessons learned:

a. Perfection is not a goal
b. It is better to be consistent than correct
c. Widen ownership early and often
d. Seek consensus but also define areas where it cannot be reached
e. Background work prior to meetings is critical
f. Draft definitions of all terms being used in as much detail as possible
g. Find minimal essential items for consensus
h. Begin timeline at the end with publication and work back
i. Process drives the result – use neutral drivers
j. You are judged by your claims

3. A number of participants reviewed the background and history of the development and use of different criteria for the myositis syndromes.

a. Fred Miller reviewed the history of the published criteria for the idiopathic inflammatory myopathies and how have they been tested for sensitivity and specificity. He emphasized the history of a dozen papers, spanning over three decades, and that most criteria were based on clinical impressions rather than data analyses and none have been fully tested for sensitivity or specificity using appropriately powered studies against all the appropriate disease confounders. He also stressed that the most commonly utilized criteria of Bohan and Peter are often misapplied by not first eliminating other forms of myopathy, but that there are a number of problems with these criteria relating to lack of details in their application (see attached PowerPoint file 01 Miller IIM criteria overview).

b. Jessica Hoogendijk reviewed criteria that have been used in published randomized controlled clinical trials with poly- and dermatomyositis patients emphasizing that most of the few studies to date used Bohan and Peter criteria (see attached PowerPoint file 02 Hoogendijk PM DM RTC criteria).

c. Ingrid Lundberg summarized the criteria that have been used in published studies on muscle biopsy characteristics in patients with poly- and dermatomyositis emphasizing that many criteria have been used, however, in many cases they have not been specified (see attached PowerPoint file 03 Lundberg PM DM Bx research criteria).

d. Tony Amato summarized how the different characteristics in the criteria sets have been defined and how have they been tested for performance. He also emphasized the problems with the Bohan and Peter criteria in that they do not specifically distinguish inclusion body myositis, all dystrophies and statin myopathies from PM and DM (see attached PowerPoint file 04 Amato IIM criteria review).

e. Lisa Rider reviewed the criteria that have been used in children with myositis. Bohan and Peter criteria have been most widely used, but have often been misapplied. There is no consistency in the field or within study types (basic vs. clinical research) as to the criteria applied. The work of Clarissa Pilkington and the UK Network for JDM to develop new diagnostic criteria for JDM was also reviewed. (see attached PowerPoint file 05 Rider JIIM criteria review).

f. Fred Miller described experience from the International Myositis Assessment and Clinical Studies group (IMACS), which has worked to achieve international multidisciplinary consensus on the conduct and reporting of myositis studies. He emphasized that applying a combination of Delphi and Nominal Group Technique approaches in an iterative fashion has worked well in these settings and may be applicable for this project (see attached PowerPoint file 06 Miller IMACS approaches).

4. Ingrid Lundberg and Matthew Liang led the group in discussing why this project is needed and in defining the goals of the project. After some dialogue about the differences among diagnostic criteria, classification criteria and nomenclature, and how these terms are sometimes confused or used differently in various contexts, the group came to the following consensus:

a. It was decided that this project is needed because of the lack of information on sensitivity and specificity of current criteria, because of the many different unvalidated criteria that are now being used, and due to the availability of new technologies and approaches today that have resulted in new opportunities to revise our thinking and definitions of myositis.

b. It was decided that a combined effort addressing both adult-onset and childhood-onset myositis would be ideal.

c. It was decided that there should be two primary goals for the project:

i. Criteria should be developed for use by basic and clinical researchers that separate the idiopathic inflammatory myopathies from all other muscle diseases with high sensitivity and specificity; and
ii. Criteria should be developed for use by basic and clinical researchers that separate the major forms of the idiopathic inflammatory myopathies from each other with high sensitivity and specificity.

5. Ingrid Lundberg and Matthew Liang led the group in defining some aspects of what the process for the development of these criteria should be.

a. It was decided that, given the rarity of the disease and need for funding, as many professional groups as possible should be recruited to this effort including: the ACR; EULAR; IMACS; the European Neuromuscular Centre (ENMC); the American and European Neurology societies, e.g. European Federation of Neurological societies (EFNS); The Muscle Study Group; pediatric groups including PRINTO, CARRA, and the European JDM group; Muscular Dystrophy Association (MDA) clinic directors; The Myositis Association (TMA); and Dermatology groups (as suggested by Drs. Vicki Worth, Jeff Callen, Joe Jorizzo, Cynthia Magro and Richard Sontheimer).

b. Specific individuals who should be asked to participate include: Drs. Anthony Bohan, James Peter, Marinos Dalakas, Robert Griggs, Rich Barohn, John Kissel, Rabi Tawil, Michael McDermott, Ira Targoff, Chet Oddis, Paul Plotz, Andrew Engel, Kate Bushby, Eric Hoffman and the Synergy group, Steve Greenberg, Tanimoto and colleagues, Lauren Pachman, selected myopathologists such as Kondi Wong (Armed Forces Institute of Pathology) and possible radiologists such as Jim Fleckenstein.

c. The process should include the development of an extensive glossary with standardized nomenclature.

