safeMinds
Sensible Action For Ending Mercury-Induced Neurological Disorders

NOT-MH-08-021

September 30, 2008

Dr. Thomas Insel, MD
Chairman, Interagency Autism Coordinating Committee
National Institute of Mental Health
6001 Executive Boulevard
Bethesda, MD 20892-9669

Re: Comments on Draft IACC Strategic Plan for Autism Research.

Dear Dr. Insel,

Safeminds submits the following comments urging significant changes to the draft strategic plan. The autism community worked with Congress to enact the Combating Autism Act (CAA) of 2006, P.L. 109-416. The CAA authorized $744 million over five years to expand and intensify autism basic and clinical research conducted by NIH to "investigate the cause (including possible environmental causes), diagnosis or rule out, early detection, prevention, services, supports, intervention, and treatment of autism spectrum disorder." Congress directed the Interagency Autism Coordinating Committee to develop, submit, and annually update a comprehensive Strategic Plan (SP) with a budget for the conduct of this research.

Safeminds has worked within the severe constraints imposed on development of the draft SP to achieve the best possible plan responsive to the ASD crisis, the needs of the community for effective treatments, and the mandate from Congress. Safeminds submitted comments in response to the two RFI's in January, submitted "gap" initiatives, participated in the Sacramento townhall meeting in May, attended all of the public meetings of the IACC and workgroups, submitted (through Ms. Redwood) edits to the July 1 preliminary draft, offered suggestions and critique of process issues, and generally served as a resource for education relating to the crucial research and process issues addressed in the draft plan.

In its present form, the draft is seriously deficient and is an inadequate response to a poorly specified crisis, to the needs of the community, and to the mandate from Congress. This is due in part to serious flaws in the process, violations of FACA, violations of the letter and spirit of CAA, and failure to fully utilize the resources of the community. It is our hope that these substantive deficiencies can be corrected in this round of public comment which might possibly render moot the procedural violations. Safeminds remains committed to work with IACC to achieve the best possible SP, one that is responsive to the tasks set by Congress and meets the needs of the community to harness the power of science and medicine to find the cause of autism, treat and support existing cases, and prevent the factors leading to new cases. Strong community support for the SP is essential for its success.

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The community can enthusiastically support a SP that ensures progress toward Congressional goals with all deliberate speed. Therefore, the SP must be much more than an unprioritized listing of interesting research topics relating to autism (as was the "autism roadmap" developed in 2003). The SP must address at a minimum: (1) a mission statement incorporating the goals set by Congress; (2) specific goals; (3) analysis of past and present research, accomplishments, and gaps (including unfunded projects as a measure of demand); (4) a prioritized plan for present and future research initiatives that specifically includes a focus on environmental causes including vaccines; (5) changes to the funding process to reduce delay, rely on mechanisms such as special emphasis panels with defined budgets and research targets, and increase community participation in funding decisions; (6) transparency, accountability and performance metrics; (7) a justified research budget driven by scientific opportunity and demand; and (8) collaboration and partnerships with non-NIH public and private research funders. The SP must strategically justify necessary resources, prioritize research questions, and be accountable and transparent. The community must have an effective plan to take back to Congress to obtain the necessary appropriations. Accordingly, in addition to the above, the SP must address the following major issues:

The SP Must Clearly Express Strategic Doctrine.

The first task in developing the SP should have been development and IACC approval of strategic doctrine in response to the mandate from CAA. Instead, the process launched immediately into a lengthy list of research initiatives of a fairly general and obvious nature, unprioritized, and, in essence, a rehash of the 2004 autism roadmap. At a minimum, in order to be responsive to CAA and to the needs of the community, the SP must begin by clearly articulating the following doctrine: (1) autism is a national health emergency that requires a crisis-level response; (2) autism is a biological disorder triggered in genetically susceptible individuals by environmental factors; (3) new cases of autism can and should be prevented by identification and elimination of environmental causes; and (4) autism is treatable. Based on a recognition of these principles, the research emphasis must be placed on environmental etiology, biological mechanisms and disease process, and treatment.

