The Interagency Autism Coordinating Committee Strategic Plan for Autism Spectrum Disorder Research

August 15, 2008

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Introduction

Autism spectrum disorders (ASD) share a diverse combination of core clinical characteristics of impairment in verbal and nonverbal communication skills and social interactions, and restricted, repetitive, and stereotyped patterns of behavior. Current Centers for Disease Control and Prevention (CDC) estimates of the prevalence rates of ASD are as high as 6.7 children per 1,000 (1 in 150) (CDC, 2007). Over the past decade, research addressing all aspects of ASD has expanded significantly due to greater availability of resources, scientific progress and opportunities, and wider appreciation of the individual, family, and societal costs of ASD. Yet, the needs of the communities affected by ASD remain urgent.

To improve coordination and accelerate the pace of scientific discovery in ASD research, Congress passed the Combating Autism Act (CAA) of 2006 (P.L. 109-416), which requires the Interagency Autism Coordinating Committee (IACC) to develop and annually update a strategic plan for ASD research.

Driven by both the sense of urgency and a spirit of collaboration, the IACC developed this initial Strategic Plan for ASD Research, which is focused on the unique needs of individuals with ASD and their families, as well as other consumers of these efforts. The Strategic Plan was developed through extensive and iterative input from members of the public, academic, and advocacy communities (see Appendix A for a full description of the planning process). In developing the Strategic Plan, the IACC:

- Identified recent investments and accomplishments in ASD research
- Assessed the strengths, weaknesses, opportunities, and gaps in the ASD research enterprise
- Gathered ideas for research opportunities from a diverse group of stakeholders
- Convened four scientific workshops with broad public participation to identify research opportunities
- Convened expert workgroups to recommend research objectives and strategies

The Strategic Plan incorporates this array of input in two main sections. First, the foundation of the plan - vision, mission, core values, and crosscutting themes – is described. The remainder of the plan is organized around six critical questions asked by individuals and families living with ASD.

- **When should I be concerned?**
- **How can I understand what is happening?**
- **What caused this to happen and can this be prevented?**
- **Which treatments and interventions will help?**
- **Where can I turn for services?**
- **What does the future hold?**

Each question is followed by a brief discussion of what we currently know and need from research, an aspirational goal, research opportunities and objectives. This six-question framework was chosen by the IACC to emphasize the need for consumer-focused research that addresses the most pressing questions of individuals and families living with ASD, and to link these questions to specific research efforts.

Vision Statement
The Strategic Plan will accelerate and inspire research that will profoundly improve the health and well being of every individual on the autism spectrum across the lifespan. The plan will set the standard for public-private coordination and community engagement.

Mission Statement
The purpose of the Strategic Plan is to focus, coordinate, and accelerate high quality research and scientific discovery in partnership with stakeholders to answer the urgent questions and needs of individuals on the autism spectrum and their families.

Core Values
The IACC adopted these core values and emphasized their importance for the Strategic Plan development and implementation:

Sense of Urgency – We will focus on what steps we can take to respond rapidly and efficiently to the needs and challenges of individuals and families affected by ASD.

Excellence – We will pursue innovative basic and clinical research of the highest quality to protect the safety and advance the interests of those affected by ASD.

Spirit of Collaboration – We will treat others with respect, listen to diverse views with open minds, and foster discussions where participants can comfortably offer opposing opinions.

Consumer-focused – We will focus on making a difference in the lives of people affected by ASD, including individuals with ASD, their families, medical practitioners, educators, and scientists.

Partnerships in Action – We will value cross-disciplinary approaches, data sharing, teamwork, and partnerships with clearly defined roles and responsibilities.

Accountability – We will develop SMART (Specific, Measurable, Achievable, Realistic, and Time-bound) research objectives aligned with funding priorities and develop systems for evaluation and course corrections.

Crosscutting Themes

The Strategic Plan for ASD Research is designed to highlight the most promising research ideas, while appreciating the inherent unpredictability of research. These ideas form the basis for the research opportunities and objectives of the Strategic Plan. In the process of gathering ideas from ASD stakeholders for this Plan, certain themes emerged repeatedly. These themes are highlighted here to emphasize their importance across the six-question framework.

Heterogeneity: Although certain core features are present at varying degrees among all individuals with ASD—i.e., social impairments, communication difficulties, and stereotyped behaviors—considerable heterogeneity exists as well. In the context of ASD, the term heterogeneity refers to the constellation of behavioral and medical conditions and symptoms that may accompany the disorder. The spectrum includes individuals with ASD who are nonverbal and cannot live independently, and others who find gainful employment and live independently. There is little reason to assume that this spectrum identifies a single disorder. Rather, the spectrum encompasses a range of disorders. The heterogeneity of ASD poses both challenges and opportunities to researchers: challenges, because there are likely to be many different causal factors and trajectories for ASD subtypes, and opportunities, because recognition of the variety of ASD phenotypes can lead to more appropriate diagnosis, more precisely targeted treatments, and can increase public awareness about the diversity inherent in ASD. Heterogeneity has a profound impact on the priorities and tactics of ASD research, because any given study must either focus on a particular focal point on the spectrum, or must be sufficiently complex and resourced to encompass a broader range along the spectrum. Acknowledging heterogeneity also has implications for intervention. With multiple causes and symptoms, there likely will be multiple ways and approaches to intervene (e.g., medical, behavioral, nutritional, etc.) In so doing, the ASD field will be more strategically positioned to determine what works best for which individuals.

Prevention: It is critical for research to identify the methods and approaches that can be used to prevent the challenges and disabilities of ASD. Indeed, a goal for ASD research is to develop the state of knowledge to a level similar to what is now available in fields such as cardiology. No longer do we need to wait for someone to suffer a heart attack before providing life-saving treatments. Rather, early interventions are applied upon the detection of risk factors so as to preempt these more serious consequences. Having sound research on the risk factors and the environmental triggers for ASD ultimately may allow us to prevent the development of the disorder in some children at risk or preempt the most serious disabilities in those affected.

Earlier Detection: ASD is a developmental brain disorder that is currently diagnosed by the observation of core behavioral symptoms. As with many neurodevelopmental disorders, brain dysfunction may precede abnormal behavior by months or even years. However, without biomarkers to detect individuals either with or "at risk" for ASD during pre- or neonatal periods, diagnosis must

rely on behavioral observations long after birth. As a result, intervention efforts may miss a critical developmental window. Until recently, most children with ASD in the United States (U.S.) did not receive a diagnosis until school age, and diagnosis was further delayed among disadvantaged or rural populations (Mandell, 2007). It is critical that the field enhance methods for detecting ASD earlier in life, in order to bring about earlier intervention. Furthermore, a recurrent theme expressed during the scientific workshops for the Plan was the need for biomarkers to identify ASD risk before the behavioral manifestations and the delayed developmental trajectory are established.

Lifespan Perspective: Historically, ASD has been characterized as a disorder of childhood. Although most individuals with ASD will not outgrow their diagnosis, their symptoms will change in form and severity over time. There was great support during the development of this Plan for more research on ASD in older individuals, especially the need for practical strategies for increasing the quality of life and functioning of adolescents and adults with ASD. As individuals with ASD advocate for themselves and expand our knowledge of their experiences and needs, they become partners in the research effort.

Data Sharing: Data sharing allows researchers to: (a) validate the research results of other investigators; (b) pool standardized information collected by many different researchers to facilitate rapid progress; and, (c) use data collected by others to explore hypotheses not considered by the original investigators. The expectations for data sharing have increased with the recognition that larger samples are needed to answer many research questions and with the sense of urgency for making progress. Databases for neuroimaging scans and genomic sequence are already proving important for ASD research. Wide adoption of a standardized data sharing system like that being implemented by the National Database for Autism Research (NDAR) can provide the necessary infrastructure to combine important research participant data and thereby propel ASD research forward.

