3rd Meeting of the Down Syndrome Consortium: *A Public-Private Partnership*

July 23, 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)*
Presentation attached

Dr. Maddox welcomed everyone to the third meeting of the Down Syndrome Consortium (DSC). She reported on the planned 50th anniversary of the NICHD and described an anniversary celebration that took place on Capitol Hill, during which on Down syndrome (DS) supporter, Rep. Cathy McMorris Rodgers, was recognized with an award.

Dr. Maddox moved on to how working with the DS community has helped NICHD. This improved interaction has allowed the Institute to hear more about the science occurring in the field. As an example of this, Dr. Maddox spoke of Roger Reeves' phenome project, which he presented to the DS Working Group. NICHD welcomes any opportunities to present, attend conventions and meetings, and collaborate.

Updates

Michelle Sie Whitten, Global Down Syndrome Foundation (GDSF), noted that the Linda Crnic Institute for Down Syndrome (LCI) has a new executive director, Tom Blumenthal. GDSF has additional funds that could be used to leverage public-private partnerships. GDSF hired Alzheimer's disease researcher Huntington Potter, who will be creating a clinical care center.

Deanna Tharpe, Down Syndrome Affiliates in Action (DSAIA), currently has about 80 affiliates. They also had an exhibit booth at the National Down Syndrome Congress (NDSC) meeting. They will have a leadership conference February 21–24, 2013, in Cincinnati. Requests for Proposals have already been opened, and Ms. Tharpe welcomed the opportunity to have Dr. Maddox speak at the event.

Michelle Livingston, LCI, reported that as the new executive director settles in, she would report back to him on DSC activities.

Mitchell Levitz, self-advocate, University Center for Excellence in Developmental Disabilities at the Westchester Institute for Human Development, reported that the center is also working on a research-to-practice health publication, which will come out soon. Mr. Levitz explained that his office has a program called Parent to Parent, which assists families of children with disabilities and special health needs by matching up parents with similar situations.

David Tolleson, NDSC, reported that NDSC had more than 3,000 people attend the recent meeting, from 15 different countries, 48 states, and Puerto Rico.

Beth Finkelstein was representing Jon Colman of the National Down Syndrome Society (NDSS). She announced that the NDSS website would be relaunched in late summer or early fall. It will be a great

resource and continue to provide clinical information. NDSS also received a large private grant to do a public education program on aging and DS.

Dr. Laurie Ryan, National Institute on Aging (NIA), reported that their activities have centered on the National Alzheimer's Project Act. The focus of their summit was to look at the pathway to treatment and ultimately prevention. The summit focused on everything from target validation to clinical trials to repurposing existing drugs. On July 30, an international database will go live to allow users to see what projects are being funded. Dr. Ryan felt these efforts will be critical in tough financial times.

Dr. Robert Schoen, Research Down Syndrome (RDS), reported that RDS is in its third year of raising funds.

Dr. Lisa Gilotty, National Institute of Mental Health (NIMH), reported that NIMH has a funding announcement for research into mental illness in individuals with intellectual and developmental disabilities (IDDs), including DS. The announcement covers a broad range of mental illnesses, with particular focus on depression and anxiety.

Dr. Marilyn Bull, American Academy of Pediatrics (AAP), reported that they published an update to their health care guidelines last August. The goal is to implement these guidelines and enhance awareness among clinicians and families on the aspects that will improve the health care of children through age 21. A Spanish version of the guidelines will be available by mid-August. Another major need is a parent-friendly version of the guidelines that provides an age-based outline and directions with attention to health literacy. Yvonne Maddox, NICHD, asked whether it would be possible for the DSC to be involved in the development of the more family-friendly version of the AAP guidelines. Dr. Bull was open to discussing a collaborative effort.

Dr. Cara Long, National Institute of Neurological Disorders and Stroke (NINDS), attended in place of Bob Riddle. Dr. Long noted that NINDS is funding some translational projects, including a project with Balance Therapeutics for a GABAA receptor antagonist for the treatment of cognitive impairment in DS. There is also some work being done looking at which specific genes are causing the particular features of DS.

Dr. George Capone, Down Syndrome Medical Interest Group (DSMIG), reported that DSMIG recently incorporated. Its 501(c)(3) status is pending. DSMIG has existed as a forum or colloquium for people who administer and operate clinics to meet once a year to discuss health care and health care guideline areas of common interest or concern. It also helps create consensus for best practices when a particular area is lacking the evidence. DSMIG does not endorse anyone's research studies but provides researchers and groups with a platform to present their findings.

Dr. Malcolm Smith, National Cancer Institute (NCI), reported that NCI supports research relating to DS and leukemias that arise in children with DS. Children with DS also get acute lymphoblastic leukemia (ALL), and primary research indicates that children with DS are more sensitive to the toxic effects of the drugs used to treat ALL, so special treatments need to be used for these children; this is another ongoing clinical trial. Dr. Smith remarked that acute myeloid leukemia and ALL have a distinctive biology, so there are grants out to understand the biology of these leukemias, which could lead to better ways of treating them.

