U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

FULL COMMITTEE MEETING

TUESDAY, NOVEMBER 10, 2009

The Committee met in Conference Rooms A1/A2 of the Neuroscience Center, 6001 Executive Boulevard in Rockville, Maryland, at 9:00 a.m., Thomas Insel, Chair, presiding.

PRESENT:

THOMAS R. INSEL, M.D., IACC Chair, National Institute of Mental Health

DELLA HANN, Ph.D., IACC Executive Secretary, Office of Autism Research Coordination, National Institute of Mental Health

SUSAN DANIELS, Ph.D., Office of Autism Research Coordination, National Institute of Mental Health

JAMES F. BATTEY, M.D., Ph.D., National Institute on Deafness and Other Communication Disorders

ELLEN W. BLACKWELL, M.S.W., Centers for Medicare and Medicaid Services

CHRIS DeGRAW, M.D., M.P.H., Health Resources and Services Administration (For Dr. Peter van Dyck)

LEE GROSSMAN, Autism Society

PRESENT (continued):

ALAN GUTTMACHER, M.D., National Institutes of Health (For Dr. Francis Collins)

DEBORAH HIRTZ, M.D., National Institute of Neurological Disorders and Stroke (For Dr. Walter Koroshetz)

GAIL R. HOULE, Ph.D., U.S. Department of Education

JENNIFER JOHNSON, Ed.D., Administration for Children and Families

WALTER KOROSHETZ, M.D., National Institute of Neurological Disorders and Stroke

CINDY LAWLER, Ph.D., National Institute of Environmental Health Sciences (For Dr. Linda Birnbaum)

CHRISTINE McKEE, J.D.

LYN REDWOOD, R.N., M.S.N., Coalition for SafeMinds

SUSAN SHURIN, M.D., National Institute for Child Health and Development

ALISON TEPPER SINGER, M.B.A., Autism Science Foundation

ED TREVATHAN, M.D., M.P.H. National Center on Birth Defects and Developmental Disabilities

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PROCEEDINGS

9:00 a.m.

Dr. Insel: Good morning, everyone. Let me welcome you to an extra meeting here of the Interagency Autism Coordinating Committee.

This was a meeting set up at our last opportunity to be together on October 23rd where it became clear that we had a lot more work to do on updating the Strategic Plan. So, we've put in place this special meeting for just that purpose.

Because of the late date for scheduling, there are a few people who are not going to be able to join us from the Committee. So, Henry Claypool will not be with us today. Chris McKee and Jennifer Johnson will both be arriving, but will be here late.

And I think we have most of the other group, except that Stephen Shore who was going to be joining us by phone has had a

personal issue come up and won't be able to do that either. Or if he does, it will be later in the day.

So, let's go around and do a quick round of introductions so those who are listening in can know who's with us today at the table. And I'll start.

This is Tom Insel from NIMH, and I'm chairing the committee.

Dr. Hann: Good morning. I'm Della Hann. I serve as the Acting Director for the Office of Autism Research Coordination and serve as the designated Federal official for this committee.

Dr. Daniels: Hello. I'm Susan Daniels, and I'm the Deputy Director of the Office of Autism Research Coordination in NIMH.

Ms. Blackwell: Ellen Blackwell, Disabled and Elderly Health Programs Group, Centers for Medicare and Medicaid services. I'm also a parent.

Dr. Trevathan: Ed Trevathan. I represent the CDC and direct the National Center on Birth Defects and Developmental Disabilities.

Ms. Singer: Alison Singer. I am the President of the Autism Science Foundation, and also the parent of a 12-year-old daughter with autism. I also have an older brother diagnosed with autism.

Ms. Shurin: Susan Shurin. I'm Acting Director of the National Institute of Child Health and Human Development, and Deputy Director of the National Heart, Lung and Blood Institute.

Dr. Battey: Jim Battey, Director of the National Institute on Deafness and Other communication Disorders.

Dr. DeGraw: Chris DeGraw representing HRSA for Dr. Peter van Dyck.

Dr. Guttmacher: Alan Guttmacher. I'm the Acting Director of the National Human Genome Research Institute at the NIH.

Dr. Insel: So, let me just interrupt for a second because Dr. Guttmacher is new to the Committee.

There's a chair on the Committee for the Director of NIH, and Dr. Zerhouni, I think, came once, Dr. Collins had wanted to be here on a regular basis, but his schedule is just not going to permit it. So, he's asked Dr. Guttmacher to sit in representing the Office of the Director for NIH.

So, Alan, it's a pleasure to have you here.

Dr. Guttmacher: It's nice to be here, Tom. And I think I should say Francis, I think, selected me for this not so much for my acting directorship of NHGRI as that I am a pediatrician and had a long interest in autism actually that predates - and I'm probably the only person around the table who actually knew Leo Kanner who first described autism in 1943.

Ms. Redwood: Hi. Lyn Redwood, Coalition for SafeMinds.

Dr. Lawler: Cindy Lawler representing National Institute of Environmental Health Sciences.

Dr. Koroshetz: Walter Koroshetz, I'm the Deputy at NINDS, and I am a neurologist. And the specialty was in mostly adults, but I was vice-chair of neurology at Mass General and oversaw child neurology as well.

They were pretty much on automatic pilot.

Mr. Grossman: I'm Lee Grossman, President and CEO of the Autism Society and also the dad of a young man with autism.

Dr. Insel: Okay. Well, welcome, everyone. We've got a pretty packed agenda here today. I hope that by the end of the day that we'll have made some of the major decisions about what would go in for updating the plan.

I want to have a conversation in a

few minutes about how we attack this and what the threshold should be for changing the plan. But before we do that, we have two orders of business.

One is we have public comment from now until 9:30, and then we also want to have a chance for you to look at the minutes so that we can get the approval from the October 23rd minutes.

So, let's move into our public comment period and let me ask Susan to get a microphone going. The first public comment I have down here is from Jim Moody.

Mr. Moody: Good morning, Dr. Insel, and members of the Committee. Thank you for the opportunity to give comment.

The Strategic Plan, useful tool or unfulfilled opportunity? The heart of the Combating Autism Act was the Strategic Plan, research, budget and annual updates.

This mechanism was designed to bring rigor and discipline to the process of

expanding and focusing research to achieve the goals of prevention and treating autism.

Epidemic denial has gotten in the way of achieving the primary purposes of this plan. The Plan must include a call upon President Obama to declare a national health emergency for autism.

Autism prevalence has jumped from one in 10,000 during the early 1980s, to one in 91 most recently released in pediatrics during the past three decades. Yet, CDC's official count is still a decade late.

Concerns over adult prevalence and the precise boundaries of autisms must not interfere with the urgent need for identification of environmental triggers so that new cases can be prevented and treatments for existing cases can be implemented.

The families deserve a response on the scale of SARS, lead-poisoned toys, tainted peanuts and spinach and swine flu and a re-engineered process akin to a NASA or the

Manhattan Project.

IACC is still operating on a schedule of years and decades while families need answers now.

High-ranking public officials have bragged recently that they meet on Swine Flu daily. Yet, IACC struggles having more than four meetings a year.

Why not meet weekly, if necessary, and which high-ranking officials can claim that they focus daily on preventing and treating autism?

The plan talks about research on X environmental factors and on Y treatments, but these remained unidentified. How long must the families wait for this research?

The CAA called for increased public participation in decisions relating to autism, yet the small DoD, CDMRP program remains far ahead of this very important goal.

The Senate Report called for an autism advisory board. This also remains

unfulfilled.

A rigorous cost of disease study must be done and compared with demand for competent science to determine how much and how rapidly the autism research budget must be increased.

Take the politics out of vaccine research. Vaccine court began quietly compensating autism cases, many of which are secret decisions, in 1991.

A Merck memo from Maurice Hilleman, the noted vaccinologist, identified vaccine mercury and safer alternatives in 1991. Sir Michael Rutter first published on vaccine-caused autism in a 1994 paper, Wakefield's 1998 case series. And Bernard and colleagues 1999 review of the similarities between autism and mercury poisoning came relatively late to this debate, yet they get all the, quote, blame or credit, as you will.

Do vaccines cause autism? As a matter of science, clinical medicine and law,

the answer is a definite yes. What remains is the body count, how to prevent new cases of vaccine-caused autism, how to treat and compensate the unintended victims of our one-size-fits-all vaccination national experiment.

A comprehensive program of vaccine research was removed and unlawfully deleted from the plan last January supposedly to obtain the expert input from NVAC, the National Vaccine Advisory Committee.

The claim of conflict of interest preventing HHS from funding vaccines because it might help families obtain just compensation for their cases in vaccine court, is baseless.

As perhaps the best proof that fear and politics are being used to defeat sound and necessary science on vaccine safety and our vaccines links to autism.

The only way to end the controversy, not whether, but how many and how future injuries can be prevented, is with the

comprehensive program of IACC-funded vaccine research beginning with an immediate and ongoing comparison of vaccinated and unvaccinated children.

In conclusion, stop the talk and start the cure. Thank you.

Dr. Insel: Thank you.

Paula Durbin-Westby.

Ms. Westby: Am I on? Thank you for this opportunity to comment on updating the IACC Strategic Plan. I'm representing the Autistic Self-Advocacy Network.

My comments on October 23rd focused on ethical issues, concerns about the appropriateness of early intervention and associated research, permissions for acquisition of biological materials and the IACC's recommended budget being skewed severely in favor of research into causes and prevention rather than practical and appropriate intervention such as improvements in educational intervention supports and

services.

I've had an opportunity through IACC Scientific Workshop Panel Process to make some language changes and suggestions that I think should apply throughout the Strategic Plan.

Since I was on Panel 1, when should I be concerned, I will use that section of the 2009 Strategic Plan as an example of changes ASAN would like to see incorporated throughout the entire 2010 Plan.

Many of these changes reflect either more accurate and useful terminology, or more respectful language that does not introduce an undertone of disrespect, fatalism or excess pathologizing of autism.

The first one, anywhere the term "high risk" is used to characterize the likelihood of siblings also being on the autism spectrum, the language should be changed to that "high likelihood" rather than "high risk."

"Abnormal" should be changed to "atypical," as we have done for the Panel 1 final document, I believe, during our last phone call.

Anywhere interventions are mentioned, the use of the qualifier appropriate should be inserted addressing our community's concern about intervention for the sake of intervention, and especially in the light of disregard and dismissal of autistic input into the research process to date.

Rather than "early warning signs," we strongly suggest "early indicators" which is more accurate and does not introduce negative value judgments into identifying indicators of autism or atypical development.

Instead of "symptoms," "characteristics and conditions" are more appropriate since autism is not a disease process, but a neurobiological difference.

The use of the term "and concept of severity" is questionable for several

reasons. First, severity is often contextual over both time and other things like situation and location.

What is being looked at when using the severity criterion, is how observable the autistic characteristic is. Whether or not a characteristic is observable and to what degree does not necessarily correlate with other aspects of the person.

And I'm making a change from my written comments here, if you're following them. We prefer the term "variability," which indicates that both abilities and disabilities can be present in the same person, and that abilities and disabilities can change over time whether permanently or temporarily in the presence of other factors such as external environment. This refers to variability of autistic traits.

Again, the focus needs to be on improving quality of life and not necessarily on reducing autistic traits.

Where the concept of severity if used, it must be tempered with research into autistic strengths and also neutral characteristics, and not just on negative, severe characteristics.

I've made another language change from "pathology" throughout the document to "differences in neurobiology cognition," which is more specific and avoids the concept that all autistic differences are pathological. Many of them are not.

I've rewritten the first section of the Strategic Plan with its three sub-questions under when should I be concerned.

What are the early indicators of ASD rather than what are the early warning signs?

I left the second sub-question the same. Are there typical characteristics that are part of an ASD diagnosis?

And then how much variation is there in characteristics and pattern of

abilities and disabilities over time and depending on context.

In addition, undue focus should not be placed on losing symptoms of autism without qualifying language indicating that the loss could also be due to learning of skills. And certainly should not indicate at this early stage in research, that these research subjects or children have become non-autistic especially in the light of reports that many of the subjects still retain co-occurring symptoms or conditions often found in autistic people such as OCD, anxiety, ADHD, et cetera.

And the public should not be encouraged to think that loss of autistic symptoms means loss of autism.

I've changed the sentence in Panel 1's draft to "Finally, evidence is emerging that some children lose explicit characteristics of ASD."

Although it is not clear whether

that loss of autistic characteristics is permanent throughout the life span or whether it reflects learning skills rather than losing characteristics.

I've reformulated one of the research opportunities to "Inclusion of bioethical and other ethical considerations into the diagnosis and screening process," which could also be used throughout the Strategic Plan, "including, but not limited to consideration of the implications of genetic testing and detection of maternal antibodies."

Maternal antibodies is an emerging area of concern for us which is reflected nowhere in the current plan or suggested revisions, to my knowledge.

NIMH and other grant-making institutions should not fund research that uses or promotes the use of restraints, aversives and seclusion.

There's a growing movement in society away from the use of these measures

reflected in current legislative efforts to ban their use. They're used disproportionately against people with disabilities, including autism and other developmental intellectual and behavioral disabilities.

In no case should researchers applying for grants to study this area of restraints and aversives to further their use or legitimize that use, be allowed access to Federal funds including from private and Federal partnerships.

Research that promotes restraint reduction and elimination should be funded as a high priority in order to keep autistic and people with other disabilities safe.

Research into communication differences must be given higher priority than it was given in the 2009 Strategic Plan. There was a mention of picture exchange communication systems, which does not address the communication needs of everyone on the

spectrum.

It doesn't address the needs of people who use communication technology or systems part time as a supplement to speech and/or writing or the need for systems that are flexible enough to accommodate a wide variety of changing communication needs.

And it does not address the needs of people who use non-symbol and/or non-language-based communication systems.

Every person communicates in some form, but that communication is often not well understood. And to this date, has been under researched.

To separate autistics into verbal and non-verbal categories and leave it at that is to miss a critically important area for research far surpassing in practical importance to the finding of yet another autism gene or maternal antibody.

The need for all autistics to communicate in ways that others can

understand, is crucial for our empowerment, life chances, access to basic needs, and for the chance to engage in reciprocal communication with people who do not easily access our various ways of communicating what do autistics want, ways of communicating that work for us and that allow us to communicate effectively with a wide range of other people.

What do parents of autistic people want? Ways of communicating with us.

A glance at comments online and in news media indicate that more parents are interested in being able to communicate with their autistic children, including adult offspring who are not to be written off in research, than are interested in what genes are responsible for autism.

Finally, in order to accomplish the goal of achieving the best possible outcome for all people on the autism spectrum, autistic adults should be consulted and should participate in all levels and tasks of

research on autism.

We have a perspective that focuses away from questionable cures and elimination of autism, and we should be given a seat on the Interagency Autism Coordinating Committee. Nothing about us without us. Thank you.

Dr. Insel: Thank you. I remind the Committee that all the comments are in your packages, as well as written documents.

Ms. Walker: Good morning. I'm Katherine Walker, mother to seven-year-old Adam who is recovering from PDDNOS. I am a Government Affairs Committee member representing SafeMinds.

Adam has responded tremendously well to toxic metal detoxification and biochemical correction. In other words, we have been cleaning out the toxic heavy metals in his body, and bringing his body's biochemical makeup into balance in order to attempt recovery from regression into PDDNOS.

My husband and I thank God for the

progress Adam has made, and are thankful to all those who have helped us along this long and arduous journey.

I thank the Committee for the opportunity to speak today on the behalf of my family and the families SafeMinds represents.

We offer public comment in hopes that the Committee will respond to the many requests SafeMinds and the autism community have sent the IACC with regard to vaccine safety research and the lack of Federal member support of public members who were outvoted last year on the expansion of investigations of toxins, biomarker and treatment objectives.

Government statements regarding the uncertainty of autism's rise to one in a hundred ignore the growing body of research indicating that not only is the rise real, it is likely that environmental factors are driving the increase in prevalence.

The Strategic Plan must incorporate this data, and respond with

greater urgency in addressing the needs of those with autism.

The word "anecdotal" must be a positive mile marker for the funding of treatment research in discovering which individuals are more likely to respond to one treatment versus another.

Expanding the number of toxins and other environmental factors to be investigated is reasonable to enable much needed understanding of causation, treatment and prevention.

Increasing biomarker and treatment objectives will bring up much closer to these goals. We request these expansions as they reflect the corresponding urgency required of this committee by the community.

Additionally, we remind the Committee that expertise requested by IACC of the National Vaccine Advisory Committee was delivered in July to assist in determining the validity of vaccine objectives removed from

the Strategic Plan and which were inserted in the draft plan document provided by Lee Grossman to the IACC on October 23rd.

As is well known, the NVAC Report made autism-specific recommendations that must now be integrated into the Strategic Plan in accordance with the intent of the Combating Autism Act and the 1986 congressional mandate for safer childhood vaccines which requires research to reduce vaccine-adverse effects.

Former NIH Director Dr. Healy has stated, quote, 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.

Dr. Louis Cooper, a former AAP president, and Dr. Samuel Katz, a former ACIP chair, also recognized the vaccine safety research deficits and wrote in Newsweek, “There has been grossly insufficient investment in research on the safety of

immunization."

Vaccine court has quietly awarded compensation for vaccine injuries resulting in autism since 1991. Over 1300 awards for vaccine injury have been made.

Messaging from this committee should not be that the vaccine-injured are an acceptable collateral damage not worth of investigation.

These two objectives are budgeted at $16 million representing a fraction of the IACC budget. We acknowledge Dr. Lawler's recent statement regarding animal and cell models being the bread and butter for NIEHS in discovering pathways and mechanisms.

We note NVAC has agreed on this point with regard to vaccine research. We appreciate Dr. Insel's recognition during the Committee's last meeting that panel recommendations were not meant to be the sole source used for improving the Strategic Plan as NVAC's expertise was recognized by the full

committee months ago.

Indeed it is unlikely that Panel 3's expertise exceeds that of NVAC since the plan panel was purposely made to be diverse enough to address more than vaccines.

We also acknowledge that Panel 3 members themselves have noted a lack of toxicological expertise and the Panel's inability to fully address other aspects of causation and prevention. We recommend the correction of this oversight in future planning.

With the rise in voluntary unvaccinated populations as noted by NVAC, CDC and the Institute for Vaccine Safety, perceived impediments and ethics are without foundation in terms of conducting a comparative population study for critically needed baseline information on vaccines and their effects.

This is a study former CDC Director, Dr. Julie Gerberding, believed could

be done. Vaccine research as acknowledged by NVAC, will require an array of ongoing studies. Incorporating active recruitment protocols in current studies such as NCS, with commiserate monies to obtain medically-verified vaccine records must also be implemented.

Dr. Duane Alexander estimated the cost for NCS to gather these records, at 28 million.

Additionally, protocols are easily added to assure statistical power and are a wise investment in closing existing vaccine safety research gaps.

In closing, our community expects scientific curiosity to supersede policy concerns as this committee is first and foremost a research committee.

In this committee's acknowledgment of HRSA's conflicts of interest, vaccine research objectives must be independent from vested interests and have independent

oversight.

We have loudly and repeatedly made clear the need for this research, as has the NVAC and numerous members of Congress and public health officials.

Thus, I leave you with a quote from Dr. Albert Einstein. "The world is a dangerous place not because of those who do evil, but because of those who look on and do nothing."

It is now up to this committee to do something. Thank you.

Dr. Insel: Thank you.

Dr. Kerry Lane.

Dr. Lane: Good morning. My name is Dr. Kerry Lane. I'm a board certified anesthesiologist. I practice in West Palm Beach, Florida.

My talk today is entitled "Glutathione Loss by Gliotoxin and Acetaminophen Results in Metal Intoxication and Oxidative Stress Causing Autism."

Acetaminophen toxicity in the liver is well established. One of the known toxic effects of this commonly-used drugs is depletion of the most important antioxidant glutathione.

Disease states like the depletion of glutathione and excessive amounts of oxidized glutathione versus reduced glutathione include diabetes, atherosclerosis, AIDS, Alzheimer's and pregnancy-induced hypertension.

Regressive autism is a condition that has defied a definitive pathobiology to date. The 53 attachments I have enclosed reveal that acetaminophen by exacerbating an already depleted glutathione antioxidant system due to a preexisting condition, triggers autism in the peri-vaccination period by reducing glutathione levels to below a critical level.

Adequate glutathione levels are crucial to the effective functioning of the

metallothionein system.

The metallothionein system is involved in the metabolism of metals, as is glutathione. However, the metallothionein system is especially critical to the metabolism of zinc in the brain.

In states of depleted glutathione and excess oxidized glutathione, free zinc is released in brain cells. This free zinc is toxic to the mitochondria causing cellular hypoxia and a generalized neurological malfunctioning we now recognize as autism.

It appears acetaminophen alone is not enough to cause autism. The comorbid pathobiologies due to the creation of a state of abnormal gastrointestinal biology due to antibiotic administration to the infant, this allows a replacement of the normal GI flora with yeast overgrowth by Candida species and others.

Many yeast and fungi produce micro toxins which have been shown to be

pathological to man and animal alike.

Recent interest has focused on a mycotoxin known as gliotoxin, which has been shown to be immunosuppressive by killing CD4 cells, along with a multitude of other deleterious effects.

Gliotoxin has been shown to form adducts with glutathione essentially removing glutathione from the pool of bioavailable antioxidants. Over 50 percent of Candida species have been shown to produce gliotoxin.

If we envision the sequence of events that results in an undesirable yeast and GI tract causing a depletion of glutathione and generalized oxidative stress followed by vaccination that includes a metal adjuvant, possibly mercury or aluminum, followed by the administration of acetaminophen as an antipyretic to an infant at a critical period of neurodevelopment, we can envision the pathobiology of autism.

The 53 references I have attached

from peer review articles are a roadmap to the above-described pathobiology.

I suggest IACC act with all due haste to make this material public so the autism epidemic can be properly managed.

Additionally, this is directed to the AIDS syndrome which also involves depletion of glutathione. It would seem acetaminophen is inappropriate in this setting, and possibly in most settings. Thank you.

Dr. Insel: Thank you. And final comments are from Dr. Anita Sostek.

Dr. Sostek: Good morning. I'm Anita Miller-Sostek, Vice-President for Scientific Review and Operations at Autism Speaks presenting statement of Autism Speaks on vaccine safety research and the IACC Strategic Plan.

Autism Speaks is the nation's largest autism science and advocacy organization. We are dedicated to funding

global biomedical research into the causes, prevention, treatments and cure for autism, to raising public awareness about autism and its effects on individuals, families and society, and to bringing hope to all who deal with the hardships of this disorder.

Consistent with these purposes, we make the following statement: in enacting the Combating Autism Act, Congress intended that the Federal Government examine potential links between vaccines and autism.

During the Senate debate over the Combating Autism Act, Mike Enzi, Chairman of the Senate Health Education Labor and Pensions Committee, instructed that no research avenue should be eliminated, including biomedical research examining potential links between vaccines, vaccine components and autism spectrum disorder. That was in August of 2006.

In the House, Joe Barton, Chairman of the House Energy and Commerce Committee was

equally clear. The legislation rightfully calls for renewed efforts to study all possible causes of autism, including vaccines and other environmental causes.

The important thing to understand is that there were no preconceived notions contained in this bill. The bill language is clear in that we should follow every avenue that science opens to us in searching for a cure. Also December 2006.

Beyond this clear directive of the Combating Autism Act, Autism Speaks supports rigorous evidence-based scientific research into all aspects of autism for potential causes, including both genetic and environmental factors, to diagnosis and treatments.

As such, we strongly urge that further vaccine safety research be included in the Strategic Plan for autism spectrum disorder research.

Comprehensive good science should

be the standard in all areas studied, and there are aspects of vaccine safety research that have not yet been and should be considered.

It is also essential that all scientific research recommended by the IACC and funded by the NIH be rigorous and evidence-based to engender the trust of the scientific, medical and entire Autism Speaks community.

Without a solid foundation that supports confidence in scientific conclusions, the entire portfolio of scientific research is at risk of losing community support.

Further, vaccine safety research will increase both a level of confidence in the safety of our nation's vaccine program and the rate of participation which is absolutely crucial for the prevention of serious infectious diseases.

Autism Speaks calls on the IACC to consider the importance of evidence-based

science and trust, and to remain true to the critical legislative purpose of the Combating Autism Act, and asks the IACC to include vaccine safety research in the Strategic Plan. Thank you.

Dr. Insel: Thank you, and thanks to all of the members of the public who joined us to provide these comments.

These will be part of the written record of the Committee meeting and will be available just as you have them in your folders now.

We're going to move on with the rest of the agenda. There are a number of issues we need to get to. The first being the approval of minutes from the October 23rd meeting.

Those are also in your packet. If you'll let us know if you have any corrections, revisions, suggestions, Ellen?

Ms. Blackwell: Actually, I did ask for a correction. There's an error on page

10. I asked that the word "person" be substituted for "patient," and the minutes are incorrect.

So, if you guys could just fix that.

Dr. Insel: Other comments or suggestions from the minutes?

Can I have a motion for approval with the one recommended change?

In favor. Opposed. Abstain. They're passed.

Good morning, Chris. Welcome. And we're going to move on then to now talking about the strategies for updating the Strategic Plan.

Before we do this, Della wanted to take you through some of what you have in your packet here.

Dr. Hann: All right. You have a number of materials in your packet, and I just wanted to make you aware of them.

In addition to the oral public

comment that you just heard, the Committee also received a number of written public comments. And those are also in your packets.

You will see that you are provided the line edits for each of the chapters that each of the wonderful liaisons helped us to create. Those are also in your packets for today's discussion.

There is a comment that we received just yesterday from Henry Claypool who was unable to be here today. That is also in your comment to take into consideration.

And then the last two documents I wanted to draw your attention to were materials prepared by my office to try to help show with regard to the recent funding through the American Recovery Act and how the - with that funding, as well as the FY08 funding that we received not only from NIH, but also the other organizations, how that's matching in terms of the objectives.

So, there's actually two packets

of that. One is sort of a short reference, and the other is a little longer with actual titles of projects. So, we just wanted to let you know that that's also available for your consideration.

Dr. Insel: Okay. Let's start on this discussion about updating the Plan. I left our last meeting thinking that it would be worth taking some time at the beginning of this meeting to figure out what it is we're really about here and what we want to do in terms of updating.

So, this is really conversation at 30,000 feet before we get down into the weeds of the actual line edits and the changes. And it may have been useful to have done this at the beginning of the last meeting, but as we talked about it, I thought maybe it would be more helpful to get started to see where this took us, and then to step back with some idea of what the process would be like.

Mindful that we're doing this for

the first time, and we're required by law to do it every year, so what we're really working on here is a process that we will be going through probably every November or every October in subsequent years. So, I want to think with you about what we're trying to accomplish. I'll remind you that if we go back to the original mission statement, that the goal of the Plan was to focus, to coordinate and accelerate high-quality research and discovery.

So, those are the three words that I kept going back to in thinking about the update. Do the changes, do the recommendations help us to focus, do they help us to coordinate and do they help us to accelerate? It's clear that there are many different uses that the Plan will be put to, and maybe each of us coming from a different perspective, sees this as a plan that will do different things.

I think for many of the people at

NIH, this is a plan that was meant to guide the research community. So, what will be important is not only what it says we will be doing, but also what it says we will not be doing. So, sometimes in that case, a few focused objectives are going to be very helpful.

On the other hand, if you're in the realm of advocating for more funding for research, then having a longer list and having very high budget numbers may be more useful. So, there are many, many different purposes that this plan could be put to. Again, I just want to keep us with our focus or with our attention on the mission, because I think the focus, coordination and acceleration have got to be what at the end of the day we ask ourselves whether we've done a better job or a worse job of that.

The annual update as it shows here, is something that we are required to do by law. We use a set of data with which to do

this. And the concept that I think many of us had going into it was that the reason for the update was that we were making rapid progress.

And so, you wanted to do mid-course corrections as new information became available. And that information should be out of the summary of advances, some of it will come from scientific workshops so that we can hear about work that hasn't yet been published, some should be reflected by the portfolio analysis that tells us what we have and have not already funded so that we can be aware of gaps and opportunities, and then also public comment as we've heard this morning, which is an important piece of deciding what may need to be changed in the Plan as we go forward.

In this first year, we deferred a number of issues from January that we simply said we didn't have time to dig into and there were things that we would have to come back to. So, this first update will clearly have

to consider those as well. And we'll have to use this first update to really develop the process that we want to use in subsequent years, and I point this out because the Committee itself may be changing.

It wouldn't be surprising now that we have a new secretary, that she will want to change the membership of the Committee in various ways. And certainly the science will change. There are opportunities in science today that we didn't have a year ago. And we will hear about some of those, I think, in the course of the day. But what will be really important is to stay on top of those so that we have a living document that moves quickly as the science changes, but realizing also that the perspectives that are on the Committee may also change as the membership changes over the next few years.

So, I've tried to find a way to summarize what I think we were struggling with at the last meeting, because I felt there was

a certain tension as we tried to do this. And I'm not sure that I can resolve the tension, but I thought there may be some value in putting it on the table and asking you to think with me about it and decide how we want to do this in the course of the rest of the day.

The first is certainly one around the scope of what we're doing. Are we really just tweaking the Plan, are we rewriting it? What do we mean by an update? I was a little surprised at the end of our last discussion when I went home and I discovered that there were 33 new objectives in a Plan that had only started with about 30 or 35, depending on how you break them up.

So, that felt like more than a tweak. It felt like more than an update. That felt like really changing in a profound way, the objectives that were in the Plan. And the question from that I think people who are using this to guide the scientific

community will have to ask is, is that helpful or hurtful? Is that helping us to focus the scientific community on the high priorities, or is it just going to be confusing and it's going to lead to research community saying these guys don't have any idea what they really want us to do, and so why should we pay attention to it anyway.

It's also probably worth thinking about whether some of the original objectives have been completed or at least have been completely funded in the way that we had intended. And that's the purpose of having this portfolio analysis that Lyn asked for last time. I think it's really going to be important as we look at this plan if in fact of the original 35 or 30 objectives, if 20 of them had been completed in the first seven months, that may be the very best reason for developing a whole new set.