Resources: In addition to data sharing, research often depends on the availability and quality of research resources, such as access to scientific instruments and repositories of biospecimens. An important resource, paradoxically, is the identification and assessment of individuals who do *not* have the disorder, as a basis for comparison. Such comparison groups serve a critical role in interpreting ASD research and findings. Moreover, human resources such as adequate numbers of well-trained researchers and administrators are vital to these efforts. This need cannot be understated.

Public-Private Partnerships: A strength of current ASD research is the degree of private involvement and investment in research funding from advocacy groups and committed stakeholders. In addition, the amount of research dollars awarded by the U.S. government for ASD research has grown rapidly over the past ten years. There is currently a great willingness on the part of government agencies and private organizations to collaborate on the development and implementation of the Strategic Plan for ASD Research. In fact, the Strategic Plan is built on the

premise that the public and private sectors will work collaboratively to better leverage resources to advance the research opportunities and objectives put forth in the plan.

Community Engagement in ASD Research: Individuals with ASD, their families, their educators, and their care providers have vital roles to play in shaping, participating in, and disseminating research. Their insights and perspectives are needed in order for interventions and services to be developed that will have maximal impact and have the strongest evidence and means for real-world uptake and utilization.

I. WHEN SHOULD I BE CONCERNED?

- **What are the early warnings signs?**
- **Are there typical characteristics that are part of an ASD diagnosis?**
- **How much variation is there in symptoms and severity associated with ASD?**

What do we know?
A child's primary caregivers are often first to identify the signs of ASD. There may be delays or plateaus in a child's attainment of developmental milestones, such as the onset of speech and pretend play. In other cases, the first signs of ASD occur in young children who appear to regress after they seem to have been developing normally. Current diagnostic criteria and classifications of ASD represent progress in identifying a core set of developmental symptoms that, in the past, might have been attributed to other disorders because of more narrowly defined ASD evaluation criteria.

The diagnosis of ASD can be reliably made by age three, because the core symptoms emerge by that time. However, most children eventually diagnosed with ASD exhibit signs of abnormal development well before the age of two. Recent studies of children at high risk because of a family history of ASD suggest that many cases of autism can be detected by 12 months of age using simple behavioral tests, such as response to calling the child's name or ease of engaging the child in jointly looking at an object (Landa et al., 2007).

A number of screening tools have been developed for detecting autism, for children of varied ages and different levels of clinical severity. A video glossary of early red flags of ASD in young children has been developed to help families and professionals learn how to identify subtle differences in development that may indicate areas of concern (Wetherby, 2007). In terms of diagnosis, there is emerging evidence that tools can be developed with sufficiently high sensitivity and specificity to support epidemiologic and risk factor studies.

What do we need?
Most cases of autism and related disorders are not diagnosed until after a child's third birthday, and yet early intervention can have a critical influence on the future course of ASD. At least three issues have limited the use of early interventions. First, it remains difficult to diagnose ASD in very young children because there is considerable healthy variation in the age at which infants and toddlers reach typical developmental milestones (e.g. speech). Delays do not always indicate the presence of a disorder. Pediatricians recognize that most children who are slow to walk or talk will catch up in the second year. Second, diagnosis of an ASD in a person of any age is currently based on behavioral and cognitive signs, reflecting abnormal brain development, but not on detection of brain or other biological differences that may be present before the emergence of the behavioral or cognitive signs. Biomarkers can potentially identify individuals with ASD, or infants who will subsequently develop or are already developing subtle signs of ASD, so that providers can initiate intensive early intervention strategies to address or possibly preempt developmental delay. Third, children with ASD

develop along different trajectories. Some show abnormal behavior soon after birth, others develop normally for the first year or longer and then regress, while others appear to later improve significantly.

Although families are eager for guidance, more research is needed to better answer the question of when developmental variation should become cause for concern. We need studies that test both new and current diagnostic and screening methods and that integrate both developmental and biologic approaches in community-based setting. In particular, studies need to be designed to validate methods in underrepresented minorities and disadvantaged populations. Such studies could increase our understanding of barriers to diagnosis and access to services. Taken together, earlier identification coupled with increased access to interventions and services could reduce disparities in health care and service provision, and ultimately improve outcomes for individuals with ASD.

Scientific studies of ASD require the reliable diagnosis of participants but this can be a time consuming and labor intensive process. Therefore, streamlined diagnostic approaches that facilitate the enrollment of research participants are needed. Researchers also need ASD measures that are easy to administer and are sensitive to changes in clinical status. With regard to heterogeneity, identifying characteristics that are specific to certain ASD subpopulations could potentially identify neurobiological and genetic markers and improve our understanding of more global causal and intervention mechanisms.

ASPIRATIONAL GOAL: CHILDREN WITH OR AT RISK FOR ASD WILL BE IDENTIFIED BY 24 MONTHS AND RECEIVE APPROPRIATE INTERVENTIONS

Research Opportunities

- ASD screening instruments and approaches for use in community settings to identify individuals who require diagnostic evaluation.
- Sensitive and efficient clinical diagnostic tools for diagnosing` ASD in widely diverse populations, including underrepresented racial and ethnic groups, females, younger and older age groups.
- ASD measures that are easy to administer and that are sensitive to incremental changes in both core and associated ASD symptoms. Such measures can be used to help track the clinical course of individuals with ASD, monitor responses to interventions, and provide information about the broader autism phenotype.
- Detailed criteria for specific ASD sub-types in order to better describe the variations in symptoms and severity and study how these variations relate to underlying pathology, intervention strategies, and outcomes.
- ASD subpopulations and associated biobehavioral markers that provide early indication of ASD risk and opportunities for early intervention.

- Protocols for genetic testing in routine clinical practice in order to identify individuals at risk for ASD. Identification of individuals with genetic variations associated with ASD will facilitate intensive studies of ASD subpopulations with shared genetic risk factors to characterize common phenotypic and biological features.

Short-Term Objectives

- Develop, with existing tools, at least one efficient diagnostic instrument (e.g., briefer, less time intensive) that is valid in diverse populations for use in large-scale studies by 2011.
- Validate and improve the sensitivity and specificity of existing screening tools for detecting ASD through studies of the following community populations that are diverse in terms of age, socio-economic status, race, ethnicity and level of functioning by 2012.
    - School aged children
    - General population (vs. clinical population)

Long-Term Objectives

- Validate a panel of biomarkers that separately, or in combination with behavioral measures, accurately identify, before age 2, one or more subtypes of children at risk for developing ASD by 2014.
- Develop five measures of behavioral and/or biological heterogeneity in children or adults with ASD, beyond variation in intellectual disability, that clearly relate to etiology and risk, treatment response and/or outcome by 2015.
- Identify and develop measures to assess at least three continuous dimensions of ASD symptoms and severity that can be used to assess response to intervention for individuals with ASD across the lifespan by 2016.
- Effectively disseminate at least one valid and efficient diagnostic instrument (e.g., briefer, less time intensive) in general clinical practice by 2016.

II. HOW CAN I UNDERSTAND WHAT IS HAPPENING?

- **What is happening early in development?**
- **Are there known biological differences that help explain ASD symptoms?**
- **Are there subgroups of people with ASD that have been identified?**

What do we know?
Researchers, clinicians, and families have long posed questions about the possible biological bases of ASD. Clinicians classify ASD as a developmental brain disorder based on the behavioral features required for diagnosis. Little evidence exists, however, for a specific neurological abnormality beyond reports of an exuberant and transient pattern of brain or head growth (Akshoomoff et al., 2002; Dawson et al., 2007; Hazlett et al. 2005). While many scientists believe that the behavioral features of ASD result from atypical brain wiring or connections in synapses, they have not reached a consensus on a specific neural variance associated with ASD. Nevertheless, there are some promising leads, and projects are underway that have the potential to provide biological signatures of some forms of ASD.