Dr. George Jesien, Association of University Centers on Disabilities (AUCD), reported that AUCD has partnered with the National Association of State Directors of Developmental Disorders to look at critical policy areas, including community living. Dr. Jesien also noted that AUCD is working with the John Merck Fund, which has begun an IDD translational research program. A call for proposals, with the

requirement that the project focus on either DS or Fragile X syndrome, resulted in approximately 100 proposals.

Dr. Michael Harpold, Down Syndrome Research and Treatment Foundation (DSRTF), reported that DSRTF and RDS came together behind the same scientific strategy, the same advisory board, and essentially the same grants program in order to accelerate the development of treatments for those with DS. DSRTF and RDS have funded slightly more than $1.3 million for the coming year, which covers approximately 24 primary investigators. Dr. Harpold emphasized the importance of being efficient in funding and of setting priorities. Roche Pharmaceuticals is involved in a clinical trial looking at the safety and tolerability of its new investigational drug, an inverse agonist and slightly more selective than antagonists. Additionally, Roche has committed to performing parallel studies, required by the Food and Drug Administration, on individuals less than 18 years of age. In order to continue to see these clinical trials for the development of therapeutics, more patients need to be recruited. Dr. Harpold remarked that he attended an Alzheimer's summit and was pleased to see that the community knew about the connection between DS and Alzheimer's and that they supported involving DS in some of their plans and programs.

Lisa Kaeser, NICHD, thanked everyone for their great work. She noted that National Institutes of Health (NIH) Director Francis Collins recently received two questions about DS, one in March at a Senate appropriations meeting, and one in June at a House Energy and Commerce hearing. This is another way of keeping DS on the front burner, especially for Congress. Ms. Kaeser pointed out that the website is not on the agenda today. Discussion at the last meeting produced a number of comments that are being taken very seriously, so efforts have been pulled back to approach the website differently. The group will receive updates at future meetings.

Progress on the NIH DS Registry

Melissa Parisi, NICHD
Presentation attached

Dr. Parisi provided an update on the NIH DS patient registry. The registry will

- Improve understanding of DS and issues faced by individuals and families,
- Facilitate contact with national organizations,
- Identify health gaps and challenges,
- Improve opportunities for clinical research participation,
- Have the potential to link to biorepositories and other resources,
- Facilitate recruitment for clinical trials, and
- Encourage pharmaceutical companies to develop treatments.

Issues surrounding a patient registry include content, structure, governance, ownership, and host options. The DSC Registry Subcommittee has been active in working to identify the best model(s) for a patient registry for the DS community.

Key principles to consider when developing a patient registry include the following:

- Start simple.
- Have participants enter own data.
- Utilize existing common data elements and established platforms.
- Employ unique identifiers to protect confidentiality and facilitate future linkages to research data and biobanks.
- Develop an outreach and marketing strategy in advance.
- Determine policies for access to information.

- Anticipate a need for dedicated core staff.
- Identify a governance board to develop and implement policies related to the registry.
    - Identify a research and operations board to develop registry materials and manage registry personnel.

Dr. Parisi explained that NICHD committed $250,000 of fiscal year (FY) 2012 funds for initial costs to create the registry. A solicitation was developed, and Lockheed-Martin, utilizing a parent contract, sent out a request for proposals to key registry vendors. Three proposals have been received.

Dr. Parisi presented a funding plan for FY 2014 and beyond.

- Each DSC member would contribute according to its resources.
    - For example, if an organization has an annual revenue of more than $1 million per year, their contribution should be $15,000 to $25,000 per year.
    - Nominal fees or waiver of fees could be given in special cases.

Dr. Parisi noted that after evaluating the other registries and their starting costs, it was reasonable to assume $100,000 to $200,000 per year. Dr. Parisi requested feedback from the group regarding the establishment of the two boards and the funding plan.

Discussion

The group asked whether the proposed funding plan was a typical funding model used for other conditions, such as autism or rare diseases, and whether there would be matching funds from NICHD. Dr. Maddox remarked that before addressing the funding model, it is important to focus on the recognition that this is being called a DSC registry. From the earliest stages, it is important to determine who owns the registry and is responsible for it. If everyone agrees that this should be the DSC, then discussion can move on to look at contributions in terms of sustainability.

- Dr. Maddox said that the Institute was willing to contribute the funds to get the project started and isn't opposed to funding it in the future, but it is important not to preclude or exclude others from providing funds.

Another question was how fast the registry should be populated.

- It was emphasized that budgets change from year to year.
- Intellectual property may come out of this effort, and it would be reasonable for people who develop patents to give back to the project itself.
- Everyone's input is just as valuable as, if not more valuable than, monetary commitments. Dr. Maddox encouraged everyone to continue to provide feedback to keep the registry headed in the right direction.
- The registry will be launched before October 1, since it is using FY 2012 money, which allows some time to continue thinking about sustainability and next steps.

