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Examining the Federal Response to Autism Spectrum Disorders

Witness before the
House Oversight and Government Reform
Subcommittee on Government Operations
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Introduction

Good morning Chairman Mica, Ranking Member Connolly, and distinguished Members of the Subcommittee. I am Dr. Tom Insel, Director of the National Institute of Mental Health (NIMH) at the National Institutes of Health (NIH). I have served as the Chair of the Interagency Autism Coordinating Committee (IACC), created by the Children's Health Act of 2000, re-established by the Combating Autism Act of 2006 (CAA), and reauthorized by the Combating Autism Reauthorization Act of 2011 (CARA), since my arrival at NIMH in 2002.

First, I'd like to thank you for the opportunity to share with you today some of the exciting progress we have seen since the passage of the CAA and the inception of the IACC. We at NIH are very grateful for the strong support that you in the Congress have always shown for NIH and the thousands of researchers around the country who are working to advance biomedical research in support of people living with a wide array of diseases, disorders and disabilities. As Chair of the IACC, I'd like to express the gratitude of all the Federal Agencies represented on the committee for your continued support for our efforts on autism spectrum disorder and related disabilities. I am here to provide an update on the Federal response to autism, including the work that has been done by the IACC to coordinate Federal activities and foster public-private collaboration, and to provide a snapshot of the considerable progress being made in autism research. More details on the specific programs and projects funded by the various Federal Agencies involved in the autism effort can be found in the recently submitted *Report to Congress on Activities Related to Autism Spectrum Disorder and Other Developmental Disabilities Under the Combating Autism Act of 2006 and Combating Autism Reauthorization Act of 2011 (FY2010-FY2012)*.

Background on Autism Spectrum Disorder (ASD)

Autism spectrum disorder (ASD – also referred to as “autism” interchangeably in this testimony) is a neurodevelopmental condition characterized by deficits in social interaction and social communication, along with restricted interests and repetitive behaviors— sometimes

accompanied by additional features such as intellectual disability or language impairments. With varying degrees of severity in these symptoms, autism is a heterogeneous condition that affects some with only mild impairments and others with profound disabilities. Like many other neurodevelopmental disorders, autism is thought to be caused by a combination of genetic and environmental factors—in this case, by genes and environmental factors that influence the development of the brain. Currently, there are only a small number of proven causes of ASD, including genetic mutations associated with several well-characterized genetic disorders such as Rett Syndrome, tuberous sclerosis and Fragile X, and other rare genetic syndromes. While each of these causative mutations is rare, the discovery of different rare mutations associated with ASD is increasing so quickly that in a recent report, the American College of Medical Genetics and Genomics (ACMG) strongly expressed their support for genetic testing to be routinely provided for individuals who have autism without a known cause, because currently available tests are likely to be able to identify a specific genetic mutation underlying autism symptoms in an estimated 30-40 percent of individuals. Identification of contributing gene mutations could result in benefits for the individual, including better targeted intervention strategies and awareness of additional health conditions for which he/she may carry an elevated risk.

Prevalence of ASD

The most recent report from the Centers for Disease Control and Prevention (CDC) estimates that one in 68 children (1.5 percent of eight-year-olds) in the United States has been identified with an ASD, which is an increase from the estimated prevalence of one in 88 (1.1 percent of eight-year-olds in 2008) reported in 2012. The data reported this year, for children who were eight years old in 2010, show that three major aspects of the picture of ASD have remained the same. First, ASD is almost five times more common among boys than girls – with one in 42 boys and one in 189 girls identified. Second, white children are more likely to be identified with ASD than black or Hispanic children. And third, most children with ASD are not diagnosed until after age four, even though ASD can be diagnosed as early as age two. Interestingly, this latest study emphasized an emerging trend. In the 2014 report, nearly half of children with an ASD were found to have average or above-average intellectual ability (an IQ of 85 and above) compared to only one third of children a decade ago. It could be that we are getting better at identifying these children, there could be a growing number of children with ASD and higher intellectual ability, or it may be a combination of the two.