The development of sophisticated magnetic resonance imaging (MRI) methods has enabled researchers to accurately visualize many aspects of brain structure and functioning. For example, many children and adults with ASD perceive and analyze the visual information conveyed by facial expression differently than do other people (Spezio et al., 2007). Other researchers have employed MRI methods to investigate differences in brain anatomy between individuals with and without ASD, and have found differences in the density of white and gray matter, in some cases linked to specific symptoms of ASD (Craig et al., 2007).

Frequently, people with ASD experience co-occurring behavioral and medical symptoms or conditions such as immunological and metabolic abnormalities and gastrointestinal symptoms. In the case of the immune system, a number of hypotheses concerning how disruptions might contribute to ASD and other neurodevelopmental disorders have emerged in recent years. Some recent findings suggest that the immune systems of parents and their children may affect early brain development and the onset and fluctuation of symptoms in some children with ASD (Pardo, et al, 2005). For example, research on the effect of maternal antibodies, proteins produced as part of the immune response, on an array of fetal brain proteins suggested that in some cases maternal antibodies could interfere with normal brain development (Braunschweig, et al, 2008).

Exploring the neural basis of ASD requires access to biospecimens of individuals with and without ASD. Some progress has been made to establish the necessary infrastructure for the collection and preservation of post-mortem tissue from individuals with ASD, through the efforts of the National Autism Brain Bank, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Brain and Tissue Bank, the Autism Tissue Program and the Autism Brain Project. In addition, advocacy organizations such as Autism Speaks have made efforts in the U.S. and internationally to promote tissue donation.

What do we need?
One of the greatest barriers to progress in determining the biological bases of ASD has been the heterogeneity of the spectrum. A clear need exists to advance understanding of the many phenotypes of ASD, including studies that link genotype to phenotype, investigations of natural and treated history, analyses of genetic interaction with environmental exposures, and studies of co-occurring medical conditions.

To determine the earliest discernable onset of ASD, experts have expressed the need for an intensive, multidisciplinary study starting at early ages that examines biomedical, neurodevelopmental, and behavioral trajectories of children with ASD. A parallel multidisciplinary analysis of typically developing children would be especially enlightening, as limited normative information is currently available. Understanding early trajectories may lead to targeted interventions aimed at mitigating behavioral and medical challenges and improving outcomes through adulthood.

Another understudied arena of ASD research is gender differences. Many studies of autism preferentially enroll males, which, due to a 4:1 increased prevalence, are easier recruit. Without additional information about the biological features of ASD in females, it remains unclear whether the course of ASD is similar and whether currently used interventions are appropriate for females. It is critical to determine whether the gender ratio is accurate and whether gender is related to protective factors, diagnosis, and trajectory.

Many in the field have highlighted the need to establish nationally coordinated strategies for the collection and preservation of post-mortem tissue from both individuals with and without ASD. The existing brain and tissue bank resources have insufficient numbers of well-preserved brains, and the specimens include a number of varying co-occurring conditions and are of limited developmental range. Furthermore, there are few matched controls available for the resources in the existing repositories.

ASPIRATIONAL GOAL: DISCOVER HOW ASD AFFECTS DEVELOPMENT WHICH WILL LEAD TO TARGETED AND PERSONALIZED INTERVENTIONS

Research Opportunities

- Multi-disciplinary, longitudinal, biobehavioral studies of children, youths, and adults beginning during infancy that characterize developmental trajectories and identify ASD risk factors, subgroups, and potential biological targets for intervention. Such studies could include:
    - High-risk siblings of children, youths, and adults with ASD, children without a family history of ASD, and typically developing children
    - Multi-disciplinary assessments of brain imaging, metabolic and immune markers, microbiomics, electrophysiology, and behavior
- Research on females with ASD to better characterize clinical, biological and protective features.

- Human and animal studies that examine immune, infectious and environmental factors in the occurrence of ASD.
- An international public-private collaboration to expand current postmortem brain and other tissue resources (e.g., skin fibroblasts) to increase the acquisition, quality, type and availability of biomaterials relevant to studying the pathology of ASD.

Short-Term Objectives

- Establish an international network of brain and other tissue (e.g., skin fibroblasts) acquisition sites with standardized protocols for phenotyping, collection and distribution of tissue by 2010.
- Support at least four research projects to identify mechanisms of metabolic and/or immune system interactions with the central nervous system that may underlie the development of ASD during prenatal-postnatal life by 2010.
- Launch three studies that specifically focus on the neurodevelopment of females with ASD by 2011.

Long-Term Objectives

- Complete a large-scale, multi-disciplinary, collaborative project that longitudinally and comprehensively examines how the biological, clinical, and developmental profiles of children, youths, and adults with ASD change over time as compared to typically developing individuals by 2020.

III. WHAT CAUSED THIS TO HAPPEN AND CAN THIS BE PREVENTED?

- **Is there something in my genetic or family history that poses a risk for ASD?**
- **How might genetics and/or the environment influence the occurrence of ASD?**
- **Could an exposure to something in the environment lead to the development of ASD?**

What do we know?
As with many complex disorders, causation is generally thought to involve some forms of genetic risk interacting with some forms of non-genetic environmental exposure (e.g., hormonal and reproductive factors, paternal age, birth weight, stress during preconception/pregnancy, infections, and toxicants). The balance of genetic risk and environmental exposure likely varies across the spectrum of ASD.

The greatly increased concordance of strictly defined autism in monozygotic (identical) twins (70 - 90%) compared to dizygotic (fraternal) twins (0-10%) argues for the importance of genetic factors (Bailey, et al., 1995; Steffenburg, et al., 1989). Moreover, there are subpopulations of those diagnosed with ASD that have a known genetic mutation, often associated with a genetic disorder, such as Fragile X syndrome, Rett syndrome, or tuberous sclerosis. Using new technology that reveals gaps and extra copies in DNA sequences, researchers have found that some people with ASD have deletions and duplications of genetic material not found in their parents' DNA (Sebat et al., 2007). Recent research has revealed additional mutations of specific genomic regions (15q21 and 16p11) (Marshall, et al., 2008, Weiss, et al., 2008). These findings have contributed to new hypotheses about the inheritance of ASD. In families with just one affected member, spontaneous deletions and duplications may be causal factors of ASD.

Taken together, these genetic structural abnormalities account for 10-20% of ASD cases, yet individually each abnormality accounts for only 1-2% of cases (Abrahams & Geschwind, 2008). This suggests that the genetic factors in ASD may involve many rare mutations. Possible models include: (a) additional genetic mutations to be discovered; (b) multiple genetic variations each conferring a small increased risk; and, (c) many forms of ASD with different genetic contributions.

Progress in identifying susceptibility genes has been made possible due to collaborations and resources, both public and private, including: the National Institute of Mental Health (NIMH) Center for Collaborative Genetic Studies; the Collaborative Programs of Excellence in Autism (CPEA) co-sponsored by NICHD and the National Institute on Deafness and Other Communication Disorders (NIDCD); the National Institute of Environmental Health Sciences (NIEHS) Childhood Autism Risks from Genetics and the Environment (CHARGE) study; the Autism Genetic Resource Exchange (AGRE) sponsored by Cure Autism Now (CAN) with a large consortium of researchers assembled by Autism Speaks/National Alliance for Autism Research; CDC's Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE); the Norwegian cohort study supported by the National Institute of Neurological Disorders

and Stroke (NINDS); and the Simons Foundation Collection. In addition, existing research resources in toxicology could be tapped to provide important infrastructure for studying some forms of environmental risk.