1. Autism Is a National Health Emergency Requiring a Crisis-Level Response.

There has been an explosion in the rate of childhood autism and related disorders in the United States. Despite imperfect surveillance systems, less than ideal prospective evidence and a fragmentary base of prevalence surveys, there is no responsible way to interpret the reported rise in disease frequency as anything less than a true increase; an order of magnitude increase in childhood autism rates cannot be explained as a mere artifact of changes in diagnostic practices and greater awareness. No persuasive evidence supports the conclusion that increased autism rates are an artifact of increased awareness, and indeed, any hypotheses to that effect must not be given the benefit of the doubt and assumed as a default policy position but rather require high levels of proof before they can be considered as serious claims. Instead, precaution requires that, in light of these alarming increases, autism be considered a national and global health emergency requiring significant resources, diligent investigation of its increasing frequency and aggressive management. This dramatic rise in prevalence imposes huge and growing direct and indirect costs on society as a whole and on affected families in particular. Ganz (2006) estimated the lifetime cost of care for an individual with autism at $3.2 million and the annual cost to society at $35 billion.

Strategic goal: prevent new cases of autism and reduce the rate of autism in cohorts of newborn children by over 90%.

2. Autism is a Biologic Disorder With a Primary Environmental Etiology.

Historically, the leading priority for autism research funded by NIH has been placed on research into inherited genetic risk factors. Although there are many reasons for this, the weight of the evidence suggests that these investments have not yielded results that will provide the kind of urgent breakthroughs required to respond to this health crisis. The increased concordance of autism in monozygotic (identical) twins compared to dizygotic (fraternal) twins has been used to argue for the importance of inherited genetic factors in autism but these findings are based on old studies that examined birth cohorts born before the rapid increases in autism rates. In addition, large investments in full genome scans for autism (most recently the largest genome scan ever conducted, the Autism Genome Project Consortium) have failed to yield reproducible results that support the role for inheritance in any region of the genome. While investigation of inherited factors in autism has contributed to some interesting hypotheses about the biology of ASD, and there continue to be extensive privately funded research projects in this area, this research is unlikely to lead to meaningful interventions for many years and therefore does not deserve the funding priority it has heretofore received.

Strategic goal: conduct research in areas likely to provide benefits to living children and adults.

3. New Cases of Autism Should Be Prevented By Identifying Environmental Etiology

There is a clear need for a high priority on investigating environmental factors in light of the increases in autism rates. These increases also help explain why there has been so little success in the search for heritable risk factors. We need to take on a more innovative view of the interactions between genes and the environment in order to make research on both genes and the environment more productive. Meaningful exposures can occur from prenatal period through infancy and the changes in the brain are most notable after infancy. Some are born autistic but many develop normally as infants and then regress. In light of the increases and the observations we see in children, it's important to leave no stone unturned in the investigation of environmental exposures.

An environmental factor or combination of factors contributes to disease causality. These factors can interact with susceptibility genes. Timing of exposure during development is also an important consideration, and relevant exposures may occur pre- or post-natally. Even low level exposures can result in alterations to development that can lead to symptoms of autism. Research on the role of environmental agents must be the priority for understanding the new case rates, and can be a fruitful approach for both treatment and prevention. This research should include continued investigation of controversial environmental exposures such as childhood vaccines, vaccine preservative and environmental mercury exposures, as well as other environmental toxins such as organophosphates and pyrethrins. We need to consider the best ways to inform epidemiology with toxicology, while also developing the disciplines of predictive toxicology, in order to get answers rapidly.

The CAA required NIH to "expand, intensify, and coordinate" basic and clinical research to investigate "cause (including possible environmental causes), diagnosis or rule out, early detection, prevention, services, supports, intervention, and treatment of autism spectrum disorder." 42 U.S.C. 284g. Prevention is an attractive goal in terms of the direct and indirect cost of autism and the burden it imposes on individuals, families and society as a whole. The sharp rise in autism rates can only be fully explained by environmental factor causality (interacting with genetic susceptibility), these environmental triggers can be identified and eliminated, thereby preventing disease spread and potentially ameliorating the condition in existing cases.

Although NIMH Director Insel stated to Congress[1] that prevention is a goal of NIH autism research, a glaring absence from both the draft mission[2] and vision[3] statements presented by Dr. Insel at IMFAR is an express commitment to "prevention." This absence reflects the irremediable failure of NIMH to develop an acceptable SP and demonstrates a fundamental need to overhaul the SP exercise. Any acceptable SP must come to grips with the fundamental nature of this disorder. As you clearly articulated during the first IACC meeting on November 30, autism is both preventable and treatable. The SP must incorporate this vision.