Overall, does the upward trend in CDC prevalence estimates over the last several years represent a true increase in the number of children with ASD, or does it reflect more children with ASD being detected due to improvements in awareness, screening and other factors? The answer – it is possible that both contribute. Clearly, the numbers indicate that there is, and there will continue to be, an increasing need for services to address the wide variety of needs among children being diagnosed with ASD and progressing toward adulthood.

IACC Coordination Activities

As autism is a complex condition that impacts individuals and families across the lifespan and in all areas of their lives—including health, education, and service needs—a coordinated Federal response to address all of these areas is underway. The IACC was established by the Congress to coordinate efforts across multiple Federal departments and agencies as well as private organizations to support autism-related research and serve the autism community. The CAA outlines the membership of the IACC, composed of both Federal Agency officials and public members representing a variety of stakeholder groups within the autism community, including adults on the autism spectrum, family members of children and adults with ASD, leaders of national advocacy organizations, researchers, clinicians, educators, and other community providers. Participation of both Federal and public members on the IACC helps to ensure that a wide range of ideas and perspectives are represented in the committee’s deliberations.

The CAA charges the IACC with a number of tasks to facilitate coordination, such as developing and annually updating an interagency strategic plan for autism research, preparing an annual report summarizing the latest advances in autism research, monitoring and exchanging information about the wide array of autism-related activities being undertaken by Federal Agencies, providing a forum for public input on issues related to ASD, and providing advice to the Secretary of Health and Human Services (HHS) to help guide autism efforts. To fulfill this charge, the IACC released its first *Strategic Plan for ASD Research* in 2009, followed by annual updates that refined and expanded the original set of *Strategic Plan* objectives, and provided updates on progress that had occurred since the *Plan* was launched. Note that the IACC does not have a charge or a budget to implement research or services programs. As a Federal advisory

committee composed of Federal agency officials, private funders, and other community stakeholders, the role of the IACC is advisory in nature and is limited to coordination, monitoring, and providing advice to the Secretary of HHS regarding emerging issues and specific actions that may be warranted in order to better meet the needs of the community.

In 2013, the IACC undertook the most comprehensive review of the *Strategic Plan* to date, taking advantage of the extensive five-year portfolio analysis data collected by the Office of Autism Research Coordination (OARC) for the IACC. Detailed information available and accessible to the public through an online database about projects that have been funded, by both government and private funders on an annual basis, is vital for the autism field. Using portfolio analysis data, the IACC was able to provide a five-year accounting of the implementation of the *Plan*, tracking the number of projects funded and dollars committed toward each of the 78 individual objectives since the inception of the *Plan*. In this review, the committee found that, to varying degrees, progress has been made toward nearly all of the 78 objectives in the *Plan* in the past five years. Most of these objectives represent broad-based goals such as research on new diagnostic, therapeutic, or services approaches, requiring the support of multiple projects and the activity of multiple Federal and private funders.

In addition to the IACC's *Strategic Plan*, which has served as a guide for Federal Agencies and private partner organizations in planning their research activities, the committee has also been successful in fostering public-private partnerships to advance autism research and effect change in areas of critical need identified by the community. For example, in 2011, a mother of a child with autism from the Somali-American community in Minneapolis, Minnesota gave public comment at an IACC meeting, asking the committee to support research to understand if there might be a higher prevalence of autism in the Somali-American community in that city. The IACC responded to this community concern by fostering a collaboration between CDC, NIH, and the private autism organization, Autism Speaks to answer this question. The three groups collaboratively funded a project to examine the prevalence of autism among children of different ethnic groups in the Minneapolis area. Findings showed that, one in 32 Somali children in Minneapolis were identified as having ASD. This estimate is about the same as for White

children, but higher than for Black and Hispanic children in Minneapolis. Overall, the combined prevalence for the Minneapolis children was one in 48, which is higher than CDC's most recently published ASD prevalence estimate of one in 68. Somali children with ASD were also found to be more likely to have intellectual disability than children with ASD in all other racial and ethnic groups in Minneapolis (100 percent of the Somali-American children with ASD who had IQ records on file showed an intellectual disability in comparison to only 20-30 percent of children with ASD in other ethnic groups). The community in Minneapolis is now using these findings to make improvements for children and families.