But in the absence of that evidence, I think we may want to ask ourselves

how many more items do we want to put on the agenda. And if we're putting new items on, how do we prioritize the list? How do we communicate to people that this is the first thing that needs to be done? I think the most difficult piece of this will be if we have an ever growing laundry list of objectives, it will become very difficult for the funders to decide what should be left out in funding so that they can use whatever dollars are available to prioritize to the highest level those objectives we most want.

The other thing that will come up, and it came up last time, and I think it will come up today again, and we heard this a bit even in the public comment already, is what we want in these objectives, how much do we want to specify.

I think we used the example last time that we don't specify the actual genes we want people to study who are doing whole genome association or Candidate gene studies,

do we want to specify which environmental factors or which therapeutics or which interventions of various sorts we expect people to pursue, or do we want to stay for the Plan, at a broader level and expect the scientific community to come up with the very best, we'll say, small-grain projects, the projects that actually go after deciding which Candidate gene or which intervention are the ones that needs to be followed. So, the Plan here could be to say the five RCTs, five randomized clinical trials in adults, without having to say trials that do the following things.

This is just really a question that I'd love to hear the Committee's thoughts about. The other question that will come up, and we heard this a little bit last time, is this sort of boundary between what is science and what is service. And you'll see this - when we originally did the Plan, the values that we talked about were discovery,

scientific excellence, but we also noted that we needed to be consumer focused and we needed to have an emphasis on urgency. So, that was part of the tension.

There's also this comment that we made originally that I think we need to keep in the forefront of the conversation today, and that was that we wanted our objectives to be accountable. And we use this metric of SMART, Specific Measurable Achievable Realistic and Time-bound. Those are acronyms that one would only expect to find in the government, but actually I think that particular acronym came to us from outside. But if we are looking for objectives that can be accountable, I want us to make sure that we are using the right language and the right kind of framing of the goals so that in fact we'll know when we've done it.

There are certain pieces that have come into the Plan and the update that I think we just need to talk about. The use of

demonstration projects is usually outside of what research agencies do. And whether that is research or services, I'd love to hear the Committee's thought about that. It's certainly conceivable that a large part of what's in here, including some of the things that have come into the update, could inform a different sort of plan that would really be focused on the needs for services, and better and different services, that could be quite separate from a plan that's more discovery-based and more focused on research, including services research.

So, I'll leave it at that. I really only wanted to introduce the issues and not resolve them. But I do want to get a sense from the Committee before we jump into the details here, about what I'll call basically the threshold for what you think will be worth including in an update.

What we've done up until now is to scan the community, scan the portfolios, get

lots of public input, but now is where the rubber hits the road. You could decide not to do anything different than what we had in January. You could decide to completely scrap what we had in January and start over.

What I'm asking is for what we've received from the various inputs that we've had, where do you want to set the bar for making a change in the 2010 plan?

Dr. Koroshetz: I could throw a comment out and maybe ask people who have done strategic plans before for other organizations, the - I think the responsibility when you put a strategic plan together is - the next responsibility is not to rewrite it, but to evaluate it to know what got done, what didn't get done. Potentially, what should be dropped and what should be added. And those - that, I think, is the core. And I think as you go out past that, you diffuse the messages and I think you become less effective with your plan.

So, I mean if you're running a business, you do a strategic plan, you want that strategic plan to then work and be effective so the next year it's not rewriting a strategic plan, it's like all right, this is what we said we wanted to do, what did we get done, all right, that's the problem, how do we solve the problem.

So, I think that's generally in a business you focus after, you know, you may do another one five or ten years when things change, but I think people who rewrite strategic plans every year don't - their organizations don't go anywhere. They just poop out.

So, I would urge being focused and being self-critical about what we put in and what happened, were we naive or did we hit a roadblock that needs to be moved through and get kind of more kind of into the progress as opposed to - otherwise it gets to be a political document and not a research

document.

I think Tom was getting at that, that different people have different purposes. So, that's something that you got to be honest with. What is it that you want?

I think the NIH people are going to want -- and the government people are interested in finding treatments, and that's a hard-nosed, grind-it-out, Boston Celtic-type defense. And that's what I think I would like to be involved in.

Dr. Insel: Susan.

Ms. Shurin: Yes, I think it's important to keep in mind what a strategic plan is, and I think Walter really sort of hit on this. It really is a plan of action that's designed to achieve a particular goal, and it focuses much more on the how than on the what.

My institute, Heart, Lung and Blood, did a strategic plan a couple of years ago, and we cover heart, lung and blood research. As you can imagine given the

breadth of that since it goes from the most basic molecular biology in genomics into big epidemiologic studies, the Strategic Plan doesn't list all of that.

The Strategic Plan is actually at a fairly high level. And the way then that is implemented plays out differently in the different areas, and it also changes with time, but we don't change our strategic plan with time. The Strategic Plan stays the same. The implementation phase and the way that we actually are making investments is really what changes. And we anticipate in another, I don't know, five years or so we'll probably really go through the entire planning process of individual people who contributed, and there were about 600, so there were really a lot, may not be getting exactly what they want out of how the Strategic Plan plays out, but I think everybody agrees on the general direction.

Everybody came in saying that

their own particular area of research was the most important, and that's what you would hope that they believe. And we really took all of that to sort of say here's the general direction that we're going. I think it loses its utility as a strategic plan if it's constantly - if you're constantly reworking it. If it requires constant reworking, I think it really does raise the question of whether you got the direction right in the first place. And it should be constituted in such a way that it can encompass within it a number of different ways of playing out and actually doing the implementation.

So, the what piece in terms of how it gets played out, doesn't need to be incompatible with the how piece, which is really what the strategic action is.

The word itself derives from, I think, the Greek for general. It's a military term. And it's sort of like how are you going to move forward. And the different components

of the Army are going to move forward in different ways, but the general direction really ought to be the same.

Dr. Insel: So, so far we've had a basketball and a military analogy.

Lee.

Mr. Grossman: Well, I'm glad you brought that up. Being an avid Steelers fan, I prefer the Pittsburgh Steelers defense of dominate and confuse the enemy. And in some ways. I feel as though in this strategic plan and having worked on a number of business strategic plans, that this is confusing. Our aspirational goals are stated, but there's really no timeline for them.

Generally in the business world when you draw up a strategic plan, you do put out goals there, but they're defined by a certain year of when you will accomplish that. And then you work back developing the processes that will meet those specific timelines.

I mean I'm looking at one of the aspirational goals for the Panel 3 that I worked on, which are admirable. "Causes of ASD will be discovered that inform prognosis and produce effective treatments, services and supports and lead to improving the quality of life of all those that are affected by ASD."

It would be much more productive and much effective if we put a time frame on that. And by doing that and with all the aspirational goals, we should be coordinating all aspects of the Strategic Plan so that it is working in concert together towards the very defined time-limited goals that we have set. Right now without a timeline, I feel that it's pretty nebulous, and all of these goals kind of stand alone. And I don't see them working towards a focus of pulling it together because one goal begets another in terms of really getting to the answers that we need. So, that's kind of where I am.

It is hard to go back and re-

tweak, and it almost makes the efforts that we've gone through in the past - well, we've been at this a year and three-quarters. There's too much good work that's been done for us to change that. But with that said, I still feel like we're floundering and that we don't have it here.

Part of that also is I think that the political aspects of what we're considering here also come into play with the fact that we really don't have that discrete and that concrete timeline that we should have with the processes in place. Because with that, I think that everybody would be again working together more closely putting differences aside to achieve a goal.

Anyway, that's my perception on it and I'll take other analogies.

Dr. Insel: Can I just ask you to clarify? Because in the original version, every objective was as it says up here, time-bound. The aspirational statements were not.

They were meant to be, I think, much more general and mostly inspiring rather than accountable in the way that we have on the screen right now.

I'm not sure I understand what you're feeling. Is it that we need to make the aspirations as well time-bound, or is it that you're concerned that some of the updates don't yet have timing as part of their goal?

Mr. Grossman: Well, I think that the long-term aspirational goal should be time-bound. That whatever it is that we decide that we're going to do, that we will accomplish that by X date. I liken this to what NIH did, and I am paraphrasing some of this, did for HIV/AIDS. There was a timeline set that they would find a vaccine by a certain date.

Dr. Insel: 2003.

Mr. Grossman: Right. And they still don't have it, but look what's happened in the meantime in terms of longevity and

responding to the needs of that community. It's been incredible. And that's one of the keys about these aspirational goals. It doesn't necessarily mean that you're going to achieve them, but you have a line in the sand that you're shooting for and you put all the resources together for that.

The short-term and long-term objectives that we have in there which are time-bound and have monies identified to them, I think that we've all been a little bit concerned if we're going to; A, get the money for them and, B, hit those timelines.

At some point - and to me it's not so much the money part and the time part even though those are very important, I just don't see everything working together having these goals at the top and everything that's underneath it working towards accomplishing what we've defined as the goals that we want to reach.

Lyn.

Ms. Redwood: Yes, Tom. I wanted to respond first to Walter and Susan in that when we started this process last year, it was very difficult. And we were struggling, I think, to the very end. And there were several things that were deferred.

And we were told at the time, that this is Version 1.1. And don't worry, because we're going to circle right back around to this next year for Version 2.0.

And the things that we've missed that we sort of rushed and we didn't have the appropriate input or information were delayed, thinking that we would be updating this again as we've done.

So, just to give you a little bit of background on that, that's why we went through and we tackled the process that we did, the Strategic Mining Subcommittee.

Tom, I also wanted to respond to two of the things that you mentioned. One was the addition of 33 new objectives.

I'm really concerned with the recent data that's come out of OCDC in the National Children's Health Survey that one in every 91 children now has autism, and one in every 58 boys. That's an epidemic.

That is the national emergency that Jim Moody referred to, and I just don't think that 33 objectives captures that. I mean I think that we should double our number of objectives based on the fact that our numbers have just doubled since the last time that we were discussing it. It was one in 150 when we came up with the first plan.

So, I don't really think that that runs the risk of confusing the scientific community. I think we need everything we can to throw at this the way Lee was saying to respond to it like the AIDS epidemic, like SARS, like spinach contamination, like H1N1.

The other thing I wanted to respond to was you asked whether or not we should have broad initiatives or be very

specific, and I think we really need both.

I think we need broad initiatives for coming up with hypotheses about what's causing autism. But then I think once we have some of those hints, we need to get very specific with testing hypotheses.

So, I don't think that's an either/or. I think it's a both.

Dr. Insel: other thoughts or comments from the rest of the group?

So, Lyn, I'll respond. I think that the concern I had in looking at it wasn't so much the total number of objectives. But as I read through especially with all the updates, it was difficult to see the focus.

I felt that we had lost the sense of priorities of communicating to people this is what must be done now. Instead it was becoming a very long list of many, many, many things that people could do.

I was just thinking about this because we had a strategic plan that we did

for my institute, and it's mostly been useful in telling people what not to do.

Because we left a lot of things off there that we were currently doing that people - lots of people were very interested in continuing to do, we felt that much of our current activity needed to shift.

And so what we did was to make a very tight plan with very few objectives, and to funnel all of the work towards exactly the things that we felt needed to be accomplished in the next five years. Very accountable, very measurable, very deliverable, and I think it's working.

Scientists do not like to be told what to do, but they will respond if you explain to them where the needs are, where the funding is going to be.

What I was concerned about in looking at going from 30 to 65, or now I think it's going to be more like 75 objectives, is that this has something for everyone.

Now, maybe that's good and maybe the Committee wants to do that and to sort of let a thousand flowers bloom, but that's not necessarily the best way to get to a particular point that you want to be.

And so, I just use that as an example of how we struggled with some of the same issues and ended up actually - and it was pretty painful that we ended up saying let's really focus this down, let's make this a priority list, not a laundry list.

And that is what people don't like to do because it's uncomfortable, and yet sometimes that is where you have the greatest impact.

Ms. Redwood: Tom, would it not be possible to take the initiatives we have now and rank them in priorities in the Plan? I mean that might be a way to handle that in terms of pointing scientists toward what's the most important to us now.

Dr. Insel: That's a great idea, I

think, for the Committee to consider.

Susan.

Ms. Shurin: One of the things that sometimes helps with this, your comment about the hypothesis piece, it's important to have the hypotheses, but they don't necessarily belong in the Strategic Plan.

And I think one of the key things is to sort of figure out what do you put in the Strategic Plan, and what comes in someplace else.

What often helps if you're trying to really get that focus, is to try to group all of those so that you have categories, perhaps, of some of these priorities.

The difficulty with trying to rank them is that everybody is going to rank them somewhat differently. I think then it becomes very crucial who's at the table in terms of making that ranking, which may not actually be how we end up making decisions about investment of resources because there may be

things that are aspirational that are not actually key, current scientific opportunities. Therefore, may not quite be ready for investment right now.

So, I think the key issue is just sort of to try to get the direction right and to set it up so that you can use this to get more into the details so that this is sort of the framework upon which you can get into the other things. All of which are absolutely essential.

You don't do research without, I mean it either generates or is testing a hypothesis, and so absolutely it's completely essential.

This may not be the place where you lay that out. What you lay out here is sort of a general direction, and then expect that you're going to be filling that in.

Dr. Insel: Alison.

Ms. Singer: I think one outcome of our decision up front when we were talking

about how to revise the Plan, was the decision to look at each chapter individually and appoint panelists who focused individually on each chapter.

Because I think when you read all of the chapters now together versus last year's strategic plan, it feels much more siloed.

Last year when we wrote the original plan, we had one person who sort of brought it all together and wrote a more cohesive storyline than I think is present in the current plan where I think everyone really focused in on their individual question, but maybe didn't look at the bigger picture. And also didn't really look at where their question fit within the broader framework.

So, I think that's something that we might want to think about for next year is in addition to looking at each individual chapter, we really need to make sure that the plan is a cohesive whole and has a message, a

key message to deliver.

Dr. Insel: Let me add one more thing to Lyn's comments about for those of you who weren't involved in the Plan last year. We really pushed to get this done by the end of January, because we wanted to have something to deliver to the new administration.

And I think that was a good idea in retrospect, but we realized at the time, as she said, that several issues had to be deferred.

We also heard fairly quickly, I think, in several of the scientific workshops that were held the past few months, that there were some important topics that didn't get included, that needed to be thought about more deeply, and some of them actually cross multiple objectives.

For instance, the emphasis on adults which is an emerging priority for the community. Even though we heard about it last

year, we didn't find a way to really incorporate that in the Plan in the way that we might have.

There were a few other areas as well that two or three of the different panels recommended now be included.

So, I don't want you to interpret anything I've said to say that we shouldn't make any changes and the Plan we have was perfect.

We had said last year that the Plan we have was imperfect, and in some ways would need to be revisited very quickly.

I was concerned though that some of the topics that we put up for deferral that we said would be the basis for updating, actually got very little attention in the subsequent discussions from the scientific workshops.

We had to go back to them multiple times and say oh, by the way, we know you have all these wonderful, new things you'd like us

to consider, but we do need you to give us your best sense about these items that were deferred from last year because we have to decide what to do with them.

So, as we revisit this, we're going to need to keep that in mind as well, but there were about five or six topics for the Plan that we said we would take on soon after January to be able to decide whether they would go into Version 2.0.

Walter.

Dr. Koroshetz: I think it's probably too late, but just thinking this through I would wonder whether the right - or one right way to do this would have been to basically add to the sections, you know, this is what was accomplished with regards to what we had asked for, this is where our stumbling blocks are. And then an additional point, bullets or things that we think that should be added to the Plan as new bullets, but those are basically - they're explained as new

items.

I think some of it's stylistic in the sense that the way it's written, it looks like it's like a whole new redo as opposed to - it's like people don't know what they're doing, you know. They rewrote the whole thing.

If we had something - which I think the Plan is pretty good. I mean it looks really good. Especially glossy is great. But it really - it looks pretty good to me.

So, I think to build off of it as opposed to rewriting it might have been the better way to go, and then just isolate, you know.

And over time since we're going to be doing this every year, you have a process. You need to have X, Y and Z. Then you get a new bullet. If you have X and Y, we wait until next year until you get the Z. Then we add it, and then maybe things drop off.

It will be nice to have some kind of a process by which it's a living document that goes from year to year and people can track it as opposed to having to rewrite it, read it all and it seems different.

So, some kind of trackable thing over time would be good.

Dr. Insel: Alan.

Dr. Guttmacher: yes, to state the obvious, or what I'm hearing from a number of people, I think while we clearly do want to set a standard for the process that we'll follow in future years, this is a unique year, I think, hearing something about the way the Plan was originally done last year with some time pressure, etcetera.

So, while I personally would not think that we want to massively rewrite it, there were these clearly deferred issues that we need, I think we have responsibility to take up.

One would hope, though, that that

is a onetime event. We may defer something this time, but one would hope it would be a much smaller list than would have happened the first time. So, there may be some things we're going to do here which I would think would be necessary for 2.0, but not necessary for 2.2 or whatever would follow this.

So, I think that's one thing we should kind of keep in mind as we go forward with it.

I also, you know, I looked at the Plan when it first came out months ago, and then re-looked at it in the last few days, and I must say I agree with Walter. It's pretty impressive.

Now, that's not to say that there aren't some ways it could be improved, but I think the other thing I would ask, and again as someone new to the process, it sounds like some of what's being brought up, not a lot, is rehashing fights that you undoubtedly spent a lot of time and a lot of effort hashing out

last year.

I would think we would probably want to take those off the table unless there was some new, compelling science within the last year that really changed things.

With the exception of that, the battles were fought once, there's enough other stuff to do. We probably shouldn't just re-fight the same battles, but should take on new ones. And that is the deferred issues and things like that.

Dr. Insel: Ellen.

Ms. Blackwell: At least as far as the last chapters of the Plan are concerned, Chapters 5 and 6, I think that we did have an opportunity in the succeeding year to collect a lot of public comment about services and about adults that we didn't have in Version 1.

So, part of our goal in making those revisions was to include all of the input that we got from the public and that we didn't have a chance to get in Version 1.

Dr. Insel: Jim.

Dr. Battey: I'd like an opportunity to agree with what Alan said. I think it's fine this time because we did defer a number of subjects for the Plan to get twice the length it was the first time around.

But if you do that every single time you revise it, you know what I mean? You can do the math. It's going to get pretty long. And it will get so long that no one will pay any attention to it.

Dr. Insel: Cindy.

Dr. Lawler: I agree with both of those two, and I like the idea of in future years as we go forward, keeping this fairly intact plan that we have for the second year, and then adding onto it. And maybe based on what's happened in the last year, we could identify objectives that mirror renewed emphasis because maybe there wasn't enough funded on that objective. And then adding new objectives that represent new scientific

opportunities over the past year, but that those be sort of clearly separate from the Plan itself which maintains its integrity at least from the second year going forward.

Because I think, you know, I agree there was - it was more than an incremental change the second year, and that's reasonable to expect given it's the state of flux, but now I think we are in a good position to make more deliberate, separate adjustments moving forward.

Ms. Redwood: I just want to capitalize on that. I think we're also in a good position from what Walter was saying, in that we now have funding information which we didn't have when we started this process.

So, I think it will make it much easier moving forward next year to be able to tweak this, because we didn't have that information when we started this.

Dr. Insel: Chris.

Ms. McKee: I'm a little nervous

about having the second rewrite, the siloed version, to be the final version then that we go forward with because Alison was talking about the next year bringing it back together.

So, if we're going to do this just this once and really hit it, I think it needs to come back together a little bit.

Dr. Insel: Did other people have that experience as well in looking at it in its current form, that it looks more Balkanized and less integrated?

So, the message from the Committee is that we do need to - it has to have a common voice.

The other thing along with that that I noticed in reading it again last night, was that many of the text revisions are in the section What Do We Know? But they have nothing to do with a new discovery or new information. They're really about what we need.

And it's really What Do We Know?

Should be driving the revision, because we've learned something that we didn't know last year. And therefore, we have to change objectives in some way.

I think if you look at what we've really learned over the last six months, seven months since we did the Plan - I guess it's nine months now, the list is actually fairly short.

There are a few things that we can put into What Do We Know that we didn't know in 2008, and that is worth including. But most of that text as I read it, were about what we consider to be new needs. Which tells you something about this updating process that it was driven much more not so much by the - a better understanding of the biology or a better group of discoveries, but much more by a better understanding of the needs and of what we were hearing from many different stakeholders.

Other thoughts about this?

Susan.

Ms. Shurin: Coming back to Ellen's comment, I think the key thing as I look at this, that looks as though it really needs emphasis over the first version of the Plan, is the issue of adults.

That that seemed to be the biggest - not that it's new knowledge, but it's a different emphasis in the sense that the primary emphasis at least originally was on children.

And you don't want to lose that focus, but the fact that there are key issues that we hadn't really identified there.

So that's, in many ways, that seems to me to be the major sort of point that perhaps ought to get highlighted really primarily because it does actually have an impact on the priorities. That that becomes a somewhat higher priority item than it might be otherwise.

Dr. Insel: Lee.

Mr. Grossman: Yes, I'm glad that we transitioned well into this new section, because I did want to ask about services and to get some clarification or further information on your thoughts on just this question about do we need a separate plan for services.

Dr. Insel: Let's throw that open to the Committee. I think we will wrestle with this when we get to Sections 5 and 6, but what does the group feel about this?

Mr. Grossman: Since I brought it up, if you don't mind, I do think that we need a separate plan for services primarily because I think that there is many stakeholders that would be involved in service delivery that just aren't at the table.

I don't know how we would accomplish that through the current membership of this committee, but there are many people that really should be involved in this that are impacted by anything that we do in

services that are actually on the field doing the work behind us and their voice really is not represented on this committee.

I mean there are many examples of that. The teachers, speech pathologists, the people working at State levels like developmental disabilities divisions, labor, Department of Labor.

Dr. Insel: Housing.

Mr. Grossman: Housing and transportation and the justice system, and I can go on forever. A long list.

Dr. Insel: Others have a sense about that? Ellen.

Ms. Blackwell: I guess I don't like to disagree with Lee, but I think if you take services out of the Plan, I guess to me that might actually have the boomerang effect.

It might actually disassociate the importance of services in adults in the world of autism.

I mean I guess I'd have to ask why

are CMS and SAMHSA and HRSA and education here if we're not talking about services?

And maybe some of the stakeholders aren't here, but I can say that we brought them into our discussions. We had a DD person with us when we talked at our scientific workshops, and we certainly talked about workforce issues and education issues and the issues that we mentioned, housing and training, the issues with the criminal justice system.

So I guess to me, taking off Chapters 5 and 6 would be very odd in the progression of how the questions are designed.

Dr. Insel: I think the question isn't whether to leave them in or take them off. I don't think anybody - I haven't heard anybody recommend that we remove those chapters.

The question is, I had it up here, is how much of what we want to do in the service arena is actually research, and how

much of it is much more focused on the service needs.

This research plan should by no means be the full scope of what the IACC encourages or gets involved with. I mean the whole - I would think it's maybe half.

There's another half of what we have to do that's not science that's really important that has to do with service provision and policy. And those are all issues that require our focus every bit as much as looking at etiology or doing randomized clinical trials.

Mr. Grossman: And that's how I interpreted it. Is that if - looking at this as a research plan, we need the practicality of service delivery and policy development to become as important.

And if we are looking at this plan that's in front of us as strictly a research document, then that's why I was advocating for services to be separate.

And in that regard if it is part of the Plan in terms of research element, I would not disagree with that.

Dr. Insel: Gail.

Dr. Houle: Yes, I would hate to see services desegregated from the Plan. I think that perhaps the focus on research to practice and knowledge utilization could be beefed up so that services could be positively impacted by the Plan in a way that it's not now.

And I'm also wondering if we could bring to bear some of the NIH expertise in that area.

Don't you have a services research unit at NIH? No?

Dr. Insel: Well, our institute has a large services research portfolio which - some of which is involved with autism. Particularly the work of David Mandel, people like that.

Dr. Houle: Right.

Dr. Insel: But again, there's a difference between services research and service delivery.

Dr. Houle: Yes.

Dr. Insel: And there is sometimes a gray zone in between that I think we could easily get stuck in.

And I only bring it up here because as we get into those items later for Numbers 5 and 6, we want to find a clear boundary, I think, where we stay focused on the research side of this and not begin to get involved in the tremendous - really, the universe of need out there for service provision.

Dr. Houle: Well, I do know that there tends to be a dichotomy between research and services, and sometimes the bridge is the knowledge utilization.

And so to keep it in the forefront of the research community may move services further.

Dr. Insel: I guess one final comment about this. I want to just make sure that what we're talking about here is the research plan. And I just can't emphasize enough that that's not the full scope of what the IACC should be thinking about.

And so, we don't need to make this plan cover all of the needs that we have for autism. It really is going to cover the needs on the side of, as it says in the mission, what discoveries need to be made for progress.

And we'll still when we finish this, have to really buckle down and think about the service needs.

Ed.

Dr. Trevathan: Yes, just listening to all of this, I have to say I do have going back to your first question and some of Walter's comments, I think at least for the questions that don't address services in adults, I do have concerns about the rewriting and have, you know, when we had - when I've

been on a number of strategic planning groups, we're rewritten things every three, five or even five to ten years.

I think I am concerned about taking the focus off and making the document be less relevant by constantly rewriting it.

On the other hand, I think it's quite different when we're looking at what we have inserted in here in the adults and services which were clearly lacking the previous plan.

The issue with services, I mean I think I agree with Lee and Alan and all, is that there is such a huge need to address services that's really not research that I think that tends to bleed into these discussions because we all feel it so desperately and realize it's such an important problem.

So, I know that it's not our mandate or our authority to really address that issue of services apart from research.

But to the degree that the IACC can point out that the service needs are tremendous maybe could drive a separate group to address services apart from research.

But having the overlap between the services research and services delivery and implementation could be something very valuable that we could address.

Dr. Insel: I saw a couple of other hands up.

Anybody?

Have we talked this to death? Is there anything else that people want to talk about before we get started on the actual work?

All right. So before we take a break, let's just think about what's in front of us. We've got the six original questions, we have a seventh chapter that we want you to look at as well.

We deferred Chapter 3 or Goal 3 from last time, because Lee wasn't here. We

have already spent some time on 1, 2, 4, 5 and 6.

I don't think we talked about 7, because we didn't have it last time, but we do need to look at that. And actually, that may be the other major discussion for today as this is a whole piece of this plan that wasn't in the original version, and yet we keep hearing about the need to go back to the mission, the coordination part that's not actually in the Plan.

So, we have lots of objectives, but no discussion about coordination, workforce and the issues around surveillance. So, one possibility now that's on the table, is to - rather than try to work that into either Number 1 or Number 6, is to think about whether that ought to get some attention in a small addendum here a little bit like what Walter was suggesting where you have a couple of pages to say this is something that we really could add in.

So, my recommendation is that we take a short break and then we come back and start with Number 3, if that's okay with everybody. And then go from 3 to 7. And then we hopefully finish that in the morning and then use the afternoon to do 1, 2, 4, 5 and 6. Okay? All right.

Let's reconvene in about ten minutes.

(Whereupon, the meeting went off the record at 10:26 a.m. and resumed at 10:38 a.m.)

Dr. Insel: We're going to get started. So as we just discussed, what we'll do is begin with Chapter 3 or Objective 3 which was deferred from last time. And I'm going to turn this over to Lee Grossman to walk us through the reports you have.

You should have the line edits in front of you in many different colors so there's a chance to just do this with revision by revision.

Lee, why don't you take it from there?

Mr. Grossman: Oh, goody. Well, thank you and I have to apologize for this getting in a little late, but I think that most people would agree that of any of the panels, this one was probably the hardest to tackle.

From the 23rd to today, there were a lot of difficulties that our group had because we just had - we wanted to go back and really look at this again, take the comments that were given at the workshop, and make sure that those were as well reflected in this document.

And I have to thank the other people that were a part of this panel, Craig Newschaffer, Matthew State, Robin Hanson, Sue Swedo, Lars Perner and Jeff Sell for their incredible work in the last couple weeks.

Half our group had the flu. A couple of the people in the group were six

hours time difference away for a majority of this time frame. So, there was quite a bit of work that everybody had to do under extraordinary circumstances, including working through most of the weekend to complete this and to meet the 10:00 a.m. deadline yesterday morning.

Some of the things that should be pointed out, this was a struggle for us. We weren't in total agreement. There was not consensus on some of the aspects of what we had discussed and what we were tasked to do.

And as a result, there are some parts in this plan that do reflect where there was not consensus. There was much, much back and forth between all of us in terms of comments, edits, revisions and this was quite an effort.

At the end of the day, this reflects, I think, what most of us believe was what we wanted to present to the IACC, and that we in no means believe that this document

should stand alone in front of the Panel. And this is really a document that we are recommending to the IACC and for them to carry forth and to finalize.

When I was trying to listen in on the call on the 23rd, it was very, very difficult. So, I'm not really sure of the process that was involved with everybody going through this.

Was it line by - oh, it was line by line. Okay.

Well, you all have the document in front of you and I'm not sure - have people reviewed this?

Okay. Because I mean I think it would be very time consuming to go line by line. And perhaps if there are points that people want to bring up, I can address those specifically as best I can and see if I can reflect the opinions of the Panel.

Ms. Singer: I think we want to go line by line.

Mr. Grossman: Okay. Well, page 1, line 2, as you can see, there were some additions made to the bullet point there. And it's the same thing for the first three bullet points. The Panel decided to add "or the consequences of ASD that impact quality of life."

Dr. Insel: Alison, go ahead.

Ms. Singer: This struck me as an example of where certain panels proceeded differently than other panels in that these introductory statements in Chapter 3 differ dramatically in their form from the introductory statements throughout the rest of the Plan.

I think it's inherent in all of the statements throughout the Plan in all of the chapters, that the idea is to focus on quality of life.

We had talked about that at the last meeting, that that was sort of an uber-goal. And I think to include that here

implies that it's not part of all of the other introductory statements. So, I would suggest removing that clause.

I also think that the last item in the introductory statement here is much more detailed than any of the other introductory statements found elsewhere in the Plan. And I think it, again, leads to inconsistency throughout the document.

Dr. Insel: Ellen.

Ms. Blackwell: I agree. Although I certainly support quality of life, I think it would be better to put these first three back the way they were.

I thought that the fourth bullet was more of a research question. The fifth one I felt should be eliminated.

