2nd Meeting of the Down Syndrome Consortium:
A Public-Private Partnership
February 28, 2012

6100 Executive Boulevard
5th Floor Conference Room
Rockville, Maryland

Welcome and Introductions
Yvonne Maddox, Eunice Kennedy Shriver *National Institute of Child Health and Human Development (NICHD)*

Dr. Maddox, Deputy Director of NICHD of the National Institutes of Health (NIH), welcomed the group to the second meeting of the Down Syndrome Consortium (DSC) at 12 p.m.

Updates
Dr. George Jesien, Association of University Centers on Disabilities (AUCD), reported that AUCD is working with the John Merck Fund, which is switching its research scholarship program to a spend-down of about $15 million over the next 10 years. The Fund has decided to focus on Down syndrome (DS) and fragile X syndrome. In addition, AUCD will hold a series of self-advocacy summits in the form of four regional meetings. Information can be found on the website at http://www.aucd.org.

Dr. Bob Riddle, National Institute of Neurological Disorders and Stroke (NINDS), explained that his Branch's piece of the NIH portfolio focuses on issues relating to cognitive function in both the normal state and the state affected by DS.

Mitchell Levitz, self-advocate at the University Center for Excellence in Developmental Disabilities at the Westchester Institute for Human Development, explained that he works within the community support network and is actively engaged with numerous organizations.

Michelle Livingston, Global Down Syndrome Foundation (GDSF), reported that the GDSF Washington, D.C., gala will take place in spring 2013. The foundation is focusing on advocacy efforts and improving its website.

Dr. Edward McCabe, **Linda Crnic Institute for Down Syndrome (LCI),** reported that the institute is growing, and that Huntington Potter will be joining the team in August. Dr. Potter is investigating the relationship between classical Alzheimer's disease and DS and has an active clinical trial relating to Alzheimer's.

Dr. Margaret Nygren, American Association on Intellectual and Developmental Disabilities (AAIDD), reported that AAIDD recently released the user's guide to its terminology and classification manual. AAIDD is engaged with those developing the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* on the diagnosis and classification of intellectual disability and autism. AAIDD has produced a number of free webinars and is working on building more educational content.

Dr. Michael Harpold, Down Syndrome Research and Treatment Foundation (DSRTF), reported that DSRTF has funded an additional round of grants for research that addresses not only basic mechanisms but also downstream thinking on how these could be proven in clinical studies. Another focus has been to

engage the pharmaceutical industry; for example, Roche USA announced an initiation of a clinical trial for a novel drug.

Jon Colman, National Down Syndrome Society (NDSS), reported that this week is the society's Buddy Walk on Washington and day on Capitol Hill. They have hired Sara Weir, previously of GlaxoSmithKline, who brings a lot of research experience. The society will be making a number of investments across its program areas over the next few years.

Dr. Frank Avenilla, National Institute of Mental Health (NIMH), represented Lisa Gilotty at the meeting. He reported that NIMH continues to encourage basic research on the overlap between autism and DS and related disorders. He highlighted a grant aimed at developing effective tools for monitoring and assessing progress for parents and children with intellectual disabilities.

Dr. Marilyn Bull, American Academy of Pediatrics (AAP), reported on the release of DS care guidelines last summer. Additionally, she reported that strategies for approaching DS were discussed during a meeting.

Janelle Nanavati, Special Olympics International, reported on student-led (disabled and non-disabled co-investigators) participatory action research performed with the Department of Education. The goal is for students to learn from their peers with intellectual disabilities what an inclusive school environment feels like to them. There is also ongoing planning for the Special Olympics 2013 games in South Korea, which will include an embedded symposium on the needs of individuals with intellectual disabilities.

David Tolleson, National Down Syndrome Congress (NDSC), reported that NDSC continues to work on a number of initiatives. Its 40th national convention takes place July 19–22. Registration opens next week. The hotel block has already been filled twice.

Deanna Tharpe, Down Syndrome Affiliates in Action (DSAIA), reported that their leadership conference starts immediately after Buddy Walk. There are approximately 225 leaders from the DS community attending, including interest from Canada and Puerto Rico.

Dr. Robert Schoen, Research Down Syndrome (RDS), reported that last year was RDS's first year of actually awarding grants, and six were awarded. Dr. Schoen described a busy year on the awareness front as RDS works to establish a national program of runs or walks as a fundraising mechanism. He was pleased to have the cooperation of many first spouses across the country.