Strategic goal: identify preventable causes of autism and promising areas of intervention to improve function in affected individuals while also preventing new cases.

4. Recovery of Function is Possible With Effective Treatment.

There is no "cure" for autism. We cannot turn back the clock to reclaim the time lost to developmental injury. We also embrace the unique personality of autistic individuals and, for a few, their unique aptitudes and gifts. Our hopes for children with autism are that they: may lead independent lives; otherwise expand their capacity to learn, grow and develop; play a productive role in society; and the ability to enjoy mutually satisfying and loving relationships. Individuals diagnosed with autism are physically sick and disabled; they are not genetically defective. While they may have unusual talents, their condition is not purely behavioral or psychiatric. Substantial recovery from their deficits is possible and there is evidence in case studies of effectively complete recovery from the symptoms of autism.

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[1] Statement of Thomas B. Insel, M.D., Autism Research at the National Institutes of Health, Before the Appropriations Subcommittee on Labor, Health, and Human Services, Education, and Related Agencies, United States Senate at 7 (April 17, 2007) ("Ultimately, our goal is prevention, based on early detection of risk, understanding environmental factors that increase or decrease symptoms, and development of effective interventions before behavioral and cognitive deficits appear.")

[2] Draft 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."

[3] Draft 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."

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Autism and related disorders and their associated conditions are amenable to treatments which, if applied correctly, can result in significant improvements in function. Treatments and recovery mechanisms can be identified through systematic and thoughtful clinical practice, use of basic science, and comprehensive data analysis. With better science applied and more training of clinicians, significant improvement in function is likely. Recovery and improvement can be measured with the appropriate tools and methods. In order to accomplish meaningful recovery, however, medical intervention should be an integral component of autism support services, which also include specialized education, traditional therapies like speech and OT, innovative neural systems challenge approaches, accommodations, and life choice opportunities (housing, employment, recreation).

Strategic goal: expand therapy and treatment options for all individuals with autism and identify the most effective intervention modalities and regimens in current use.

Comments on Specific Research Questions.

I. WHEN SHOULD I BE CONCERNED?: Regression is only offered as an afterthought and the growth in autism prevalence "explained" as an improvement in diagnosis. Regression is a reality that must be recognized and used in the development of sensitive screening tools to detect subtle development differences to better support epidemiology and risk factor studies. Additionally, inclusion of data from the CDC 2007 surveillance study confirming that existing screening tools are not adequately used by pediatricians at "well baby" check-ups, as recommended by the American Academy of Pediatrics, in effectively screening and subsequently diagnosing children would more accurately describe screening issues to date. Use of these well care screenings with development and use of measurable biomarkers will allow families earlier access to early intervention by 24 months for improved long-term outcomes.

II. HOW CAN I UNDERSTAND WHAT IS HAPPENING?: Use of existing scientific data on medical conditions, such as motor and sensory problems, seizures, metabolic abnormalities, gastrointestinal pathology, mitochondrial dysfunction, inflammation and cognitive disabilities that accompany ASD is nonexistent the this plan (Valicenti-McDermott, Pardo, et al, 2005). Recognition of inquiries underway, such as those by Autism Treatment network (ATN) documenting medical features in 15 academic centers, and need for understanding early medical trajectories are necessary, as well as comparison of ASD individuals to their typical counterparts, to better assess physical and developmental differences to improve outcomes. Also absent in is the need for analyses of genetic interaction with environmental exposures. Multi-disciplinary, longitudinal, biobehavioral studies of children, beginning in infancy, characterizing neurodevelopmental and medical trajectories of development across the multiple axes of ASD phenotypes are necessary in order to identify ASD risk factors, subgroups, and potential biological targets for intervention. Children must be intensively studied during the process of development of the disorder and during phases of regressions in order to fully understand the precise developmental and biological mechanism of this disorder. Such intensive study will include some in-patient time, multiple and repeated neurological, biological, and imaging studies, and the repeated collection of biological and tissue samples.