And when I went back and looked at the - what was presented at the workshops, the bullet that I thought should be here was what are potential risk factors for ASD?

That might be the missing bullet.

Dr. Insel: Lee, I had a question on the third one.

Mr. Grossman: Yes.

Dr. Insel: So, I would agree that the additional language, I think, besides being awkward, it doesn't add information. But on the third one, the original language was "Could an exposure to something in the environment lead to the development of ASD?"

And I didn't remember that. I went back to check it and I gather that is correct.

Is that really a question that we would even need to ask at this point? Shouldn't the question be which environmental factors lead to the development of ASD?

I mean I don't think anyone in the course of any of the workshops we've had has ever questioned whether there is an environmental basis to some cases of this - or to any complex medical disorder.

I mean to even pose the question

as if we still need to wonder whether there are environmental factors involved seems to me to take us back at least ten years or more. Maybe further back than that.

Was that discussed at all in the workshop?

Mr. Grossman: Yes.

Dr. Insel: It's just an odd -

Mr. Grossman: Every line in here was discussed, and I'll try and reflect back to you the feeling of the collective wisdom of the Panel.

In adding "or the consequences of ASD then impact quality of life," the belief there was to demonstrate what was brought up by just about everybody on there that many of the documents and certainly what we were talking about did not in its original format, reflect the life span as well as the urgency of the issue.

And by explicitly stating it in there it was to draw attention towards the

overall life span impact, and that's why that was added in.

And as far as bullet number 3, I can't respond specifically to that. It shows here not as an edit from the original, so I don't know if it was in the original or not.

Dr. Insel: It was in the original. So, it's something that we all decided on in January.

Mr. Grossman: Yes.

Dr. Insel: So, we found it acceptable then, but I didn't remember us even discussing it in January. But it just struck me now in reading it more carefully, that the language doesn't seem to reflect the scientific knowledge base.

Lyn.

Ms. Redwood: Tom, I agree, and I'm wondering whether or not we could consider deleting Number 3 and using the first half of the sentence for Number 5, which is what factors such as environmental toxins, genetic

aberrations, metabolic processes, immunological-related conditions, inflammatory issues can be identified and assessed to improve the quality of life.

And then I think the second half of that sentence needs to go to services, because I do think that's combining services with what caused this to happen.

I'm wondering about this issue with the quality of life and life span perspective if that could be beefed up in the introduction, which is something that we've not talked about at all.

And if you go to the introduction, there's actually a whole section on life span perspective, so I think that we could beef that area up and possibly take it out of these bullets because it does seem a little bit lengthy and unfocused.

Mr. Grossman: Okay. And then just to respond to the last bullet that's here in the introduction and why that was specifically

put in there, is that part of what we were tasked to do on this panel was to address the notion of prevention, which we have struggled with before the workshop, and certainly afterwards, and we're all cognizant of the idea that prevention really means to enhance quality of life.

And there was this idea, and I think it was fairly unanimous from the Panel, that since we really didn't address prevention or enhancing quality of life to the degree that any of us felt comfortable with, that we wanted to explicitly state that these are issues that we need to work with.

But again, we'll defer to the full IACC's decision on any of this.

Dr. Insel: So, just focusing on the introductory, five introductory questions, anybody want to make a motion for how to alter these?

Alison.

Ms. Singer: I mean I would suggest

that we revert back to the language in the existing plan, but correct Number 3 to incorporate some of what Lyn was saying and change it to what environmental exposures contribute to the development of autism spectrum disorders.

Dr. Insel: What about Items 4 and 5 that are here?

Are you recommending we just limit it to the original three?

Ms. Singer: I'm recommending we limit it to the original three.

Dr. Insel: With that change to Number 3?

Ms. Singer: But change Number 3, yes.

Dr. Insel: Other comments for discussion?

Ms. Redwood: I guess I sort of like Number 4, because it's obvious that not all children who are all exposed to these environmental agents develop autism.

So, what is it that makes some children susceptible? I think that's an important question.

Dr. Insel: is it different than Number 2? Maybe we can ask Dr. Guttmacher who's an expert on this.

Are 2 and 4 asking the same question?

Dr. Guttmacher: To me, they would be, but of course I may not be your typical reader. I mean they're two ways of expressing the same question.

It gets back to the point I think you were making earlier, Tom, no one questions environment plays a role, no one questions the fact that genes play a role. It's the interaction of the two that really explains the whole thing if only we understood either part of that let alone the interaction.

Dr. Insel: So, would it be helpful to switch the order here so the first is about genetics, the second one says which

environmental factors lead, and the third one would be how might genetics and the environment influence the occurrence, and even if it helps to explain that and parenthetically say are there some individuals or groups more susceptible, and then you have your three items and you've, I think, captured all the ideas.

I'm mindful of trying to make sure the language is clear so that people know what we're talking about when they read it. And it's going to be read by so many different kinds of people.

But, Alan, tell us as a person who works in this area of gene environment issues, what's the best way to say it?

Dr. Guttmacher: I mean the one concept I guess that's not there, you know, I hate to revisit, is we talk about influence, but we don't talk about the interaction. It's not as though these are completely independent influences.

They may occur independently, but the influence is how they interact together specifically in an individual's life.

Dr. Insel: So, could we rewrite that to say how might genetics and the environment interact --

Dr. Guttmacher: Yes.

Dr. Insel: - to increase the risk for ASD?

Dr. Guttmacher: Yes, I think whatever you write after the interaction, you could - yes, but that's right. I would think so.

Dr. Insel: Della, could you --

Dr. Hann: So, let me see if I can summarize. I heard the first objective to read as follows: Is there something in my genetic or family history that poses a risk for ASD?

What I heard now for the second, what environmental exposures posed risks for the development of ASD.

And for the third, how might genetics and the environment interact to influence the occurrence of ASD.

Dr. Insel: Influence the risk, I thought it was.

Alan, what's the best way to say that?

Dr. Guttmacher: Influence the occurrence, is fine.

Dr. Hann: Okay. Do you want to take a vote?

Dr. Insel: Susan.

Ms. Shurin: I like that. I think that's very clear. And I think no matter where you're coming from, those three in sequence really clarify a concept.

Dr. Insel: Any other comments about this? Should we vote in favor of the change?

Dr. Hann: I see all hands are in the air for yes.

Dr. Insel: Okay.

Dr. Hann: You didn't vote for it. I'm sorry. I didn't see that.

Dr. Insel: Okay.

Dr. Hann: So, one no.

Dr. Insel: Do you want to abstain, or do you want to vote against?

A vote against. Okay.

Moving on, what do we know?

Mr. Grossman: Okay. There was quite a bit of discussion around the lines from 19 to 23. And the gist of this primarily was to - and this went through many, many rewrites. The gist of this was just to explain that there needed to be -- as this area was one that was perhaps the area that was funded more than any, that it was the feeling of the Panel that we needed to have a greater balance among all the different disciplines that are trying to address the issue of autism. And that's the final wording that we came up with.

Dr. Insel: Lee, how did that enter

under What do We Know, which is really about the science base of what we currently understand?

This sounds like it's a what do we need comment. Whether we include it or not, it just seems like it's in the wrong place.

Mr. Grossman: I'm trying to - I don't have the original wording here. But from what I recall in the original wording, it talked about - what the Panel didn't feel comfortable with was that there seemed to be just too much of an emphasis particularly and entirely around genetics research. And they wanted to demonstrate that they felt that there needed to be a balance around that.

Dr. Insel: Other comments?

Ms. Blackwell: I thought it was a little strange to mention a particular agency in this paragraph, because we look at all funders.

Dr. Lawler: I agree that it seems out of place in this particular section.

Maybe it could be mentioned later on when we talk about what we do know about environmental risk factors, you know, prefacing that with there's not as much research that's looked at potential environmental factors as a sort of a preface to we know less about environmental risk than genetic risk.

And I agree with Ellen that I'm not real comfortable talking about a priority of NIH.

Dr. Insel: Jim.

Dr. Battey: Yes, I think the comment is out of place.

Dr. Insel: Any other comments?

Lyn.

Ms. Redwood: I guess, Lee, from what I hear you saying, you're actually saying that you think there needs to be a change with regard to an emphasis on genetic research.

And I'm just wondering if like Tom said, that might not fit better under what need, because we have all the information we

know about genetics, but I'm thinking your intent is that we need to shift the focus and have it be more evenly distributed between genetic and environmental and other research; is that correct?

Mr. Grossman: Well, let me clarify. This is a reflection of our panel, it's not me. And I'm just presenting and - particularly through the majority of this even though I think that it was a collective effort in terms of what the final wording would be.

With that said, I think I believe what you're saying is right. We just wanted to note that I'd say for the Panel, they felt that there was just an imbalance in the way the funding was, is that we needed to spread around and -

Dr. Insel: Alison.

Mr. Grossman: And if it needs to be spread around and I guess to another part, then that's fine.

Dr. Insel: Alison.

Ms. Singer: I think the point that you're making is actually reflected under the What Do We Need? On page 4, line 4.

So, if you want to move this sentence from 19 to 23, into that area and replace what's currently 4 through 7, which basically says the same thing, I think that would be a better place for this statement.

Dr. Insel: So, I guess then the question would be whether you need it in both places or whether we could - because it's been added in both places.

And if we were to retain it under What Do We Need?, could we remove it from the beginning of What Do We Know?

Dr. Hann: Just a point of clarification. Page 4 that Alison just was speaking about, is actually still in the What Do We Know section.

Dr. Insel: That's right. Good point.

Dr. Lawler: So, I think we can

delete lines 19 through 23, because I think they --

Dr. Insel: Would you like to make a motion, Cindy?

Dr. Lawler: I'd like a motion to delete that, because I think the important points captured, are captured elsewhere in the document at more appropriate points in time.

PARTICIPANT: I'll second Cindy's motion.

Dr. Insel: All in favor?

Dr. Lawler: 14.

Dr. Insel: Opposed and abstentions? One abstention, one opposed.

(Ms. Redwood opposed.)

(Mr. Grossman abstained.)

Dr. Insel: Moving on to page 2.

Mr. Grossman: Page 2, lines 3 through 6, that language was submitted just to further clarify that section.

Dr. Insel: So, I don't want to dominate this, but I thought there was a

misunderstanding of the science here.

What it says is that "In many cases the same genetic variation does not result in an ASD phenotype, suggesting that the mutation is not deterministic, and some genes seem to increase risk but have low penetrance," which is true. But for a Strategic Plan or for the scientific future, what's most important is that when people have a mutation but don't have the phenotype, they may have protective variants which are what everybody is looking for in cancer, because those are where you find your targets for therapeutics.

So, this comes out sounding as if it's a problem when it's a huge opportunity. You salivate to find people who have a mutation, but don't have the phenotype, so that you can use them to figure out how to develop new therapeutics.

So, I'm concerned that the wording as it is now doesn't provide what is really a

very hopeful observation.

Dr. Battey: In fact, there are two explanations for low penetrance. One is environmental influences, and the other is what we call genetic modifiers which is allelic variation and other loci that essentially modify the phenotype.

And I don't think the language that's up there is clear at all from the standpoint of science.

Dr. Lawler: Tom, how would we word that to reflect it as an opportunity?

Dr. Insel: I would word it as understand - let's see. In many cases the same genetic variation dos not result in an ASD phenotype, suggesting possible modifiers or protective variants that could be important therapeutic targets.

Dr. Lawler: Just including in there environmental factors, because they could be modifiers as well.

Dr. Insel: Right. Exactly. That's

great, actually. That would be, I think, even more informative.

So, if you said possible genetic or environmental modifiers, that could be important therapeutic targets, because the environmental modifiers could be the same way.

Ms. Blackwell: I have a comment about the first part of that sentence, "understanding of which has led to the identification of possible therapies."

I found it a little bit confusing because we haven't used the word "therapy" anywhere else in the document, and I just think we should strike it.

I think if we substituted the sentence you just suggested, that would be great.

Dr. Insel: Well, I suspect what the Committee was thinking about, the Panel, was the mGluR5 antagonist trial which has been in the newspaper the last two weeks, which again is something we didn't have last year

when we did the original Strategic Plan.

That's for children with Fragile X, and there's a lot of interest in whether since 50 percent of those kids meet criteria for ASD, that in treating Fragile X we'll have a new therapy, I think that is the right word, for autism as well.

We don't know. It's too early to say, but it's certainly the case that understanding those syndromal versions of autism has now given us apramycin, mGluR5 antagonists and also the beginning of a therapeutic strategy for Rett as well.

Ms. Blackwell: We say understanding which may lead to identification of possible interventions for certain people with autism or something like that?

Ms. Singer: Or maybe you want to use the word "therapeutics," because I think Ellen uses the word "therapy" as more educational in her section.

So for internal consistency, we

might want to use therapeutics.

Dr. Insel: Or medications?

Dr. Hann: Or saying "therapeutics" in the next sentence as well in the newly-constructed sentence.

Dr. Battey: It seems to me really what you're talking about is interventions, right? Whether they be a drug, whether they be a behavioral therapy or whatever they might be.

Dr. Insel: Right. But the interventions for Fragile X, Rett and tuberous sclerosis, if you take out Rett, for Fragile X and tuberous sclerosis are in fact drugs. So, they are medications.

So, I would just call them that if that's what you're really talking about. And then there's no question that we're using this to develop a new form of behavior therapy.

Dr. Guttmacher: That makes sense to me. But in the new sentence which we created where we have "therapeutics," in fact

since "environment" is in there, it might be better saying "preventions," because one could imagine it's biologically pointing to some change you might make in the environment to ameliorate things as well as simply medications.

I agree with you the ones that have been shown so far for those other diseases, those are drugs, the interventions for the new sentence.

Dr. Insel: Yes. Okay. I gotcha. So, maybe that would solve our problem here. This is so crazy to edit this by committee.

So, we use therapeutics in the first case where we're talking about the syndromes. And we'd use interventions in the second case.

PARTICIPANT: Use medications in the first one since you all just talked about medications applicable for the other diseases.

Dr. Insel: Either way, but interventions is the appropriate in the second

case.

PARTICIPANT: For the second one, correct.

Dr. Insel: Della, can you read this to us?

Dr. Hann: Yes. I'll try.

Picking up then the last parenthetical for the sentence after tuberous sclerosis, "understanding of which has led to identification of possible medications in autism." Then "in many cases the same genetic variation does not result in an ASD phenotype, suggesting possible genetic or environmental modifiers that could be important intervention targets."

Ms. Singer: I would take out the word "in autism" after "medications," because they're referring to Fragile X and --

Dr. Insel: Okay. Do we want to have a motion for this? In favor for these changes?

PARTICIPANT: 14.

Dr. Insel: Opposed. Abstentions. Moving on.

Mr. Grossman: Let me just state here that pages 2 and 3 were constructed primarily by the people on our panel that had the most experience in genetics, and they put the new terminology in as clarification over what was in the original plan.

In all honesty, I don't know much about this. So, I'm not going to be able to respond except to say that the people on the Panel that did have this experience felt that it - and that goes down to the - it's the bottom of page 3, felt that it was reflective of the most current information.

Dr. Insel: I can't remember the first authors. A lot of this has come out in the last two weeks, so we do want to make sure they've captured the right references, but the concepts aren't any different.

Dr. Houle: So, you would add those references to it so that it would be --

Dr. Insel: It may be that Weiss, et al., is the paper from last week in nature.

Did they get it?

Dr. Houle: I would think that would be important if it's vetted or read by the authors whose citations are used, that it be accurately interpreted and up to date.

Dr. Battey: So, we need the Committee to look at this and decide whether this is what you want in the document.

I did have a comment that there's kind of a problem listing genes that have been identified, is that it's a moving target and it could easily be incomplete next week or another article to be published.

So, I'm not sure that you necessarily need to list the specific identify of genes where allelic variation contributes to the pathogenesis of autism.

Dr. Insel: This is the same issue about grain size that we talked about before.

The other comment I had was I can

sort of picture what your committee must have been like, Lee, because there tends to be this interest in editorializing.

I'm not sure why they had to say that genetics research has been highly productive leading to the identification. They could have just said recent genetics research has identified common variations and changes in chromosomal structure, provided the references, and I think the read would have gotten the same idea.

Mr. Grossman: As I said, this was written by the people with the genetic experience. I'm sure that they wanted to highlight themselves.

Dr. Guttmacher: On behalf of the genetics committee, I would say that's a friendly amendment to remove the editorializing.

Mr. Grossman: sure. The degree of information that's placed in here is not really unlike what the original wording is

where we did have specific genomic regions identified in the Plan.

I could see the point about taking them out, so that would be perhaps a good modification from the original plan as well.

Dr. Battey: I think it's important to note that gene discovery has taken place, and taken place recently. But again, that is clearly a moving target and all the genes have clearly not been found. There are still more out there to be identified, and I just think you run the risk of having a plan, language in the Plan that is no longer accurate and up to date.

Ms. Redwood: I think that also is contradictory where it says highly productive in a small number of cases. So that to me, sounds somewhat contradictory.

Dr. Insel: So, could we come up with some language? If we were to say recent genetics research has identified common

genetic - so, we take out the whole highly productive thing. Has identified common genetic variations. And you'd have the references. Changes in chromosomal structure in specific genomic regions.

And then we can leave what was originally there, but we add another reference. And rare mutations in genes, leaving out the part, Jim, that you feel might be out of date soon.

In a small number of cases contributing to ASD, and that would be the final sentence with lots of references. So, if anybody really wants to dig into this, they'll know where to find it.

I mean I don't think this has to be a textbook of autism genetics, but - Walter.

Dr. Koroshetz: Well, I'm just thinking that we don't capture the actual, interesting thing, which is that the genes actually are in the same pathway that -

Dr. Insel: Yes.

Dr. Koroshetz: - and they're not like structural so that they offer a chance of reversibility.

Dr. Insel: You could parenthetically say synaptic proteins instead of listing all the individual ones, since they all happen to be the same family.

Dr. Koroshetz: I think to Lyn's point, that's what makes it actually really important because although it's a small number of cases all pointing to the same spot, and that spot might be although maybe different proteins, that same spot may affect all of autism. That's the exciting part.

Dr. Battey: I agree with Walter.

Dr. Insel: Jim, can you give Walter some language to say that? So where it says "rare mutations in genes," what would you want to say?

Dr. Battey: Gene associated with synaptic connectivity.

Dr. Insel: For other people around the table, does that mean anything?

Is that language okay?

Okay. Della, do you want to read this to us?

Dr. Hann: Okay.

Dr. Insel: You don't have to read all the references. Just the text.

Dr. Hann: Thank you. So, recent genetics research has identified common genetic variations, changes in chromosomal structure in specific genomic regions, and rare mutations in genes associated with synaptic connectivity in a small number of cases.

Dr. Insel: Do you need that small number? As Lyn was saying, that sounds like it's redundant.

You've already said it's rare mutations in genes associated with synaptic connectivity, so I think you can leave out the -

Dr. Battey: Once you say "rare," it's a small number of cases by definition.

Dr. Hann: Right.

Dr. Insel: And there should be commas somewhere in that sentence.

Dr. Hann: Yes.

Dr. Insel: Okay. In favor. Opposed. Abstentions.

Dr. Hann: Unanimous.

Mr. Grossman: So, that brings us down to 20 through 22.

Dr. Insel: Can I ask a - this is a semantic issue maybe, and maybe it's silly. But in line 18 and 19, what causes these spontaneous deletions and duplications is not clear and could be due to environmental exposures.

Shouldn't it be exposures to environmental toxins?

Cindy, when people say "environmental exposures," what does that - does that mean the same thing as exposures to

environmental toxins or -

Dr. Lawler: I'm fine with this wording.

Dr. Insel: Okay. Forget it. Let's move on. Okay.

Any comments on 20 through 22?

The 30 percent number, it doesn't show up in the Geschwind reference which is on line 1 of the next - so, Abrahams & Geschwind.

Dr. Guttmacher: There's also a distinction between the old language "accounts for" and are "involved in." And without having recently read that reference, though I've read it before, I'm not sure that we - we are not at a point in 2009 that we know yet what percentage of cases these gene variants, et cetera, are involved in. And it could be a much higher number than 30 percent, possibly.

Dr. Battey: That's exactly the case. There could be genetic changes in the promoter region in the introns that have not yet been tracked, where that allelic variation

in fact contributes to the onset of autism.

Dr. Guttmacher: Right.

Dr. Battey: So, I think saying a number is dangerous here.

Dr. Guttmacher: Unless we want to say at least percent. Either that or I would avoid a number in substantial fraction or something, proportion.

Dr. Insel: Yes, what we had before was 10 to 20 percent, but, Alan, you're not comfortable with that?

Dr. Guttmacher: It's the "accounts for" which somehow sounds a little more forceful or something than "contributes to."

But, yes, I think if I had been here a year ago, I would have had qualms because we just don't know it and to put an upper limit. I think we've demonstrated a lower limit.

I also agree with the phrase at the end that each one of them seems to only account for a small percentage where the one

or two could end up being three someday, but it's never going to be a huge number, presumably.

But in total, I don't think we know what that number is.

Dr. Insel: Yes. Well, the literature now is using the term - David Ledbedder who's been doing probably most of this, is using the term 15 to 16 percent of children seen in ASD clinics will have one of these factors.

Dr. Guttmacher: Things we know how to look at, look for today.

Dr. Insel: Right.

Dr. Guttmacher: Right. And that's my concern is, is Jim's really saying in terms of promoter regions or someplace that we may not be looking yet.

Dr. Insel: Well, so would you feel better if - or maybe you don't want any number. I hear that, but I'm concerned if the only number that shows up is one to two

percent of cases, it suggests that this is a trivially small -

Dr. Guttmacher: It could say a substantial proportion or something.

Dr. Insel: So, you're saying at least ten percent or -

Dr. Guttmacher: Yes.

Dr. Insel: At least ten percent would be okay?

Dr. Guttmacher: Yes.

Dr. Insel: That's defendable by the current -

Dr. Guttmacher: Right.

Dr. Insel: - state of knowledge. It's consistent with Abrahams & Geschwind - actually, Geschwind in the Cell paper from 2008, uses the term ten percent.

Dr. Guttmacher: Yes.

Dr. Insel: Or he says in at least ten percent.

Dr. Guttmacher: Right.

Dr. Insel: So, one to two percent

can remain, a case found in no more than about one to two percent of cases. They're not recommending a change there.

Other changes in this - I mean there's a lot here going onto the next page.

Dr. Lawler: I think an obvious omission is an explanation in terms of environmental interaction with genetic risk.

And if you just read line 1, in addition in those instances in which common genetic variations have been associated, risk conferred have been quite modest, this suggests that genetic factors may involve many different genes and multiple types of mutations and/or modification by environmental exposure.

So, either include that modification by environmental exposures there, or have as one of the models that modification of genetic risk from environmental exposure as D.

I mean I know this whole section

is focused on genetics, but it just really seems like an omission to go back to the initial aspirational goals.

I mean we really need to understand the interplay and to not consider that. Even in a section that's focused on genetics, it seems like an omission to me.

Dr. Insel: Cindy, I didn't know when we were going to get into this issue. And I didn't think we were going to get into it now, but I had a real serious concern about this from the get-go that the chapter continually talks about genetics and environment as if they're two different problems with different skill sets and different approaches.

And that may have been even more fair to do a year ago or 18 months ago, but I think we're now smacking the new era of epigenetics where if you really want to look for environmental exposures, you do it at a molecular level and you use the tools of high

throughput biology.

And we now know in the last six months how to do this much better than we did back in January.

I just think that missing out on talking about that, it's really almost nowhere in this whole chapter, is a terrible omission for the field because it's probably the most important thing we want to communicate to people, is that going forward we want to use these kinds of tools to look at environmental exposures, and I don't think we say that explicitly. We dance around it a bit.

So, it's probably not in the What Do We Know section except if you wanted to add something about we now have the tools to do this in a more precise way, but certainly we could put it in the What Do We Need and into the Research Opportunity section, and it's not there.

It's sort of sad. I think your group got kind of wrapped around a whole set

of issues which were probably more important two years ago, but today we actually could deal with them in a more sophisticated way.

So, I don't know if we want to change the language here. What's the sense of the group?

We certainly will have to address this as we get into the What Do We Need area.

Dr. Guttmacher: I think it makes sense to address it later, but I do think that Cindy's suggestion since it is about a suggestion, you know, that part really isn't about what we know, it's about what we knows suggests to us. And I think she's right that it suggests environment as being part of it there.

Dr. Insel: That would be the D - yes, go ahead.

Dr. Koroshetz: So, I was going to say that the common genetic variations never confer a large risk. It's always modest risk.

So, I was going to say since

common genetic variations confer only modest increase in risk, this suggests that the genetic factors in ASD may involve many different genes and interaction with the environment or genetic environmental interaction.

Dr. Insel: Anything else on this section?

Okay. Della, can you read it to us?

Dr. Hann: No, can't. Walter.

Dr. Koroshetz: It's okay. So, it comes after the Geschwind thing. So, it says since common genetic variations confer only modest increase in risk, this suggests that genetic factors in ASD may involve many different genes and genetic environmental interactions.

Dr. Insel: And then Cindy added in another item under A, B, C and there's D as well.

Dr. Lawler: Yes, I don't know if

we need both.

Dr. Insel: Okay.

Dr. Lawler: I think it either needs to be - I'm fine with Walter's edit.

Dr. Insel: Okay. So, Della wants you to say it again, hopefully, in the same way.

Dr. Koroshetz: I was hoping to get away from it because there is a grammatical problem the way I say it.

Dr. Insel: We can get to the grammar later, but we just want to get the concept right.

Dr. Koroshetz: Okay. Since common genetic variations confer only modest increase in risk, this suggests that the genetic factors in ASD may involve many different genes and interactions between genes and environment.

Dr. Insel: I'm just reading the rest of it.

Is there anything else that you

wanted, that the group wants to change, because there's another five or six lines added.

Okay. Can we put this to a vote, Della?

Dr. Hann: I like this role I get to play here. Okay. So, let me just back up because we had a change on page 2 as well that said taken together, rare genetic mutations, chromosomal abnormalities and submicroscopic deletions, duplications of genetic material are involved in at least ten percent of ASD cases.

And then the rest of the sentence stands as proposed. Then we moved over. We agreed to the next insertion. There's a sentence that was inserted that begins with "In addition."

It is the next sentence that we just - Walter has helped us very much with, and let's see if I can do justice to what you've said.

Since common genetic variations confer only modest increases in risk, this suggests that the genetic factors in ASD may involve many different genes and interactions between genes and environment, with some grammatical kind of things.

Dr. Insel: Do you need the sentence "in addition" in those instances, or is that just understood?

So, you're replacing that sentence?

Dr. Hann: Replacing that sentence. All right.

Dr. Insel: Okay. And then the rest of this stands as is. Okay.

In favor. Opposed. I think it's -

Dr. Hann: I think it's unanimous as well.

Dr. Insel: Anyone opposed or abstain? Okay. Moving on.

(Unanimous.)

Mr. Grossman: There were a couple additions on five, and then we can move from seven to 12 for consideration. Again, that was all addition -

Dr. Hann: Wait.

Mr. Grossman: We're on page 3. So, what I was referring to is lines 7 through 12.

Dr. Insel: I think we just voted on that.

Mr. Grossman: We struck all that?

Dr. Insel: No, I thought we agreed to it. It's in.

Mr. Grossman: Okay. So, that's been entirely -

Dr. Insel: Yes.

Mr. Grossman: Great.

Dr. Insel: Victory.

Mr. Grossman: Great.

Dr. Insel: Moving on.

Mr. Grossman: There's an addition on line 19.

Dr. Insel: Could all of that paragraph move to Chapter 7 where we talk about the infrastructure? Do we need it in here?

Dr. Battey: I question whether or not we need it at all. I think if people are looking to the Plan to guide them as to what the next research opportunity ought to be, this paragraph doesn't help.

Dr. Insel: So, Jim, are you making a motion?

Dr. Battey: Yes, I move we strike it.

Dr. Insel: Okay. All right.

Do we have other points of view on this or - the Plan is getting shorter by the moment.

In favor of taking out the whole paragraph?

Dr. Guttmacher: I have a point of view even though I may be in favor of taking it out. I'm just trying to figure this out.

But the one point I think that paragraph makes is that there are many parties involved, including different federal agencies and non-federal organizations as well.

Now, that may be suffused enough in the report that we don't need this specific section to get that point across, but I think that is a useful point.

Dr. Insel: Yes, I think where this is likely to come up again is when we talk about the need for various repositories. And what becomes clear is that we built this whole framework for DNA repositories. We haven't done so well in many other arenas.

And so, we may want to revive this at some point when we get to Chapter 7. But I think for right now in terms of what do we know in this chapter, one has to ask why is it here?

In favor of striking it all entirely?

Dr. Hann: Appears to be unanimous.

Dr. Insel: Any opposed or abstains? Okay. Moving on.

Ms. Redwood: Tom, if we do bring this up in Chapter 7, it mentions the National Alliance for Autism Research which I don't think is in existence anymore. So, I think it needs to be updated.

Dr. Insel: Certainly does. Okay. So, if we revive it, we'll have to fix it.

So, we're up to page 4, line 4.

Mr. Grossman: The Panel's inclusion in this addition was mainly reflective of the fact, and I'll quote from a comment, this was in response to the proposed edit that environmental research has been chronically underfunded.

Dr. Insel: So, any questions or issues, four through eight?

Dr. Koroshetz: I'm not convinced - what's the progress in identifying environmental - I don't know that we have any progress to stand on.

I think I would definitely say it's a much harder research to do and has been less activity.

Dr. Insel: Could we add references there, Walter? If we put in references, would you feel better that actually documented like the organophosphate finding from last summer, those kinds of things?

I mean there are - we can find you some pretty good - but it is striking with all the references that were under the genetics piece, that this is under-referenced, and we can help with that.

Maybe we can do that later.

Dr. Koroshetz: Certainly, if you're going to refer to specific papers in terms of genetic factors, you ought to refer to specific papers in terms of environmental factors, or not refer to specific papers for either.

Dr. Insel: But are we okay with the language four through eight?

All right. In favor of including these changes?

Anyone opposed? Abstaining? Okay. Moving on.

Dr. Hann: Unanimous.

Dr. Insel: Thank you, Della. 12 and 13.