Research on environmental risk factors is less well developed. An Institute of Medicine workshop held in 2007 summarized what is known and what is needed in this field (Institute of Medicine of the National Academies, 2007). Numerous epidemiological studies have found no relationship between ASD and vaccines containing the mercury based preservative, thimerosal (Immunization Safety Review Committee, 2004). Some parents, however, remain concerned that ASD is linked or caused by vaccination. In addition, a number of other environmental agents are being explored through research that are known or suspected to influence early development of the brain and nervous system. Recent studies suggest factors such as paternal age, exposure to infections, hormones, and other biological agents may confer environmental risk. These findings require further investigation and testing, some of which is ongoing through the CADDRE Program, the Norwegian cohort study, the CHARGE study, and the Children's Centers for Environmental Health and Disease Prevention supported by NIEHS and the Environmental Protection Agency (EPA).

What do we need?

Most scientists believe that risk factors for ASD are both genetic and environmental. However, few studies have ruled in or ruled out specific environmental factors. While there are reports of associations of ASD with exposure to medications or toxicants prenatally, and to infections after birth, it is still not known whether any specific factor is necessary or sufficient to cause ASD. Hampering these efforts is a lack of consensus in the research community about how to define the environment, as well as the best approach for staging studies to examine environmental factors. Some researchers believe that it is important to study a large number of exposures, or classes of exposure, that are known to affect brain development. Others support more tightly focused studies of one exposure or a limited number of exposures, with greatest biologic plausibility for interacting with known or suspected biologic or genetic ASD risk factors. In addition, it is also important to design studies that assess environmental exposure during the most relevant exposure windows: pregnancy and early development.

Research studies on risk factors for ASD require large sample sizes to disentangle the many possible genetic and environmental factors that contribute to and help explain ASD. For other complex disorders, large DNA collections, i.e. >20,000 samples, have been necessary to detect the full genetic risk architecture. There are no genetic repositories of this size for ASD. Similarly, large birth cohort studies in which biological samples have been collected throughout pregnancy and early postnatal life may be essential for detecting the interplay of environmental exposures and genetic factors that lead to ASD. As a complement to these large-scale studies, research on critical high-risk sub-populations (e.g., subsequent pregnancies in families with ASD, those with elevated exposure to specific environmental factors, older parents) could provide leverage in identifying genetic and environmental risk factors.

ASPIRATIONAL GOAL: CAUSES OF ASD WILL BE DISCOVERED THAT INFORM PROGNOSIS AND TREATMENTS AND LEAD TO PREVENTION/PREEMPTION OF THE CHALLENGES AND DISABILITIES OF ASD

Research Opportunities

- Genetic sequence variations in ASD and the symptom profiles associated with these variations.
- Family studies of the broader autism phenotype that can inform and define the heritability of ASD.
- Standardized methods for collecting and storing biospecimen resources from well-characterized individuals with ASD as well as a comparison group for use in biologic, environmental and genetic studies of ASD.
- Case-control studies of unique subpopulations of people living with ASD that identify novel risk factors.
- Monitor the scientific literature regarding possible associations of vaccines and other environmental factors (e.g., ultrasound, pesticides, pollutants) with ASD to identify emerging opportunities for research and indicated studies.
- Environmental and biological risk factors during pre- and early post-natal development in "at risk" samples.
- Cross-disciplinary collaborative efforts to identify and analyze biological mechanisms that underlie the interplay of genetic and environmental factors relevant to the risk and development of ASD.
- Convene ASD researchers on a regular basis to develop strategies and approaches for understanding gene – environment interactions.
- Exposure assessment -- efficient and accurate measures of key exposures for us in population and clinic based studies and standards for sample collection, storage, and analysis of biological materials.

Short-Term Objectives

- Initiate studies on at least five environmental factors identified in the recommendations from the 2007 IOM report "Autism and the Environment: Challenges and Opportunities for Research" as potential causes of ASD by 2010.
- Coordinate and implement the inclusion of approximately 20,000 subjects for genome-wide association studies, as well as a sample of 1,200 for sequencing studies to examine more than 50 candidate genes by 2011.
- Within the highest priority categories of exposures for ASD, validate and standardize at least three measures for identifying markers of environmental exposure in biospecimens by 2011.

Long-Term Objectives

- Determine the effect of at least five environmental factors on the risk for subtypes of ASD in the pre- and early postnatal period of development by 2012.
- Conduct a multi-site study of the subsequent pregnancies of 1000 women with a child with ASD to assess the impact of environmental factors in a period most relevant to the progression of ASD by 2014.
- Identify genetic risk factors in at least 50% of children with ASD by 2014.
- Support ancillary studies within one or more large-scale, population-based epidemiological studies, to collect nested, case-control data on environmental factors during preconception, and during prenatal and early postnatal development, as well as genetic data, that could be pooled (as needed), to analyze targets for potential gene/environment interactions by 2015.

IV. WHICH TREATMENTS AND INTERVENTIONS WILL HELP?

- **When should treatments or interventions be started?**
- **What are the medical issues I need to know about?**
- **How do I know that treatments are both safe and effective?**

What do we know?
While autism spectrum disorders are defined and diagnosed by deficits in core behaviors, there are often associated symptoms or conditions, both behavioral and medical, which can accompany the disorder. Some examples are seizures, gastrointestinal symptoms, and sleep disturbances. There is increasing recognition that such co-occurring symptoms can influence the trajectory and severity of ASD and need to be considered as targets for treatment.

A wide range of treatment and intervention options are available for children and adults with ASD that can target core symptoms, ameliorate associated symptoms, and prevent further disability. For example, interventions such as speech therapy facilitate language development, pragmatic communication and social interaction. Occupational therapy can address problems with sensory integration and motor planning. Both types of therapy can promote the development of life skills, which help individuals with ASD to gain more independence. Individuals with ASD can benefit from adaptive technologies, such as the use of keyboards and computers that promote expressive communication skills, and visual representation tools such as the Picture Exchange Communication System (PECS) that assist those with little or no language to communicate more effectively. For pre-school and school age children, public school systems and private schools can provide essential interventions including curricula that are individualized to the child, testing for cognitive and academic strengths and weaknesses, and special education services with lower teacher to student ratios, to name a few. For all of these interventions, there is a range of improvement, with some individuals making profound gains and others showing little response. We do not know how to predict which individuals will benefit from any of the available treatments.

Of the numerous behavioral interventions currently in use, little scientific evidence from randomized controlled trials (RCT) supports their efficacy. Behavioral therapies, such as Applied Behavior Analysis (ABA), which are based on principles of reinforcement and repetition, have been used since the 1960s and have been studied most extensively. Controlled trials have shown ABA to be effective for improving social skills and language when provided for at least 25-40 hours per week for 2 years (Lord & McGee, 2001). Efficacy is greatest when behavioral interventions are used early, but improved skills have been reported with adolescents and adults (Weiss & Harris, 2001; McClannahan et al., 2002).

Medications to improve some of the symptoms associated with autism have been studied. However, thus far, no medication has been shown in controlled trials to enhance social behavior or communication. In 2006, risperidone became the first Food and Drug Administration (FDA)-approved pharmacologic therapy for certain symptoms of autism.

First introduced in 1993 as medication used to treat symptoms of schizophrenia, risperidone has now been shown to be effective as a treatment of irritability and aggression seen in some children with ASD. Selective serotonin reuptake inhibitors have had mixed results in decreasing certain repetitive and stereotyped behaviors (Kolevzon et al., 2006). Other biological and pharmacological treatments that have been investigated in small studies and may warrant fuller attention include omega-3 fatty acids, memantine, oxytocin, and pioglitazone (Ammiger et al., 2007; Chez et al., 2007; Hollander et al., 2007; Boris et al., 2007)

There are other treatments in wide use that have not been studied in randomized controlled trials. These include nutritional supplements and diets (e.g. gluten-casein free diets), and chelation. One such treatment, the neuropeptide, secretin, that had been reported to improve symptoms of ASD was studied in a placebo-controlled trial and found to be ineffective (Esch & Carr, 2004).