Wandering behavior associated with ASD—the tendency for a child with ASD to wander away from a caregiver or safe place into an unsafe environment—has become a national issue in the autism community due to its often tragic outcomes, including accidental injuries and deaths. Children with ASD and other developmental disabilities are at higher risk of wandering away from caregivers and safe areas than are children without these conditions or with other cognitive disabilities. To address this issue, which also was first raised at the IACC through public comment, the IACC launched an effort to reduce the incidence of wandering-related injuries and fatalities by supporting the CDC to propose the adoption of a code intended to capture information about individuals, with any condition classified in the ICD, who wander. The intention was to provide a way to document and understand this behavior, and to support the development of approaches to reduce the risk of wandering-related injuries and fatalities. The measure was adopted and the code is now in use. Discussion at the IACC meeting also resulted in an IACC public member initiating coordination among private organizations to support a study to assess the prevalence as well as qualitative aspects of wandering behavior in the autism community using an established interactive virtual network (IAN – the Interactive Autism Network) of people with ASD and their families. The study, conducted within the short timeframe of a few months, resulted in the publication of an analytical report about the prevalence of autism-related wandering that helped raise awareness of the issue in the community and provided some initial figures to support the need for further research in this area. Many private organizations have mobilized to assist in efforts to raise awareness and provide tools and training to help keep children with ASD safe and to give needed support to families.

Research Highlights

With the coordination provided by the IACC and its *Strategic Plan*, NIH and other agencies within HHS and other Federal departments have been working collaboratively to tackle the challenges of supporting research on this profoundly complex condition. Investment in ASD research over the last decade has increased 90 percent to \$190 million in Fiscal Year 2014.

Some of the most important research investments related to ASD have not been specific to ASD but have created tools or resources for studying brain development, new insights about the immune system, or research on the microbiome that may transform ASD research. I'd like to share just a few examples of the scientific progress that has been made toward understanding autism and developing new clinical approaches over the past five years. This brief survey cannot do justice to the many areas, from immunology to social science, that are revealing new insights about ASD.

We're currently at a pivotal moment in the field of brain research as an explosion of new technologies enables scientists to analyze brain anatomy and function in ways that have never before been possible. At the same time, the world of autism research is also rapidly evolving. Since 2009, over 11,000 articles on autism research have been published in scientific journals—more than double the number published in the preceding five years. The increase in availability of large, shared data sets through venues such as the NIH's National Database for Autism Research (NDAR), which provides access to data from more than 70,000 research participants, with appropriate privacy protections, is enabling scientists around the globe to get involved in autism research. In fact, ASD research is on the cutting edge of data sharing in biomedical research as all NIH-funded scientists are expected to deposit clinical data in NDAR. This approach provides unprecedented transparency and access to accelerate scientific progress. And through the use of a global unique identifier (GUID) for each individual whose de-identified data is housed in the database, NDAR precludes duplication of data from a given individual who might be enrolled in multiple studies.

The technology advances that are revolutionizing neuroscience are rapidly being incorporated into the autism field, with the promise of greatly deepening our understanding of autism.

One ground-breaking new method developed by NIH-funded researchers, called CLARITY, takes intact postmortem human brain samples, donated with appropriate consent, and replaces the lipids (or fat) in the brain with a clear hydrogel, holding all of the brain structures in place, but making them transparent. Until now, access to deep brain structures could only be achieved by slicing the tissue into very thin sections, so cells and molecules were only studied in two dimensions. This new technique preserves the connections between neurons and between larger brain regions, enabling researchers to visualize actual brain structures in 3-D, down to the level of individual nerve fibers, neuronal cell bodies, their extensions, and even molecules. Applying CLARITY to a post-mortem brain sample taken from a person with autism revealed an unusual pattern of connectivity between neuronal structures. This technique will likely reveal a whole new level of information about connectivity in the autism brain, helping us to better understand the circuitry and neurochemistry underlying autism-related symptoms, and offering opportunities to develop novel interventions to enhance brain function.