Request for Information (RFI): DS Research Plan Discussion

Dr. Oster-Granite, NICHD

- The DS research plan was developed in 2007 but needs revisions.
- It is important to talk to others not in the room to determine whether their perception is that what needs to be done is being done. An RFI was issued to capture this:
    - The aim is to be simple, concise, and accessible, so responses were gathered from the general population on expectations and what they would like to see in a 5-year research plan.
    - The draft includes a link to the original research plan, information on a request for applications soliciting factors that affect cognitive function, and the two successful grants

that were awarded for studies examining and identifying biomarkers predictive of risk for progression to dementia in adults with DS.
    - The draft needs to get out as soon as possible so that the next time that the DSC meets, there can be some concrete information gathered from the responses.
    - Since the first DS research plan was released, NIH has received approximately 600 grant applications.
    - NICHD has funded 21 percent of its grants received, which is twice the average for most NIH Institutes and Centers.
- Dr. Maddox commented that the last time that an RFI went out on the research plan, NICHD responded to each and every response. She said that DSC members would be called upon in many ways, from reacting to the plan being developed to disseminating the plan.
    - Ms. Kaeser remarked that any responses to the RFI itself will be very helpful. The aim is to make the RFI understandable to the general DS community.
    - There was concern that some of the language in the RFI was not conducive to receiving feedback from the DS community. It would be better to adapt the document and make it understandable to the entire population.
    - Dr. Maddox said that while the RFI is being issued for DS groups to respond, it is also geared toward the general public. She felt that where organizations are concerned, there could be a benefit in collective response as proposed, but this should not preclude additional comments.

What's Next in the Field of DS Research?

Yvonne Maddox, NICHD
Presentation attached

The operational planning session for 2014 will be taking place in the next 2½ weeks. Dr. Maddox wanted to get a sense from the group on areas of focus for the future. She wondered whether it might be time for the NICHD to put out another initiative on DS. Issues proposed and discussed follow:

- Cognition and memory.
- Social justice and the disparity in life span for African Americans.
- Families' access to data. Families often express that there is a lack of a good knowledge base and recommendations surrounding pervasive health issues that occur in the lifetime of people with these disorders.
    - It was pointed out that in the current budget climate, it is difficult to get funding for research tools.
    - GDSF conducted a small survey that asked respondents about their priorities in terms of improving the health of their children with DS. The number one issue for parents was language and communication, followed by education.
    - Mr. Levitz commented on the number of individuals with DS whom he knows who are actively involved in research projects on topics such as nutrition and health. It is important to keep an eye on the type of language being used so that everyone can understand it.
- Outcome measures in relation to clinical trials.

Registry Launch

- Dr. Maddox explained that once a subcontractor is selected, NICHD will prepare a press release. She will be in touch with DSC members as the launch date approaches so that they have time to make their own press releases or connect to the NICHD release.
- Would it be a good idea to pull together a webinar for DSC members before the registry launches so that they all feel knowledgeable and prepared to share the information with their membership?

- Mr. Levitz commented that October is National DS Awareness Month.
- Dr. Maddox asked the DSC for input on other types of individuals who should be included as candidates for membership of the governance boards for the registry.
    - Mr. Tolleson commented that the affiliates represented by the organizations around the room deal with families with a number of disorders, including mosaic DS.
- Regarding therapeutics, in the DS field, it is often hard to think past the point of phase I trials, and NIH is not typically involved in phases II and III.
- Dr. Ryan said that they have been fairly successful in getting Alzheimer's therapeutics through phases II and III, but they are finding that phases I and IIa can be tough. NIH cannot be averse to involving companies in the development of therapeutics.
- Ms. Whitten considered it the job of DSC members to communicate transparently the activities and results of the meeting.
    - The meeting minutes are public and posted on the website.
    - Dr. Maddox added that people are free to share anything that transpires at the meetings, and everyone is encouraged to use the information from the meeting to impact and benefit the DS community broadly.

Dr. Maddox concluded the meeting and thanked everyone for their participation.

Attendees

Malcolm Smith, NCI
George Capone, DSMIG
Cara Long, NINDS
Lisa Gilotty, NIMH
Laurie Ryan, NIA
Beth Finkelstein, NDSS
Michelle Sie Whitten, GDSF
Michele Lloyd-Puryear, NICHD
Marilyn Bull, AAP
Michael Harpold, DSRTF
George Jesien, AUCD
Lisa Kaeser, NICHD
Mitchell Levitz, self-advocate, University Center for Excellence in Developmental Disabilities at the Westchester Institute for Human Development
Michelle Livingston, GDSF
Yvonne Maddox, NICHD
Melissa Parisi, NICHD
Robert Schoen, RDS
Charlene Schramm, National Heart, Lung, and Blood Institute
David Tolleson, NDSC
Deanna Tharpe, DSAIA