Mr. Grossman: the Panel here wanted to reflect the varying opinions on the IOM report. That's why that was placed in there.

Dr. Insel: Comments, questions.

Dr. Battey: Looks accurate to me.

Dr. Insel: Alison.

Ms. Singer: I think that starting at line 13 and going through the following page on line 13, I think this is really an example of what Dr. Guttmacher was saying before where this is just really a rewrite of what we discussed and had in the previous strategic plan. And I think actually the way it's written in the existing version of the

Strategic Plan really reflects the breadth of the discussion that took place not only at this table, but at the Panel workshop.

So, my suggestion would be this is an area where I think we want to stick with the original language.

Ms. Redwood: I have to say I disagree with that because I think this is a modifier regarding those epidemiological-based studies that is very accurate, and I think that what we had in the previous plan was not totally reflective of the 2004 IOM report.

Ms. Singer: So, are you saying that there have been new studies since we last developed this plan that would speak to changing this sentence?

Ms. Redwood: No, what I'm saying is that the rewrites from line 14 down to line 16 is actually part of the 2004 Institute of Medicine report. It just wasn't included.

Ms. Singer: Right. We looked at exact language last year, and we decided not

to include it.

Ms. Redwood: I'm just saying I think this reflects better the report than deciding not to include it.

Mr. Grossman: And from the Panel's perspective when they were looking at this as what we believe we were tasked to do, we thought this, and I would agree with Lyn, is that was the consensus, the overall consensus that this was more reflective of the report.

Dr. Insel: Other comments or thoughts about this?

Ellen.

Ms. Blackwell: I'm not comfortable with the last sentence. In particular, lots of issues related to autism get public attention, and it just seems misplaced in this document.

Ms. Singer: I have a question for Lee. I mean are you saying that the discussion of the Panel members subsequent to the actual workshops reflected that? Because

the notes I took at the scientific workshops for Panel 3, they're pretty - there was disagreement, but the majority were in favor of leaving the existing report.

Mr. Grossman: After the workshop so that we could be reflective of all the diversity of opinions that were expressed there, we asked people to go back and review the entire document. And from that, this is what we came up with.

Ms. Singer: So, you're saying that on the phone call subsequent to the workshop, some of the panelists changed their mind?

Mr. Grossman: I'm not sure if I understand you. Prior to the workshop -

Ms. Singer: And after the workshops on the phone call where you worked on the language, you're saying that some of the panelists changed their point of view?

Mr. Grossman: Yes. Everybody had an opportunity to respond and comment on everything that you see in here, and they did.

And this was something that there was - I would say I can't remember any dissension around this -

Dr. Insel: Let me see if I can find some middle ground here. If you start at line 13 and you go through the first sentence: however, the IOM report acknowledged that the existing population-based studies were limited in their ability to detect associations that are limited to small, susceptible subpopulations - I think we might want to rework this a little bit - that could be more genetically vulnerable.

So, then if you simply said the IOM report acknowledged that there may be susceptible subpopulations that could be genetically vulnerable to environmental exposure, something like that, and you leave out the rest of this and you don't put in the specifics of any particular kind of exposure, would that work better?

Would that still address the

concerns of the Panel, address the full range of what the IOM report suggested without implicating Congress or anybody else in the rest of the language?

Dr. Battey: Yes, I think that's better.

Ms. Redwood: Tom, the only thing with that is that you're removing the large epidemiological-based studies. And that's primarily what the report was based on, so I think it's important to include that language.

CHAR INSEL: I wasn't removing that. I didn't think I was anyway. It's in line 14.

We just have to do something with using "limited" twice in one sentence. We'll have to make the language a little bit cleaner, but I thought that the concept that you wanted in here was that epidemiology has its limits. And the IOM report recognized that.

And what they said was the

epidemiological evidence isn't there, but that's all we have to look at here, right?

But I think the rest of it, and especially the business about vaccines and autism, we get into in many other parts of this. I'm not sure we have to do it here as well. It will come up in the next paragraph and be on that later in the document.

So, does that - if we make that change, we drop the rest of the language and just have the sentence from 13 to 15, Della, do you want to try to read that?

Dr. Hann: Here's what I heard. However, the IOM report acknowledged that the existing population-based studies were limited in their ability to detect small, susceptible subpopulations that could be genetically vulnerable - excuse me - more genetically vulnerable.

Dr. Battey: I like that. Move to make that change.

Dr. Insel: Okay. Second. In

favor. Opposed.

Dr. Hann: One opposed.

Dr. Insel: Any abstentions. Okay. We're moving on.

Mr. Grossman: Page 5, I guess we'll consider one through -

Dr. Insel: There is no sentence following that. We deleted everything from 15 down. We're moving on to page 5, line 1.

Mr. Grossman: Which I would probably take as a whole since it's a very long-running sentence from lines 1 through 4.

Dr. Insel: Comments, questions.

Ms. Redwood: Motion to accept.

Dr. Insel: Second?

Dr. Battey: Second.

Dr. Insel: All in favor. Opposed. Abstained. One abstention. Otherwise, the motion carries.

So, we're up to now line 10.

Mr. Grossman: It was inserted to reflect the lack of consensus that the Panel

had around this issue.

Dr. Insel: Do we need that? I mean we already have the lack of consensus in the public. Do we need to tell the world that the Panel also had the same lack of consensus? Maybe that's useful. I don't know.

Jim.

Dr. Battey: I think that sentence is unnecessary.

Dr. Insel: See lots of head-shaking as well.

All right. Do I have a motion to delete it?

Dr. Battey: So moved.

Dr. Insel: Second.

Dr. Battey: Second.

Dr. Insel: Okay. In favor of deleting the sentence. Opposed.

Dr. Hann: One opposed.

Dr. Insel: Abstentions. You'll have a different panel next year, Lee. We promise.

(Off-mic comment.)

Dr. Insel: I'm sure. I can imagine that they would want to make sure their views were included here.

Okay. We're moving on.

Mr. Grossman: There were some small changes in 14 and 15. And we might as well consider 19. The EARLI study was included in there as well.

Dr. Insel: Any discussion about any of this? Okay to include? All the heads are nodding. Okay. Let's keep moving to page 6.

Mr. Grossman: There were some slight additions on lines 7 and 8.

Dr. Guttmacher: I'm a little unclear by the phrase "need to be replicated" as opposed to have not been replicated.

Dr. Insel: And at the beginning of the sentence it says that these are reports, and the end of the sentence calls them studies, which are somewhat different.

So, is what the Panel really meant that, however, these observations need to be replicated with rigorous studies, something like that, or need to be verified or validated, or need to be the subject of rigorous study?

Do you remember what they were thinking?

Mr. Grossman: I'm seeing what comments are here, and there aren't any.

Ms. Redwood: It actually makes more sense to me if we just put a period after postnatally unless -

Ms. Singer: I do think it's important that if there's things that have been identified, that we try to replicate those studies and determine if it's accurate.

So, I do think it's something we need, and it's in the What Do We Need Section.

Dr. Insel: Exactly. So, I mean the reason it's in here is because we're saying there's a need associated with the

observation. I just wanted to make sure that it's clear that these are not real studies that are being reported, but they're observations.

Dr. Guttmacher: Right. And I just want to make clear that if we say they haven't been -

Dr. Insel: Right.

Dr. Guttmacher: - then it sort of implies that gee, we can't really believe until they have been.

If we say they need to be then as a declaration of this group, it seems to me that that - I'm not sure how high a priority it rises to, but then the group is declaring not only is there not such verification, but that there is a desire to have such.

Dr. Koroshetz: How about just changing that last sentence to; however, these reports need to be - to rigorous scientific evaluation.

Dr. Insel: How about just need to

be the subject of rigorous study?

Dr. Koroshetz: These reports need to be subject to rigorous study.

Dr. Hann: Okay. So, what I have then are the reports of associations of ASD with exposure to medications, toxicants, infections prenatally or postnatally; however these reports need to be subject to scientific study.

But I guess to take a prerogative, and I think Alison often says it, does that mean that -

(Off-mic comment.)

Dr. Battey: Why don't we just say additional studies rather than rigorous studies, again, not to impugn the studies that have already taken place.

Dr. Hann: To additional study?

Dr. Insel: Additional study. Okay.

In favor?

Dr. Koroshetz: Wait. One

question. Should the maternal antibody stuff be in here?

Dr. Insel: Now, want to add that in, Walter?

Dr. Koroshetz: No.

Dr. Insel: Okay. So, that's an additional -

Dr. Hann: Isn't that somewhere else?

Dr. Insel: Hold up.

Ms. Singer: It's in Section 2, but we can put it here if you want.

Dr. Insel: Okay. Can you read this?

Dr. Hann: Okay. There are reports of associations of ASD with exposure to medications, maternal antibodies, toxicants and infections prenatally and postnatally. However, these reports needs to be subject to additional study.

Dr. Insel: In favor. Opposed. Abstained.

Dr. Hann: Lyn, is that an opposition?

Ms. Redwood: No, I just was delayed.

Dr. Insel: Just delayed in favor. Unanimous. So, we're moving on to line 10, 11, 12?

Mr. Grossman: 10 through 12 under What Do We Need.

Dr. Insel: Can that go into Research Opportunities instead of What Do We Need, just as a bullet?

Dr. Lawler: Or maybe in the Research Resources in the new chapter, because I'm not sure. I was going to ask Lee for some specificity about -

Dr. Insel: Sounds like Chapter 7.

Dr. Lawler: Yes.

Dr. Insel: Let's boot that to Chapter 7 if you're okay with that.

Mr. Grossman: I mean the thinking of the Panel was that there was ongoing

research in other areas of toxicology outside of autism, and that we could piggyback on that.

Dr. Lawler: But that's probably something that could be covered in Chapter 7, or you think it still needs -

Dr. Insel: Cindy, you're the expert. What do you think?

Dr. Lawler: I think we're going to need to elaborate it more if we keep it in this particular section.

Dr. Insel: Maybe it does go into resources and opportunities that are available for developing infrastructure.

Dr. Lawler: Right.

Dr. Insel: Would you want to help us with that if -

Dr. Lawler: Yes.

Dr. Insel: So, motion is to punt on this and put it into a separate chapter.

In favor.

PARTICIPANT: So moved.

Dr. Insel: Opposed. Abstain. Moving on. Line 20.

Mr. Grossman: It goes over to the next page.

Dr. Battey: I don't think it's necessary. I would take it out.

Dr. Lawler: Again, part of it could - we could circle back to it in Chapter 7 -

Dr. Insel: Okay.

Dr. Lawler: - with the reanalysis of biospecimens.

Dr. Insel: All right. So, what's the group want to do? In favor of deleting it?

Dr. Battey: Move to delete.

Dr. Insel: All in favor of deleting? Opposed.

Dr. Hann: There are two opposed.

Dr. Insel: And abstentions. One abstention.

Dr. Hann: One abstention.

Dr. Insel: The motion carries and we're moving on to page 7, line 7.

Mr. Grossman: Page 7, line 7 - starts at line 6.

Dr. Insel: I just don't understand what it was that the Panel was asking for.

I understand the first part, coordinating with NVAC, but what's line 8 and 9 mean?

What do they want?

Mr. Grossman: Well, this is one of those areas where we wrestled on the wording, and I would - my sense of the Panel was that this was an issue that we couldn't get consensus on regarding vaccine safety. And we wanted to put some wording in here that the IACC would consider if they wanted to address this.

There was some discussion about if too much emphasis had been put on the NVAC. And there were some comments made about the NVAC not having the research monies to go

forward.

And since IACC had it, is it something that they should reconsider?

Dr. Insel: So, the IACC and NVAC have virtually the same budget, which is almost zero. So, there's no IACC research money.

I thought what - let me read this to you and see if this is what the Panel wanted, because I just was confused.

It looked like it was either two completely different concepts in one sentence, or it was one sentence that didn't have the right conjunction.

"To address public concerns regarding a possible vaccine/ASD link, it will be important for the IACC to continue to coordinate with the NVAC."

And then what I thought they were saying was that they want us to continue to coordinate with the NVAC to ensure that whatever comes out is informed by the best

science on neurodevelopment and ASD risk.

Is that what they were asking for, or do they want something around health surveillance?

Mr. Grossman: It seemed to be a further explanation or just more - a stronger linkage between what NVAC was doing with what we are trying to accomplish there in terms of driving - there was concern that there was too much of a void between what NVAC was doing and what some of the members felt that the IACC should be doing.

So, they wanted to draw a closer, collaborative effort between the two.

Dr. Battey: I think you can accomplish that goal if you simply end the sentence after the NVAC in parentheses and don't include the rest of it.

Ms. Redwood: Tom, I'm a little confused by this because this was actually from last year's plan. And at the time, we did want to coordinate with NVAC. And shortly

thereafter in the first part of this year, we set up a meeting - actually, I think it was July 15th - where we met with all the members of NVAC.

NVAC has completed their work and they have a document, the National Vaccine Advisory Committee's Recommendations on the Centers for Disease Control, Prevention, Immunization Safety Office. This is their draft five-year scientific agenda.

So, we've already done that. Does it really need to be in the Plan now, or should we just move forward with what was discussed at the meetings and the recommendations by NVAC? Because this, to me, has already happened.

Dr. Insel: So, remind me. I thought that when we met with them, that one of the recommendations was to have a third party, they were talking about potentially Institute of Medicine body, look at feasibility questions and how best to pursue

issues around vaccines and autism.

So, when I read this, I thought what this meant was that we should continue to work with them to figure out how that could be done and to make sure that whatever is done, has people involved to actually keep autism in the forefront so it doesn't become like that report about vaccine safety much more generically.

Ms. Redwood: Yes, and no. If you read the minutes to the meeting, actually, this was a quote from, you. Dr. Insel said that members of the IACC may struggle with the recommendation that the question of a feasibility for a vaccinated and unvaccinated study be booted to another committee such as the Institute of Medicine. He asked if it would be beneficial to release a Request for Proposals to see whether a well-designed study could be proposed.

And then Dr. Carlson said it would be possible for an investigator-initiated

study to be funded and would not require a committee's actions.

Dr. William Rob supported the idea of issuing an RFP, calling it a wonderful pragmatic tool with relatively low risk. And in the worst case scenario, no high-quality proposals would be received.

Dr. Insel: Right. So, that's very much the way I felt about it then and I still do, that we don't need an endless series of meetings to continue to look at the same question.

But I do believe that what the NVAC is intending to do, is to actually mount an additional - I think it's a meeting. I think it's an IOM session to look at this question.

They felt that this was one of their items on their to do list that came out of that joint meeting we had with them, and they have come to us asking for our support in this.

And it's not something that I'm particularly enthusiastic about. But if they do it, I think they ought to do it with people who are informed about autism so this does become a group that has, as it says here, the - includes developmental assessments and outcomes to inform ASD research.

So, again, why I was asking what it was that the Panel meant by this, is I was confused whether the second half of this sentence had anything to do with the NVAC.

And if it did, the only thing I could figure out was that it was about the next steps that the NVAC was going to take and to make sure that it was autism related, or if this is something completely unrelated to NVAC and had to do with asking the IACC to support efforts in public health surveillance of vaccine safety.

And I just still don't know what it is that the Panel is recommending, because those are two very different things.

Ms. Blackwell: Tom, could you reread the suggestion that you started out with that talked about to ensure that the best science -

Dr. Insel: Yes, this is based - and this is, again, at variance with what Lyn was saying, but it's based on my sense that the NVAC does intend to do something further that was in response to our original request around the feasibility question.

What they've said to us was that they didn't think it was ethical to do such a study of vax versus unvax, but they also recognized that there may be a need to look at this more fully, and they were willing to think with us about putting together a third party to explore it.

And Lyn's quite right. At the meeting, I wasn't very enthusiastic about that. What I thought this was saying is that we should continue to work with them. And if we're going to work with them, it would be -

so, it would be important for the IACC to continue to coordinate with the NVAC and to ensure that the best science and neurodevelopment in ASD risk are part of whatever it is they come up with.

That's not the right language, but something like that.

I thought our role here is to bring the best science on autism to whatever it is the NVAC decides to do.

Ms. Redwood: I guess what I'm asking, Tom, is you also say that you felt spending another year in panels discussing feasibility would not address the urgency felt by parents currently grappling with immunizing siblings of their autistic children. And so, I'm asking whether or not this really needs to go to another IOM report.

If you actually read the NVAC report that came out, what they're suggesting, the type of studies being suggested would be an observational study of populations looking

at natural variation in vaccination schedules. And this would be ones that have chosen not to vaccinate, it would not be a random controlled study, and where some children were vaccinated, vaccination is declined through parental intent.

And we have states now that have between five to six percent of children that are unvaccinated, so I don't think it would be very difficult to find enough children to be in this study.

And, let's see, they go on to say importantly it might be difficult to control for co-founders in the study of health outcomes of vaccinated/unvaccinated populations. The baseline health and social characteristics may be different, but meaningful results may be difficult to obtain, but they still are endorsing that this feasibility study be done, in their report.

Dr. Insel: So, what they mean by a feasibility study, Lyn, as I remember it, was

that this is something they want to hand over to a third party like the IOM, to tell us how it could be done.

And what I was saying was - I think actually you and I are saying the same thing. Do we really want to wait another year and have another IOM report at great expense to tell us how this could be done, rather than just deciding what could be done and figuring out a way to move forward with this.

Taking your comments seriously, I mean one might argue for just deleting this whole section about the NVAC and saying, as you've mentioned, they've done their report, we've had our meeting with them, and perhaps we don't need to go back to them for yet another long conversation and another IOM effort.

Well, I'm open to whatever the Committee wants to do. I just have to say that my comments at that meeting really reflect my own view. I wasn't speaking on

behalf of the whole committee.

I personally just don't see that taking another year and having another set of meetings is the answer to this question, but that's why -

Ms. Redwood: Do you want to make that as a motion?

Dr. Insel: Well, that's why I'm focusing on this paragraph. Because if the Panel is saying continue to work with the NVAC and do a lot more stuff with them, you know, I'm trying to get a sense of what it is they were telling us they want.

I mean maybe the motion would be to strike this whole section and forget about the NVAC, and move into questions about what we can do in response to the interest that we keep talking about in doing more on the environmental factors.

What's the sense of the group?

Dr. Houle: Tom, I'm not sure that we need that much detail, but I'm not sure

what the downside would be of continuing to communicate and coordinate with the NVAC considering the nature of the work that they do.

Dr. Insel: So, should we just end the sentence after NVAC, as someone suggested, and not worry about the rest of this?

Dr. Battey: Yes, I support that.

Dr. Trevathan: I would too. And I'll just add I think part of what the discussion we had with NVAC that led to some of the additions here, was really related to what you said, Tom, was that we want to make sure that we emphasize to the NVAC the importance of having experts that they consult with and get expertise of - get the expertise of those that really know developmental neurology and autism, and have that expertise inform what they do.

I think that's been heard and is actually what is accomplished in part by us continuing to have open dialog with the NVAC.

So, I would say that's accomplished by ending the sentence after NVAC with a period.

Dr. Insel: Is that a motion or -

Dr. Battey: So moved.

Dr. Trevathan: Yes, so moved.

Dr. Insel: Now, let's talk about this because I want to make sure that we're not rushing through this.

Is there something we're missing here by not specifying what it is we want to do with our continuing work with the NVAC?

I don't think we're committing ourselves to anything, but I just want to make sure we're not losing something in this process.

Gail.

Dr. Houle: Well, we have many directives that we coordinate with other agencies. And we've, in fact, sometimes had to clarify the legal definition of coordination, say, with DoD and the autism

work that they are doing. And it in no way takes the primary responsibility away from the agency who was the primary charge.

It just is a statement to include consideration and coordinate with the work of the other agencies who could have valuable - valuably inform what you are doing.

Dr. Insel: So, would you change the language at all or -

Dr. Houle: I would leave it as coordinating with the NVAC, because I think that the nature of the work that they do is something that we want to keep abreast of.

Dr. Insel: So, do we have a motion what to do here, because we need to keep moving.

Dr. Battey: Yes, end the sentence after NVAC and delete everything else.

Dr. Trevathan: Second.

Dr. Insel: What about the original language about what the NVAC is? Do you want to leave that in? You don't want to change

that?

Dr. Battey: I think it's innocuous.

Dr. Insel: Okay. In favor of stopping the sentence after NVAC? Opposed.

Dr. Hann: One opposed.

Dr. Insel: One opposed, and any abstentions. None. Okay. Moving on.

Mr. Grossman: Okay. We're going to now look at lines 15 on page 7, to line 1 on page 8. And this is describing examples of topics to be included. And we're probably going to want to chunk this out line by line, I would imagine.

Dr. Insel: So, again, the question just going back to the conversation we had, all of this is in reference to our interaction with the NVAC, yes?

Do we need to even go there? If we've just said that we're going to coordinate with the NVAC -

Dr. Hann: I thought we agreed to

delete this.

Dr. Insel: No, I don't think we talked about it.

Ms. Redwood: Tom, these are specific - these are not the specific recommendations of NVAC. These were specific recommendations of Panel 3.

Dr. Insel: Right. So, these are examples of topics that could be of mutual interest between IACC and NVAC.

Mr. Grossman: Right.

Dr. Insel: Do we need that?

Ms. Redwood: I guess I viewed it more, Tom, as this is the IACC workgroup's recommendations with regard to what should be studied.

And one of the things we were saying about NVAC, is that they lacked expertise in autism. So, I see this as our contribution to what we think would be important to look at with regard to vaccine research as it relates to autism.

Ms. Singer: I don't recall these particular topics being brought up at the Panel discussion. And I think we can capture this with the sentence that we brought up earlier, which is that the topics would be to ensure that the best science on neurodevelopment and ASD risk is included in NVAC's discussions.

Mr. Grossman: Just to represent the Panel on this, is that everybody on the Panel had agreed to this section. So, I'm just making you aware of that.

Ms. Redwood: And I listened in on both of those phone calls, and these items were discussed on the phone calls, not as much during the actual committee meeting.

Dr. Hann: Okay. So, what am I hearing? Am I hearing then that we just voted to stop the previous section after "the NVAC Committee." And then have the next sentence, "the NVAC is a Federal advisory committee," essentially saying what NVAC is. That's where

we stopped in the previous section.

So, the question would be are we saying then that the next sentence is acceptable to keep as was originally proposed by the Committee?

The communication between IACC and NVAC permits, so on and so forth, and then examples of the topics. Because examples of the topics were examples of the dialogue between IACC and NVAC.

Dr. Insel: So, it made sense, I think, to do that last year when we were trying to propose what we would be doing with NVAC?

Why do we need to continue to list the things that we're going to discuss with them?

I guess I'm just lost here about what we're trying to accomplish here.

Dr. Battey: I would be in favor of deleting the entire sentence that starts "examples."

Ms. Blackwell: I actually liked Alison's suggestion, and it could be substituted under this sentence that starts "communication."

Ms. Singer: Right. So, I would suggest that we replace the sentence or that we eliminate the sentence that starts with "examples," and add that what we want to coordinate and communicate with them about is - the reason we want to continue to be involved with them is to ensure that the best science on neurodevelopment and autism and ASD risk is included in their decision-making process.

Dr. Insel: Discussion?

Ms. Redwood: Again, I think it's important to include because this is what the Panel 3 came up with and this is our contribution to NVAC as being autism experts in terms of what studies we think would be important to be done to be able to answer these questions.

So, I would make a motion that it be retained.

Dr. Insel: Other discussion?

Does anyone want to make a - so, we have one motion to retain all of the language that came from the Panel. The other motion is to delete everything after the word "examples," and to include something about scientific - the best science on neurodevelopment and autism, ASD risk.

So, we can simply vote between those two motions. Let me ask how many people want to retain the original language.

The original language is what you see in blue. So, it's lines 15 through -

Dr. Hann: Original edits.

Dr. Insel: Yes, the original edits. I'm sorry. So, these are the edits that came from the Panel.

So, to accept the Panel's recommendations?

Dr. Hann: Four to retain the

language.

Dr. Insel: And to delete all of this beyond line 13?

Dr. Hann: Ten.

Dr. Insel: And then there's a recommendation to include some language which we'll leave to OARC, that will specify that the mutual interest includes our providing them with the best science on neurodevelopment and ASD risk.

Mr. Grossman: Okay. On to page - lines 13 and 14. There's an addition there.

Ms. Redwood: I don't think it's necessary to have that in there to specify there's several studies that this could be accomplished.

Dr. Hann: Do I have a motion to delete?

Dr. Insel: I move to delete.

Dr. Hann: Okay. Second? All in favor of deleting? Any opposed? Any abstention?

Okay. Unanimous. It's gone.

Mr. Grossman: Okay. Lines 18, 19 refer primarily to gene/environmental interactions.

Dr. Battey: This has got to be at least the fourth time that that's been mentioned in this section. I don't know what good comes from that redundancy, so I would move to remove the language.

Dr. Hann: To all of the language, or as well as the parenthetical that's ending on line 18?

Dr. Battey: I would take out all the blue text on lines 18 and 19.

Dr. Hann: Okay.

Dr. Trevathan: Second.

Dr. Hann: All in favor of deletion? Eleven.

Those not in favor? Two.

Any abstentions?

So, the section beginning on 18 through 19 has been deleted. I think that

leaves us now with 20 -

Mr. Grossman: 20 through three on the next page, which is just describing the EARLI study.

Dr. Hann: Comments?

Dr. Trevathan: It's a great study, but I guess why do we need to have all these individual examples, I mean other than the obvious that you've explained already.

Dr. Battey: I completely concur with that sentiment.

Dr. Hann: Okay.

Dr. Battey: I would eliminate it.

Dr. Hann: To eliminate, anybody have a second?

Dr. Trevathan: Second.

Dr. Hann: Second. Those in favor of eliminating? Okay. Any abstentions? Any not in favor?

It was unanimous to delete.

Mr. Grossman: Okay. We're now on page 9, lines 4 through 10. The Panel was

primarily wanting to emphasize the heterogeneity in this section.

Dr. Hann: Comments? Discussion? I think there was one member who would move to strike it.

Dr. Battey: Yes, I believe it's redundant with statements that had been made throughout the section. Move to eliminate it.

Dr. Trevathan: Second.

Dr. Hann: Okay. Those in favor of deleting this paragraph? We have eight in favor of deleting.

Those not in favor, four.

Any abstentions? Two.

Mr. Grossman: Okay.

Dr. Hann: Motion carries to delete.

Mr. Grossman: Next for consideration are lines 11 through 17.

Ms. Singer: I would suggest that lines 11 through 17 be moved into Chapter 7 which is specifically now focused on exactly

these types of information, communication and infrastructure issues.

Dr. Battey: I second that motion.

Dr. Hann: Discussion?

Okay. Vote to move this section to the new Chapter 7? Those in favor? It looks like it's unanimous.

Any opposed? None opposed.

Any abstained? None abstained.

Motion carries.

Dr. Insel: Okay. Lines 18 through 19 on the aspirational goal. The term "prevention" which was originally what we were trying to highlight in Chapter 3, it's in the title, somehow got lost as all these changes were made.

Was there a discussion from the Panel that they didn't want to talk about prevention or what was the issue?

Mr. Grossman: Well, they did want to talk about prevention. They were having issues with the term "prevention." And trying

to be cognizant of some of the comments that were made at the workshop and the connotations that prevention may have, there was a seemingly unanimous decision to as we were referring to prevention, that it was truly talking about enhancing quality of life.

When the term "prevention" was to be used specifically, was to address amelioration of comorbid medical conditions that might be associated with ASD.

So, in terms of how this was looked at, there was a discussion that went on about how we would certainly put this into context. With those aspirational goals, though, the feeling of the Panel was that it needed to be far reaching and address life span.

Dr. Insel: Somehow I think we've lost something in this, though, because if you were really trying to be aspirational, and not just for autism, but in any area of medicine, the first thing you think about is reducing

morbidity and mortality through prevention.

That is the one thing that we can point to over and over again. And if we're not going to do it in this chapter, I don't know where it will happen.

I mean especially after we've just had this whole section saying that our environmental triggers and that we can figure out now how to know who's susceptible, why wouldn't you speak to that as what you aspire to is that you'll be able to prevent ASD by making sure people don't get exposed to something that could cause it.

Am I missing something here? Is there a way which that is offensive to part of the community or what -- Alison.

Ms. Singer: No, I completely agree and I think we were reflective of the concerns expressed by the community when we added the phrase "prevention of the challenges and disabilities" so that we're clear that we're not referring to prevention of individuals.

I also question the addition of the term "services and supports" in this aspirational goal, because I think these particular set of research studies really do not speak to services and supports. I think there are other studies elsewhere in the Plan that do, but just these do not.

Mr. Grossman: The discussion that we had on the Panel was like where do we bridge this research? And that's why they felt that it was important to throw services and supports in there so that there would be this translation from research to actually making it applicable on a day-to-day basis.

Ms. Singer: But what you're describing is the side effect of the silos that we -- we knew this might happen when we decided to take a chapter-by-chapter approach. Not every chapter needs to talk about services and support in translation.

I think we capture it in the sort of overall umbrella themes throughout the

document, but what you're describing is exactly what we referred to earlier.

Dr. Insel: The same with treatment.

Ms. Singer: I don't think it needs to be here.

Dr. Insel: We don't need it. I mean this is about causes and prevention, and it's not about treatments or service delivery.

Ms. Redwood: Can I move that we put the aspirational goal that we had in here, back?

Ms. Singer: I second.

Dr. Hann: Okay. Any further discussion?

Okay. Those in favor of restoring the original language? Those opposed? One. Any abstentions? What was that? Christine, what did --

Ms. McKee: What was deleted, are we putting back in that the prevention preemption of the challenges and disabilities,

that section?

Dr. Hann: Yes, the original language. Just to be clear, the original language was causes of ASD will be discovered that inform prognosis and treatments and lead to prevention/preemption of the challenges and disabilities of ASD.

Ms. Singer: Not of ASD, but of the challenges.

Ms. McKee: Of the challenges. Okay. Thank you.

Dr. Hann: So, the motion carries to restore to the original language.

Mr. Grossman: Moving on to page 10, research opportunities, epigenetics was added to line 2.

Dr. Lawler: This is a case where I'm really surprised that I think this is the only point in this section that we even talk about, epigenetics.