III. WHAT CAUSED THIS TO HAPPEN AND CAN THIS BE PREVENTED?: The draft is biased toward prenatal onset and should recognize the likelihood of multiple trajectories in autism, including postnatal onset,

regression and postnatal influences. Detection should extend to a continuum of time points, and trajectory research should include an understanding of the biology underlying disease/symptom onset.

Historically, the leading priority for autism research funded by NIH has been placed on genetic research, which has yielded no reproducible results, while other research has identified a cause in "rare cases" and there is a growing body of anecdotal evidence of recovery. "Rare" and anecdotal evidence of recovery are not leveraged in this plan, or use these cases as a starting point for new research initiatives. Due to this lower priority, research on environmental risk factors is less well developed. Wording should be revised to recognize the innovative and novel approaches currently in place, or being developed by the field. The current wording suggests that cutting edge developments are only occurring in the area of genetics.

The most frequently cited environmental toxin is mercury. Numerous studies that indicate a potential role for mercury exposure in autism (Palmer et al, 2006 and 2008, Windham et al, 2006, DeSoto & Hitlan 2008, Holmes et al, 2003, Austin, 2008, Young, 2008), a finding that receives support in animal studies as well (Hornig et al, 2004, Laurente et al 2007). The draft must specifically include vaccine research as this is the only specific research topic addressed in the legislative history of the CAA and the intent of Congress. The document should reference the known shortfalls of the epidemiological studies commonly cited to rule out vaccines in autism and state that the issue is open.

Environmental research in ASD must build on the substantial pre-existing environmental research infrastructure and informatics, as risk factors are likely to be pertinent to both brain development and chronic systemic features, such as inflammation and oxidative stress (James 2004), in subgroups of ASD.

IV. WHICH TREATMENTS AND INTERVENTIONS WILL HELP?: This section must encompass accumulating evidence suggesting that the breadth of this disorder extends well beyond the behavioral diagnosis with multiple systemic issues influencing vulnerability, onset and severity of symptoms and behaviors. Care models like those of the ATN support the possibility that both the core behaviors and medical issues have a convergent mechanistic basis that, if identified, could provide new insights into treatment targets, candidate genes, and strategies for prevention. Large-scale multidisciplinary RCTs to develop and test the efficacy of comprehensive interventions will identify which elements are most effective in reducing or ameliorating symptoms for which children and should be fast tracked to facilitate translational treatment research.

Obstacles to conducting treatment research, such as the review process, need to be addressed. An increase in improved research designs are needed that consider subgroups of responders versus the aggregate treatment response with recognition that treatment response can inform phenotype studies. Shared treatment databases will move the field forward.

<u>Critical Flaws in the Planning Process</u>.

Without major revision, anything approved by IACC may be subject to legal challenge and a restart of the process. Some of the more serious flaws in the development of the SP include: appointment of Joyce Chung, wife of legendary epidemic-denier Roy Grinker, as head of the Autism Team; members of science workshops and workgroups were not appointed by IACC, the IACC community members were prohibited from collaborating outside formal meetings; secret email voting and discussions; "public" comments not made

public; refusal to provide background information necessary to formulate the plan; community input was ignored; selection of workshop and workgroup members with disqualifying bias and lack of diversity; abrogation of IACC's obligation to make key decisions to an internal bureaucracy; and "community" participation in making crucial decisions regarding funding priorities and specific initiatives was limited to organizations and interests that privately fund autism research (especially relating to genetics). Genetics was over-represented while several relevant fields were underrepresented at the science workshops, including immunology, virology, gastroenterology, toxicology, and clinical care. The second workgroup was arbitrarily terminated although it stated its desire to complete and extend its work. "Gap" initiatives were submitted but not circulated to the full IACC for review and basically ignored by the Autism Team. In particular, there was a systematic effort to exclude vaccine-specific research despite repeated public comment and community support that such research was absolutely necessary.

The inclusion of the broader autism community during this process has been severely limited, with consensus from town meetings regarding mercury and vaccines ignored and absent in research objectives. Individuals with autism, their families, their teachers and their caregivers have insights and perspectives needed to inform research design and evaluation and must be integral to this process. Dismissive wording when referring to parent observations should be removed. The final draft of the SP should include an analysis of the cost of disease, recognize the serious increase in prevalence, and calculate the social ROI for the SP initiatives.