What do we need?

Efficacious interventions are needed across the lifespan, from early development shortly after the detection of risk or diagnosis, through childhood, school age, adolescent, adult, and senior phases of life. Going forward, attention is needed to develop and test the efficacy of comprehensive interventions, and to identify which elements are most effective in reducing or ameliorating symptoms for which persons. Intervention research should collect information about the mode of delivery, intensity, duration, and dose as well as unique characteristics of the individuals with ASD (e.g., behavioral, biological, genetic) in an effort to develop more personalized interventions, treatments, services and supports, and help inform basic research about additional targets for study. This research will require large-scale multidisciplinary RCTs.

Special attention is needed on co-occurring medical issues, developing pharmacological treatments, and testing interventions that are in wide use, (e.g., nutritional supplements) but for which little rigorous efficacy data exist (Levy & Hyman, 2003). Medical issues, such as gastrointestinal symptoms and sleep disorders, may influence the effectiveness of interventions designed to affect the core symptoms of ASD. Similarly, interventions that focus on medical issues may also affect or reduce core symptoms. Animal models and/or cell lines relevant to autism are needed to develop new or test existing pharmacological agents for ASD, understand the mechanisms of action, and serve as a first-step in testing drug safety. Such model systems research may be crucial in leveraging the pharmaceutical industry to develop medications that target the core symptoms of ASD.

While some people with ASD have been reported to show marked improvement in their symptoms, little is known about the characteristics of these individuals or the types of interventions they have received that may help to explain these changes. Studies of these individuals may provide an opportunity for discovering important clues with regard to risk factors and intervention strategies for specific ASD subgroups.

ASPIRATIONAL GOAL: INTERVENTIONS WILL BE DEVELOPED THAT ARE EFFECTIVE FOR REDUCING BOTH CORE AND ASSOCIATED SYMPTOMS, FOR BUILDING ADAPTIVE SKILLS, AND FOR PREVENTING THE DISABILITIES ASSOCIATED WITH ASD

Research Opportunities

- Large scale studies that directly compare interventions and combinations of interventions to identify what works best for which individuals and how much it will cost.
    - Best practice models that are being used in community-based ASD intervention programs.
    - Clinical trials that assess the safety and efficacy of widely used interventions that have not been rigorously studied for use in ASD populations.
- Interventions that improve functioning and quality of life for older children and adults with ASD.
- Early interventions that aim to prevent the development of ASD in very young "at risk" children and reduce family burden.
- Innovative treatments that specifically target symptom clusters unique to ASD.
- Animal models and/or cellular lines that can be used to test efficacy and/or safety of ASD interventions and treatments.
- Strategies that facilitate rapid translation of promising basic scientific discoveries and community practices into clinical research and trials.
- Methods of treating co-existing medical or psychiatric conditions and assess how such methods affect ASD symptoms and severity.
- Early interventions that may enhance neural plasticity and adaptive brain reorganization thereby promoting significant behavioral improvement of ASD.

Short-Term Objectives

- Launch four research projects that seek to identify biological signatures that measure significant improvement in ASD core symptoms across the lifespan by 2010.
- Support three randomized controlled trials that address co-occurring medical conditions associated with ASD by 2010.
- Conduct five randomized controlled trials of early intervention for infants and toddlers by 2011.
- Launch three randomized controlled trials of interventions for school-aged and/or adolescents by 2012.

- Standardize and validate three model systems (e.g. cellular and/or animal) that replicate features of ASD and will allow identification of specific molecular targets or neural circuits amenable to existing or new interventions by 2012.
- Test safety and efficacy of five widely used interventions (e.g., nutrition, medications, medical procedures, etc.) that have not been rigorously studied for use in ASD by 2012.
- Complete two multi-site randomized controlled trials of comprehensive early intervention that address core symptoms, family functioning and community involvement by 2013.

Long-Term Objectives

- Complete randomized controlled trials in humans on three medication targeting core symptoms by 2014.
- Develop interventions for siblings of people with ASD with the goal of reducing risk recurrence by at least 30% by 2014.

V. WHERE CAN I TURN FOR SERVICES?

- **What types of services and supports should I seek and where can I find them?**
- **What is my state or local government doing to provide services for ASD?**
- **What is the cost of interventions and how will it be paid?**

What do we know?

Discovery of new diagnostic tests and efficacious interventions is necessary but not sufficient to reach the bold vision for this Strategic Plan. To fulfill the mission to "profoundly improve the health and well being of every individual on the autism spectrum across the lifespan," scientific discoveries must be implemented in clinical practice and supported by public policy. , The gap between knowledge and action can only be overcome by an aggressive focus on engaging families and the services community in the research process, disseminating research findings into the community, and helping individuals and families identify what will work best for them.

The communities in which children are diagnosed vary tremendously in their ability to meet the needs of individuals with ASD (Shattuck & Grosse, 2007). School districts vary in their ability to identify and provide appropriate educational and related programs for children with ASD (Mandell & Palmer, 2005; Palmer, Blanchard, Jean, & Mandell, 2005). States vary in the policies they have developed to organize, finance and deliver care to these individuals. Even within local and state jurisdictions with generous policies to support ASD interventions, the professional infrastructure or capacity is often inadequate to provide timely diagnosis and appropriate care.

These differences in policies, resources and organization result in marked differences in the treated prevalence of ASD across geographic areas, the types of services and support that are received, and the associated financial burden to families (Fujiura, 1994; Ganz, 2007; Jarbrink, Fombonne, & Knapp, 2003; Mandell et al., 2008; Ruble, Heflinger, Renfrew, & Saunders, 2005; Stahmer & Mandell, 2007). In general, children with ASD have a much more difficult time accessing appropriate care than children with other special healthcare needs (Krauss, Gulley, Sciegaj, & Wells, 2003). Data are still lacking on how these differences in policy and infrastructure relate to the differences in care received, and in turn how these differences affect outcomes for children and families.

What do we need?

A new health services research field of implementation science is emerging to: (a) evaluate the effectiveness of interventions in community settings; (b) identify the most effective means of disseminating research into widespread clinical practice; and, (c) define the best ways for research to inform policy on ASD services and supports. Integral to success, will be community engagement in shaping, participating, and disseminating ASD research.

An initial part of this process is the assessment of needs and costs. Care for developmental disorders is financed largely by federal, state and local agencies in both the health care and education sectors. Because there are significant regional differences in ASD resources, describing this varied landscape across states and localities in the U.S. will provide important baseline data for those with ASD and policy makers so they can appropriately seek and plan for services respectively. Research can also define the cost-effectiveness of evidence-based practices and thereby provide the data needed by various payers and policymakers.

In addition to disseminating best practices from ASD treatment and intervention research studies to community settings, so called bench to bedside translation, the other kind of translation, bedside to bench, could take and test promising community practices in rigorously designed research trials. Using a participatory action model, families and communities can be empowered to become partners in research that can in turn inform policy.

ASPIRATIONAL GOAL: COMMUNITIES WILL IMPLEMENT HIGH QUALITY, EVIDENCE-BASED AND COST EFFECTIVE SERVICES AND SUPPORTS ACROSS THE LIFESPAN FOR PEOPLE WITH ASD

Research Opportunities

- Annual State of the State review of policies, services and supports for individuals with ASD and their families.
- Effective dissemination of evidence-based practices for people with ASD at the community level.
- Cost-effectiveness studies of interventions and services for individuals with ASD across the lifespan.
- Studies that characterize current ASD diagnostic and service utilization patterns in community settings that also examine the relationship between the likelihood of a diagnosis and services availability for ASD.
- Improved and coordinated methods for tracking trends in ASD prevalence across the lifespan of diverse populations.