Another project supported by the NIH that has had a recent and profound impact on autism research is the BrainSpan Atlas of the Developing Human Brain. This atlas provides a map of gene expression over the course of fetal and post-natal brain development. Two very recent studies examined groups of genes related to autism using this atlas. Previously, when studied in the context of the adult brain, these genes didn't appear to have anything in common except that they all were identified as genes that contribute to risk of developing autism. Researchers decided to examine the expression of these genes during development using the BrainSpan Atlas to find out whether they could discern any identifiable patterns – either spatial or temporal. Remarkably, when the gene expression patterns were studied in the developing brain using the database, these seemingly unrelated autism genes were revealed to have very important things in common; they were expressed in the same region of the brain at the same time, around the mid-point of fetal development. This reinforces the evidence that pregnancy/fetal development is a key window for the development of autism. Additional studies—such as a recent study from the

University of California at San Diego that found scattered patches of disorganized brain cells in the deep layers of the brain cortex in samples from children with autism—also converge on the second trimester of fetal development as a critical time-point in the development of autism, indicating that the origins of autism are present before birth.

If autism begins before birth, why are we making the diagnosis after age 3? A number of new scientific findings from prospective longitudinal studies are helping us make significant progress in the area of early identification. For example, NIH-funded researchers using eye-tracking technology determined that children who later go on to develop autism exhibit a distinct pattern of decline in eye contact with caregivers that is detectable between the ages of two to six months of age. In another study, in slightly older infants and toddlers with autism, from 14-42 months of age, the use of eye-tracking technology revealed pronounced differences in attention to social cues; when given a choice between watching a video of a friendly human face interacting with them versus one showing a moving geometric pattern, the children who eventually developed autism preferred to focus on the geometric pattern. Other studies have demonstrated that children who later develop autism show measurable differences in repetitive behaviors (such as hand flapping or rocking back and forth) and in visual attention to objects (“sticky attention” – in which children with ASD tend to stare at an object after picking up for a longer period of time than typically developing children) by the age of 12 months, as well as visible differences in the development and structure of the white matter tracts that connect different parts of the brain in infants at the age of six months. With these and other new findings, we hope that in the future it will be possible to design tests or biomarkers to help us identify children who are on the path to autism within the first year, opening the door to early interventions that can help reduce the severity of disabling symptoms.

Do we have effective early interventions? Recent studies have also begun to demonstrate that early behavioral interventions can have lasting positive effects. A randomized controlled trial of a treatment called Interpersonal Synchrony, in which a child is assisted in sharing both social actions and attention, showed that this technique enhances eye contact and social awareness, and that these skills can be applied to new situations. The fact that a child who receives this therapy

develops new social behaviors indicates that the brain is “plastic” or able to adapt and remodel itself to learn new skills and that behavioral therapy is actually changing the way that child’s brain processes social information. In another study, researchers evaluated children receiving the Early Start Denver Model therapy approach, or ESDM. ESDM focuses on social exchange, social attention, social engagement, and positive affect. Randomized trials have shown that this intervention results in significant improvement in IQ, language, and adaptive behaviors. Very compelling new evidence has also shown that this technique results in “normalized” patterns of brain activity, as measured by electroencephalography, and that these patterns correlate with improvement in behavioral outcomes. This suggests that ESDM is actually remodeling the brain to respond to social stimuli in a different way—perhaps by strengthening existing neuronal circuits or building new ones to compensate in areas where function is reduced—and this adaptation results in improved social behaviors.