I mean that really is one sort of clear example of a case where there has been

significant progress and it provides a nice model for how environmental factors can interface with the genome, and it just seems that it's not reflected anywhere.

This is a single bullet, and this bullet doesn't even refer to environment in epigenetics. Just refers to genetics and epigenetics and I'm just curious.

Was there any discussion of this and it just didn't make it into this document or --

Mr. Grossman: That's a good question. I don't have a good answer for it.

Dr. Battey: Could I ask the question as to whether or not the term "epigenetics" is going to be widely understood by a lay audience without some explanation as to what it means?

Dr. Insel: Would it be possible to -- I know we don't want to backtrack at all, but since it's not anywhere in the document, if maybe Cindy could help us to put in three

sentences in the What Do We Know section about this new area and define what epigenetics is and why this is so important in bridging genomics and environmental --

Dr. Battey: This is where the environment meets the DNA.

Dr. Insel: Exactly.

Dr. Battey: The epigenetics.

Dr. Insel: So, we're going to have to come back at the end of January anyway to look at this. But, Cindy, if you could do that, then it would provide some basis by which to say this is a research opportunity.

Dr. Lawler: Okay.

Dr. Insel: And it is under What Do We Know because it's new stuff that we can -- and you can cite, you know, there are two or three, I mean there's a recent nature piece on the human epigenome that's just been out a month, but that would be a great reference to have in here.

Dr. Lawler: I'll have to do that,

and I'll run it by Jim. I know he's one of the leads on the Roadmap.

Dr. Battey: There have been some spectacular advances in epigenetics in the last year. So it's entirely appropriate, I think, to add it in.

The community is in the process of discovering new types of epigenetic marks that actually we didn't even know existed a year ago.

Dr. Insel: I mean you could argue that that's the most important thing to put in the update of the Plan. Because if there's one thing that's changed in science in the last 12 months, that's probably the most profound difference.

And it's highly relevant not yet so much in the autism research community, but it should be. And this could be one of the places where the Plan could be very helpful.

Dr. Battey: It's the first time this morning that we've talked about something

that's driven by new science.

Ms. Redwood: This is a little off topic, but this brings up a big concern that we just really didn't have some of the expertise that we needed on these Panels. And I think we need to when we move forward next year, look at this process a little bit more closely in terms of what are the scientific advances and who do we need there to help represent those advances, it could be just a vote among committee members.

Dr. Insel: Yes, I mean we'll talk about this later, I think, but you could argue that we should have had people from cancer biology or other areas of medicine that are far ahead of autism to be talking to us about what we need in the autism research community, right?

So, I think we learned a lesson in this that we can do better next year. Okay.

We need to finish this up, so let's move quickly.

Dr. Hann: So, do I take that then that the proposal to have Cindy and Jim work on some language that would probably fall at the end of the What Do We Know section so that you all can review it, everybody is in favor?

And in the What Do We Need as well? So, in two places, essentially in the What Do We Know and What Do We Need, that you all will provide some additional language.

Is anyone opposed to that idea? Okay. Thank you.

Dr. Insel: Is there anything in the research opportunities that anybody wants to change? These are fairly minor recommendations.

So, can we look at them en bloc?

Dr. Battey: Move to accept the changes.

Dr. Insel: Any discussion or question?

Ms. Blackwell: Actually, I do have one. On page 11, I think you should strike

the piece about seeking to improve quality of life for those with ASD, and then it would be fine. Just put a period after "treatment studies."

I'm sorry. It's lines 7 and 8.

Dr. Insel: So, with that change, any other discussion?

Dr. Hann: Okay. Those in favor of accepting with that one change? Anyone opposed? Any abstentions? Motion carries.

Dr. Insel: Okay. We want to plow through here and get this finished. So, can we move on to the objectives, Lee?

Mr. Grossman: Sure.

Dr. Insel: We've got about two more pages.

Mr. Grossman: Yes. We're up to about line 17 on page 11. There were a couple of additions there.

Dr. Battey: Could I ask where the figure of $56 million came from?

Mr. Grossman: Yes, you can.

Dr. Battey: Is there any explanation?

Mr. Grossman: Where did we get those figures? Jeff put that in? Oh, okay.

I think that most of the figures were put in as placeholders just for the IACC's consideration. There wasn't any discussion of any significance around any of the dollar amounts.

Dr. Battey: It seems pretty arbitrary to me.

Dr. Insel: Was there a reason to take out the number of studies? We had last agreed that we would do 20, and they --

Mr. Grossman: It was five. The discussion was five versus 20, and it seemed like we couldn't agree on anything except multiple.

Ms. Redwood: If we want this plan to be measurable, I think it would be important to sort of have a number, because multiple could be from three to 30.

Dr. Insel: I agree. This goes back to the business about being accountable. We want to have time -- didn't want to be time-bound, we want to be quantifiable so we know when we've done it.

Dr. Battey: So, why not substitute for multiple, at least five?

Dr. Insel: That's where we were. That's where we started.

Ms. Redwood: If we doubled the budget, could we go to ten?

Dr. Insel: Do we know --

Ms. Redwood: If we're saying that the environment is hugely important, I don't think this is an area we should shortchange investigating.

Dr. Battey: I think the question is how many studies can the current research community embrace at any given point in time. And I'm not sure that they can embrace a lot more than five.

Dr. Hann: One of the comments I

recall from the phone exchange on this topic was the importance of looking at multiple factors. So while it may be only five or whatever number studies that the Committee feels like, but that the importance was to be in a given study, to potentially be looking at more than one factor.

So, I don't know if that helps in your deliberations, but that was something that was discussed by the Panelists.

Mr. Grossman: And for whatever it's worth, the Panel was having an issue with a limited number and five being too small.

Ms. Redwood: I'll make a motion for ten.

Dr. Hann: Is that for, just to be clear, is the ten for the number of studies or for the number of factors?

Dr. Insel: So, Lyn, I'm just looking at what we have here for our portfolio analysis. And if I'm reading this right, which may not be the case, it looks like there

are about 12 currently funded.

Ms. Redwood: Are those studies that we just started with ARRA, or these are ongoing studies like EARLI and CHARGE or MARBLES.

Dr. Hann: No, this is not just ARRA. This is ARRA in combination with what was the existing -- that came through through the existing portfolio analysis.

And from looking at this and conferring with the folks who actually did the hard, heavy lifting on this, I believe for Objective 3-1 in the Plan as it was written last year, through the portfolio analysis and ARRA funding, there are currently 22 projects underway. For that fiscal year, 8.1 million.

Mr. Grossman: Lyn, I accept your idea of having at least ten.

Ms. Redwood: I just wondered. I think it's great we have this funding information now, but I think we need to apply it across the whole plan. And I'm wondering

if that's something we could start January 1st and start Strategic Planning early in the year and really look at it closely to see -- Della is shaking her head no.

Dr. Hann: Well, the difficulty we have is that the NIH data frequently is not available until February or March for the entire portfolio.

We were able to gather what we had done for ARRA early, but for the entire portfolio for NIH, we will be limited to a different point in time.

Dr. Insel: But I think that the request makes sense. I mean this is so difficult to do this blind, and this is a great example.

I mean you wonder about all the other things we're going to talk about today, how many things we're actually currently doing, and it's kind of odd that we're arguing between whether to do five or ten, Lyn. We're already doing 22, so --

Dr. Battey: But Lyn makes a good point. I don't know of too many planning exercises that don't begin with an analysis of where we stand at the present time.

Dr. Insel: But we've done that, Jim. The problem is we haven't chosen the data for this conversation. So it's in front of us, and it's one of the things we ought to be looking at as we go.

Let's get back to this particular item, though, because the original language said at least five. Lyn is recommending that we change it to be at least ten. We are doing far more than that now, and the group clearly wants to emphasize environmental factors.

So, how do you want to handle the specific language for this item?

Group, come on. Don't let me down here. We've got to get this done.

Dr. Johnson: I'm okay with at least ten, but I would like one of the scientists to talk a little bit about the

estimated cost.

Dr. Insel: Well, we'll do the cost later. We turn that over to program and --

Dr. Hann: We also last year, we had at least five. And it was at 23.6. And if you're doubling that, then that would be another way to approach it too.

Dr. Insel: Though we're doing 22 at a much, much lower budget than that, so I'm not sure how it scales.

So, Chris.

Ms. McKee: Is there any indication of what -- has anyone lined this up with what's identified in the recommendations of the --

Dr. Insel: No, that's not been done. So, I actually count 14, not 22. But of the 14, I'm not sure how many of those are specific to the IOM report.

Ms. McKee: That language would be inconsistent. I don't want to get into --

Dr. Insel: Yes, that's a good

point, and maybe there's a way to soften that. If people think that the IOM report is out of date and that there are more things that should be done and not limited to what we came up with in 2006, that's worth considering.

So, can we get a motion here of how you want to handle this, because we need to keep going and get this finished.

Ms. Redwood: I made a motion to retain the original language with the exception of increasing the number of studies to ten and doubling the budget.

Dr. Insel: Can we get a second?

Ms. Singer: Singer.

Dr. Insel: In Favor? Opposed? Abstention? We're moving on.

(Unanimous.)

Mr. Grossman: Okay. Page 12, line 9. And again this might be some redundancy that's been put into the wording.

Ms. Singer: What is the heterogeneous group that you're referring to?

Mr. Grossman: They were just referring to those with ASD.

Dr. Insel: Yes, I agree it wasn't clear what the reference was to. I'm not sure it helps to put it in.

Ms. Singer: I think we can take that out.

Dr. Hann: Motion to delete heterogeneous group. Any opposed? Motion carries.

(Unanimous.)

Mr. Grossman: Line 11, "racially and" was added.

Dr. Insel: Any problem with that, Group? Everybody is shaking their heads yes. Okay. We're going to keep going.

Mr. Grossman: And then we'll consider lines 14 through 19.

Dr. Lawler: Okay. I've had a lot of trouble trying to unpack all the different ideas that are in that bullet that starts on line 14. So, I'm going to need some help from

you, Lee, and other members of the Committee to try to understand what the intent was there because it seems like there's lots of different things mixed together.

If we could come up with a kernel of what is really needed, that would be helpful.

Mr. Grossman: From the Panel's perspective, there were a lot of different colors in this area, which meant that there were numerous edits and additions to it.

Dr. Insel: Again, keeping this idea that we're looking for smart objectives, I got lost. I read this many, many times. And at the end, I still couldn't figure out how we'd know that we'd done it and how many, you know, in what time period or in how many studies.

It was just I didn't see how this added to other bullets that are in there. Maybe I was missing something.

Dr. Battey: I would move to delete

it.

Dr. Hann: Is there a second? Yes.

Those in favor of deleting? Any opposed? One opposed. Any abstain? Motion carries to delete.

Mr. Grossman: And then the next addition from 20 on page 12, to 3 on page 13.

Dr. Koroshetz: So, I think that this, I mean I don't quite understand all of it, but I think it gets to a lot of the things that kind of didn't quite fit, but are emphasizing the phenotypic variation. The underpinnings for that variation.

So, I think that sounded like a good addition. I'm not sure if the wording is right.

Ms. Redwood: Motion to keep the new language?

Dr. Hann: We need the number of studies as well. The Panel did not recommend a number.

Dr. Koroshetz: Five. We have

five.

Dr. Hann: I hear five. I feel like I'm at an auction. Okay. So, that would be to initiate five studies to understand factors contributing to phenotypic variation across --

Dr. Insel: I hate to do it this way. I think this is just not intellectually valid. We should be thinking about this much more carefully.

Is this one of these things we want to defer, because we don't have -- I'm just concerned that they haven't given us the information we need about what needs to be done.

What's the sense of the group?

Dr. Trevathan: I think we need more understanding of what they're describing and what we're voting on. I'm not -- maybe someone can explain it quickly. I'm not sure I understand what they're requesting.

Mr. Grossman: It was primarily

around the objective of looking at phenotypical variations and to get that launched, but I would think that we probably have already funded studies around.

Dr. Insel: I think we're all doing that. I mean it's every one of the studies on genotype is looking at phenotype breakdowns, and the Simons Simplex Collection is all about that.

I mean we could put it in. It's already done. I'm not sure that there's any added value in having it, but if people think that it would be useful to include an objective on this --

Ms. Singer: We have a similar objective in Section 2 as well.

Ms. Redwood: Tom, the only question, though, is with this Simons Simplex, are they looking at all these things that are listed like developmental trajectories, co-occurring conditions, response to interventions?

I think that's what - they're really trying to tease out the phenotypic variation, and I don't know that that's really reflected. Maybe it is. I just don't remember that that level of detail is reflected in here, and I think it's very important.

Dr. Insel: Then maybe what we need to do is to wrap that into these other, you know, the other objectives where we're talking about the importance of doing genetic studies where you understand the subgroups and the phenotypes and to put that parenthetical language in.

Maybe there's not -- there isn't a really good bullet on genetic studies, is there?

Dr. Guttmacher: It does seem like that's a nubbin of this, is it's sort of a hortatory if you're doing genetic studies, make sure you are in fact looking at these factors when you do them, not just use

genetics to look at causation of ASD per se.

Dr. Insel: So, Alan, what about moving that language up to the first bullet at the top of the page, coordinate and implement the inclusion of subjects. And then to also request that there's an attempt to look at phenotypic variation along these dimensions.

Dr. Guttmacher: Yes.

Dr. Insel: You think OARC could do that for us and put the language together so that we don't have to -- because it's not clear how many steps we're talking about or how these would be different from further genetic studies.

I think if I understand you, Lee, the point was that the Panel wanted that kind of information to come out of the genetic studies that are being done.

So, rather than saying all right, let's do a whole new set, let's make sure the people who are doing studies now collect this kind of information.

Is that fair?

Mr. Grossman: Yes, I think that's a good move to put that under that first bullet.

There was some discussion around the response to interventions and if the other studies were really looking at that, but we didn't get very involved in that dialogue.

Dr. Insel: Okay. Do we need to vote on this, Della, or --

Dr. Hann: Yes, we do.

Dr. Insel: Okay. Go ahead then.

Dr. Hann: So, the motion what I've heard is that do we delete the bullet beginning with "initiate X studies to understand factors contributing to phenotypic variation" and move the idea of what we mean by phenotypic variation and add it to the first bullet at the top of page 12 that needs to be included in the genetic studies?

Dr. Koroshetz: I hate to prolong this, but maybe I'm on the wrong boat here.

So, I didn't consider this as a genetic question. I considered it as understand the factors contributing to phenotypic variation. So, why do some people have epilepsy, others don't? Why do some people have poor IQ, others don't? Why do some people have GI problems?

So, those are the --

Dr. Insel: So, I read this completely differently, Walter. I thought this was in the 16p11 cohort, you have 50 kids and 25 have seizures, and 25 don't. Why is that?

That's not the way you read it? I thought it was selecting for genetic subgroup and then understanding the variation of the phenotype.

Dr. Koroshetz: So, I thought that was one part of it.

Dr. Insel: If we can't figure out what it is, we're in real trouble for the rest of the community.

Ms. Redwood: It actually says "genetic variation," but I think Walter brings up a really good point in that that would be an additional study that would look at phenotypic variation that didn't involve genetics. I think that's important too.

Dr. Insel: Can we put this off until Version 3.0? I just think that it doesn't -- we don't have it developed enough to really understand what this is about, but it might be useful to at least include this information about which clinical features we want people to be focusing on in the genetic studies that are in the other bullet. Okay.

Della.

Dr. Hann: Okay. So, do I hear the vote to do that? Essentially, to take what is listed now under the bullet that seems to be going away that describes the kind of clinical features, cognitive behavioral features that are important to study, and include that information in the bullet at the top of page

12 which --

Dr. Battey: So moved.

Dr. Hann: And a second? Second. Those in favor? Anyone opposed? One opposed. Any abstentions? The motion carries.

Dr. Insel: So, we've saved the best until last.

Mr. Grossman: Yes. This is the last items for consideration, and from four to 11 are two separate sections that were put in by the Panel. There was not consensus around this, but there was agreement from the Panel that it should be included for consideration by the IACC.

And these specifically pertain to research and studies around vaccines.

Dr. Insel: It says the majority of Panel members did not agree with the following, but they thought it was important for the IACC to know that some Panel members strongly supported the addition of these.

Mr. Grossman: Right.

Dr. Insel: So, what's the sense of the group?

Dr. Lawler: So, Lee, my recollection was that the IACC committee members to begin to address the vaccine issue, they did make some recommendations of the kinds of studies that would be helpful. And those were ones that we had deleted from an earlier version of -- I guess it was What Do We Need or What Do We Know.

But they talked about doing studies looking at response of children with autism to immune challenges and sort of monitoring post-vaccine responses in children with, in individuals with an ASD looking at vaccination status and understanding the limitations, but looking at it in some of the ongoing studies where you could begin to make those comparisons.

So, my understanding was there was a lot of discussion and that was seen as a reasonable approach and one that would replace

these two objectives that were on the table from last year.

That was my understanding from being at the scientific workshop and --

Dr. Battey: I think it's clear that environmental factors play a huge role in the etiology of autism.

It's not clear to me that the vaccine issue needs to be highlighted. I think it is one of many environmental factors where more research is needed.

And for that reason, I would favor deleting the language in lines 4 through 11.

Dr. Houle: Lee, I guess my question is in terms of the decision rules of what to include and what not to include, would different decision rules apply to these two bullets?

Mr. Grossman: No, not really.

Dr. Houle: So, the rest were minority opinions as well?

Mr. Grossman: Well, on this one

specifically there was a feeling among some of the Panel that there were concerns expressed at the workshop by public comment and by some of the people that were at the workshop, that this is an item that the IACC should reconsider.

They did discuss the fact that as this was looked at last year and was taken off the Strategic Plan, and that's how it came about to be placed back on here.

Dr. Houle: As a person who was at the scientific workshop, I think it is important to note that it was the scientists that non-concurred with these recommendations. That would Hanson, Swedo, State, Newschaffer and Landis.

The people on the Panel, I believe, who non-concurred were Hanson, Swedo -- Sue Swedo gave a long speech. Craig Newschaffer, Matthew State and Story Landis.

I believe that was the group. Alison, you were there.

Ms. Singer: I agree. They did not think that there needed to be devotion of new resources to vaccine studies is what I took away from the Panel discussion.

Dr. Lawler: But again I want to make the point I think they did see value in some recommendations. It was just the type of studies that would be most useful, and it would be in the best interest of moving the science forward.

So, it's not that they voted to delete these. I think they came up with some alternative recommendations that I had described before about looking at -- not just at vaccines, but looking at immune challenges.

If you have some evidence already that there may be some immune alterations in some children with autism, perhaps it makes sense to look at the issue of immune stressors. And vaccinations would be one of those.

Naturally-acquired illnesses would

be another, and there would be ways to look at that and move the science forward.

Mr. Grossman: Yes, and I guess I have to take some offense to that portrayal of who did and who did not support this.

There wasn't a vote that was taken at the scientific workshop regarding that. And there were discussions that were held where everybody was in agreement that this should be put forward as a minority opinion.

So, if there's any consensus, that was a strong consensus.

Ms. Redwood: I want to concur.

(Off-mic comments.)

Mr. Grossman: Well, it was part of the discussion.

Ms. Redwood: And also --

Mr. Grossman: It wasn't the majority of the people that were on the call. And there was also some discussion as to would this be presented as a minority opinion, and that was the terminology that was brought

forward.

Dr. Insel: Lyn.

Ms. Redwood: I just want to agree with the statement that Cindy was making, and I was on both of the calls. And there was a lot of discussion around this, and they did feel as though the studies that were mentioned over -- that were excluded before that described the type of studies that would be important, is what they thought should move forward.

So, I think that as you were saying, Cindy, to look at the immune system if we know that there's some children who are at more risk because of some type of mitochondrial abnormality or susceptibility, and that when they receive multiple vaccinations in one day, they may go into mitochondrial dysfunction.

I think that's important to look at, and that's what the Committee was trying to get at.

So, I would make a motion that we take the item on page 12, bullet number 1, 2, 3, 4, 5, and move that over into a short-term goal replacing Short-Term Goal Number -- the first bullet that's highlighted in blue.

Dr. Lawler: Wait a minute. Say that again.

Ms. Redwood: Page 12. Look and see if that's the one you're referring to, Cindy.

Dr. Lawler: My understanding from the workshop is there were a series of recommendations, and coordinating with NVAC was one of those. But another one was looking at using individuals with ASD and looking at response to immune challenges, monitoring post-vaccine events in children with ASD as a lower priority because of the limitations in interpretation using existing studies whether they be the SEED study, CHARGE, EARLI, to compare autism risk in vaccinated, unvaccinated or alternatively vaccinated

children knowing that there would be little power and there's some limitations to how you interpret that.

But that was the kinds of studies that they recommended, and those are captured as part of what's in blue on page 7.

Ms. Redwood: So, the blue part on page 7 instead of "strategies," would start with "studies."

Dr. Lawler: Yes. Studies that better characterize response, and going through line 21.

Dr. Insel: So, Cindy, is the way to forward here to stay more generic and to say for this bullet we have one notion here to just nix it completely. The other possibility is to say to study subpopulations to look for factors that make people susceptible to specific environmental events or environmental precipitants, something like that, without going into the details of the -- without sort of prejudging for the scientific community,

which of those factors somebody might want to look at?

I would assume that vaccines would be one of them.

Dr. Battey: I would support that.

Ms. Redwood: Tom, I know researchers who have mentioned vaccines in their proposals, and they get nixed. So, I guess I have concerns if it's not specifically identified, then they're not going to get studied because it's not a popular subject to investigate it, obviously.

Dr. Insel: What you might want to do is to encourage people to look at a whole range of factors of which this could be one of them, right?

Ms. Redwood: I think that's important, but it's important that we specify vaccines and not just say environment. Because otherwise vaccines will not be incorporated into those studies.

Dr. Insel: Walter, use your

microphone.

Dr. Koroshetz: Potential compromise as the language on page 7, uses the generic term immune challenges.

So, that was your proposal to move that sentence on page 7 to take the place of -

Dr. Insel: Cindy, could you actually do that? Could you come up with some language and just if you paste that in, what would it look like?

Dr. Lawler: I'm not good at editing on the fly. So, I think if we go back to page 7, and then - let's see.

The studies that better characterize response to immune challenges. And then in parentheses, including vaccination as well as naturally-acquired illnesses. And then either the same bullet or separate bullet, studies measuring post-vaccine response in children already diagnosed incorporating those measures into existing or new studies and assessment of how

epidemiologic studies can - well, I don't know about that.

Dr. Insel: So, I want to go back to this issue about focus, focus, focus. I think there's too much there.

And what I thought I heard from Lyn and what I heard from the Panel, was this comes up over and over again. Nobody is claiming that vaccines cause all cases of autism. We're looking for whether there's a subpopulation.

Whether it's response to an immune challenge, response to an infectious agent, response to something else we don't know about, but whether there's a way to be able to detect subpopulations that may be more susceptible to a range of things.

And it may be that if we use the last part of that bullet and we graft in this business of response to immune challenges and we can spell out what those might be, including acquired illnesses and vaccination,

that could be a way to spell this out so that people understand what it is we're looking for without saying we're looking for a thousand different factors here.

Dr. Hann: Okay. Do you want to take a stab at - well, what I've heard and I was sitting here scribbling and listening at the same time, this is not final, by any means, support studies to investigate subpopulations that may be more susceptible to environmental exposures, including the study of susceptibility or something having to do with the immune system.

I'm having difficulty with the words right now, but sort of looking at a new challenge. I am, but it needs to be streamlined because it's so verbose at this moment.

Walter, you need your mic.

Dr. Koroshetz: Couldn't it be support research to identify potentially susceptible subgroups and to better

characterize the response, e.g., immunological, behavioral, symptomatic, developmental, to immune challenges.

Dr. Insel: I think you want to define the subgroup in terms of their response to an immune challenge, and there may be something else in there as well. But the immune challenge would include naturally-acquired illnesses and potentially vaccination or something like that.

Ms. Singer: What subgroups are we referring to?

Dr. Insel: We're talking about -

Dr. Hann: That are susceptible to environmental exposures.

Dr. Insel: So, these would be kids who may be considered to have a more regressive picture or something like that, or potentially kids who just have an exacerbation with an environmental challenge of some sort.

Ms. Singer: And is such a group well defined in the literature?

Ms. Redwood: Actually, if you look at some of the research of Jill James with lower glutathione levels, then those children would be more susceptible to vaccine injury because some of their natural detox mechanisms aren't working appropriately.

So, yes, there are subgroups defined.

Dr. Insel: Would you feel better if it was to say support studies to determine if there are subpopulations that are vulnerable to environmental challenge?

Ms. Singer: I think that -

Dr. Battey: That sounds good to me.

Dr. Hann: Okay. Say that again, Tom.

Dr. Insel: Because that doesn't beg the question. It simply says this is a question worth pursuing.

Dr. Hann: Say it again.

Dr. Insel: Support studies to

determine if there are subpopulations who are more susceptible to -

Dr. Hann: Immune challenge?

Dr. Insel: To immune challenge. And then I would put in there in parentheses, acquired infections/vaccination and perhaps something else. Is there - or autoimmune.

Dr. Lawler: I like that. I think that's a good compromise.

Dr. Hann: Okay. Let me try to - I'm like doing my own version of shorthand or so.

A support study to determine if there are subpopulations that are more susceptible to immune challenge. And then in parentheses, e.g., infections, vaccines, autoimmune.

Ms. Blackwell: Can I ask a question?

Did we cover the environmental events in the words immune challenges? Because we kind of lost that somewhere along

the way.

Ms. Redwood: I think we've got environment throughout this.

Ms. Singer: Maybe it should be more susceptible to environmental challenge rather than immune challenge, is what Ellen is saying.

Dr. Lawler: I'd like to at least include as an example, immune challenge is a really important -

Ms. Singer: So, maybe it's environmental challenge, and then in parentheses -

Dr. Lawler: - including immune challenge.

Ms. Singer: - immune challenge.

Dr. Insel: But then would an acquired infection be an immune - would that be an environmental challenge?

Ms. Singer: Could it be an environmental event that -

Dr. Insel: Environmental

exposures? How about environmental exposures? Is that better?

Dr. Lawler: I just think we need to have -

Dr. Insel: And have some examples?

Dr. Lawler: As immune challenges, an example of environmental exposures?

Dr. Insel: Yes, including immune challenges such as -

Dr. Lawler: Okay. Della, can you read that back?

Dr. Hann: Okay. Support studies to determine that there are subpopulations that are more susceptible to environmental exposures.

Ms. Singer: For example, immune challenges.

Dr. Hann: E.g., immune challenges.

Ms. Singer: Immune challenges.

Dr. Hann: Such as naturally-acquired infections, vaccinations. Such as immune challenges related to infections,

vaccines or underlying autoimmune -

Dr. Insel: That puts the question on the table, and it makes this a place that people can do an RFA if they want, that can support research.

Other issues or questions about this? Let's put this to a vote.

Dr. Hann: Okay. So what I hear, and correct me if I'm wrong, the vote is that we would accept the new language which - please, do I have to read it again?

The new language which is to support studies to determine if there are subpopulations that are more susceptible to environmental exposures such as immune challenges related to infections, vaccines or underlying autoimmune problems.

That would replace the red bullets that appear on page 13. There are two of them, but that language will replace both of those.

And then I do have to beg and ask

you how many studies such as this that you're interested in.

Ms. Redwood: Della, what about - I was seeing that as replacing the study that's highlighted in blue, and then still considering the following bullet on epidemiological studies to look at health outcomes.

Dr. Hann: Okay. How about if we try it this way? Why don't we vote to see if people are comfortable with the wording, and then we'll go through and determine which ones are going to be either kept or deleted.

So, the new language, those in favor of the new language? I see 14. All in favor of new language.

Okay. Those in favor of keeping that which is now highlighted in red and blue, essentially it has a blue highlight over it, it begins support the investigation of the effects of vaccine, vaccine components, etcetera.

Those in favor of keeping the language? Those in favor of deleting that language? Twelve. Those opposed?

We're voting to delete it.

Dr. Insel: So, we've basically replaced it. But in this case, we're making sure you want to do the replacement.

Ms. Redwood: Right.

Dr. Hann: So, what I heard was a vote of 12 to delete. Any opposed? One opposed. Any abstentions?

Okay. Motion carries to delete.

The next set of language is the next bullet which is in red. Support the initiation of an epidemiological study to determine if the health outcomes, including ASD, among various subpopulations with vaccinated, unvaccinated and alternatively vaccinated groups at an estimated cost of 10 million.

Discussion?

Dr. Trevathan: Maybe just can you

clarify - maybe I'm just a little confused.

So, your comment about the majority of Panel members do not agree with the following recommendations noted in red, that includes, etcetera, I won't read the whole comment, that includes this bullet as well?

So, your clarification about the previous bullet applies to this one as well.

Dr. Battey: I move to delete that bullet.

Dr. Insel: So, I want to say something about this because I wasn't part of the Panel discussion.

We're moving ahead with something that looks quite a bit like this already, using an HMO network. At least that's the intention.

That's not a reason why it has to be in the Plan, nor is it a reason why it shouldn't be in the Plan. It's just I thought it might be useful to know.

We're looking at it in a somewhat different way. We're looking at what we'd like to do, and this is not yet complete. So, it's the intention, is to look at health outcomes of family members where there's at least one child with ASD in the family.

And this will be an observational study. It's just looking at administrative databases to get a sense of whether siblings, and for that matter parents, have health outcomes of interest.

In this case, the question about vaccination is actually an interesting independent variable because we already know that a large number of these siblings don't have the full vaccination schedule.

So, I just thought I should put that out on the table. Whatever it is the IACC decides to do, we will probably have data that will be pertinent to the question within a couple of years, maybe less, based on these very large administrative datasets.

That's not a reason why it has to be included here. But if it's not included, we're still going to go ahead and do this.

Dr. Battey: There's a motion on the floor.

Dr. Insel: Second?

Ms. Singer: Second.

Dr. Hann: Those in favor of the motion to delete this bullet? Nine. Those opposed? Four. And one abstained.

Motion carries to delete.

Dr. Insel: We have come to the end of Panel 3. Thank you, Lee.

Mr. Grossman: On behalf of Panel 3, thank you all for your patience.