Short-Term Objectives

- Initiate a “state of the states” assessment of existing state programs and supports for people and families living with ASD by 2009.
- Support two studies that assess how variations and access to services affect family functioning in diverse populations by 2012.

Long-Term Objectives

- Test four methods to improve dissemination of effective interventions in diverse community settings by 2013.

- Test the efficacy and cost-effectiveness of three evidence-based services for people with ASD of all ages in community settings by 2015.

VI. WHAT DOES THE FUTURE HOLD?

- **What will my family member be like when he/she gets older?**
- **What is known about adults with ASD and how can I plan for the future?**
- **How does American society support individuals with ASD?**

What do we know?
An overarching goal of ASD research is to enable individuals with ASD to lead fulfilling and productive lives in the community. We are in critical need of information about the current landscape for adults with ASD. Longitudinal studies designed to capture the range of possible outcomes for adults with ASD are best suited to inform public policy decision-making, service and support delivery, and funding strategies. Also it is important is to improve public understanding of ASD in adults, including older adults, so that they may receive support from their neighbors and communities, to help them lead fulfilling and productive lives.

ASD poses economic and social costs for individuals, families, and society at large. Although ASD symptoms vary greatly in character and severity, the disorder occurs in all ethnic and socioeconomic groups and affects every age group. Some scientists and economists have estimated that the combined direct and indirect costs to provide care for all Americans with ASD during their lifetimes exceeds $35 billion, and that each individual accrues approximately $3 million in costs over his or her lifetime (Ganz, 2007). Families often incur large debts related to medical and educational services not covered through public programs or medical and dental insurance. In addition to financial challenges, ASD can lead to emotional hardships for individuals and families throughout life.

What do we need?
Although considerable research has focused on the earliest phase of ASD, through optimized diagnosis and early intervention, far less effort has addressed the adolescent, adult, and older adult phases of life. Minimal guidance exists for individuals and families about the trajectories of ASD across the lifespan. Although the general assumption is that higher functioning children can sometimes excel as adults, and children with more narrowly defined autistic disorder grow up to become adults who are lower functioning, the evidence base for these ideas is lacking. Scientists have not yet identified key prognostic factors or detailed information about how adults with ASD currently function and how they are best supported.

There are a number of areas in which prevalence studies could be improved: continued estimation and evaluation of prevalence in the same population over time; assessment of ASD prevalence in the context of other neurodevelopmental disorders; collection of data beyond core ASD symptoms, including genetic data and co-occurring medical, dental, and behavioral conditions; and expansion of studies across ages.

More research is needed to tailor treatments, interventions, services and supports to the evolving needs of school-age children, adolescents transitioning to adulthood, and adults

with autism. There is a need to address co-occurring conditions and developmental changes that coincide with transitions from adolescence to adulthood, to better assess functional outcomes (e.g., school-to-work, independent living, access to healthcare, including oral health care) in older individuals, and to develop improved quality-of-life measures for adults with ASD that assess dimensions other than intelligence and language skill. There is little information about the number of adults with ASD within the criminal justice system.

Finally, merging and analyzing health care, education, and social services administrative databases that include information about individuals with ASD will facilitate the study of whether early diagnosis, entry to services, and type of intervention, affects the course of ASD over time. Methods for merging such databases and linking investigator-recruited samples to these merged databases have been used in other populations and in specific locales with success.

ASPIRATIONAL GOAL: ADVANCES IN INTERVENTION, EDUCATION, AND SERVICES WILL SUPPORT AND ENABLE INDIVIDUALS ON THE AUTISM SPECTRUM TO LEAD FULFILLING AND PRODUCTIVE LIVES IN THE COMMUNITY

Research Opportunities

- Longitudinal studies of both people with ASD and their families to follow trajectories that account for clinical, psychosocial and biological heterogeneity.
- The scope and impact of ASD in adults, including how to diagnose ASD in adulthood, their needs during critical life transitions, assessment of functional and legal outcomes, family relationships, and co-occurring health issues.
- Use of existing administrative databases for information relevant to diagnosis, course, interventions and long-term outcomes for ASD.

Short-Term Objectives

- Develop and have available to the research community means by which to merge or link databases that allow for tracking the involvement of individuals in ASD research by 2010.
- Launch at least two studies to assess and characterize variation in adults living with ASD (e.g. social and daily functioning, demographic, medical and legal status) by 2011.
- Conduct at least two clinical trials to test the efficacy and cost-effectiveness of interventions, services and supports to optimize daily functioning (e.g., educational, vocational, recreational, and social experiences) for adolescents, adults, or seniors living with ASD by 2012.

Long-Term Objectives

- Develop at least two community-based interventions with individual specificity that improves outcomes, as measured by educational, occupational, and social achievements by 2015.

- Develop and have available to the research community means by which to merge or link administrative databases that allow for tracking the involvement of individuals living with ASD research in health care, education, and social services by 2018.

Development Process for the IACC
Strategic Plan for Autism Spectrum Disorder Research

Introduction
As a federal advisory committee established by the Combating Autism Act of 2006, the IACC is mandated to develop and annually update a strategic plan for the conduct of, and support for, ASD research, including proposed budgetary requirements.

Overview of the Strategic Planning Process
At its inaugural meeting in November 2007, the IACC approved a process for developing the initial version of the Strategic Plan for ASD Research. The process resulted in a strategic plan that includes a set of research opportunities and objectives. The IACC will monitor the implementation of the strategic plan over the next several years and update the plan annually. To help facilitate and accomplish the strategic planning steps, the IACC formed workgroups and convened scientific workshops. The strategic planning process incorporates several opportunities for public input and stakeholder participation.

The strategic plan includes the IACC's goals and objectives for services research related to ASD. Concurrent with the strategic planning process, the IACC formed the Services Subcommittee to assess and improve services and supports for people with ASD. This subcommittee's work complements the Strategic Plan, by extending beyond services research to improving access to and delivery of services and supports.

Steps in the Strategic Planning Process

November 2007	**IACC Approved Strategic Planning Process**
December 2007	**Strategic Planning (SP) Workgroup Formed**
Dec 2007 – Jan 2008	**Solicited Public Input on ASD Research Priorities**
January 2008	**Four Scientific Workshops Convened**
February 2008	**First SP Workgroup Meeting Held**
March 2008	**IACC Reviewed and Modified SP Process**
April 2008	**Second SP Workgroup Meeting Held**
May 2008	**Town Hall Meeting Held**
June 2008	**Short- and Long-Term Objectives Developed**

The IACC approved the formation of a Strategic Planning (SP) Workgroup at its meeting on November 30, 2007. The purpose of the workgroup was to facilitate the development of the Strategic Plan for ASD Research. The workgroup members included scientific experts, representatives from private ASD research funding organizations and advocacy groups, program officials, and a subset of IACC members.

The SP Workgroup helped organize four scientific workshops to identify high priority research opportunities in the domains of Biology, Treatment, Diagnosis, and Risk Factors. The workgroup oversaw the process for selecting workshop participants based on diverse viewpoints and expertise. IACC members had the option to nominate workshop participants and to observe or participate in workshops.

Request for Information (RFI) for Public Input on ASD Research Priorities
The purpose of the RFI was to seek input from ASD stakeholders about high-priority research questions as a first step in receiving broad input at the beginning stages of strategic plan development.

Dissemination of the RFI

- The RFI (NOT-MH-08-003) was posted in the National Institutes of Health (NIH) Guide on December 19, 2007. Responses were accepted through January 4, 2008.
- The electronic link to the RFI was sent to a wide range of advocacy, research, and professional organizations, IACC members, the IACC strategic planning workgroups, the NIH autism listserv, and an email distribution list from the NIMH Office of Constituency Relations and Public Liaison.
- Autism societies and advocacy organization were asked to post the RFI on their websites or otherwise disseminate the RFI among their membership.