The Research Budget Must Be Significantly Increased to Respond to Both Crisis and Opportunity.

CAA tasked IACC to "develop and annually update a strategic plan for the conduct of, and support for, autism spectrum disorder research, including proposed budgetary requirements, and submit to the Congress such strategic plan and any updates to such plan." 42 U.S.C. 280i-2(b)(5), (6). The Senate HELP Committee report (S. Rep. No. 109-318, emphasis added) was quite specific[4] in the reason for and expected contents of this autism research budget: "To increase the accountability and focus on autism spectrum disorder at the National

[4] Rather than simply a listing of interesting studies, Congress required rigorous analysis of past achievements and future priorities in the SP: "Further, in crafting the specific strategic plan, the committee encourages the director to:

> Determine and establish priorities among critical scientific questions related to autism spectrum disorder;
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> Specify the short and long-range objectives to be achieved, and estimate the resources needed to achieve these objectives;
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> Evaluate the sufficiency of existing research programs on autism spectrum disorder to meet the specified objectives and establish objectives, timelines, and criteria for evaluating future research programs; and
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> Make recommendations for changes to existing research programs on autism spectrum disorder, including potential consolidation of research activities if such consolidation would improve program efficiencies and outcomes."
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> S. Rep. 109-318 at 13.

Institutes of Health (NIH), the committee specifically authorizes a strategic plan related to autism spectrum disorder. In requiring the Director of the NIH to develop a strategic plan for autism spectrum disorder, the committee wants to ensure that this plan provides not only an outline of key research activities and questions but also ties those activities to specific budgetary outlays to improve the transparency of the planning process… In reporting on the expected spending and providing an analysis of what was previously expended, the committee strongly encourages the director to provide such dollar amounts using clear and consistent methods for determining the monetary allocation."

Despite this clear requirement,[5] the NIMH has repeatedly claimed "there is no new money" and forbidden both the science panels and workgroups from addressing budget requirements. The July 1 draft contained no budget information. Ultimately, the third workgroup proposed budgets for each of the 35 initiatives but these figures were fairly arbitrary and not the product of rigorous analysis, especially given the general nature of many of the initiatives. Arbitrary limits were placed on the number of studies undertaken under each of the initiatives by the workshop chairs and/or the Autism Team. These limitations are severe in light of the crisis of autism and the opportunity to perform good science.

The draft budget released after the September 9th meeting of the third workgroup is woefully inadequate as a response to the challenges and opportunities of the autism epidemic. Although initially reluctant, the Autism Team eventually accepted the requirement in the CAA that it provide a research budget as part of the SP. How much should be spent on autism research? The answer is simple: as much money as is needed to effectively treat existing cases and prevent new ones. Given the enormous direct and indirect financial burden of autism on society, now growing exponentially, a "cost of disease" analysis should be performed and included in the plan to determine how much "should" be spent. This is the same general analysis used to "justify" each new vaccine in terms of the "benefits" of preventing an infectious disease and must be similarly used in the creation of a plan addressing the autism crisis. The budget must also consider the demand from the scientific community for funding for autism-related research. Such an analysis would require, at a minimum, a review of proposals submitted to NIH during recent years that were not funded due to lack of money. This information was requested but never provided to IACC.

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[5] In doubling the President's budget proposal for FY09 autism spending, Senator Dodd explained: "It continues to be a challenge to determine how much Federal funding is actually going to study the causes of and treatments for autism. In fact, some estimates are that actual NIH funding for research specific to autism is less than half of what is being reported. That is why this amendment is so critical. It will redouble our Federal commitment to funding autism, the fastest-growing developmental disability in the U.S. At a time when the number of children and families living with autism has grown exponentially, the President's budget proposes to freeze Federal spending on autism at levels that are insufficient to make the kind of discoveries in autism that are needed. . . . There are so many unanswered questions about autism. And it will require a major scale-up in funding to bring us closer to answering them. We should close no doors on promising avenues of research into the causes of autism and my amendment allows all biomedical research opportunities on autism to be pursued. The amendment I am offering would enable us to redouble our efforts on autism research and treatment services by increasing funding for research, treatments, education and interventions by $197 million in fiscal year 2009 and I urge my colleagues to support the amendment. Again, I emphasize it is the fastest growing developmental disability in our country. The number of children who will be born with autism is increasing every day in this country." 154 Cong. Rec. S1971 (March 12, 2008).