Pharmacological treatments for autism are in earlier stages of development, but work has intensified in this area. In 2008, only six drug treatment clinical trials were underway. That number is now around 100. ASD is a relatively new area for clinical trials research. Working out the design and the appropriate outcome measures has been an ongoing discussion between NIH and FDA as well as with colleagues at Autism Speaks and scientists involved in ASD clinical trials in Europe. These discussions are helping us to improve trial design and ensure the highest rigor of science along with the best protection of participants. As the dialogue continues and ongoing clinical trials proceed, we expect to have more rapid progress on medications and other interventions for autism in the near future.

In order for a medical treatment to be effective, it must address the problem at hand. What we know as “autism” is really a collection of conditions, and the causes of autism are likely to differ from person to person. The ultimate goal for autism treatments is that they will soon be defined by biological indicators of the underlying cause, or biomarkers, which will help with both diagnosis and the development of effective treatments. Some of the remarkable findings we’ve already discussed have begun to define biomarkers of autism. Because of the potential for biomarkers to be such a powerful tool in efforts to identify autism early and address core

symptoms, several large national and international efforts to accelerate the discovery of autism biomarkers have been launched. The Foundation for the NIH manages the Biomarkers Consortium, which is a private-public partnership to identify and develop biomarkers to help prevent, diagnose, and treat a variety of conditions such as autism. The Biomarkers Consortium has organized a targeted search for and refinement of biomarkers for ASD, which will unite funding agencies, academic researchers, and pharmaceutical companies. The Consortium is also working with international partners from European Autism Interventions - A Multicentre Study for Developing New Medications, which is the largest single grant for autism in the world at over \$38 million, to focus discovery of autism biomarkers with the ultimate goal of creating effective and personalized treatments for autism.

NIH continues to support its Autism Centers of Excellence (ACE) program, which was expanded under the Combating Autism Act. The ACE program is composed of both individual research centers at a single institution and networks of research teams at different institutions working together to solve a common scientific problem. The ACEs are designed to conduct intensive and coordinated research programs into the causes of ASD and to develop and disseminate new interventions and treatments. In 2012, NIH made nine new ACE awards—three centers and six networks—to be funded over five years. In 2013, two additional networks were awarded. The newly awarded ACEs will address a variety of critical research areas, such as using brain imaging technology to chart brain development of children at risk for ASD; identifying potential environmental and familial factors that may confer autism risk; investigating sex differences in ASD; evaluating the effectiveness of widely-used treatments to improve social interaction and communication, including exploring mechanisms of verbal communication and new interventions for minimally verbal children with ASD; and developing effective in-school and at-home interventions for children with ASD.

Finally, I'd like to share an update on services research. Recent studies in this arena, as well as the most recent *IACC Strategic Plan Update*, have highlighted areas of significant services needs for people all across the spectrum, including the need for transition services and adult services that can provide much-needed supports once an individual ages out of the educational system.

Research has suggested that people with ASD are often under-employed due to difficulties in obtaining and maintaining meaningful employment, as well as due to income limits prescribed for those who receive Social Security Disability Insurance benefits. Health disparities and lack of adequate independent living opportunities for people on the autism spectrum are two other common themes in autism services research.

While services research is not the primary focus of the NIH mission, NIH does support a small number of autism services research grants, and recently launched a series of three initiatives to support research on services implementation across the lifespan, with the goals of addressing the challenges of improving outcomes for children, adolescents, and adults. The first initiative targets models for coordination of ASD identification, evaluation, and early intervention services for children with ASD within the first two years of life, including tests of the feasibility and effectiveness of interventions across settings. The second focuses on models to assist adolescents with ASD to transition to adult supports and services while preventing lapses in services and supports. The third addresses development of adult ASD service strategies that concern areas of employment and training, social relationships, physical and mental health, and independent functioning, including community housing and safety, alone or in combination, with the ultimate goal of improving behavioral, functional, and health outcomes. Awards for all three initiatives are expected in 2014.