Dr. Charlene Schramm, National Heart, Lung, and Blood Institute (NHLBI), reported on involvement in a number of research portfolios, including sleep disorders.

Dr. Melissa Parisi, NICHD, will report on the registry subcommittee progress later in the meeting.

NICHD Report: Background and Future

Yvonne Maddox, NICHD
Presentation attached

Dr. Maddox reported on the activities and next steps of NICHD, particularly how they relate to individuals with DS and the DSC. This year marks the 50th anniversary of NICHD. Dr. Maddox said that NICHD originally focused mainly on human development across the lifespan, intellectual and developmental disabilities (IDDs), and key processes during pregnancy, with special interest in pregnancy outcomes. Since then, however, NICHD has expanded and extended its scope to women's health and a range of behavioral and social sciences.

Dr. Maddox reported on the NICHD Visioning process. She reported that IDDs were a key topic as the research community and stakeholders expressed a desire to see more engagement with the communities, families, and patient populations regarding research.

Another subject was the need for biorepositories. Dr. Maddox noted that the DS contact registry is a valuable and appropriate next step for the group and NICHD.

Dr. Maddox informed the group that the aims of the 50th Anniversary were to showcase NICHD's past accomplishments while focusing on future goals, specifically how best to put a limited budget into play over the next 10 years. NICHD understands the importance of engaging its stakeholders, the community at large, and the lay community especially. Dr. Maddox noted that NICHD is working to increase and better understand volunteerism; NICHD staff will be engaging in 10 areas of volunteering related specifically to NICHD's mission and community stakeholders. Such outreach underscores the importance of partnerships and collaboration to help NICHD and NIH as a whole and is directly connected to maintaining and identifying the highest priority areas of research, such as DS.

As part of its 50th anniversary, NICHD is compiling a set of slides that reflect its past accomplishments. Dr. Maddox asked that members present or let a member of NICHD present the slides at annual or regional meetings over the next year.

Discussion

It was suggested that the 2011 funding numbers be revisited, and that a grants analysis be performed assessing categorization, as the results might help improve communication with researchers and the community. It was suggested that at least two projects tied to DS were not included in the list of related projects. Dr. Maddox responded that this discussion was very helpful. It was noted that these lists are compiled largely through a keyword search, so it is important to mention DS in project titles.

The NIH Grant Process

Bob Riddle, NINDS

Dr. Riddle provided a brief description of the NIH process for supporting biomedical research. This was an overview and not specific to DS.

NIH supports a spectrum of biomedical research, from basic and disease-based science to translational and clinical research. The overall goal of NIH is to encourage and support the best research. Dr. Riddle explained that given limited funds, the question becomes how to effectively support the best research. While each of NIH's 27 Institutes and Centers (ICs) is distinct and has distinct processes, there exist several overarching principles: The vast majority of research should be investigator-initiated, a small number of focused studies should be solicited, and all grants should be peer reviewed.

Dr. Riddle provided an overview of the grant preparation and review process, specifically noting that NIH is well-equipped to help researchers with the pre-submission process, and these resources should be utilized.

The NIH peer-review process has undergone some changes in the last few years. Dr. Riddle emphasized that the idea of allowing peers to review and determine the best science to move forward is critical.

Discussion

The discussion began with the concept of including individuals with DS in the peer-review process.

A DSC member felt that there were fewer individuals with an understanding of DS research being involved in the peer-review process. Dr. Maddox noted that there are two approaches that can be taken to improve the review process. One is training the researcher to write and submit a better application. The other side is to train more people to be interested in this type of research and get more involved in study sections. It is important that they hear from consortia such as the DSC on what particular area of research is worth focus.

Mr. Levitz said that the research process is very complicated, and it would be better if an effort were made to make it easier for people in the community to understand.

Report from the Contact Registry Subcommittee

Melissa Parisi, NICHD
Slides attached

The Contact Registry Committee was created at the first meeting of the DSC with the overarching goal to identify the best model for a contact registry for the DS community.