For example, and to illustrate the inadequacy of the funding, five projects relating to environmental cause are proposed for the next five years at a funding level of $24 million. Why limit these studies to only five, none of which specifically mentions vaccines? The plan should propose as many as are needed to identify the pre-natal and post-natal exposures that trigger ASD without arbitrary limits. The budget proposes a handful of treatment studies and clinical trials over five years and in doing so falls far short of studying the effectiveness of the dozens of behavioral and medical interventions currently used by parents. It's difficult to have confidence in NIH's treatment research agenda in light of the recent cancellation of a clinical trial on the books for two years and then dropped for safety reasons. The fact that thousands of parents are using various forms of chelation with success more than justifies rigorous study of this intervention, particularly if there are legitimate safety concerns.

Notwithstanding the above comments on the need for a significantly increased research budget for ASD with a comprehensive justification, Safeminds has proposed modifications to the research budget within its current format and constraints (reserving our objections) for the guidance of IACC in achieving the best possible allocation of available resources. These budget recommendations and suggested changes in the initiatives are set forth in the accompanying spreadsheet.

The SP Must Specifically Research Vaccines as a Potential Cause of Autism:

The CAA specifically listed 13 scientific fields that should be included in the research plan: pathology, developmental neurobiology, genetics, epigenetics, pharmacology, nutrition, immunology, neuroimmunology, neurobehavioral development, endocrinology, gastroenterology, and toxicology. Both House[6] and Senate[7] legislative history singled out a single research opportunity, vaccines, transcending many of these fields. Considerable public input (from the January request for written comments, following the IACC March 14 request to fill any "gaps," and the May 3 town hall meeting in Sacramento) insisted that the research agenda

[6] House Chairman Barton added: "With respect to possible environmental or external causes of autism, some have suggested a link exists between autism and childhood vaccines. . . . I recognize that there is much that we do not know about the biological pathways and origins of this disorder, and that further investigation into all possible causes of autism is needed. This legislation is not designed to predetermine the outcome of scientific research. Rather, the legislation rightfully calls for renewed efforts to study all possible causes of autism-including vaccines and other environmental causes. Simply put, we should leave no stone unturned in our efforts to find a cure, whether it means exploring possible environmental factors, paternal age, genetic factors, or any other factors that may hold answers." 152 Cong. Rec. H8787 (December 6, 2006).

[7] Senate HELP Committee Chairman Enzi explained that the CAA research mandate as: "the bill reported by the HELP Committee contemplates key research activities, including environmental research, that focus on a broad range of potential contributing factors, with meaningful public involvement and advice in setting the research agenda. However, I want to be clear that, for the purposes of biomedical research, no research avenue should be eliminated, including biomedical research examining potential links between vaccines, vaccine components, and autism spectrum disorder. . . . No stone should remain unturned in trying to learn more about this baffling disorder, especially given how little we know." 152 Cong. Rec. S8772 (Aug. 6, 2006).

must include vaccines. However, none of the 41 (revised down to 35) broad initiatives under consideration even mentions this topic.

The SP must not be ruled by implicit censorship or fear,[8] but by a sincere commitment to use science to uncover the truth about vaccines and autism. The need for vaccine-autism research is particularly urgent, especially a comprehensive retrospective and prospective comparison of the health outcomes of vaccinated versus unvaccinated children. The present vaccine schedule must be regarded as experimental because its safety with respect to chronic disease has never been validated by a customary double-blinded randomized clinical trial in either an animal or human population. CDC's comment at the July 15 IACC meeting that the science is all "done" and there is no connection between vaccines and autism is disingenuous, as the safety research has never been done, and there is no follow up for safety beyond 3-6 week is in existing "safety" studies. Whether the burden of chronic vaccine-caused disease, including autism, exceeds the benefits of preventable infectious disease is simply unknown. Dr. Insel's comment that a separate section on vaccine research in the plan would call too much attention to the issue is compelling evidence that vaccine research will not be done under the general rubric of "environmental" research unless it has a specific set of research initiatives.