Dr. Insel: Taking out nested, case-control at the very end is okay, one assumes. Okay.

Let's break for lunch. Let's bring lunch back. We are so far behind. There's a cafeteria down the hall. Grab something, come back, we'll try to get started

in 20 minutes.

(Whereupon, the meeting went off the record at 1:12 p.m. and resumed at 1:26 p.m.)

AFTERNOON SESSION

1:26 p.m.

Dr. Insel: It's almost 1:30. We're about an hour behind. Little more than that. So, I'd like to invite you to now come back to work and we'll start on the rest of the Strategic Plan.

So, we have a new chapter, Chapter 7, that we have a draft of that you've looked at.

I'm going to recommend that if it's okay with the group, that we hold off on that until we go through one through six.

Is that okay? Because I want to try to see if we can get everything else finished.

We have a good enough start on 7 that I think we can add to it as we go.

You'll see there will be a number of things that will drop out from other chapters.

So rather than doing that first, I think what we can do is begin to mark the things we want to move, and then we'll come back to it once we have a list.

So, if we go back to Chapter 1, which we've already been through once in the previous meeting, Chris, that's your chapter; is that right?

Ms. McKee: No, no.

Dr. Insel: Who -

Dr. Johnson: No, that's mine.

Dr. Insel: Jennifer. Great. So, we have some notes from that.

I also need to announce that I have a family emergency, which is why I've been getting all of these phone calls. So, I'm going to have to leave at 2:30, unfortunately. This has just come up and there's nothing I can do about it.

So, I'm hoping we'll be able to

get as much done as possible by then, and then I'm going to turn this over to Della to chair for the rest of the afternoon.

So, Jennifer, take it away.

Dr. Johnson: Okay. Thank you. I'm just trying to get myself organized here. So if you can give me another minute for that, because I have papers all over and lunch.

Okay. I think I'm ready.

We did discuss Chapter 1 at the last IACC meeting. And what we did was based on the recommendations from the IACC, take the revisions that had been done at that point in time, back to our Panel for their feedback - well, review and feedback.

And we subsequently then made additional changes to the chapter as a result of our discussions with the Panel.

Our Panelists never got involved with editing the document, so again their feedback was just general - in some cases

specific to some of the language in there, but again they were never in the document actually editing it.

There's a couple things I want to highlight for you all, and then I guess we can decide if we want to go through this line by line.

One of the things I want to highlight, I think, is something that we as a committee need to decide whether we make these changes across the Plan altogether or just specific to Chapter 1.

There were some recommendations to make some changes to some of the terms that are used in Chapter 1, which are terms that are used throughout the Plan, I think.

So again, I think we need to decide whether we would accept those changes and whether it would be changes for the entire Strategic Plan.

Throughout Chapter 1 there is use of the terms "symptoms and severity." And it

was recommended that we change that to "characteristics of ASD." That symptoms and severity had somewhat of a negative connotation, and that characteristics was a better representation or better term to use to talk about the variability that occurs in the spectrum.

Another change that was suggested was when we reference early intervention, that we include the term "appropriate early intervention." So again, a decision as to whether we would any time we reference early intervention, refer to it as appropriate early intervention.

And then another change that was suggested, and there's different terms that are used throughout the Plan, specifically in this chapter it's warning signs, red flags, risks. Those terms in general were changed to indicators of autism spectrum disorder.

So, those are the three terminology or areas in which terminology was

changed.

In terms of the specific edits to this chapter, you might have looked at this and thought that there was extensive changes based on the last copy you received of the edits to Chapter 1.

And although they look extensive, they actually are not significant. Because what ended up happening was we took what was in the What Do We Need Section and moved it to What Do We Know.

And the reason for that was that I think in this committee and also on our Panel, there's a real struggle around the context for the discussion about when should I be concerned.

And the way the chapter was set up, it was almost as if the cart was becoming before the horse and that there wasn't a context for the discussion about what are the issues that the field is dealing with when it comes to the topic of when should I be

concerned and, really, that information was in the What Do We Need section of Chapter 1.

So, it was the first paragraph, I believe, under What Do We Need that was moved to the What Do We Know to just, again, summarize where is the field currently in terms of looking at the indicators, characteristics and the issues overall with regards to the topic of when should I be concerned.

I think looking at this again after our discussions this morning, we need to be mindful of something that I think you said earlier, Tom, that I think there's a certain lack of updates to what we know to this section.

I don't think we really, truly have integrated current research and the updates in terms of what we know currently about this topic. So, that may be something to take into consideration.

And I think there's still a need

to look at the information that's in Chapters 2 and 3 and how it relates to Chapter 1, because Chapter 1 is really focusing in on the diagnostic tools, screening tools, assessment tools. And those should be based on what we discover through Chapters 2 and Chapters 3.

And I'm not sure if this fully integrates with those chapters, so I think that's just another consideration.

Let me see if there's anything else.

Again, the Panel had recommended that we better emphasize the issue of adults being missed and that they're not diagnosed with autism until they are adults, that they're missed in the early childhood phase of their life, and the issue of diversity in that we're not reaching out fully to culturally and linguistically diverse populations and that we need to do a better job with that, and the issue of co-occurring conditions that - and I think the issue is two-fold with that.

That sometimes it can be difficult to diagnose ASD if a child has co-occurring conditions that may mask the autism, or if a child is diagnosed with ASD, that co-occurring conditions may emerge over time. So, we try to tease that out a little bit more.

Finally, I just wanted to highlight for you the aspirational goal because we did talk about that.

I think that maybe was - a large part of our time was spent in this Panel overall, trying to come up with an aspirational goal that everyone could agree to.

And I'm not sure that everybody agreed to the aspirational goal that is currently in the edited version of the Strategic Plan because, again, we had some who felt that it truly should be aspirational and that we should be reaching children as early as possible as soon as they're showing any indication of ASD, that that's the point at

which they should be identified, whereas some are still concerned that there are adults on the spectrum who have not been diagnosed and they wanted to have that reflected in the goal itself.

So, we changed it to, I think, be a little bit more focused on the idea that we're catching children as early as possible. And, therefore, we won't have a need or a concern about there being adults who are not diagnosed along the spectrum because they would have been caught if we're really good at finding those indicators for anybody who may have ASD.

So, that's what I have. Do we want to go through line by line at this point in time or -

Dr. Insel: Let's see if there are general comments in response to what you've just summarized.

I have one, Jennifer. I'm still confused about the What Do We Know/What Do We

Need organization.

Dr. Johnson: Yes.

Dr. Insel: The way I read it now, the first two pages are all about - they're a little bit of a downer. And it sounds to me like it's all the things that we still need to do, and yet they're the first thing you come to under What Do We Know. We actually do know some things even with recent research about earlier detection, and that's kind of lost. It ends up being now at the very end of that section.

Dr. Johnson: Yes.

Dr. Insel: So, I just wondered whether all of that very good prose ought to be moved back to What Do We Need so that people could get some understanding of why this has been so difficult to get earlier diagnosis.

Dr. Johnson: Yes.

Dr. Insel: The other question I had, and this is back to the issue of how the

plan is organized and how some things seem to have fallen through the cracks. When we talked about this at our October 23rd meeting, we talked about biomarkers because we wanted to have biomarkers for early diagnosis and the idea that behavioral changes are a late stage of autism.

So, if we could come up with ways of detecting autism even before there was manifest behavior, that that would be a huge sign of progress and would allow for much, much earlier intervention and maybe even preemption of some of the behavioral manifestations. But I couldn't find it in here now, and I thought maybe it migrated to Chapter 2, but it's not really there either.

So, what happened to the biomarker idea?

Dr. Johnson: The biomarker is still in there, and I'm trying to remember - we did make, however, some modifications to that. And let me just find - page 8. Okay.

Dr. Insel: It's a single word and a long-term objective. It's to identify preclinical familial, behavioral and a panel of biomarkers and preclinical markers, but that has to do essentially with just associated features of autism like immune metabolic problems or medical problems. What I'm looking for are the biomarkers that would be like the test of phenylalanine, you know, something that you could do at birth of soon after birth that would identify who's at very high risk for autism itself, not just the associated features.

Dr. Johnson: And I think there is something that comes in out of the What Do You Know or What Do We Need section, and I'm just trying to find that. And the comment was that there was a researcher on our panel who felt like biomarkers, we may never get to that point where we really have a reliable set of biomarkers to do that. That it may contribute to a diagnosis, but the actual biomarkers,

we're just never going to get there.

And so, that's perhaps why it's not as explicit as you're looking for.

Dr. Insel: I just would vehemently disagree that that really should be the aspirational goal here is to identify, you know, is to think about autism as the final common pathway of lots of different biomedical problems. And you get there long after the train has gone off onto a different track, but the behavioral part of it doesn't show up until much later.

Dr. Johnson: Right.

Dr. Insel: And so, what you want to do is be able to move way up the track to be able to identify something earlier, and that is what we define as a biomarker.

In this case, a predictive biomarker or an early diagnostic biomarker.

Dr. Johnson: And the -

Dr. Insel: I'm sorry, but Deb Hirtz had her hand up, and so did Lyn.

Dr. Hirtz: So, this is a really important question and I think we should and can do both. I'm afraid that if we take - it's definitely an aspirational goal. But I'm afraid if we make it the only goal or the main goal, then we lose out on a very rich area which we could have, and that is to identify the biomarkers which would give us a very high increase in risk because that in itself would still deliver a very strong improvement in our ability to detect early and screen early. So, I wouldn't give up on that. I think that would enrich our practice greatly if we could do that, as well as identify - it would be great if we could get that PKE just like we have in PKE with a blood test and that's it.

But we can look forward to both, but the realistic goal probably sooner is identifying markers of very high risk. So, it is in there. Perhaps you want to emphasize it a little more.

Dr. Insel: Well, Deb, where is it?

Because I had trouble finding it as I was going through this.

Dr. Hirtz: Well, it's on the first page. And then as you say, on page 8.

Dr. Johnson: There is just one reference to it in the -

Dr. Insel: So, line 18. So, that would be a potential need, but it's also a research opportunity. And it doesn't show up anywhere as an objective.

We have objectives about screening, but -

Dr. Hirtz: Well, it's in long-term.

Dr. Insel: Except for the long-term objective.

Dr. Hirtz: Right, right.

Dr. Insel: I guess I feel about this the way I feel about epigenetics. I mean you would think this would be the core of what it is we're trying to do and trying to focus the field on, and yet it's barely mentioned in

the process of looking at this text. We have a lot of other stuff in here, but not something that could be really transformative.

Other comments? Jim?

Dr. Battey: I agree completely, Tom. I think that that should be a highlighted item the discovery or attempts to discover biomarkers that allow for either early diagnosis or for high risk.

Ms. Redwood: I'm really confused having compared this to the one that we've reviewed on the 23rd. They just seem so different and I sort of agree that the opening is a real downer. There's also some things in there that were in the first one that I can't find where there was -- the sentence in here "evidence is emerging that some children lose symptoms of ASD," and I think recovery is a really important thing to be included. And I couldn't find that that was then transposed over into this document. And if you look at the study that just came out with the National

Children's Health Study, there's actually something like over 30 percent of the parents in there answer that their children had been diagnosed with ASD, but they no longer had it.

So, I think that's a real important thing that we need to be looking at too.

Dr. Johnson: The notion that you're talking about, the different developmental trajectories, I think, is in there still. Again, it just may be hard to find it because of the changes that were made to the different sections.

So, let me try and find it.

It starts on page 1, line 21. And then goes over to Page 2 on line 1, 2, 3 and 4.

Just the terminology, "lose," -- because our panel really didn't come to a consensus about using the term "lose." So, we didn't want to use that terminology because there wasn't consensus around that.

Ms. Redwood: Because I think we saw some children on the 23rd that had clearly lost their diagnosis. So, I think - I don't know that I would agree with that recommendation.

Dr. Johnson: I think just in response to that, the Panel member basically said that even though the obvious, detectable - I don't even know obvious, but the observable characteristics of autism may have gone away or been lost, but there may still be other autism-like characteristics that that person is still experiencing that may be not as explicitly understood by others. But there may be some perhaps in the way they interact or understand the social setting, may still be impacted by the autism, but it's not as big of an impact that it affects their ability to interact with others.

That's just one example.

Dr. Insel: Any other general issues here before we get any deeper into it?

So, could you just explain what happened, though, between the last version and this version? So, did the Panel come back and just decide to undo a number of things that we had talked about or what -

Dr. Johnson: In terms of moving the information that was in What Do We Need or -

Dr. Insel: Well, not just that but what Lyn just brought up. That was in here, actually, the last time we looked at it.

Dr. Johnson: The lose -

Dr. Insel: And it's now listed on page 3 as a delete item.

Dr. Johnson: Yes.

Dr. Insel: And then there's a whole bunch of other language that had been in the document that's now gone.

Dr. Johnson: You know, I was actually incorrect when I started out to say that nobody had gone in to edit the document, because now I'm remembering that one person

did. And I think maybe they did make some edits to that, and I'd have to go back and look to see what specific. And I think it was maybe from those edits that we did end up taking out the term "lose." So, I apologize for that inaccuracy that I started with.

Dr. Insel: So, what does the group want to do? How do you want to handle this? Because there are a number of issues in both the objectives, as well as Jennifer was saying, you know. We struggled in the last meeting around the aspirational goal, so we'll have to probably revisit that. And then there's this language under What Do We Know/What Do We Need and some things that have been missing.

Is there a way to go through this quickly that people would be comfortable with or do you want to - because this is one of the chapters that's going to require more work. I can tell you that there are a couple of chapters that will require, I think, very

little because there are very few changes. But this one there are many new objectives and many new things that have been added, and then a number of things that have been taken out. So, should we wade into this and try to get it to a point where everybody is comfortable? What's the sense of the group?

Dr. Johnson: If I could offer something for efficiency purposes, quite honestly the decision to move some of the information that was in What Do We Need to What Do We Know, I could take it or leave it, you know. It isn't necessary. I think the problem with the What Do We Know section is that it was very awkward and it, again, didn't provide the necessary context for the whole chapter. And I think that's where our panelists were struggling with that particular section of the chapter.

When we got to the What Do We Need section, they were pretty - there weren't a lot of recommended changes to that. So, it

may be just a matter of figuring out how to situate this and introduce this chapter adequately to provide the appropriate context and I don't know if the Committee wants to get into that or not.

Ms. Redwood: Would it be possible - I'm just throwing this out there - to work with the one from the 23rd that we're familiar with? Because this is just so different and there's been so much deleted that - and we've already discussed so much back on the 23rd. I just don't know if anybody else feels the same way.

Dr. Insel: I feel that way as well. I thought we were pretty close, actually. We struggled a lot with the aspirational goal, but I thought most of the rest of the text we were pretty close with. Do we even have access to the 23rd? I have it as well. I mean do other people have it?

(Off the record comments.)

Dr. Insel: Okay. So, the problem

is that no one following along remotely would be able to see it on the screen because it's not loaded up.

Ms. Singer: So, can we come back to one after you have a chance to get it and load it in? Because I agree. I think we were - the last version we saw was a better reflection of, I think, where we wanted to be.

Dr. Insel: Even the objectives which now have become very diffuse and hard to follow. So, Jennifer, would that be okay if we circled back, got the October 23rd version -

Dr. Johnson: That's fine. Yes.

Dr. Insel: - figure out whether there's anything else that needs to be added or taken away, and can we move on to Chapter 2 then?

Ms. Singer: Okay. I was the co-liaison for Chapter 2 along with Dr. Ed Trevathan and Dr. Cathy Rice, both from the CDC.

In general, the panelists came up with really four areas where we thought the Plan should be updated. The first was really focused on developing a repository to deposit skin fibroblasts to convert them to pluripotent stem cells. That that was new technology that was not available at the time of the writing of the 2009 strategic plan.

The second area we wanted to focus on was really the need to look more closely at individuals with autism who also had cognitive disabilities. Third, the Panel felt it was important to look at studies that associated specific genotypes with functional and structural phenotypes, including behavioral phenotypes and medical phenotypes to really better understand the association between symptoms and behavior. And then fourth, the Panel wanted to look at underlying biologies of ASD by examining what was similar and different in the pathways, the biological pathways in co-occurring syndromes like

Fragile X and tuberous sclerosis syndrome. And also co-occurring conditions like epilepsy and autoimmune disorders.

So, we presented that at the last IACC meeting in October. And the feedback from the IACC at that time was to go back and clarify on four key areas. The first, the IACC asked us to separate out the objective that looked at both co-occurring conditions and underlying comorbidities. So, we separated those out and I'll get to that. The IACC asked us to look, to go back and clarify the language regarding the studies for individuals who were nonverbal. Third, the IACC asked us to clarify the language regarding regression. And fourth, we were to take out the language regarding biomarkers for diagnosis which was going to go into Section 1, and we were just to focus on biological signatures.

Our panel did have each member of the Panel review the document, make changes

directly onto the document line by line. It was quite an iterative process. There was a lot of back and forth and it was quite an exchange. But at the end, we did come up with a document that everyone felt was a good reflection of the viewpoints of all of the panelists, so I don't know if you want me to focus on all of the changes, or just the changes since the October meeting.

Dr. Insel: I think we should look at what's been done since October, because we went through this in some detail three weeks ago - two weeks ago.

Ms. Singer: Okay. So, with regard to our charge to separate the co-occurring conditions from the comorbid disorders, in the short-term objectives on page 8 starting at line 11, we separated those two. So, we have one that says launch three studies that target improved understanding of the underlying biological pathways of genetic conditions related to autism, for example, Fragile X,

Rett syndrome, Tuberous Sclerosis complex, and how these conditions inform risk assessment and individualized intervention.

And then the second part is launch three studies that target the underlying biological mechanisms of co-occurring conditions with autism, including seizures, epilepsy, sleep disorders and familial autoimmune disorders. And that was to clarify that those were two different biological pathways.

Dr. Insel: Okay. Discussion about this? And now we're looking at the whole document of Chapter 3. So, if there's anything that anybody wants to revisit -

Ms. Singer: Do you want me to -

Dr. Insel: I'm sorry. Chapter 2.

Ms. Singer: - just go through the other changes that we added or -

Dr. Insel: Were there any other changes since October?

Ms. Singer: Yes. We also

clarified with regard to regression on page 8, line 18, we clarified this short-term objective that the language now is launch two studies that focus on prospective characterization of children with reported regression to investigate potential risk factors clarifying the risk factor focus. With regard to individuals who are non-verbal, we made that change on line 7 of page 8. Launch three studies that specifically focus on non-verbal individuals with ASD. The change was "who test as having cognitive impairment."

And then finally, I think we clarified the language regarding biological signatures, that we were not intending to mean biomarkers for diagnosis, but in fact biological signatures. And we made that change on line - help me find it. Yes, page 9, line 10. Launch at least three studies which evaluate the applicability of ASD phenotype and/or biological signature findings

for performing diagnosis, risk assessment and clinical intervention.

Those were the changes since October 23rd.

Dr. Insel: I didn't understand the last part of that, Alison. You changed from biological signatures. A change from what? What was the original?

Ms. Singer: From biomarkers because there was concern that the term "biomarker" could be interpreted as biomarker for diagnosis as opposed to biological signature. And that biomarker for diagnosis was going to move to Section 1.

Dr. Insel: Okay.

Ms. Singer: Do you want to -

Dr. Insel: Ellen.

Ms. Blackwell: I wondered if we might entertain substituting intellectually disabled or intellectual disability for cognitive impairment.

Would you guys be okay with that?

Dr. Trevathan: I think some of the reason for not doing that, Ellen, is that the cognitive impairment is broader and there was concern about excluding people who had a cognitive impairment, but say their IQ wasn't less than 70 or something. So, I think that it was an attempt to be more inclusive there or broader. I don't know if that makes sense.

Dr. Insel: Just an organizational question. All of the material on biobanks and skin fibroblast collections and all that, do you want to keep that here or should that move to the infrastructure chapter?

Dr. Lawler: I think it should move to infrastructure.

Dr. Insel: Maybe, we can keep the same language, but just circle it. And then we'll do a cut and past when the time comes.

Dr. Trevathan: If the advantage to moving it to the infrastructure chapter would be to emphasize the long-term commitment to maintaining the storage of the specimens and

that sort of thing, I would think there's a major advantage doing that so we don't see this as a onetime study sort of issue.

Dr. Insel: Yes, so the issue that we have to deal with in that chapter is sustainability, and to come up with a plan that makes this more than a three-year effort. That's always the problem with these banks.

Dr. Hann: So, there's a piece, I don't know if it's related any longer with the changes, but there is something sitting in long-term as well to maintain an international network of biobanks so that -

Ms. Singer: Yes, that could move as well to Chapter 7.

Dr. Insel: And then there's a section under What Do We Need on page 5. "Many in the field have highlighted the need to establish nationally coordinated strategies."

So all that, the language is great. It's just a question of how best to organize it.

Okay. Anything else from this?

Chris?

Ms. McKee: I have a question about the one that addresses non-verbal children with ASD.

Ms. Singer: Wait, what page is this?

Ms. McKee: Page 8, line 7. I just don't know why it says "who test as having cognitive impairment" as their - are you focusing on something other than ASD? I'm not really certain why you have that qualifier on it.

Dr. Trevathan: Well, I think the discussion or the intent was that there's a feeling that there hasn't been enough research done looking at children who have co-existing cognitive impairment and ASD and so that there was a general focusing on that subgroup. So, that's the real reason. Not to say they don't have ASD. They have ASD and cognitive impairment.

Ms. Singer: The way we explained it in the What Do We Need that led to the objective was, many studies of autism preferentially enroll higher functioning individuals who do not have cognitive impairment because of their ability to cooperate and participate in study-related tasks. However, these individuals represent only a subset of all individuals with autism, and lessons learned from them may or may not be generalizable to all individuals with ASD. So, we were looking at it as sort of an under-represented population within the portfolio studies.

Dr. Insel: So, two questions to that. There are many non-verbal individuals who would not test that way, so do you really want to link those two, or is that two separate questions? And the second issue is I'm not sure what it is the studies are doing. What's the question that would be - what's the research question for these three studies?

Dr. Trevathan: Yes, I don't think

-

Ms. Singer: Go ahead.

Dr. Trevathan: Again, I wasn't there for all the discussions, but I think that the intent was to really make sure that studies in a variety of different areas included these children because they had been excluded from other studies, not a specific hypothesis.

Dr. Insel: Should we weave that into some other bullet as a group that needs to be included?

Dr. Hann: Like the next one? Functional and structural phenotypes, including behavioral and medical phenotypes, as well as individuals who are non-verbal?

Dr. Trevathan: Right. So, just include -

Dr. Insel: It's not clear from this bullet, what anybody would be doing other than studying this group, studying them for

what. So, if there's a way to just merge this with something else - and we do in various places, talk about having diverse populations or under-represented groups, and this -

Dr. Trevathan: Right.

Dr. Insel: This will come up in Panel 4 as well. This is actually the main emphasis that we heard was to include non-verbal, which has not been a group that has been studied as extensively. So, is there a way you could just link this in not as a separate bullet, but as part of an existing proposal?

Ms. Singer: I think the idea was that there are two groups that are non-verbal. There's non-verbal with cognitive impairment, and there's non-verbal without cognitive impairment. And that the research issues surrounding those two groups are different and we just wanted to make sure that this was included. I think it might have even been a response to the objectives in Section 4 which

I know focused on trying to understand why individuals who are non-verbal, but have no cognitive impairment, can better communicate. There was also just a desire by the Panel to make sure that non-verbal with cognitive impairment was not left off the table completely.

But I think you're right. It could be subsumed under another objective.

Dr. Insel: Yes. So, I mean if you just merged it with the next one and you keep those separate, so you could say including non-verbal individuals and individuals with cognitive impairment. Then people can figure out how to mix and match for whatever studies are coming up.

Dr. Trevathan: I think that would take care of that intent.

Dr. Insel: What else? Anything else from this?

Deb.

Dr. Hirtz: I just want to make a

general comment. I think these are excellent objectives and stated very well. I just wonder what we think about the tremendous overlap and repetition in so many of the questions about the need to do genetic/environmental interaction studies, to look at the autism phenotype with regard to risk factors. All of these studies are very - it's clearly the key in so many of these questions, but there's a lot of redundancy. And I just wonder how do we solve that problem, because they come up in every -- almost every question.

Dr. Insel: Yes, this is how we started the day. I think it was Alison who pointed out that we've lost the single voice here and we're really victims of a process that we created that ended up doing all of this as five separate projects. So, at the end of the day, we're going to have to have a wave that comes through and figures out how to harmonize everything and make it read like

it's one document.

But you're right. There's a lot of redundancy. There may be opportunities to actually drop some things out that come up over and over again. I think right now we just want to make sure we've got everything included that you want. And then if there's places where it can be slimmed down, you'll see that by the end of January.

Anything else on this document?

Ms. Redwood: I had some questions with the very beginning. The What - let's see. Where are we? With the What Do We Know section. There were a couple of things that were removed, and I was just curious. There was a whole paragraph that started with -- on the old document, frequently, people with ASD experience co-occurring behavioral/medical.

That on page 2, it would start with line 3, and there was a lot deleted there and it's even different than the document for the 23rd. And I was going to suggest that we

put back or put into this list of conditions, also immune system abnormalities. I think those were inadvertently overlooked, and I think they're hugely important. And I'm also wondering about the deleted comment, "While such medical symptoms may not be entirely specific to ASD, treating may have significant impact on quality of life, symptom severity and level of functioning."

I think that's important to include because those comorbid medical conditions so oftentimes get overlooked. And I also think that because a large percentage of children have these comorbid medical conditions and there are numbers greater than what we predicted in the general population, that we also need to ask the question whether or not they are secondary comorbidities or if they're potentially a manifestation of some underlying mechanism that might be implicated in the pathogenesis of autism.

And I think that's not reflected

here. And I think that's a question that people ask quite a bit about these co-occurring medical conditions. Are they really co-occurring or are they actually some actual part of the disease process that we're overlooking?

Dr. Insel: What's the sense of the Panel for this?

Was there a good reason to take this out?

Okay. So, is there an interest in putting it back in? That's the question.

Ms. Redwood: Would there also be interest in adding in a comment about these comorbidities, whether or not they are secondary or possibly an underlying mechanism of the pathogenesis of autism?

Dr. Insel: So, that was the original language. That's what it's -- so, we had that in there. So, I'm wondering if we could actually do this en bloc rather than going line by line. If we can get a few

things like this on the table that you want to go back to in the way that it was before, since it was okay before, and adding in a few of the comments that you've heard, whether we can give you enough that we could just vote for the whole chapter rather than having to go through it with each line.

What's the sense of the group? Would that be all right? I see a lot of heads shaking. Okay. So, Ed, Alison, could you come up with a sort of summary of what we'd be voting on and give us a sense of whether you think there are any outlying issues that we'd still need to think about?

Ms. Singer: Okay. Well, we went through the changes that we made to the objectives, the four changes after the October 23rd meeting. Lyn has proposed adding back the sentence which we had deleted that starts, "While such medical symptoms may not be entirely specific to ASD, treating may have significant impact on quality of life, symptom

severity and level of functioning." And then I don't know what - those are the changes since October 23rd.

Ms. Redwood: Alison, there was also a whole area in there in the document from the 23rd, about language regression that was really nice.

Ms. Singer: Where?

Ms. Redwood: It's in the old document. It's not even listed as being deleted, but it says that acute language regression may occur with or without associated autistic regression. In some studies, children with language regression and autistic regression were less likely to have associated seizures or epilepsy. And then it says we don't know the frequency of language regression with or without autistic regression in the absence of hearing loss in general. And the previous studies have been hampered by delayed referral for evaluation after onset of symptoms of regression.

I was just wondering why that was taken out too.

Dr. Trevathan: Yes. Well, I have a bias on that because I wrote the paragraph, but I think that that was - I don't think there was a reason particularly why that was taken out other than we were trying to be efficient without words and that that actually, I think as someone said, reads more like a book chapter as one of those kinds of comments we heard before.

And on page 8, the last bullet, there is a, you know, one of our specific aims here is to really look at regression. So, I don't think there's any reason why we can't add that back in.

Ms. Singer: No, we can put that back in.

Dr. Trevathan: Yes.

Ms. Redwood: I thought it was just important information and it validates why we're looking at those children more closely.

Dr. Insel: Okay. Anything else on this?

So, what they're asking for, let me make sure we've got this, is there were a number of things that were in the document on October 23rd that have disappeared, some of them show up here as delete items, but there's some that aren't included, and we want to go back to what we had on October 23rd to have that document, and then there are a few revisions.

So, one revision is that the pieces that have to do with infrastructure would migrate to Chapter 7.

Dr. Trevathan: Right.

Dr. Insel: What else?

Ms. Singer: The paragraph on language regression with and without autistic regression that was in the document on the 23rd, would be added back.

Dr. Insel: So, that would be added back, the pieces on -

Ms. Singer: This line over on page 2. The second part of the deleted sentence here that starts with, "While such medical symptoms" would be added back.

Dr. Insel: Right. There was a paragraph there that has been deleted.

Ms. Singer: And then the four changes we made to the short-term objectives were changed.

Dr. Insel: And then we'll merge those two objectives into one.

Ms. Singer: And merge the two objectives into one.

Dr. Insel: Okay.

Ms. Singer: Those are the changes.

Dr. Insel: Are we ready to vote on that?

Ms. Redwood: The only other thing suggested was some language about the medical comorbidities possibly being part of the disease itself.

Dr. Insel: So, I thought that was

in there from the 23rd, and we were going to put that back in. Yes, no?

Ms. Redwood: I just didn't hear it as one of the things mentioned now.

Dr. Insel: Okay.

Dr. Hann: This has been very, very difficult for myself and staff to follow. So, I'm going to have to ask, actually, that, Alison, if you could send to us what you are hearing as the changes, because we really can't follow this when we're jumping around between the different versions like this.

Ms. Singer: Okay.

Mr. Grossman: We understand it.

Dr. Insel: Do we understand it well enough to vote on it? Is the group - I see some people nodding, and some people's head shaking. Alison, Ed, do you want to again try to summarize what we're talking about here so that people can - because we want to be able to get the Committee's approval of a document that then we can really

give you budget requirements and all those things for January.