- The Subcommittee identified three distinct, but linked, resources that would benefit the DS community:
    - Contact registries,
    - Research databases, and
    - Biobanks.
- Contact registries are an important first step, and the subcommittee evaluated a number of different platforms representing a broad sampling of approaches.
- It is important to use common data elements in the registry. Approximately 80 percent of fields are common across registries (e.g., date of birth, address). The remaining 20 percent would focus on what is unique to a given condition, in this case DS.
- The software is open source, so it is not proprietary. Most are Web-based with a paper option for those without Web access. Data are compiled in aggregate and de-identified (specific permission is needed to gain access to identifiable information).
- Administration of the site is a key challenge.
- The value of an outreach plan to ensure individuals sign up for a registry should not be underestimated.
- The Global Rare Disease Registry (GRDR) employs a global unique patient ID (GUID). Each individual in the registry is assigned a unique identifier calculated by an algorithm. First, middle, and last names, as well as the date and place of birth, are factored in for the GUID so that it does not matter if an individual moves. A secure algorithm calculates and creates the GUIDs, and they can be invoked wherever a registry participant shows up for a given input of data. This gives continued usability linking registry and research.
- The group should consider translating the registry up front to encourage international involvement, though this may be a more important priority for the rare diseases.
- It is important to monitor startup costs to maintenance fees.
- The subcommittee suggested a structured board of governance, complemented by a research and operations advisory board with a dedicated core staff.
- One suggestion for a funding mechanism is to use a federated model with tiered-fee structure, depending on the annual revenue of a participating organization, a nominal fee or waiver for small organizations with minimal revenue, federal partners, and potential sustainability from access or user fees.

Discussion Topics, Questions, and Answers

- What are the origins of funding of GRDR? Was it peer reviewed as it originated?

- The NIH Office of Rare Diseases Research (ORDR) has a contract with PatientCrossroads. There is an open competition ending on March 10. Any organization can propose a rare disease registry. Selected applicants would be supported through the initial phase of creation and become a part of the GRDR.
- Under NIH, DS does not qualify as a rare disease, though some subsets of it may. It could be considered a neglected disorder.
- The classification of DS could depend on what ORDR was mandated to address. This would necessarily help the DSC in establishing a registry, and it could be helpful in the future as funding streams are pursued.
- Who would be involved in the outreach groups?
- Outreach groups would be any group interested in advancing understanding, research, and treatment for DS.
- Proposals need a governance process and a vetting process.
- The DSC needs to inform the community of the registry. The Consortium also needs keys to keeping the community involved, access, language, recruitment, and information protection.

Dr. Maddox Responses

- Dr. Maddox proposed that some decisions be made before the meeting ended.
- NICHD would be willing to contribute some funds. However, a federated funding approach could prove difficult, since it has not been built into the 2012 budget and other outside groups are involved.
- Where will all the funds be housed? The NICHD gift fund? The NIH Foundation?
- Who will handle administration and oversight of the registry? A sponsor? A contractor selected through a solicitation process? NICHD itself? The DSC must work on trust and transparency with the community at large.
- The Consortium need to hold a future discussion on biobanks.
- A funding proposal ought to be developed, encapsulating comments and concerns, as well as a proposal for governance and operations, and then distributed to the DSC for comment in the next few weeks.

Presentation of the Draft DS Website/Feedback from DSC Members

James King, NIH Library

Mr. King presented a draft of the DS website. He explained that the site that they are building uses Drupal, which is open source and not on any NIH server. The draft website is a baseline, and Mr. King requested feedback from DSC members, specifically on the organization, the content, the labels, and so forth.

- The website is intended for three audiences: families, clinicians, and researchers. There is also a page with basic information about the DSC and its members.
- The goal is to ensure that the site reflects the latest and best information on DS.
- The site will link to the NIH clinical trials website, and information boxes can be placed within the DS site to announce the latest clinical trials.
- The website would be made Section 508 compliant.
- Suggestions:
    - The site could consolidate all government activities in one place, such as the Centers for Disease Control and Prevention's or the Food and Drug Administration's involvement and activities with DS. Capturing Requests for Applications (RFAs), Requests for Proposals, or any other relevant funding opportunities on the site would also be particularly useful to the research community.
    - There should be research projects by individuals who have DS.

- Step outside the government structures for the website for a variety of reasons, most specifically for agility. The information websites and other strategies that are most successful are the most agile and best understand by their target audience.
- Mr. King provided the group with the Web address and secured login information so that they could review the site at their leisure and respond with any feedback. Lisa Kaeser encouraged the group to be honest with their responses.

Preparation for Revision of the NIH DS Research Plan/Portfolio Review

Mary Lou Oster-Granite, NICHD

Dr. Oster-Granite presented a history of the DS research portfolio. Currently, 19 ICs have continued to fund DS research since the DS research plan was released.