Mounting evidence from animal models, especially results presented at the preeminent autism scientific conference IMFAR in May, suggests the expanded schedule is unsafe. That pilot study showed significant neurological impairments and bowel disease in vaccinated macaques versus unvaccinated controls. Even the Institute of Medicine has left open the possibility that vaccines could cause autism in a genetically susceptible population.[9] The lead author of the only US epidemiological study relied upon by IOM published a retraction[10] of any "no causation" inference, and called for further research. In addition to the studies cited in the "gap"

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[8] Former NIH Director Bernadine Healy explained in a May 12 CBS News interview: "I think that the public health officials have been too quick to dismiss the hypothesis as irrational, . . . There is a completely expressed concern that they don't want to pursue a hypothesis because that hypothesis could be damaging to the public health community at large by scaring people. First of all, I think the public's smarter than that. The public values vaccines. But more importantly, I don't think you should ever turn your back on any scientific hypothesis because you're afraid of what it might show. . . . What we're seeing in the bulk of the population: vaccines are safe. But there may be this susceptible group. The fact that there is concern, that you don't want to know that susceptible group is a real disappointment to me. If you know that susceptible group, you can save those children. If you turn your back on the notion that there is a susceptible group… what can I say?"

[9] Determining causality with population-based methods such as epidemiological analyses requires either a well-defined at-risk population or a large effect in the general population. Absent biomarkers, well-defined risk factors, or large effect sizes, the committee cannot rule out, based on the epidemiological evidence, the possibility that vaccines contribute to autism in some small subset or very unusual circumstances. However, there is currently no evidence to support this hypothesis either." IOM, Vaccines and Autism at 11 (2004).

[10] "The article does not state that we found evidence against an association, as a negative study would. It does state, on the contrary, that additional study is recommended, which is the conclusion to which a neutral study must come. . . . A neutral study carries a very distinct message: the investigators could neither confirm nor exclude an association, and therefore more study is required. . . . The bottom line is and has always been the same: an association between thimerosal and neurological outcomes could neither be confirmed nor refuted, and therefore, more study is required." Pediatrics, 2004;113;932.

initiative for vaccine-specific research submitted in March, recent studies (Austin, 2008, Young, 2008) continue to point to a growing consensus that vaccines play a role in the etiology of autism.

The SP Must Include Specific Opportunities for Public Participation.

There must be community involvement in decisions relating to both scientific merit and programmatic relevance, a model used very successfully (encouraged and ratified by the IOM) for the newly-funded Congressionally Directed Medical Research Program for Autism.[11] Adherence to the six "values" adopted by IACC (Sense of Urgency, Spirit of Collaboration, Consumer-focused, Scientific Excellence, Partnerships in Action, and Accountability) requires significant community participation at each stage of funding decisions as well as structural reform to ensure that the "scientific excellence" will actually achieve measurable benefits in finding the cause, prevention, treatment, services, and supports for autism.

The SP Should Re-Engineer the Funding Process to Ensure Transparency and Accountability.

The CAA specifically directed IACC to "make recommendations to the Secretary regarding public participation in decisions relating to autism spectrum disorder." 42 U.S.C. 280i-2(b)(4). Funding must be re-prioritized to place greater emphasis on environmental factors as potential causes and modifiers and on treatments. IACC's review of progress in achieving the goals of the autism roadmap concluded that these areas in particular had been underfunded. Greater reliance must be placed on RFA's (with specific monetary allocations)[12] with review by special emphasis panels (as opposed to the more generalized study section review of R01 grants)[13] to ensure

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[11] http://cdmrp.army.mil/arp/default.htm. The CDMRP includes consumer input at the beginning of the annual planning cycle and during both levels of proposal review, scientific merit and program relevance, explaining: "Consumer advocates participate in setting CDMRP priorities and making funding decisions. Consumer advocates' firsthand and personal experiences with a disease provide a unique perspective that complements scientific expertise during proposal review. The Consumer perspective increases awareness of the human side of research and how it impacts survivors. Funding decisions incorporate the concerns and needs of patients, treating clinicians, and survivors, their families, and communities. Conversely, scientists impart a new understanding of the research community to the Consumers on the review panels. The mutually beneficial partnership between Consumers and scientists is a valuable aspect of the peer and programmatic review process at the CDMRP. Through 2007, Consumers have participated in more than 1,700 peer review opportunities." Strong consumer participation was recommended by the Institute of Medicine and reviewed with approval. See IOM, Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command, National Academy Press, 1993; IOM, A Review of the Department of Defense's Program for Breast Cancer Research, National Academy Press, 1997, McCaughan, S., The DOD Congressionally Directed Medical Research Program: Innovation in the Federal Funding of Biomedical Research, Clinical Cancer Research, 8:957-62 (April, 2001).