RFI Responses
A total of 542 responses were received, coming from nearly every U.S. State and from foreign countries including Canada, England, Norway, Argentina, and France. Individual respondents included parents or relatives of a child with an ASD; individuals self-identified with an ASD; professionals involved in ASD care, educators, and school staff; and researchers in ASD and other fields. Examples of organizations that responded included state autism societies; state or local departments of health, mental health, and public health; university departments; disease-specific foundations; advocacy organizations; and professional organizations. Respondents shared many personal stories and expressed a great diversity of opinions. The Treatment domain received the most responses and in general, the comments strongly supported the need for more research on ASD.

Four Scientific Workshops
Four one-day scientific workshops were organized, each focusing on one ASD research domain. The workshops took place on successive days (January 15-18, 2008) to encourage overlap between participants and to facilitate discussions at the interface of the workshop domains.

To ensure thoughtful discussions, workshop participants reviewed research accomplishments and ongoing initiatives and resources for ASD research as reported by Federal agencies and private funding organizations. Workshop participants also received a comprehensive summary of the RFI responses related to their domain.

Workshop participants considered the strengths and weaknesses underlying the current state of the science and identified opportunities, unanswered questions, and research resources needed to find solutions. Throughout the workshops, participants discussed crosscutting themes of ASD heterogeneity and trajectories, and emphasized research activities with the greatest potential to improve the lives of individuals with ASD and their families

Following extensive dialogue, the four workshops generated 41 potential research opportunities using a uniform template. Each proposed research opportunity explained the need addressed, the proposed solution, whether the proposal included a new tool or a modification of an existing resource, the impact of achieving the objective, an evaluation plan, and a timeframe.

Workshop Domains

Biology: The underlying biological processes that lead to developmental and medical problems associated with ASD. Included research in the neurosciences but was not confined to neuroscience. Researches on other organ systems, interactions between organ systems, and/or other disease processes were included as well.

Treatment: ASD treatment, intervention, and services research that aimed to reduce symptoms, promote development, and improve outcomes. Topics included development and evaluation of medical, behavioral, educational, and complementary interventions for ASD. In addition, evaluation of treatment effectiveness in real world settings, disparities in ASD treatment among specific subpopulations, practice patterns in ASD programs and services, and their cost-effectiveness were all included.

Diagnosis: The accurate and valid description and measurement of ASD (phenotype) at both the individual and population levels as well as the public health impact of ASD. In addition, this area concerned itself with the diversity of what constitutes ASD and the characteristics of the condition over the lifespan.

Risk Factors: Factors that contribute to the risk of develop an ASD at both the individual or population level. This included genetic studies of clusters or sporadic occurrences of ASD, studies focusing on environmental factors, e.g. intrauterine events or exposure to toxins, which could lead to ASD, and the interaction between these factors that increase risk for ASD.

First Strategic Planning (SP) Workgroup Meeting

The goals for the first SP workgroup meeting were to discuss the 41 research opportunities generated by the scientific workshops. Thomas Insel, M.D. who chaired the meeting, asked participants to identify ideas that they felt were missing from the research opportunities developed by the scientific workshops. Discussion also focused on how to facilitate research through high-risk, high-payoff projects; technical assistance to help write fundable research proposals; and the need to involve scientists from different disciplines in ASD research.

The SP workgroup discussed and formulated draft core values for the strategic plan and proposed a framework for organizing the research opportunities. The workgroup proposed a consumer-focused approach that would adopt the perspective of families and individuals that include a person with ASD of any age. Families ask questions such as: "When should I be concerned?" "How can I understand what is happening?" "What

caused this to happen and how can this be prevented?" "Which treatments and interventions will help?" "Where can I turn for services?" "What does the future hold?" The workgroup then categorized the 41 research opportunities using the question framework.

Second Strategic Planning (SP) Workgroup Meeting
At its March 2008 meeting, the IACC formed a new SP Workgroup to broaden workgroup representation. IACC members had the option to nominate a workgroup participant or to participate themselves. The workgroup members included scientific experts, representatives from private ASD research funding organizations and advocacy groups, professional societies, program officials, workshop chairs, and a subset of IACC members.

The main goals for the second workgroup meeting were to review 2007 ASD research funding, prioritize research opportunities within the six-question framework, and discuss budgetary requirements for the strategic plan. To facilitate broader stakeholder participation in the strategic planning process, members of the public were able to listen to the meeting via teleconference link and view slides on the Internet.

Before the workgroup met, the NIMH Autism Team coordinated the compilation of ASD research funding portfolio information for FY 2007 from major funding sources: NIH, CDC, Department of Defense, The Simons Foundation, and Autism Speaks. The Autism Team also solicited feedback from the scientific workshop participants about the degree to which ideas from the stakeholder RFI were included within the 41 research opportunities.

The SP workgroup prioritized the 41 research opportunities. This prioritization, along with recommendations that overlapping opportunities be consolidated and that an overall mission, vision, and goals for the strategic plan be developed, was forwarded to the IACC.

Regarding budgetary requirements, workgroup members discussed various topics including the need for fast track funding for high risk, high yield studies; the demand for more clinical trials infrastructure; and the relatively smaller percentage investment in treatment research reflected in the 2007 funding data. Finally, the workgroup members emphasized the role of the strategic plan in stimulating quality research to attract excellent researchers to ASD research.

IACC Town Hall Meeting
A Town Hall meeting was held on May 3, 2008 in Sacramento, CA at the University of California, Davis Medical Center to solicit additional public input regarding research priorities for the treatment of ASD.

The meeting consisted of a series of panel discussions, with opportunity for public comment after each panel. The panels were comprised of treatment researchers, clinicians, service providers and public advocacy representatives. Three IACC representatives were present at the meeting and participated in panel discussions. The morning panel was designed to stimulate discussion of a range of conventional and

alternative/complementary treatment approaches that are being used currently, with the goal of developing recommendations about research priorities for establishing safety and efficacy of these approaches. The afternoon panel was focused on discussion about the differing needs of older children and adults with ASD, with the goal of developing research recommendations for treatment and interventions that target this underserved population.

The meeting, attended by approximately 125 individuals, included parents, researchers, service providers and representatives from advocacy groups and state government. Public comments were summarized for the IACC at its May 12th meeting for consideration during development and refinement of the Strategic Plan.

Short- and Long-Term Objectives

The chairs from the four scientific workshops met by teleconference on June 10, 2008 to discuss ways to consolidate the 41 research opportunities and to provide input on short-term and long-term objectives for the Strategic Plan. These draft objectives and consolidated opportunities were subsequently reviewed and discussed by program staff from the NIH, CDC, Department of Defense, The Simons Foundation, and Autism Speaks on July 24, 2008. The cumulative input from the workshop chairs and program staff was used to formulate the short- and long-term objectives and research opportunities described in the July 1, 2008 draft of the Strategic Plan.

References:

Abrahams, BS, & Geschwind, DH. Advances in autism genetics: on the threshold of a new neurobiology. Nat Rev Genet. 2008 May;9:341-355.

Akshoomoff N, Pierce K, Courchesne. The neurobiological basis of autism from a developmental perspective. Dev Psychopath. 2002 14:613-634.

Amminger GP, Berger GE, Schäfer MR, Klier C, Friedrich MH, Feucht M. Omega-3 fatty acids supplementation in children with autism: a double-blind randomized, placebo-controlled pilot study. Biol Psychiatry. 2007 Feb 15;61(4):551-3.

Autism and Developmental Disabilities Monitoring Network Surveillance Year 2002 Principal Investigators; Centers for Disease Control and Prevention. Prevalence of autism spectrum disorders—autism and developmental disabilities monitoring network, 14 sites, United States, 2002. MMWR Surveill Summ. 2007 Feb 9;56(1):12-28.