Dr. Oster-Granite reported that in fiscal year (FY) 2009, there were $18 million in funds and an additional $4 million in American Reinvestment and Recovery Act (ARRA) funds for DS research. In FY 2009, 132 grants were received and 52 were funded, 7 of which were ARRA grants. In FY 2010, $22 million was available for NIH funding, $6 million was available through ARRA, 141 grants were received, and 12 of those funded were ARRA.

- Dr. Oster-Granite said that she runs a portfolio analysis in the NIH system on a routine basis to see what grants have come in, their scores, and grant awards.
- Actions that have been taken in an effort to stimulate the DS research community:
  - An RFA was released, and two grants have been funded under it.
    - The projects are structured to provide more information on biomarkers that might help determine who with DS is likely to get dementia.
  - The Jackson Laboratory Mutant Mouse Resource repository was recompeted and continues to supply mouse models to investigators at both NIH and private companies and support foreign grants.
  - The Brain and Tissue Bank at the University of Maryland was also recompeted and continues to be the largest repository of DS specimens available.
  - Three announcements, each titled the same, were released: an R01, an R03, and an R21.
    - The goal was to undertake a broad approach to better understanding the underlying factors in adolescents with IDDs.
    - The R01 has received six applications, with four discussed, two not discussed, and one funded.
    - The R03 has received four applications, with three not discussed and one discussed and subsequently funded.
    - The R21 has received six applications, with five not discussed and one pending review.
- A number of the goals set at the first meeting have been accomplished, and the next thing to consider is the evaluation of the research plan. Members of the trans-NIH working group, the DSC, and ad hoc members as needed could evaluate the impact of the research plan on DS research. This could be undertaken through a variety of formats, such as a workshop, a teleconference, or a state-of-the-science meeting.
- Possible future steps:
  - A Request for Information (RFI) could be issued, soliciting public evaluation of the plan to determine the best and most efficient format for receiving significant input in reevaluating the research plan.
  - It would be appropriate to invite participants from every IC that has funded DS research under the plan to participate in deciding whether there should be a research matrix, honing it if so, and deciding what items would benefit from change or further expansion.

    - The project could conclude with a face-to-face meeting and a draft of the recommendations circulated via the website.
    - An RFI could be issued seeking public comment.
- Suggestions
    - There is a significant opportunity to guide future research by simply compiling the research, identifying the gaps, and identifying NIH activities so that others can step up to the plate.
    - Noted that a number of individuals with DS have done research, and it is important to recognize those who have done extraordinary research.
    - It is important to look at what DS research has done for people living with DS. As greater emphasis is placed on translation, it is important to make an actual difference in the lives of people living with DS.
    - There could be training programs for early stage investigators to demonstrate and discuss what NIH is doing to grow the field of researchers.
    - A paucity in the more clinical literature on what is lacking within the clinical care setting is determining the progress that has occurred over the last 5 to 10 years.

As the strategic plan gets developed, Dr. Maddox suggested potentially focusing on infrastructure and therapeutics going forward. A plan that focuses on strategic ideas in a priority order could be a different approach to take, compared to the broader initial strategic plan. She noted that at the next meeting, the group will get input on next steps, the registry, and potential workshops. Given that the DSC has been meeting every 3 to 4 months, the DSC should come together again in June or July. Mr. Tolleson added that NDSC's 40th national convention will take place July 19–22.

Dr. Maddox informed the group that she would be in touch regarding the next meeting, and members should submit any ideas or suggestions to her regarding the agenda.

Attendees

Frank Avenilla, NIMH
Marilyn Bull, AAP
Jon Colman, NDSS
Diane Cooper, NIH Library, Office of Research Services
Michael Harpold, DSRTF
George Jesien, AUCD
Lisa Kaeser, NICHD
James King, NIH Library, Office of Research Services
Mitchell Levitz, self-advocate, University Center for Excellence in Developmental Disabilities at the Westchester Institute for Human Development
Michelle Livingston, GDSF
Yvonne Maddox, NICHD
Edward McCabe, LCI
Janelle Nanavati, Special Olympics International
Margaret Nygren, AAIDD
Mary Lou Oster-Granite, NICHD
Melissa Parisi, NICHD
Bob Riddle, NINDS
Robert Schoen, RDS
Charlene Schramm, NHLBI
David Tolleson, NDSC
Deanna Tharpe, DSAIA