Conclusion

As you can tell from this brief update, we have made a great deal of research progress since the enactment of the CAA in late 2006, fueled by increasing investments from the NIH annual appropriation each year and \$122 million from the American Recovery and Reinvestment Act of 2009 into the autism research effort in 2009 and 2010, shortly after the release of the original *IACC Strategic Plan*. Since reconstituting the IACC under the CAA in 2006, the committee has become an important focal point for Federal coordination and public input on Government autism activities. It has done this by holding frequent public meetings, providing data to the public via its website and publicly accessible Federal-private research project database, and regularly publishing detailed reports regarding Federal activities and research progress related to

the implementation of the *IACC Strategic Plan*. In addition, the NIH's internal Autism Coordinating Committee has played an important role in helping NIH institutes coordinate their efforts to ensure that areas of the *IACC Strategic Plan* that fall within the NIH mission are being covered, and to foster cross-institute collaborations and prevent duplicative efforts.

As a result of this investment in autism research and our intensive efforts to coordinate and to foster collaboration, over the past few years we have seen remarkable progress in autism research. We have made tremendous advances in our understanding of how autism unfolds during the course of early development, in the identification of factors that may be contributing to increased or decreased risk for autism, and in developing and testing new screening/diagnostic tools, treatments and interventions, and services approaches that can be used in a variety of populations and community settings.

With the availability of unprecedented tools and technologies, we are poised to make significant scientific discoveries that can be translated into the next generation of tools and services to improve the quality of life for people on the autism spectrum. With several promising early results, there is also a need for more replication to validate research findings. Continued focus on coordination and collaboration with external partners will be essential to help us achieve the objectives in the *IACC Strategic Plan*. With sustained support and continued public-private collaboration, the IACC and its members can continue to work steadily toward the eventual collective community goal.

I thank you for this opportunity to speak with you and look forward to addressing any questions that you may have.

Thomas R. Insel, M.D.
Director, National Institute of Mental Health

Thomas R. Insel, M.D., is Director of the National Institute of Mental Health (NIMH), the component of the National Institutes of Health charged with generating the knowledge needed to understand, treat, and prevent mental disorders. His tenure at NIMH has been distinguished by groundbreaking findings in the areas of practical clinical trials, autism research, and the role of genetics in mental illnesses. NIMH has a large autism research program, covering a wide variety of topics, from molecular mechanisms to research on services. The program emphasizes studies that will lead to improved and earlier diagnosis and the development of improved treatments. In addition to directing the NIMH, Dr. Insel chairs the Interagency Autism Coordinating Committee, a federal advisory committee appointed by the Secretary of Health and Human Services that provides advice and coordination to the federal autism research effort (since 2002). He has also served as Co-Chair for the NIH Blueprint for Neuroscience Research (since 2004) and the Acting Director of the NIH National Center for Advancing Translational Sciences (NCATS) (2011-2012). Currently, Dr. Insel is one of the leaders for the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) effort, a Presidential Initiative focused on developing new tools for understanding the brain.

Prior to his appointment as NIMH Director in the Fall 2002, Dr. Insel was Professor of Psychiatry at Emory University. There, he was founding director of the Center for Behavioral Neuroscience, one of the largest science and technology centers funded by the National Science Foundation and, concurrently, director of an NIH-funded Center for Autism Research. From 1994 to 1999, he was Director of the Yerkes Regional Primate Research Center in Atlanta. While at Emory, Dr. Insel continued the line of research he had initiated at NIMH studying the neurobiology of complex social behaviors. He has published over 250 scientific articles and four books, including the *Neurobiology of Parental Care* (with Michael Numan) in 2003.

Dr. Insel has served on numerous academic, scientific, and professional committees and boards. He is a member of the Institute of Medicine, a fellow of the American College of Neuropsychopharmacology, and is a recipient of several awards including the Outstanding Service Award from the U.S. Public Health Service. Dr. Insel graduated from the combined B.A.-M.D. program at Boston University in 1974. He did his internship at Berkshire Medical Center, Pittsfield, Massachusetts, and his residency at the Langley Porter Neuropsychiatric Institute at the University of California, San Francisco.