[12] Most recently used by CDC on June 12 to award 2008-R-VAC01, Associations of Vaccine Adverse Events and Human Genetic Variations, 2008-R-VAC01. NIH announced Research to Advance Vaccine Safety (PA-08-256) [http://grants.nih.gov/grants/guide/pa-files/PA-08-256.html].

[13] http://cdmrp.army.mil/arp/default.htm. The CDMRP includes consumer input at the beginning of the annual planning cycle and during both levels of proposal review, scientific merit and program relevance, explaining: "Consumer advocates participate in setting CDMRP priorities and making funding decisions.

that crucial scientific questions of greatest urgency and impact are matched with the funding and talent to get answers as quickly as possible.

The SP Should Include the Establishment of an Autism Advisory Board.

The SP should establish an Autism Advisory Board composed of scientists, clinicians, and advocates. This would not in any way duplicate the work of the IACC, which is broadly concerned with coordinating all federal activities relating to autism, including critical activities related to services. Rather the AAB would be concerned with the narrower scientific research agenda and the ongoing CAA mandate to annually measure performance of and update the SP. Both the House[14] and the Senate[15] recognized the usefulness of an AAB in the legislative history for the IACC. The experience of convening scientific workshops and two different workgroups this spring highlights the need for an ongoing body that brings together these three crucial sources of advice.

Consumer advocates' firsthand and personal experiences with a disease provide a unique perspective that complements scientific expertise during proposal review. The Consumer perspective increases awareness of the human side of research and how it impacts survivors. Funding decisions incorporate the concerns and needs of patients, treating clinicians, and survivors, their families, and communities. Conversely, scientists impart a new understanding of the research community to the Consumers on the review panels. The mutually beneficial partnership between Consumers and scientists is a valuable aspect of the peer and programmatic review process at the CDMRP. Through 2007, Consumers have participated in more than 1,700 peer review opportunities." Strong consumer participation was recommended by the Institute of Medicine and reviewed with approval. See IOM, Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command, National Academy Press, 1993; IOM, A Review of the Department of Defense's Program for Breast Cancer Research, National Academy Press, 1997, McCaughan, S., The DOD Congressionally Directed Medical Research Program: Innovation in the Federal Funding of Biomedical Research, Clinical Cancer Research, 8:957-62 (April, 2001).

[14] Chairman Barton explained: "The IACC has been tasked with making recommendations to the Secretary regarding the public participation in decisions relating to autism. For instance, the committee notes that the IACC may recommend providing other formal mechanisms, such as an Autism Advisory Board, to provide public feedback and interaction. Further, the Secretary may opt to provide such a mechanism under existing statutory authority, without the recommendation of the IACC. Public participation, especially among the parents and families of those affected by autism, is necessary to emphasize the human side of autism research and to ensure that Federal resources are used wisely. 152 Cong. Rec. H8787 (December 6, 2006)."

[15] "The committee further re-examined the Interagency Autism Coordinating Committee (IACC). In particular, the committee wanted to increase the amount of public participation (from two individuals) to at least six. In addition, the IACC has been tasked to make recommendations to the Secretary regarding the public participation in decisions relating to autism spectrum disorder. For instance, the committee notes that the IACC may recommend providing other, additional, formal mechanisms, such as an Autism Advisory Board, to provide additional public feedback and interaction. Further, the Secretary may opt to provide such a mechanism without the recommendation of the IACC." S. Rep. 109-318 at 17.

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In closing, considering the numerous deficits within the plan, as well as the process, expressed herein, we request that a meeting of the IACC be convened in October to address these issues. We feel strongly that this additional meeting of the IACC is justified, as it would be impossible for these concerns to be adequately addressed at the IACC's regularly scheduled meeting in November.

Sincerely,

Theresa K. Wrangham,
President