Dr. Hann: I have a suggestion if you could indulge me, and that is to go through it page by page and indicate what pages the changes are and what is being proposed to be added back in.

Ms. Singer: Okay. On page 2 we're going to add back in the sentence that right now appears deleted. The sentence begins "While such medical symptoms." We're going to also under What Do We Know, we're going to add back - do you see it, Lee, at the bottom of page 2 in the deleted? We're going to add back the paragraph that described regression. I actually think that came out as a result of one of our computer errors. I don't think we intended to take that paragraph out. So, we talked about that at length. So, I don't know why that - that should actually be in here. So, thank you for pointing that out.

And then we had four changes that

we made in the short-term objectives. Beginning on page 8 on line 7, originally this was one objective - oh, no. I'm sorry. Beginning on line 7 we're going to merge this "Launch three studies that focus on non-verbal individuals who test as having cognitive impairment." We're going to merge that with the objective that starts on line 9.

The other change we made was originally in the October 23rd document, the objective that starts on line 11 and the objective that starts on line 15 were one objective. So, the change we made was to separate them into two objectives.

On line 18 we added this objective that came directly out of the paragraph on regression. So, this new objective reads "Launch two studies that focus on prospective characterization of children with reported regression to investigate potential risk factors." And then the fourth change we made was to the long-term objectives. We added a

long-term objective on page 9, line 10. "Launch at least three studies which evaluate the applicability of ASD phenotype and/or biological signature findings for performing diagnosis, risk assessment or clinical intervention." And the change there was to change from biomarker to biological signature so that it was clear that we weren't talking about biomarkers for diagnosis.

Dr. Hann: And then I also heard recommendations to move the second long-term objective to Chapter 7?

Ms. Singer: Yes.

Dr. Hann: As well as -

Ms. Singer: And also all of the biobanking -

Dr. Hann: Right.

Ms. Singer: - to Chapter 7.

Dr. Hann: Right. To Chapter 7.

Dr. Insel: Okay. Is that a proposal? Can we get the sense of the Committee as a vote for those en bloc changes

to Chapter 2?

In favor?

Dr. Hann: We have got one, two, three, four, five, six, seven, eight, nine, ten, eleven? Eleven in favor.

Dr. Insel: Opposed and abstaining? All right. The motion carries.

Lyn.

Ms. Redwood: I just have a question for clarity. There are several times throughout this entire document where we talk about co-occurring medical conditions, and each time there are different ones listed. So, I'm just wondering like in here on the Number 3, we have seizures, epilepsy, sleep disorder, familial autoimmune, but there's no mention of metabolic, mito. So at the very beginning last time, we defined them once, and then we referred to that.

Can we do that again this time?

Ms. Singer: Yes.

Dr. Insel: Yes, that's got to be

changed. That was something we decided on the 23rd, is that we were going to move that to the front and be very clear, and then we'd have one list. Okay. Can we go on to Number 4? I know you don't want to go back to Number 3. So, we'll go to Number 4.

Lee's asking for an encore.

I did this one with Stephen Shore. So, Stephen is not able to join us, but I think I can take you through it quickly. There actually were very, very few changes from when we discussed this with you in October. So to summarize, what we told you at that point in time was that the Panel was pretty positive about the original document from January. They felt that we were missing two or three things that we didn't have, sort of like what happened with Chapter 2. There was not enough emphasis on non-verbal.

And they also realized that that was also missing from the NIH portfolio, and so they encouraged much more focus on non-

verbal, interventional studies for non-verbal populations. Also on adults, they felt that was a clear oversight. And they felt that we should have said much more about new technology. So, be thinking about interventions that were not necessarily medications or behavioral interventions, but technology interventions that could make a huge difference for function.

They also in thinking about what has changed since January, they pointed out that there really wasn't much in the way of new discoveries, but they said that we have had this wave of interest in comparative effectiveness research. So as we thought about interventions, we should be putting that into our computers and saying that we could be supporting research for decision makers more broadly, not just sort of typical RCTs.

They had made a few suggestions which we reviewed with you in January. You came up with a few additional suggestions

which we took back to the Committee. The ones that you suggested were that there was an absence of discussion of dissemination research which was something that could be done. We could argue about whether that would go into Chapter 4, Chapter 5 or Chapter 6, but they said that that was an opportunity that needed to be looked at.

You also said that we needed to consider N of 1 trials where you have multiple baselines. And we put that into the document and almost the entire panel wrote back, it was the only thing that they responded to, and they said they didn't like that idea. They didn't think we should specify that. That that was too detailed. We pushed back a little bit and then finally said well, we'll just bring this to the IACC and see what that committee wants to do.

And then you also told us that we needed to have a focus on core symptoms and on differences in different populations. Some of

which was already in there, but we tried to emphasize that even more. So, very quickly you can go through. There are not that many changes. Actually, almost no changes since what you saw in October, except that we have - well, I guess what you can see now is that we have tried to reorganize the objectives so that we've added in the studies in adults and we've moved the biosignatures, biomarkers instead of making that an independent objective, we've made that integrated with all of the clinical trials so that all trials whether they're in infants or adults or anyone in between would include a look at biomarkers.

We've added a paragraph on decision makers and CER, comparative effectiveness research, and then a few other things, but the objectives have only changed in that one respect for the most part.

So, questions?

Ellen.

Ms. Blackwell: I just had a couple

of general comments. I wondered if we could change autistic children in a couple places, to children with ASD. On page 2 where we talk about applied behavioral analysis-based therapies, if we could just perhaps get OARC to write this to clarify that there are a number of therapies that are considered to be applied behavioral analysis-based therapies. And then I noticed in the aspirational goal, and I can't recall if we talked about this at the workshops or not, Tom, but what we have in the last line is for preventing the disabilities associated with ASD. And I guess I get back to quality of life. This is where I go on board with quality of life. Could we say and for maximizing quality of life and health of people with ASD? Sort of turn that around a little bit? In the aspirational goal on page 5 instead of saying preventing disability.

Dr. Insel: What's the sense of the group?

Dr. Hann: So, Ellen, are you suggesting that it read something like this? Interventions will be developed that are effective for reducing both core and associated symptoms, for building adaptive skills, and for preventing - it wouldn't be an "and" there - preventing the disabilities associated with ASD and improving quality of life?

Ms. Blackwell: No. I was actually suggesting interventions will be developed that are effective for reducing both core and associated symptoms for building adaptive skills and maximizing quality of life and health for people with ASD.

Dr. Insel: Does that work for the group?

Okay. Deb.

Dr. Hirtz: First of all, I want to compliment you on adding the comparative effectiveness. I think this is a really good place to mention that and a place where that

could be very useful research.

I just want to make one small comment on the top of page 6. One of the big problems in doing clinical trials, particularly some of the pharmacologic trials, is that children are always - or people always have some sort of behavioral/educational interventions as well. So, it challenges - I don't know if you want to mention specifically the combination of pharmacologic and educational/behavioral interventions, which is what we have in the real world setting, and an emphasis on doing - a goal of doing trials combined.

Dr. Insel: So, we say there combinations of interventions.

Dr. Hirtz: Yes, you did. You didn't specify the - I just wanted to specify the behavioral and pharmacologic interventions together.

Dr. Insel: So, perhaps a parenthetical statement to that effect?

Dr. Hirtz: That would be fine.

Dr. Insel: Okay. Lyn.

Ms. Redwood: Tom, I had a couple of questions. One on page 3. When you talk about other treatments that are in wide use that have not been studied, you give an example of the gluten-free/casein-free diet and then chelation, but there's a lot of other things that parents are using now that I think it's important to study.

One of the things that's popular are the mitochondrial cocktails because of the increased incidence of mitochondrial disorders especially in children with regressive autism. Things like CoQ10, carnitine, carnitor. And I'm wondering whether or not those specific things might be added in there because it seems somewhat limited in terms of what might be studied.

I was also wondering on page 6 when you talk about - it's the very last bullet. Methods of treating co-existing

medical or psychiatric conditions and to assess how methods affect ASD symptoms and severities. Would it be how the treatments effect ASD symptoms and severities? And one of the things, too, that I tried to point out at the last - one of the workshop meetings, is that I believe a lot of the co-occurring medical conditions can be overlooked in children with autism because they don't have language. So, they're not able to point out certain things.

So, I'm wondering if it would be important to have some type of initiative to try to look a little bit deeper at children beyond to identify these comorbid medical conditions because - again because autism is a psychiatric disorder, I think they are oftentimes overlooked and they're a big opportunity. So, I didn't know if it would be worthwhile to mention, including some type -- in one of these somewhere to actually sort of understand how many kids do have these

underlying medical conditions.

Dr. Insel: So, I think that would come up in another chapter. This is really going to be about interventions. But on this bullet, I don't know what this wording is trying to say. I think it should probably say methods of treating co-existing medical or psychiatric conditions and assess how such treatments affect, not how such methods, right?

Ms. Redwood: Right. That was my question.

Dr. Insel: Yes, I think the wording is off. So, we can fix that.

Ms. Redwood: The last question I had was regarding the push back of N of 1 studies. That's something we heard Dr. Will Raub suggest over and over again at the Institute of Medicine meeting on autism and the environment.

And I think it's a way to do multiple baseline studies to actually assess some of these

interventions with using an N of 1, so I'm curious why the Committee members really pushed back on that issue.

Dr. Insel: Yes, I was surprised by that. And it wasn't from a single member, and they came at it from somewhat different perspectives, but I think their feeling was that we need a lot of different approaches. They didn't want to specify any one, because they felt that that would be kind of leading people in a given direction and they wanted to leave this much more open. I don't think there was anybody who could effectively critique the idea of doing N of 1 studies, because they are what they are. They're limited in what they tell you, but they can be used to provide statistically important data about clinical response in a given individual.

So, we didn't hear anybody say that that was necessarily a practice that we shouldn't support. It was simply that we shouldn't specify it. So, I had put it in,

and it came out after those comments. And I was willing to keep it in if it had just been one member of the Panel. But so many people piled on I felt that we probably needed, as Lee was saying, to respond to their wishes.

Ms. Redwood: I'd be curious to know the sense of the Committee. I know it sounds unscientific. But if an application were to come in now, do you think it would be supported without having an actual objective?

Dr. Insel: I don't think we had it in the Objective section anyway. I think we had it in the What Do We Need - I'm trying to find where we had actually added it in, but the question you're asking is whether a peer review committee would be receptive.

I don't think the Peer Review Committee will cite our plan to decide that something is worth supporting or not or in terms of measuring scientific merit, but there are good examples of people who have used multiple baseline kinds of studies to

demonstrate within subjects affects. And that can be very powerful if you do it right. So, we still see this happen. I can't think of a good study where we're supporting that now, but I wouldn't - the fact that it's not in the Plan doesn't mean that it wouldn't happen.

And they were quite clear that they just - they thought there were lots of different models that we should be considering and they didn't want to preclude thinking about lots of others by specifying that one.

So, other questions or comments about this? Is this one you want to consider en bloc as well? We have a few suggestions here. So, Ellen has given us some language change. And Lyn has suggested that when we mention other treatments that have not been studied in randomized controlled trials, we go more broadly than what we have there. We kind of get up to date on what people are doing, and she used the mitococktail as an example. But in fact, there are plenty of other things

in addition; probiotics, which is really getting to be a big deal, and lots of others.

I don't think we want to give a complete laundry list, but perhaps we could make this more inclusive. And I'll turn to OARC to help us find the right language. And then, Ellen, you've suggested that we add enhancing quality of life to the aspirational goal - I'm sorry - maximizing quality of life and health. Anything else that - there are a number of other changes that - yes, so we have Deb's combination of interventions where we specify behavior and pharmacotherapy. And that is it, I think.

Okay. Do I have a motion to accept these changes for the revision date?

Dr. Trevathan: So moved.

Dr. Insel: Second. All in favor? Opposed?

Dr. Hann: Okay. It's unanimous.

Dr. Insel: Okay. And I'm going to turn this over to Dr. Hann.

Dr. Hann: All righty. So, we've done two, three, four. That leaves five, six. Christine, I believe you're going to do five, and then we'll circle back to get one. We do now have the October 23rd version that we'll hand out at that time.

Ms. McKee: Well, Ellen and I were the co-chairs of the fifth panel which handled both Chapters 5 and 6. We had a few comments back in October that we took back to our panel, and I would say we had a lot of acquiescence by silence of our group. I think we overworked them initially, but we've made a couple of changes from the October meeting.

There are substantial changes this is document from January. And the reason for the major overhaul was because there was a unanimous opinion among our panel that what was in here was neither what we knew nor what we needed. And we had service researchers on our group, who said we missed the boat.

And one of the reasons that they

thought that happened is because when we had the original workshops, we were all under treatment. If you remember, it was biology, risk factors. Anyway, it was all under treatment. And so both interventions and the services portion and everything and it just - they said a whole lot got lost in translation.

So, we went back and tried to put some of the original intent back into the document. So, first page we just have some wordsmithing. The second page, here's where the major chunks come in. The first paragraph, this is to encompass the point brought up of the workshop about the fact that a lot of research is done in clinical studies, and we're just not getting the same positive results once we translate these to the community. And so what we really need to do is have research in community settings, figure out what works from there, and then go for dissemination.

The second paragraph there states

the basis for the research on interventions for youth and adults. Under the What We Need, the first paragraph with the large addition on page 3 talks about the challenges that we face, the finger pointing across the systems and the labyrinth of services. And the second paragraph is the solution to those challenges.

One major change that we did make since the October meeting is the language that starts off on page 4. The observational studies of current practice can play an important role in understanding - that entire paragraph was written by the services research guru. And he has some of the NIMH money, and he said he reviewed a lot of the ARRA applications. And was saying that the reason that things weren't exciting is because what the research community was proposing didn't line up with our plan.

And so, he said this is the language we need to tell the researchers what we want and how to phrase it and what to go after.

We didn't change the aspirational goal from our meeting in October. We did go through and change the research opportunities. We had a comment at our October meeting that a lot of our research opportunities looked a lot like objectives. So, we went through and pulled out a lot - three items from the Research Opportunities because they were already in the short-term objectives section.

We pulled out on page 6, the one that's highlighted in pink. Can move to Chapter 7. Talks about improved and coordinated methods for tracking trends in ASD prevalence. And we go to our short-term objectives. Not many changes there, right Ellen?

Ms. Blackwell: Well, I think one thing we neglected to do was to include the number of studies. Our group had actually taken that out, so I'm going to suggest that we put back in the ones that were already in the Plan.

Ms. McKee: Yes, there was a lot of discussion about the numbers, and they wanted to know why we kept putting numbers in the Plan. And they kept saying well, we don't need two studies. We need one really good one, and so why put two? Why not leave it open ended and see what happens? I know that fights with the whole budget. How do you budget for an amount if you don't know the number, but we had a lot of push back on putting numbers on anything.

Dr. Hann: Discussion, Alison?

Ms. Singer: One comment that I had, just a general overall comment on this, and also on Section 6, that I brought up at the October 23rd meeting and I don't see it in here, is that the goal of self-direction and self-determination is appropriate for some segments of the ASD population, but not all of them.

There are people who are so profoundly affected that they're not really

focused on self-determination. We're really still focusing on issues of safety and issues of health and I think we could reflect that if we talked a little bit more about care giving.

Because for those individuals, autism will remain a family issue in that their parents are likely to become their legal guardians when they become 21.

And I think we have to have somewhere in either Chapter 5 or Chapter 6 where we recognize that subpopulation and really speak to the issue of research that looks at best practices for ongoing care giving.

Ms. Blackwell: Although I hear you, Alison, again I have to disagree. Because really at CMS, we believe self-direction, self-determination, I mean anyone with a disability can have this, can achieve the same goal.

So, I hate to treat, you know, make assumptions about what people might be

able to do. And even the most profoundly disabled person could have family members that can put the appropriate supports and services in place to get them where they need to be.

So, I just really am adverse to not leaving our aspirational goal the way it is.

I hate to stratify people with autism into different groups, because really we have the same goals for everyone with a disability.

Ms. Singer: Well, maybe we can bridge the difference. Instead of changing what you have, maybe we can add in some goals that look at studying that determine best practices for care giving so that we're recognizing --

Dr. Hann: I'm hearing two different things a little bit, though. You mentioned aspirational goal --

Ms. Singer: Yes, I'm not looking at aspirational goals.

Dr. Hann: And I don't think that's what --

Ms. Blackwell: Well, again, I think it gets to giving people care or giving them assistance, and there is a difference.

Assistance is helping someone get where they need to be. I think most people would prefer to receive appropriate services rather than care.

So, in fact, in most of the health reform legislation you'll see language that talks about long-term services and supports, and not long-term care.

So, we're really walking away from the whole notion of care and walking towards the notion of supports.

Ms. Singer: So, maybe we can specify long-term services and supports not only for the individual with ASD, but for his or her family member.

Ms. Blackwell: I don't think anything we wrote precluded that. I mean I

think we talk a lot about --

Ms. Singer: But I would spell it out because I think there's a population where for whom that research is very much necessary. What are the best practices in terms of being a long-term services and support organizer for a person with ASD?

Ms. Blackwell: We did actually make some language changes in Chapter 6 that talk about lifelong supports. So, I don't know if you had a chance to -- that were made since October 23rd.

Ms. Singer: Okay.

Ms. Blackwell: In fact, I had a conversation with Nancy Thaler, who some of you may remember who runs the National Association for State Directors of Developmental Disabilities, NASDDS. And we talked a lot about this whole concept of lifelong services and support.

So, we tried to integrate that into Chapter 6 in particular.

Ms. Singer: Okay, just wanted to talk about it.

Ms. McKee: Alison, can we add it on page 5 and just put something in there? We have research must include services that are built upon principles of self-direction and self-determination.

Ms. Singer: Yes, that's where I was looking.

Ms. McKee: As determined by individuals or family members, something that ties in that --

Ms. Singer: I think even if you just put in all people with ASD and their family members or and their long-term guardians or however you want to describe it, should have services and supports.

I mean I think that there are caregivers who also need services and supports. And there's research that we can do to develop best practices in that area as well.

Ms. Blackwell: Wouldn't, for example, respite care be -- again, respite care would be a service that although it benefits the caregiver, it also benefits the person with the disability.

So, I guess I'm sort of getting stuck on, normally, we provide services to the person.

Ms. Singer: Well, we also provide services to the family. When you have a child in birth to three, part of your intervention plan is family training. And what I'm saying is that family training needs to be provided across the life span, not just parents of children who have zero to three, but family training is something that's ongoing.

Mr. Grossman: If I'm looking at page 5 under families, people with ASD, etcetera, are you looking for some language where all people with ASD -- it's kind of in the middle of the paragraph.

We could change all people with

ASD and their support mechanisms or something to that affect. Because it won't always be their family members, but -- and I think you do raise a good point that if we're not supporting the systems that support these people, then we're going to fall short of the goal.

And the most successful service programs are ones that are built upon not only building up the support mechanisms for the individual, but also those that are working with them.

Dr. Hann: So, should it be all people with ASD and those who support them should have the services?

All people with ASD and those who support them should have services and supports?

Ms. Blackwell: I got to tell you it's because this whole notion of giving care is really not where we are at.

I see you nodding, Jennifer. Do

you have something to add? I mean it's really about supporting people, not giving them care.

Dr. Johnson: You know, obviously this is being the administration on developmental disabilities, an issue that we come across frequently.

In our authorizing language, there is always reference to individuals with developmental disabilities and their families. Families being defined in a very broad way.

Typically thought of as parents, but we really have to think about families in broad terms.

And I agree with what you were saying in terms of the notion of self-determination and choice. That can be displayed in a variety of ways. Maybe not in the way that we always expect it to be displayed, but I don't think we want to lose that concept here regardless of level of functioning.

So, I agree that it has to be

incorporated in some way into this document. When there's reference to the services and supports, we may want to always insert long-term in there.

And I understand what you're saying, Ellen, in terms of when you talk about people with ASD, there's an assumption that is made if you're providing those long-term services and supports, that would include the extended system that is going to be engaged in that person's life, but we may need to explicitly state it and again use the term "families," but think of families as a broad definition of, again, the people who are engaged in the lives of people with ASD.

Ms. Blackwell: So, then it would read potentially all people with ASD and their families should have the --

Ms. Singer: I think it's bigger than that. I mean we have parent training when you have a child, and I don't see why parent training if you become a legal

guardian, why we would say that there's no longer a way to develop best practices for not just for habilitation.

I mean I continue to work with my brother. I am his guardian. There should be some science behind what I do with my brother the way there is with my daughter, and that's lacking right now.

So, what I'm saying is that the parent training that we offer to the parents of children, we should have similar research to build an evidence base for parent training and intervention for adults.

If you don't want to use the term "best practices in care giving," I mean we can come up with language that parallels the parent training that all of the studies now are incorporating into interventions. All of those studies now include a component based on parent training, so that parents can continue to generalize and apply those techniques when the children are not in therapy.

I don't see why we would deprive adults of the same type of science.

Dr. Johnson: I don't think that's -- at least that's not what I'm hearing that that wouldn't be the case.

We have to look at it across the age span. And obviously as a person ages, there are going to be other people in that individual's life who is going to be involved with what is happening in their life and what kind of services and supports they're getting.

We're seeing the whole emergence of siblings as key people in the lives of individuals with developmental disabilities and sibling networks forming and training going on around how are siblings transitioning as the person who supports and assists throughout that person's life span.

So, I'm hearing that that would be taken into consideration that not only parents need perhaps training, but other types of family members. How broadly you define

"family" would be included in that.

Dr. Hann: Okay. So, can we find some compromise language here to try to -- it sounds to me like people are sort of on the same page, that they're recognizing that there are very important other people who need to be taken into consideration. And what we're sort of grappling with is some sort of phrase for those other people.

Ellen, do you have a suggestion?

Ms. Blackwell: How about all people with ASD, their families and support system should have the services and supports they need?

That would be on page 5. And as I look over the objectives, I don't think including those or excluding those people is expressively stated anywhere in the short or long-term objectives.

In fact, one of them actually talks about family members, family functioning. It's the one that was already in

the Strategic Plan. Support two studies that assess how variations and access to services -- it's the second short-term objective.

Ms. McKee: Since our panel pulled all the numbers out, do we need to put them back in?

Do we have a sense from the Committee?

Let's go to the short-term objectives. We have the annual State of the States underway, and our feedback is this has to happen annually so that we can keep track of where we are.

If we just set up the baseline now, we're not measuring anything. So, conduct an annual State of the States.

We came up with support two studies that assess how variations -- two was already in there. We put it back in.

The promising practices papers, we came up with a recommendation of ten. In the promising practices papers, there are samples

in your folders if people aren't familiar with those.

Dr. Hann: Could I ask a question about those?

Most of the other objectives in the Plan are calling for research studies. So, I'm curious about this particular - I'm not saying it's not important. I'm not saying that, but I'm just not sure if it fits here as an objective, as a research objective as opposed to something that's very important for providing services, which is slightly different, if I read that.

Ms. Redwood: Well, I agree, I also think the demonstration project, which is the next short-term objective toward the very last one, isn't really a research initiative either. So, if you could address those?

Dr. Johnson: If I could ask a question, I guess I agree that the promising practice papers probably gets into the dissemination science part which may belong in

Chapter 7, which I know we're going to be talking about a little later.

I would have to disagree on the statement that the demonstration projects are not research. I think it's a different kind of research. It's still research. I mean you're evaluating the models, you're demonstrating how something might be done. And if you're demonstrating it, you're researching it.

It's efficacy at the same time, so it's not a clinical research study. It's more of applied research.

So, I would say that that is research, and I think it's very important research especially when we're talking about services when looking at the different kinds of models and how effective they are.

Ms. Redwood: I'm wondering are there other agencies doing this type of work like HRSA. I would see where it might --

Dr. Johnson: Good question.

Ms. Redwood: -- fall into their -

Dr. DeGraw: That's more in line with --

Dr. Johnson: Could you turn your microphone on? I'm sorry, Chris.

Dr. DeGraw: Yes, that is more in line with the kinds of things we should be doing, but is this report just applying to -- I don't think it is just applying to NIH research, so we do need to --

Dr. Hann: No, but it -- you're correct. It doesn't just apply to the NIH, but it is supposed to be reflective of research.

Dr. DeGraw: Yes. But I think if they initiate or just study models, you know, I don't know whether you need to have to initiate demonstration projects, but you do want to study them.

Dr. Trevathan: I was just going to say we do have a variety of -- in fact, we call them demonstration projects at CDC.

They're, say, demonstrations for certain prevention, interventions and communities or something like that.

We call them demonstration projects, and they are research. I mean they are classified as research at CDC, and I think some of them actually -- I have to go back -- we do in collaboration with HRSA.

So, in fact now that I think about it, we are. I mean some of the -- for example, the longitudinal follow-up connected to genetic and newborn screening, those could be classified as demonstration projects.

So, I think you could just -- this is just a different form of research, as Jennifer said.

Dr. DeGraw: If you want to get away from the demonstration project wording, you might want to say something like implement and evaluate models of polity and practice level, dot, dot, dot, because that's basically what it is.

When you're doing a demonstration project, the research component of it is an evaluation.

Dr. Trevathan: I'm sorry, I just -- before we get too far away, I was going to just mention that under the annual State of the States assessment, if you're looking at annual State of the States reports that have ongoing needs for infrastructure so you can do those State of the States reports, it's very similar, actually, to, I think, annual surveillance reports or something.

So, I wonder if that's something you could stick into Chapter 7 as well, because it's going to be an ongoing need and part of the infrastructure, perhaps, from which you would do services research.

Mr. Grossman: I thought when this was first discussed, though, as far as the State of the States that there would also be a needs assessment that would be not only -- no? It was never considered as a needs

assessment?

Ms. Blackwell: No. We actually talked about modeling it on the State of the States for people with developmental disabilities, and this project is now funded out of CMS.

So, I think what will happen after this, it will take us a year or two to get the first one out. But in successive years it will be much easier, because the contacts will be established at the state agency level and it will be more of a function of something that's already been established.

Mr. Grossman: Yes, I'm obviously coming into this late and missing the October 23rd meeting, but that's great having a State of the States, but I'm wondering if, you know, what are we going to do with that? Is it just counting heads?

Ms. Blackwell: Well, I think it will help us evaluate our progress every year.

Mr. Grossman: Progress against --

Ms. Blackwell: I can provide anybody with a copy of the Statement of Work if you'd like to see it.

Mr. Grossman: Yes, I was just -- maybe we're just mincing words here because I would think that a needs assessment would also have to be done so that we can identify not only what the population is, but where the states are missing on providing adequate services and what resources or infrastructure they may have to build to create what's necessary to meet the need.

I mean, is that being addressed in here?

Ms. Blackwell: You mean in the State of the States?

Mr. Grossman: Well, in the State of the States, and even in the --

Ms. Blackwell: It's much more comprehensive than you see in this one sentence here.

Mr. Grossman: Okay.

Ms. Blackwell: I believe our contract is going to be inviting you to participate, so you'll probably be learning more about this.

Dr. Houle: I wanted to say, you know, there are different examples of public and private sources that do this. There's the child trends data that's collected and put out every year and child outcomes. And that falls in the category of collection of data for research purposes and trend analysis.

And then there's also -- we put out the same kind of thing, but it's a congressionally mandated annual report to Congress by state which we collect data from states on information that Congress is interested in that relate to the goals and objectives of the program.

So, I mean there are other agencies that are doing this. Where it falls could be, you know, really questionable.

Is it practically an answer where

can I turn for services? Probably not. But it may go into the Chapter 7, and it may give some basic information on services by state.

But I'm not really sure where it would fall, this collection and reporting of data that agencies do. And it is based on outcome, child outcomes, in our case.

Mr. Grossman: Yes, I have a question for Jennifer on the promising practices, because these are generally looked at as pilots.

Can they be someway rewritten so that they are indeed research? I'll just leave it at that.

Dr. Johnson: Well, I think again that notion is getting the idea of how do we take what we know from research that works well and get it into practice? And there is research on how to do that, so that was what my question was.

Does it belong in there? Is it more -- I think it's not only applicable to

this question, but potentially applicable to other questions where we have to take what's known from research and apply it into practice.

But related to that, what I found kind of curious in looking through this is the attention paid to providers. Because when we talk about service, we of course think of the people that are going to be providing that service.

And there is some mention about training programs, but one of the things that we work on in trying to address the fragmentation that occurs in the system is to work towards interdisciplinary practice.

And I know HRSA is involved in this area as well and they support training grants to promote interdisciplinary preparation, and that's really not addressed in here.

But I think it's an important area for consideration because I think there's a

lot to learn about how do we best train the future providers to break down those barriers and the silos that exist in the field for families, for individuals with ASD and also their family members.

So, can you talk a little bit about that and the whole perspective on providers?

Ms. Blackwell: Can we add to that objective at the bottom of page 7, this whole objective to benefit the spectrum of people with ASD and promote interdisciplinary practice?

I think that would get to it, Jennifer. That's an excellent point.

Dr. Johnson: I guess my only question -- I agree with that. I guess to me, I'm wondering if we need to add something that looks at -- and I think there is -- I guess when I looked at that when you said test service training strategies, is that in service or is that personnel prep?

And that's the distinction I'm trying to make. Are we looking at researching what's happening in our personnel prep programs which oftentimes do get criticized for the quality of training that they're providing, but is there some way to look at that differently to improve what's going on in the service system?

Ms. Blackwell: I think it would be the latter that the group was trying to get at to improve training strategies.

Dr. Johnson: So, I might look to HRSA. Do we want to change service training? Because service training to me is, again, suggesting in service and not necessarily the personnel preparation, that idea that somebody is, you know, in a formal training program getting a degree and will go into the field and utilize that knowledge in some way to provide services.

Dr. DeGraw: I mean do you want to just broaden it and have it be develop and

evaluate or research methods for training pre-service and in service -- or pre-service and in service training of personnel providing services for people with autism.

Ms. Singer: And can we not add parents and legal guardians there in that sometimes it's the parents and legal guardians who are providing?

Dr. Hann: -- with what all you want into this particular one.

Ms. Blackwell: Alison, I think the intent of this one was to get to people who are paid service workers. And although that could be family members in some instances, I don't think the intent of this particular one was to get at family. It was to get at people who support people with autism as their job.