Bailey A, Le Couteur A, Gottesman I, Bolton P, Simonoff E, Yuzda E, et al. Autism as a strongly genetic disorder: evidence from a British twin study. Psychol Med. 1995 Jan;25(1):63-77.

Boris M, Kaiser CC, Goldblatt A, Elice MW, Edelson SM, Adams JB, et al. Effect of pioglitazone treatment on behavioral symptoms in autistic children. J Neuroinflammation. 2007 Jan 5;4:3.

Braunschweig D, Ashwood P, Krakowiak P, Hertz-Picciotto I, Hansen R, Croen LA, Pessah IN, Van de Water J. Autism: Maternally derived antibodies specific for fetal brain proteins. Neurotoxicology. 2008 March;29(2):226-231.

Chez MG, Burton Q, Dowling T, Chang M, Khanna P, Kramer C. Memantine as adjunctive therapy in children diagnosed with autistic spectrum disorders: an observation of initial clinical response and maintenance tolerability. J Child Neurol. 2007 May;22(5):574-9.

Craig MC, Zaman SH, Daly EM, Cutter WJ, Robertson DM, Hallahan B, et al. Women with autistic-spectrum disorder: magnetic resonance imaging study of brain anatomy. Br J Psychiatry. 2007 Sep;191:224-8.

Dawson G, Munson J, Webb SJ, Nalty T, Abbott R, Toth K. Rate of head growth decelerates and symptoms worsen in the second year of life in autism. Biol Psychiatry. 2007 Feb 15;61(4):458-64.

Esch BE, Carr JE. Secretin as a treatment for autism: a review of the evidence. J Autism Dev Disord. 2004 Oct; 34(5):543-56.

Fujiura, G. T., Roccoforte, J.A., Braddock, D. Costs of Family Care for Adults with Mental Retardation and Related Developmental Disabilities. Am J Ment Retard. 1994 99(3), 250.

Ganz ML. The lifetime distribution of the incremental societal costs of autism. Arch Pediatr Adolesc Med. 2007 Apr;161(4):343-9.

Hazlett HC, Poe M, Gerig G, Smith RG, Provenzale J, Ross A, Gilmore J, Piven J. Magnetic Resonance Imaging and Head Circumference Study of Brain Size in Autism. Arch Gen Psychiatry. 2005 Dec;62(12):1366-1376.

Hollander E, Bartz J, Chaplin W, Phillips A, Sumner J, Soorya L, et al. Oxytocin increases retention of social cognition in autism. Biol Psychiatry. 2007 Feb 15;61(4):498-503.

Immunization Safety Review Committee. Immunization Safety Review: Vaccines and Autism. Washington, DC: The National Academies Press; 2004.

Institute of Medicine of the National Academies. Forum on neuroscience and nervous system disorders autism and the environment: challenges and opportunities for research, workshop proceedings. Washington, DC: The National Academies Press; 2007.

Jarbrink, K., Fombonne, E., & Knapp, M. Measuring the parental, service and cost impacts of children with autistic spectrum disorder: A pilot study. J Autism Dev Disord. 2003 33(4), 395-402.

Kolevzon A, Mathewson KA, Hollander E. Selective serotonin reuptake inhibitors in autism: a review of efficacy and tolerability. J Clin Psychiatry. 2006 Mar; 67(3):407-14.

Krauss, M., Gulley, S., Sciegaj, M., & Wells, N. Access to specialty medical care for children with mental retardation, autism and other special health care needs. Ment Retard. 2003 41(5), 329-339.

Landa RJ, Holman KC, Garrett-Mayer E. Social and communication development in toddlers with early and later diagnosis of autism spectrum disorders. Arch Gen Psychiatry. 2007 Jul;64(7):853-64.

Levy SE, & Hyman SL. Use of complementary and alternative treatments for children with autistic spectrum disorders is increasing. Pediatr Ann. 2003 Oct;32(10):685-91.

Levy SE, Hyman SL. Use of complementary and alternative treatments for children with autistic spectrum disorders is increasing. Pediatr Ann. 2003 Oct;32(10):685-91.

Lord C, & McGee J, (Eds.). Educating Children with Autism. Washington, DC: The National Academies Press; 2001.

Mandel DS, Ittenbach RF, Levy SE, Pinto-Martin JA. Disparities in diagnosis received prior to a diagnosis of autism spectrum disorder. J Autism Dev Disord. 2007 Oct. 37(9):1795-1802.

Mandell, D., Morales, K., Marcus, S., Stahmer, A., Doshi, J., & Polsky, D. Psychotropic medication use among children with autism spectrum disorders. Pediatrics, 121(3) 2008 e441-448.

Mandell, D., & Palmer, R. Differences among states in the identification of autistic spectrum disorders. Arch Pediatr Adolesc Med. 2005 159(3), 266-269.

Marshall CR, Noor A, Vincent JB, Lionel AC, Feuk L, Skaug J, Shago M, Moessner R, Pinto D, Ren Y, Thiruvahindrapduram B, Fiebig A, Schreiber S, Friedman J, Ketelaars CEJ, Vos YJ, Ficicioglu C, Kirkpatrick S, Nicolson R, Sloman L, Summers A, Gibbons CA, Teebi A, Chitayat D, Weksberg R, Thompson A, Vardy C, Crosbie V, Luscombe S,

Baatjes R, Zwaigenbaum L, Roberts W, Fernandez B, Szatmari P, Scherer SW, Structural Variation of Chromosomes in Autism Spectrum Disorder. Am J Hum Genet. 2008 Feb:82(2):477-488.

McClannahan LE, MacDuff GS, Krantz PJ. Behavior analysis and intervention for adults with autism. Behav Modif. 2002 Jan;26(1):9-26.

Palmer, R., Blanchard, S., Jean, C., & Mandell, D. School district resources and identification of children with autistic disorder. Am J Public Health. 2005 95(1), 125-130.

Pardo CA, Vargas DL, Zimmerman AW. Immunity, neuroglia and neuroinflammation in autism. Int Rev Psychiatry. 2005 Dec;17(6):485-95.

Ruble, L., Heflinger, C., Renfrew, J., & Saunders, R. Access and service use by children with autism spectrum disorders in Medicaid managed care. J Autism Dev Disord. 2005 35(1), 3-13.

Sebat J, Lakshmi B, Malhotra D, Troge J, Lese-Martin C, Walsh T, et al. Strong association of de novo copy number mutations with autism. Science. 2007 Apr 20;316(5823):445-9.

Shattuck, P., & Grosse, S. Issues related to the diagnosis and treatment of autism spectrum disorders. Ment Retard Dev Disabil Res Rev. 2007 13, 129-135.

Spezio ML, Adolphs R, Hurley RS, Piven J. Analysis of face gaze in autism using "Bubbles". Neuropsychologia. 2007 Jan 7;45(1):144-51.

Stahmer, A., & Mandell, D. State Infant/Toddler Program Policies for Eligibility and Services Provision for Young Children with Autism. Adm Policy Ment Health. 2007 34(1), 29-37.

Steffenburg S, Gillberg C, Hellgren L, Andersson L, Gillberg IC, Jakobsson G, et al. A twin study of autism in Denmark, Finland, Iceland, Norway and Sweden. J Child Psychol Psychiatry. 1989 May;30(3):405-16.

Weiss LA, Shen Y, Korn JM, Arking DE, Miller DT, Fossdal R, et al. Association between microdeletion and microduplication at 16p11.2 and autism. N Engl J Med. 2008 Feb 14;358(7):667-75.

Weiss MJ, & Harris SL. Teaching social skills to people with autism. Behav Modif. 2001 Oct;25(5):785-802.

Wetherby AM, Watt N, Morgan L, Shumway S. Social Communication profiles of children with autism spectrum disorders late in the second year of life. J Autism Dev Disord. 2007 May:37(5):960-75.