d. It may be useful to have both retrospective and prospective parts to the study, with a maximum number of cases (possibly 10 in each sub-category of myopathy, e.g. 10 DM, 10 “PM”, 10 IBM, 10 “necrotizing myopathy”, 10 overlap, 10 myositis assoc with malignancy, 10 LGMD, 10 PROMM, etc from h. below) to be contributed by each participant to avoid excess referral bias.

e. It is likely that most cases contributed would be Caucasian, but analyses should assess for possible differences in various ethnic/racial groups.

f. Different approaches to analyze the data were discussed including heuristic methods, major and minor criteria lists, probable and definite criteria, classification and regression tree (CART) approaches, regression methods – or, if funds permit, a combination of these could be used.

g. The primary study groups need to be defined – it was decided that idiopathic inflammatory myopathies would include all forms of the myositis syndromes, particularly inclusion body myositis, polymyositis, dermatomyositis, non-specific myositis, immune-mediated necrotizing myopathy, overlap myositis and cancer-associated myositis.

h. Specific comparator groups which could be confused with idiopathic inflammatory myopathies (defined by a minimum of weakness and/or rashes) need to be defined – possibilities include:

   -Non-inflammatory inclusion body myopathies
   -Dystrophies - Limb-girdle muscular dystrophies, Fascioscapulohumeral (FSH) dystrophies, others?
   -Motor neuron and other neurologic diseases
   -Drug/toxin associated myopathies (statins, penicillamine, ethanol, etc.)
   -Metabolic myopathies
   -Mitochondrial myopathies
   -Infectious myopathies
   -Endocrine myopathies
   -Rheumatic conditions including Systemic lupus erythematosus, Rheumatoid arthritis, Fibromyalgia, Polymyalgia Rheumatica, and Scleroderma
   -Dermatologic conditions including psoriasis, eczema, infectious or allergic conditions, hydroxyurea-associated and other rashes

i. An enlarged international multispecialty steering committee of prominent researchers in the field should be defined to guide the project.

j. It may be useful to define a pathology subcommittee of at least 3 members to blindly review muscle biopsies and record findings using a specified format.

k. It was estimated that the project would cost $50,000 to $100,000, take at least 3 years to complete and require at least two meetings. Funds could possibly come from the ACR, EULAR, TMA, MDA, NIH (multiple institutes) or other European groups.

l. Milestones need to be developed to keep the project on track – estimates of the overall process include:
    - Develop data collection elements, glossary and forms by email ~ 3 months from now
    - Possible first meeting to work out details of study ~ 6-9 months from now
    - Assemble derivation cases and data entry ~ 1-2 years
    - Analyses of data ~4-6 months
    - Second meeting to review analyses of different criteria and define the most clinically sensible combination
    - Ratify criteria – ideally test them on a second population?
    - Publication – authored by a group designation with reference to a list of individual contributors that would be alphabetically listed

m. The variables to collect need to be defined – possibilities include basic demographics (gender, race, age at onset of illness), those used in the Tanimoto study (see attached PDF file Tanimoto K 1995 Classification criteria for PM DM. J Rheum), specific pathologic/immunopathologic findings, autoantibodies, HLA or other genetics, family history of autoimmunity, or magnetic resonance imaging.

n. Other as yet unresolved issues that will eventually need to be addressed include: possible training to enhance consistency in use of terms and collection of data elements; possible subcommittees for MRI, biopsies, autoantibodies; how to handle missing data (EMG, biopsies etc.); how to address international IRB and ethics issues (use a central IRB?); which of multiple statistical approaches are best; data collection and validation methods (ideally web-based).

7. To do list:

a. Summarize the meeting – Fred Miller
b. A revised proposal needs to be sent to ACR and then EULAR with a more defined scientific section. The validation process needs to be more detailed. A more specific budget per year – Ingrid Lundberg et al.
c. A letter outlining the project- Ingrid Lundberg (et a.l to augment draft) prior to contact of different groups to participate in the project.
d. Contact Neurology groups and individuals in the US for their approval, participation, and buy-in – Tony Amato
e. Contact Neurology groups and individuals in Europe for their approval, participation, and buy-in - Jessica Hoogendijk
f. Contact Pediatric groups (CARRA, PRINTO, Synergy, pediatric neurologists on US list-server) for their approval, participation, and buy-in – Lisa Rider
g. Contact European pediatric groups, neurologists for their approval, participation and buy-in (UK Network for JDM, PRES, UK neurologists)– Clarissa Pilkington
h. Contact selected Rheumatologists for their approval, participation, and buy-in – Fred Miler and Ingrid Lundberg
i. Contact IMACS members for their approval, participation and buy-in: Lisa Rider, Fred Miller, Ingrid Lundberg
j. A formal letter of participation will be approved by the steering committee and emailed/sent to all participants – Ingrid Lundberg
k. Consider applying to NIH for a clinical trial planning grant or other support - Tony Amato with Matt Liang's help

l. Develop data collection elements, glossary and forms within the next month for eventual email distribution and further comments to all participants – Ingrid Lundberg with help from all steering committee members
m. Contact Mathias and Annette Schneider in Düsseldorf for possible use of their web-based data collection system – Matt Liang
n. Define membership of the full steering committee and all participants in the study – Ingrid Lundberg with help from current steering committee members
o. Continue to think about details relating to the project and additional sources of funding – all steering committee members