Interagency Autism Coordinating Committee (IACC) Scientific Workshop Panel Three Conference Call

Strategic Plan Question III: "What Caused This to Happen and Can It Be Prevented?"

Wednesday, September 23, 2009

Call Participants: Dr. Story Landis (Co-Chair) and Mr. Lee Grossmann (Co-Chair); Panelists: Dr. Robin Hansen, Dr. Craig Newschaffer, Dr. Lars Perner and Mr. Jeffrey Sell; Dr. Della Hann and Dr. Susan Daniels (Office of Autism Research Coordination Staff)

Notes:

Dr. Story Landis, co-chair, began by inviting the panel to discuss the draft presentation, as well as the additional material distributed by Mr. Grossman and Dr. Swedo. The panelists opted to discuss Mr. Grossman's and Dr. Swedo's comments in the context of the gaps or opportunities to which they correspond, rather than address them individually.

In discussion of Gap #1[*] (taking into account ASD heterogeneity to identify risk factors), the Panel stated that more detail would be important. Dr. Newschaffer commented that he is aware of a number of studies that are already invested in phenotype measurements aimed at parsing out heterogeneity in ASD, but wondered whether the ongoing research in this area is adequate, or if the area remains a gap in light of ARRA. During the ensuing discussion, the panelists agreed that without known research results, the topic should be considered a gap. The Panel also added that under Gap #1, the slide presenter should note the need for some type of centralized coordination of research projects related to risk factors to enable crosstalk between research groups working on this topic. Though this concept is relevant to Gap #5 (integration of clinical research studies), the Panel decided that Gap #1 was the appropriate place for its inclusion.

In discussion of Gap #2 (factors that influence heterogeneity and identification of ASD subtypes), Dr. Newschaffer identified a lack of mechanisms for developing new models of identifying heterogeneity. In discussion on how to represent this, and its relevance to Question III of the Strategic Plan, the panelists agreed that this point can be presented to the Scientific Workshop though the oral portion of the presentation, but not necessarily be specified on the slides. The panel also decided to add a bullet to Gap #2 that focused on the observation of clinical ASD subtypes, examination of their shared environmental or genetic risk factors, and their co-occurring medical conditions.

The panel moved to discussing Gap #3 (assessment of vaccines as a risk factor). In reviewing the third bullet (measurement of immunological responses to vaccination), the panelists debated if the suggestions of Mr. Grossman (point #2 and #3 of the distributed document) were appropriate to collapse into this bullet. Dr. Newschaffer noted that Gap #3, Bullet #3 could be a detail associated with Gap #3, Bullet #2 (strategies to identify susceptible groups). Dr. Hansen commented that Gap #3; Bullet #3 should be expanded to include a systematic approach to measuring response to vaccinations,

[*] The numbering convention is based on the version of the slide presentation distributed by Dr. Landis immediately prior to this phone call.

including measurements of immunological, developmental and behavioral responses. The panel agreed to adjust the language to reflect Dr. Hansen's comments, and to ensure that the bullet does not focus specifically on high-risk populations, such as younger siblings of people with ASD.

Mr. Grossman commented that he would like to see the research go further by following identification of high risk children with a standardized protocol involving changes in the vaccine schedule that would be protect those children from potential adverse effects. Dr. Hansen added, however, that since the relationship between autism and vaccines is not clear, one must also consider the potential risk that changes in the vaccine schedule could worsen health for high risk children. She said that the causes of the high risk status need to be determined before it is determined what environmental factors may need to be changed. Dr. Newschaffer noted that performing this type of research is premature at this point, as these high-risk subgroups still need to be identified. The Panel also recommended adding a bullet to the Gap #3 Opportunities that addresses the active, prospective identification of risk factors that may predispose children to sensitivity or adverse reactions to vaccines. The panel recommended noting the need for research on alternative vaccination schedules as being a point of disagreement within the panel. While some panelists felt that this topic needs immediate research, others felt that without a larger evidence base, the research, as it relates to autism, is premature.

During the Panel discussion of Gap 3, Bullet #1 (studies of vaccinated versus unvaccinated children), Dr. Newschaffer noted that comparisons are important and there are upcoming studies that will soon begin to collect data on vaccination. He added that this topic appropriately belongs in the realm of vaccine safety research or a public health surveillance effort, and that such efforts could include neurodevelopmental endpoints such as autism. Dr. Newschaffer did not recommend changing the current bullet, but rather than proposing development of new studies, that the focus should be using the data that is currently or soon to be collected on vaccinations to build an evidence base that can guide where the field needs to go with respect to autism. He said that the focus of studies should remain on identification of susceptible groups. The Panel raised the issue of who will track the collection and coordination of the analysis of these data. Mr. Sell commented that addressing this question using retrospective studies will yield quicker results than the prospective fashion described by Dr. Newschaffer, and he recommended listing vaccinated vs. unvaccinated studies as a gap. As the Panel did not reach consensus on this issue, Dr. Landis agreed to modify to the bullet to include Dr. Newschaffer's comments, and to bring this issue before the Scientific Workshop for discussion.

The Panel turned to discussing Gap #4 (identification of factors that are protective and/or confer resilience). During its discussion, the Panel agreed that identification of protective factors represented the inverse of identifying risk factors, and when stated as such, is currently being addressed. The Panel decided to remove Gap #4 and its corresponding opportunity, but to mention the idea of resilience in the oral presentation.

The panelists debated Gap #5 (comparing and combining clinical research data). Dr. Hansen added the word "sufficient" to Gap #5, Bullet #1, to read "Research community lack *sufficient* common data elements, collection forms and measures." The Panel commented that one way to accomplish this scale

of information exchange is to conduct meetings that can generate common data points, but wanted to keep the content of the bullets as written.

Under the discussion of Gap #6 (efforts to translate risk factors into prevention strategies), Dr. Newschaffer noted that there is a need to facilitate earlier replication of novel study findings. The Panel decided to include the need for replication under the Gap section, and its subsequent translation into new knowledge in the Research Opportunities section of Question III.

The Panel thought the opportunities associated with Gaps #1 and #2 were well-articulated and should remain. The panelists also recommended that the opportunities for Gap #3 be expanded to include a bullet about how the data on vaccine risk is being collected, which would create a link to the new ideas on public health surveillance added to Gap #3 earlier in the phone call.

While discussing the opportunities associated with Gap #5 (comparing and combining clinical research data), the Panel debated the suggestion made by Dr. Swedo, to prioritize the augmentation of existing longitudinal studies to ensure that they capture all variables of interest (including full clinical phenotyping in genetic studies, the banking of biomedical specimens as well as DNA, and an adequate assessment of environmental exposures and response to vaccinations in the younger sibling studies). Mr. Grossman mentioned that the suggestion he had distributed was broader in scope, but the Panel should decide on how to proceed. Dr. Landis indicated that she would incorporate these ideas into the bullets and distribute to the Panel for their comments.

Dr. Newschaffer raised several issues that included the development of research methods to identify novel environmental risk factors, status updates on the collection and storage of biosamples, and the modification of large-scale genetic studies to include a gene-by-environment component. In response to these issues, Dr. Landis commented that before there is research that can identify novel environmental risk factors, there need to be validated collection methods that can retrospectively assess environmental exposures. Both the National Institute of Environmental Health and Safety (NIEHS) and the National Toxicology Center also maintain lists of toxicants that can influence pre- and post-natal development. Dr. Landis also informed the Panel that the collection of biosamples and maintenance of biobanks falls under the purview of Question II of the Strategic Plan, and that while the major barrier the Panel encountered was having complete information with regard to currently funded projects because of the unavailability of ARRA data. Dr. Landis, however, reminded the panel that this workshop activity will be an annual event, providing ongoing opportunities to evaluate progress on the plan.

The panelists nominated Dr. Susan Swedo and Mr. Jeffery Sell to present the panel's slide presentation at the Scientific Workshop, and that they can decide how they would like to divide their responsibilities for the presentation. The Panel also decided to create a list of topics to bring to the attention of other panels.

The meeting closed with thanks to the group for their participation, an encouragement for the Panel to continue to think about issues related to any question of the Strategic Plan, and that all panelists would have an opportunity to share any new ideas at the Scientific Workshop. The Scientific Workshop is

scheduled to take place at the North Bethesda Marriot (Bethesda, MD) on Wednesday, September 30, 2009 and Thursday, October 1, 2009. The Panel 3 discussion will begin at 3:30 p.m. on Wednesday, September 30, 2009.

ACTION ITEMS:

- Submit list of studies collecting vaccine data to Dr. Landis (Craig Newschaffer)
- Revise draft presentation from the meeting summary, create talking points for the oral presentation, and distribute to all panelists (Story Landis)
- Review draft presentation (All Panelists)
- Submit final presentation to Dr. Susan Daniels no later than 12:00 p.m., Monday, September 28, 2009 (Story Landis)
- Panel 3 Slide presenters: Mr. Jeff Sell and Dr. Susan Swedo