Dr. DeGraw: I would say, though, at least from her perspective, that we ought to include families. Because in our models of training it includes families as both teachers and students, so -- and trainees, so I think

it should be developed, whatever it is, models of pre-service and in service training for personnel, including families, providing services for people with autism.

Dr. Hann: Again, I'm going to ask someone -- maybe Chris is the one to try to pull this all together.

Could you give it a shot right now? Or Ellen is scribbling. Okay.

Ms. Blackwell: Develop and evaluate --

Dr. Johnson: Pre-service and in service.

Ms. Blackwell: Pre-service and in service.

Dr. Johnson: Training strategies?

Ms. Blackwell: No, it's just training, I think.

Dr. Johnson: I don't know if evidence base should be in there somewhere or it applies -- I'm trying to tie the research to the training piece.

So there's two -- so, you want to do the research on the efficacy of the training itself, but you also want to figure out how best to train people in the current research that tells us what's best in practice.

Dr. Hann: That's like the dissemination pieces of it. So, what is this one supposed to be?

Ms. McKee: It was drafted as the first one, but I understand that there might be another piece here from what Jennifer has said.

Dr. Johnson: Well, why don't we focus on the one that's really, the pre-service and in service training and researching the most effective strategies for providing in service and pre-service.

Dr. Hann: So, evaluate. Is the word we're looking for is to evaluate? Evaluate - is it methods? Evaluate methods for pre-service and in service training to

increase, and then keep the rest of this with the end of it being promoting interdisciplinary practices?

Dr. Johnson: Yes.

Dr. Hann: Now, Chris, I'm going to turn to you. This is a bona fide research topic that HRSA would be interested in?

Dr. DeGraw: Yes, I think so.

Dr. Hann: Okay. Just double checking.

Dr. DeGraw: No, I think it would be in our research program and within our training programs.

Ms. Blackwell: The only thing I think we might have missed was that our group was really focused on that there are some models out there already. So, that's why they had us put in develop if necessary.

So if we just say evaluate, does that limit us to what's already out there?

Dr. Johnson: Well, you could change it, I guess. And if you're going to

evaluate those models that exist, I guess that would lead to replication or development of more or expansion of programs.

So, it's sort of like you have to evaluate what's out there currently before you can know whether you have to develop more, refine that or expand that.

Dr. DeGraw: I think I'd keep the develop if necessary, because there's going to be -- you have to concurrently new strategies as well as looking at while you're looking at the old ones.

Dr. Hann: So, would a possibility be something like evaluate new and existing pre-service and in service training to increase skill level in service providers, including direct support workers, educational staff, public service workers to benefit the spectrum of people with ASD and to promote interdisciplinary practice.

Ms. Singer: But we want to add in there parents and legal guardians.

Dr. Hann: Got it. I thought there was a piece missing.

Dr. Johnson: If I could make one other comment about Chapter 5, and I think what ended up happening is you probably were struggling with the same kind of issues that I was struggling with in Chapter 1 where I think some of what is in here reflects more of what is needed versus what is known.

And so I guess the question to me is whether -- or what is it that we know about services currently. Do we not know a whole lot, or do we basically know that there's a lot that's needed?

So, where does it fit? Does it fit in the What Do We Know or does it fit in the What Do We Need?

Ms. McKee: We struggled with that as well, yes. We don't know a lot, we need a lot, but what we know is what we're doing isn't working. And so that's why we have these two massive paragraphs that we put in

there to say we've done a lot of studies on clinical practice, we have not done them in the communities. That's what needs to happen because what's being provided is simply not adequate.

Dr. Johnson: So, I might suggest that that then move to the What Do We Need section because that better reflects that we really don't know much at this point in time about services and the effectiveness of the services.

Ms. McKee: Jennifer, you don't think that's on page 4 in with the studies?

Dr. Johnson: Well, I was looking I guess specifically at -- well, specifically on page 2. And I guess we don't have line numbers, but the two blue paragraphs there.

I mean I don't know. I could look at the whole -- I mean what do we know about services and how much is it -- yes, we don't know anything.

Dr. Hann: We know we need them.

We know we want them better connected.

Okay. How about this? Why don't I walk through in terms of what I've heard the Committee discuss in terms of, in addition to the changes proposed by the folks who worked on this, what has been suggested to date by this group.

Page 1, I haven't heard any additional changes or modifications over and above what the Panel has provided.

Page 2 is the same. There's been discussion, but there's been no recommended changes to page 2.

Page 3, that also is the same. There's been no recommended changes to page 3.

Same with 4.

Page 5 in the middle of the page, there is a paragraph that begins with families, people with ASD. And then there's a blue section right there and we've modified that. Particularly the sentence beginning with all people.

It now reads "All people with ASD, their families and support systems should have," and then it continues as written.

Ms. Blackwell: On page 5, you're going to want to move that State of the State. Didn't we talk about moving it to Chapter 7?

Dr. Hann: Yes. Thank you, Ellen.

Page 6, the area that is highlighted in pink would be moving also to Chapter 7.

The first short-term objective will be moving to Chapter 7. And the last objective on that page about the promising practice papers will be going to Chapter 7.

Ms. Blackwell: Also that you would restore the numbers of studies --

Dr. Hann: Correct.

Ms. Blackwell: -- that were in the previous version of the Plan?

Dr. Hann: That is correct. Restoring the numbers.

Page 7, I had actually a question

before I move on. Where it says conduct a study, is that to conduct once?

Ms. Blackwell: Correct. I think Christine and I were going to suggest that we initiate two demonstration projects, but I don't quite know how to work that language into implement models of policy and practice level of coordination, which was what Chris had suggested.

Dr. Hann: Right. Because that was the change for this one, was to implement and evaluate models of policy. There, I guess one could argue, you could say, the numbers of models potentially.

Ms. Blackwell: Okay.

Dr. Hann: Implement and evaluate X number of models of policy and practice level coordination.

Ms. Blackwell: I think we were suggesting two.

Dr. Hann: Two. The other change on this page has to do with the last bullet

which we spent some time on, good time, but I'm trying now to resurrect what I have here.

Evaluate new and existing pre-service and in-service training methods to increase skill levels in service providers, including direct support workers, parents and legal guardians, education staff and public service workers to benefit the spectrum of people with ASD and to promote interdisciplinary practice.

Okay. I'm seeing heads nodding.

Do I have a motion to accept the changes? And I think there was a second. There were sort of two hands up.

All those in favor of accepting those changes? Any opposition? Any abstention? The vote is unanimous.

Okay. We're on a roll. I know we've been going a long time, but we're really on a roll. So, I really would like to get through six, and then we can have a very short break and come back and discuss seven, if

that's okay with everyone. And one, you're right.

Ms. Shurin: Della, could I ask about Chapter 7? It seems like we've had a whole lot of let's move this to Chapter 7, let's move this to Chapter 7.

So, right now even if we look at what we have, it isn't Chapter 7 at all. So, even though I know everybody wants to tidy this up today and be all done, could we not consider the possibility of putting everything in Chapter 7 that's going to go there that we've talked about, and then do either a teleconference call or an e-mail?

I mean I don't think anybody has argued about any of the things that are going in 7, it's just that's where they best go.

So, I don't envision a lot of controversy, but I think it's kind of premature, shall we say, to review 7 when it isn't what we're going to be reviewing?

Dr. Hann: Alison.

Ms. Singer: The only thing that concerns me is that right now Chapter 7 is the collective wisdom of two people. And I would really appreciate it, and I think Cathy would appreciate it as well, if before we continue to develop Chapter 7, if we could just get some general feedback that we're either on the totally wrong track or we're on the right track.

So, maybe not spend as much time on Chapter 7, but a little bit of input I think would appreciated before we go down -- if we're going down the wrong path, I don't want to continue down it.

Dr. Hann: I understand. Does that sit well with everyone else that we'll have essentially today a general discussion of 7 in terms of its direction, and that we will have to have another get-together, essentially, to look at that and potentially anything else that isn't cleared up here today?

Speaking of the potential get-

together, it will likely be December the 11th.

Dr. Trevathan: Well, I'll say what others are thinking, including someone sitting next to me.

So, if it's just -- or someone sitting on both sides of me, and across from me.

(Laughter.)

Dr. Hann: You're surrounded.

Dr. Trevathan: Why am I doing this?

So, the question is if it's just on Question 7 that we will be getting together again, especially for those of us that travel a long way to get here, is there a way we can -- if we, for example say, as Alison has requested, that it's going in the right direction given the additions, can we have the Question 7 through teleconference?

Dr. Hann: Yes.

Dr. Trevathan: All right.

Ms. Singer: Especially because a

lot of the items that will move into 7 have already been approved in other sections.

Dr. Trevathan: Correct.

Ms. Singer: It's just a cosmetic correction.

Dr. Trevathan: Correct.

Dr. Hann: Right. Because I think what I would like -- so, let's move through 6, actually, quickly right now, take a short break, come back, do 1, then have the discussion as to 7 and how we wish to proceed essentially for the remainder of the update. Okay?

So, Ellen.

Ms. Blackwell: Okay. Chapter 6. This chapter, the comment we received at the October 23rd meeting was to modify the title a little bit, which we did. The chapter previously read What Does the Future Hold? Now, it says What Does the Future Hold Particularly For Adults?

That's what Christine and I felt

embraced the comment of the group on the 23rd.

Some minor edits to the first page. Generally, our group's thought about this chapter was that they really wanted to focus on -- or they felt like the chapter already focused on transitioning youth and adults although it was unclear. Particularly wanted to look at the transition from the educational system to the developmental disability system.

The group wanted to respond to a lot of public comments that we had about community integration, housing issues and the use of psychotropic medications to control challenging behaviors.

They wanted to get at the issue of life-long supports, and also comparative effectiveness research. So, the changes that were made I think pretty much get to that.

I tried to modify some of the language that was strictly aimed at adults in the October 23rd version.

Just as I look at these pages, these are pretty -- I mean I think most of you have seen these already.

Chapter 10, the last paragraph on Chapter 10 sort of sums --

Dr. Hann : On page 10.

Ms. Blackwell: Page 10, I'm sorry. Chapter 10 -- I'm sorry, talk about a Freudian slip there. The last paragraph on page 10 sort of summed up a lot of the issues that came up in public comment.

The aspirational goal, we've modified this a little bit. We changed satisfying relationships to meaningful relationships, but we like this aspirational goal better.

We would want to ask that the Committee restore the numbers that were in the previous short and long-term objectives.

We changed the research opportunities to follow your request to make them a little bit broader and more general.

I think we might want to talk about the third bullet on page 12, which is develop a method to identify adults across the spectrum who may not be diagnosed or are misdiagnosed.

Is that something that would belong in Chapter 7 or do we want to leave it here in Chapter 6?

It's at the bottom of page 12. Or is this something that goes in the chapter on diagnosis?

Ms. Singer: I don't think it's Chapter 7. I don't think it's infrastructure.

Ms. Blackwell: Okay. We'll just leave it in 6. That's fine.

I think on page 13, it seemed to me a minute ago you weren't crazy about the language that used the word "demonstration project," so we may want to say initiate a model at the state and local level or evaluate a model at the state and local level. Sounds like that might be more palatable to the

group.

And then at the bottom of page 13 restore the "at least two interventions." And by the way, our objective in both Chapter 5 and Chapter 6 was not to substantially change any of the objectives that were in the previous plan. We felt that some of them needed clarification.

So we didn't change them, I don't think, in any really substantial way. We just tried to clarify them especially because we knew that several of them had been funded with the Recovery Act money.

On page 14 we have one study. The next bullet is a study that looks at psychopharmaceutical medications, especially as they're used to control behavior in adults.

And then the last bullet goes to actually the first bullet which talked about developing effective services and supports.

So comments, questions?

Dr. Johnson: This is Jennifer. In

this chapter, there is references to self-determination, and that would be an element of what's promoted in the research.

One of the things that we're coming to know is that there has been training that's been done. People in general, understand the concept of self-determination, but they lack the skills to apply that in their lives. And we're now supporting a project that is hoping to scale up self-determination so that people can better apply those self-determination skills in their lives.

So, I don't know if that was anything that was ever -- I don't see it popping out at me in this chapter. But I don't know if it's there and I'm missing it or if it was discussed within your panel, but certainly I think there's probably more research that needs to be done to understand how much is being promoted, how much people on the autism spectrum disorder have -- are

utilizing that again in their daily lives to support their living in the community.

Ms. Blackwell: If you take a look at the first short-term objective, Jennifer, we put it into one of the examples.

Dr. Johnson: Okay. When I read that, I didn't get that. But if that's what's intended, I could have just missed it.

Ms. Blackwell: I think one of the group's concerns was that -- I guess this sort of goes to what Alison expressed earlier that people with -- some people with autism may not have equal access to the same -- I mean I'd like to think that they do, but you're going to need a very supportive family member to help you self-direct your services, but there may be people with autism that it is the only way they can get quality services.

So, our group was really interested especially in the adult population, at looking at self-direction in adults. So, I don't know if that does come through.

Ms. Singer: Since we're talking about the first short-term objective, I wanted to add safety as one of the examples.

Dr. Johnson: And maybe it would help if we added something to the short-term objective not only to assess and characterize variation and all of those things, but related outcomes.

What are we seeing as a result of some of these things that would be more closely looked at. If they have better access to integrated employment, are they more likely to sustain employment? If there're supports for community inclusion again, do they have a better quality of life? And I know that's another question in here is to look at quality of life indicators.

Dr. Hann: Maybe I'm just confused, but launching studies to assess and characterize variation in quality of life for adults on the ASD spectrum, I understand that. And now you've added outcomes as a function

of different services that they've received?

I'm trying to understand --

Dr. Johnson: Well, it may be just because I'm not getting the objective completely.

So as I understand it, the purpose is to conduct studies that basically would be a rubric or a taxonomy or something like that to talk about the quality of life.

Am I understanding that correctly?

Dr. Hann: But as a function of what?

Dr. Johnson: Looking at these integrated employment, community inclusion, self-determination, relationship.

Dr. Hann: So, a different -- so, I'm trying to figure out that collection. Collectively, what is that? That's different service models?

Ms. Singer: To me, it would be, the way I read it, was to really try to understand best practice. What are the best

practices in employment, in inclusion, self-determination and in safety, and how can we implement them?

Dr. Johnson: And see, how I read it is that there is currently we know a lot of variation in practice, so we want to know what that variation is. And I would want to know what that variation, what is that leading to? What kind of outcomes are people experiencing?

Ms. Singer: I would want to know within that variation, which are the good ones and which ones are the ones that we don't have to be bothered with.

Dr. Johnson: Right.

Ms. Blackwell: We actually didn't change this language much from what it said in the first variation of the plan.

So, can you make a suggestion as to how you think it should read?

Dr. Hann: In the original plan, which one was this one, Ellen?

Ms. Blackwell: The second one.

Dr. Hann: The second one read, launch at least two studies to assess and characterize variation in adults living with ASD such as social and daily functioning, demographic, medical, legal status. Right. That's how it read before.

Ms. Singer: Maybe we can say launch studies to characterize and assess variation -- well, variation in the quality of life for adults on the ASD spectrum. Then list the items, and then put comma, and determine best practices so that there's an outcome.

Ms. Blackwell: I'm good with that. I was ready to move on to another. I'm sorry.

PARTICIPANT: I was wondering if issues related to post-secondary education came up in your group. That certainly is an emerging area of practice.

And I think for people with ASD,

we're seeing a lot of them in post-secondary education settings. Some getting supports, some not getting supports.

So, did that come up and is that an area worth looking more into?

Ms. Blackwell: I think we talked about it a little bit in terms of making sure that we included everyone on the spectrum in the adult group, but I don't remember other than talking about transition, that it was a specific issue for us.

Do you, Christine?

Ms. McKee: No.

Ms. Singer: On page 13, the top bullet point, I think that's another area where we can -- where it says provision of specialized training for direct care staff, I think we could add parents and legal guardians there as well.

Dr. Houle: I think back to Jennifer's point in the post-secondary education. Where you listed the examples on

page 12, short-term objective, bullet 1, you could put integrated employment and educational opportunities.

Dr. Hann: Do you want to say post-secondary educational opportunities?

Dr. Houle: Yes, that's fine.

Dr. Johnson: I'm sorry. Where were you, Gail?

Dr. Houle: Page 12, short-term objectives, bullet 1 examples. Adding those three words to integrated employment and post-secondary educational opportunities.

Dr. Johnson: The only other comment that I have is on page 13 in that first bullet where it says conduct a study to measure and improve the quality of care.

Given the conversation we had earlier about the use of the term "care," is that health care or are we talking about the long-term services and supports?

Ms. Blackwell: Let's say life-long supports. The quality of life-long supports.

Thank you, Jennifer. I thought I had them all out of there.

Dr. Hann: Okay. So then the last short-term, Ellen, you were suggesting that we think of that too in terms of different wording?

Ms. Blackwell: Didn't Chris suggest using the word models, focusing on models, evaluating models?

Dr. Hann: At the state and local level in which existing programs --

Ms. Blackwell: Evaluate models at the state and local level in which -- is that --

Dr. Hann: Okay. I think I must just have a brain freeze with the short-term objective 1. Because the way it was written in the past, in the prior version, it really was sort of demographic factors, and these are not any longer demographic factors.

So, I'm just having some difficulty trying to understand what this is

about, but maybe it's just me.

Ms. Singer: I mean, you could put in demographic factors as one of the examples. So, the three we would be adding to the list would be demographic factors, post-secondary educational opportunities and safety.

Dr. Johnson: I think that they're not demographic factors in the traditional definition of demographics, but what they are is characteristics of the service delivery system and options.

Dr. Hann: So, launch studies to assess and characterize variation in the quality of life for adults on the ASD spectrum as it relates to characteristics of the service system environment or something like that such as integrated employment, community inclusion, so on and so forth.

Ms. Singer: But then we were going to add, comma, and determine best practices.

Dr. Hann: That's okay. I think that will still fit. I think that would still

fit.

So, as it relates to characteristics of the service -- what did you say?

Dr. Houle: I called it characteristics of the service or components of the service delivery system.

Dr. Hann: Thank you. Okay. That makes me feel better. Thank you.

Ms. McKee: Della, if you look at the autism research funding, it looks like something was funded under this the way it used to be written than what it is. Autism in the second half of the life span, behavior, daily living, service needs.

Dr. Hann: Yes. So, in the past it had two studies. It said launch at least two.

Do you want to keep the numbers from the --

PARTICIPANT: The numbers go back in.

Dr. Johnson: Okay. I just have

one more. I'm sorry.

Dr. Hann: No, no.

Dr. Johnson: Back on page 12, the second short-term objective where it says conduct comparative effectiveness research, I'm just wondering if we want to be doing research on community-based interventions.

Do you want to use that as a descriptor of what kind of --

Ms. Blackwell: Yes, that would be great.

Dr. Hann: So, where would that go? I'm sorry.

Ms. Blackwell: In between examine and interventions; is that correct?

Dr. Hann: Community-based interventions.

So, Ellen, to the -- I noticed, did your group consider that the rewrites and additions under long-term objectives really were rewrites of the existing ones, that they weren't being lost?

Ms. Blackwell: They tried really hard to make sure. We all tried really hard to make sure that the integrity of the original -- because we knew that some of them had been funded, so we were hoping that we would be able to clarify at a good time.

Dr. Hann: So along those lines, the very last one. Implement a demonstration to test effective services and supports resulting from comparative effectiveness research. I'm not sure what that means.

Ms. Blackwell: Well, one of the first objectives that was in the old plan, was it's the second bullet under short-term objectives. That was to identify the community-based intervention services and supports.

Dr. Hann: Right.

Ms. Blackwell: Right. So, David Mandell asked for an objective to test them after they were identified.

Dr. Hann: I see.

Ms. Blackwell: It's a subsequent -- it's Part 2.

Dr. Hann: Okay.

Ms. Blackwell: I think his point was that it's one thing to develop them, but it's something else to test them.

Dr. Hann: In the real world.

Ms. Blackwell: Right.

Dr. Hann: So, it's -- I'm trying to remember the words. I don't think anyone is here that's in that division to help me with the words.

There are words that go with that in terms of like sort of testing the fidelity and so forth like that of interventions in real world settings and so forth, but there's a cache of words that are used with that particular area.

Deb, does that sound familiar to you at all?

(No response.)

Dr. Hann: You might want to play

with those words a little bit just because I think I know what he's trying to say.

It's like you can find out all kinds of interesting things. But when you take it to the real world where you don't have a lot of the protections in place from your trial and so forth, it may or may not work.

Dr. Hirtz: I think implementation research is probably a good, general term.

Dr. Johnson: Is it translational research? Is that what you're looking for?

Dr. Hirtz: Well, no, because translational has two meanings. One is bench to bedside and one is also -- if you modify it by saying translational from clinical trial to craft this.

So, I think implementation research might be different.

Dr. Hann: Okay. Is there any further discussion? And I'm going to walk through this one like we did the previous one. Okay.

Based on what I heard, was to accept the changes that had been recommended for page 1, 2, 3, which is 10, 4, and then beginning with the objectives to reinsert the numbers of studies that had been there from the past.

Short-term objective 1, remodified the language to launch two studies to assess and characterize variation in the quality of life for adults on the ASD spectrum related to characteristics of the service delivery system such as. And then we have our parenthetical which now also includes post-secondary opportunities, right?

Can't read my own scribbles. Education. I thought there was a missing word. Educational opportunities.

We also included the issues of safety in that as well, and best practices, and determining best practices.

The next one, there was one change to conduct comparative effectiveness research

that includes a cost-effectiveness component to examine community-based interventions. And the rest remains the same.

Next page, the first full bullet, conduct a study to measure and improve the quality of lifelong supports being delivered. And then that continues on, specialized training for direct care staff, parents and families, including assessments and development of ASD-specific training, if necessary.

Ms. Singer: Since we've added parent, we're going to add parents and legal guardians there, and it may need to be more than one study now. It may need to be two, because the training that's appropriate for parents and legal guardians may not be the same training that's appropriate for direct service providers.

Ms. McKee: You say conduct at least one study, right?

Dr. Hann: Conduct at least one.

Okay.

The next bullet we're keeping, basically, but we're going to modify the words a little bit to match previous wording that the Committee had suggested. So, it's evaluate models at the state and local level for existing programs to assist people with disabilities and meet the needs of transitioning youth and adults. I would imagine that's evaluate at least one. Okay.

Then the next set of changes actually is the final bullet, and we're going to talk about implementation research. So, to conduct implementation research to test the results from comparative effectiveness research in -- it's not real world. There's another phrase that's used for that, but essentially real world settings, including a cost effectiveness component, etcetera.

Lyn, you acted like you had a question.

Ms. Redwood: I was just looking at

the middle bullet, the conduct a study to evaluate current practices leading to the use of psychopharmaceutical medications and their effectiveness in the treatment of comorbid, and I was wondering if we could put psychiatric conditions.

Since there are psychopharmaceutical drugs, we would be treating psychiatric conditions. No? Give me an example what you're wanting to get out with that.

Ms. Blackwell: I think we received a lot of comments from the public about drugs being used to control behavior. So, this was to get at how are drugs that are created for one use being used for another.

And maybe it isn't expressed the right way. If anyone has a suggestion --

Ms. Redwood: If it's behavior, would it be a comorbid condition? I guess that's what I'm just trying to wrap my head around.

It sounds like they're misprescribing or they're using drugs the way they're not intended.

Dr. Trevathan: Well, I wasn't part of the discussion, but since I am -- I mean, we have a couple child neurologists at the table, so we'll see if there's an agreement, but there are a lot of uses of some of these psychopharmaceutical drugs for treatments of a variety of different manifestations and behaviors and autism and autism spectrum disorders and related conditions, for which they're in the communities, for which there's no really solid evidence much less FDA indication or clinical trial evidence.

I assume this is what they were getting into, right?

And I think one of the issues is that if you say, well, we're going to define these as psychiatric, then clinicians will look at a child and say, yes, I would like to try X drug on this child for this purpose, but

won't agree that the treatment -- that the indication that they're using the drug for is actually psychiatric or not.

So, what's psychiatric, what's not, what's the borderline between neurobehavioral manifestations and true psychiatric disorders becomes very blurred.

Somehow, I wonder if you could just say the use of medications for treatment of behaviors and other manifestations, you know, just use of medications for treatments for behavior because they also use anti-epileptic drugs in these situations sometimes too, for example.

Ms. Redwood: It sounds like an important initiative. I wasn't certain what you were trying to get at.

Dr. Trevathan: Does that fit what they were discussing?

Ms. Blackwell: Yes. And not only did we get this in the public comment, but out group felt it was really important especially

in the adult population, especially in the older adult population, actually.

So, you want this to say -- wait. Let me read it back. Conduct a study to evaluate current practices leading to the use of medications and their effectiveness in the treatment of -- I would actually say for specific behavioral issues with adults.

Maybe somebody else has a suggestion.

Ms. Singer: I would just take out psychopharmaceutical and leave the rest, because also we have adults with comorbid seizure disorder who are on off-label drugs --

Dr. Trevathan: Right.

Ms. Singer: -- they're on beta blockers for epilepsy.

Dr. Trevathan: And I assume they were also - I don't know if they were intending this, the group, but there's also been concern that children with autism may have different adverse affects of, for

example, anti-epileptic drugs. Adults as well.

So, I don't know. That may be part of what they were getting at. So, you could get all that if you just took out psychopharmaceutical and left the rest.

Ms. Blackwell: So, would it be because you expressed that children might fall into this area as well, would it be appropriate to think about moving this to Chapter 4? I mean, that's what I -- not this specific objective. I mean our group was concerned with the use of medications in adults, but --

Ms. Redwood: Well, could it just be changed to those with ASD, and then we're not specifying an age?

Ms. Blackwell: Yes.

Dr. Trevathan: And then put it in 4, is that what you --

Dr. Hann: Okay. So, I'm trying to -- so, conduct a study to evaluate current

practices -- conduct, I guess, at least one study to evaluate current practices leading to the use of medications and their effectiveness in the treatment of comorbid conditions or specific behavioral issues, period.

Obviously, it's in people with ASD. In people with ASD?

Ms. Redwood: I hate to bring this up, but I also think there's big concerns with the use of aversives and also physical restraints. And I know there's been several cases where children have died due to physical restraints, and I know that's not reflected here. But whether or not that's something, I don't know how you would research that, but I just wanted to mention that that's a huge concern in the community, too.

Dr. Houle: Would that fall under the safety issues?

Ms. Blackwell: I think if you go back to the chapter on services, we did bring up -- didn't we bring up safety in the

aspirational goal?

I think it's in the aspirational goal on Chapter 5.

Dr. Hann: But it is an interesting thought to consider here, conduct a study to evaluate current practices leading to the use and safety of medications and their effectiveness.

Because that would pull in, Ed, what you were talking about too in terms of the adverse reactions potentially looking different, patterns of reactions being different.

So, while it doesn't directly address the issue you raised, it does bring in the safety issue.

Okay. So, we have, conduct a study to evaluate current practices leading to the use and safety of medications and their effectiveness in the treatment of comorbid conditions or specific behavioral issues in people with ASD.

Ms. Blackwell: Conduct at least one study.

Dr. Hann: Yes, thank you. Okay. Those in favor of the changes we've just discussed for this chapter?

(Laughter.)

Dr. Hann: Those opposed? Any abstentions? It carries. You've just earned a break, but please try to keep it short because I do want us to be able to talk about Chapter 1 and at least have a brief discussion about what we're going to do with 7 before we adjourn.

(Whereupon, the above-entitled matter went off the record at 3:48 p.m. and resumed at 3:58 p.m.)

Dr. Hann: Jennifer, why don't we go ahead and get started? During the break, everyone should have received at their place, a hard copy of the version of Chapter 1 that was discussed at the October IACC meeting.

Dr. Johnson: Okay. So, what I was

trying to do during our break is do a little bit of a crosswalk between the version from October 23rd, and the version from today so I could point out some of the differences.

Again, I think what threw us off, including myself, and maybe perhaps most myself, is the information that's in What Do We Know. And I think the bottom line is that perhaps we don't know a whole lot currently about the early warning signs, and so maybe there's just not a lot to put in the What Do We Know section.

I think also the introductory sentence, a child's primary caregivers are often the first to identify the signs of ASD, I'm going to actually suggest that we just take that out and start with current diagnostic criteria to really focus on what it is that we know, because I don't even know how well we know who's really first to notice signs of ASD, if it is primary caregivers, if it's pediatricians, if it's -- and if

caregivers are considered family members or early care and education providers.

So, we might just really want to focus this on what is it that we know about diagnosis and assessment.

I think the other thing that confused this first part was the whole notion that children may be missed, and that people might reach adulthood before they receive a diagnosis.

So again, we may just want to move all of that into the What Do We Need section because right now there isn't really anything we know. We just know that it's a need.

And again, I think that's what threw people off and why this section appeared to me that we needed more of a context of what led up to what came next in the chapter.

So, do we want to have a discussion about that at this point in time or -

Dr. Hann: So, actually what might

be helpful, and obviously the Committee needs to decide if it is truly helpful, is to just sort of take page 1 from the October version, comparing it to the page 1 over here.

Jennifer, what I hear you saying is, first of all, the first page for today, the November version, had made changes to the three bulleted questions that follow beneath When Should I Be Concerned.

Are you suggesting we go back to the original version of those questions, or should we keep the November version?

Dr. Johnson: Well, I think that we should consider the November version because those changes were specific changes and language recommended by the Panel.

And I, again, talked about those as being general changes in language that we may want to consider adopting for the Plan in its entirety, not just for Chapter 1.

So, when we use terms like risks or warning signs or red flags, do we want to

consistently use the term indicators instead?

When we use terms like symptoms and severity, do we want to use characteristics instead?

So, that's the question I think up before the Panel -- I mean --

Dr. Hann: Alison.

Ms. Singer: I think in the introductory bullets you've really changed the meaning of introductory bullet Number 3 by adding over time, because now it implies you're looking at variation in an individual over time, when what we had originally intended was to really get at the heterogeneity.

Dr. Johnson: And I think that brings up another issue that the Committee needs to decide upon is, where should this chapter be focused? Should it be focused on that initial diagnosis or should it be concerned with changes that occur over time. And is that something that's dealt with in

Chapter 6, or should it be in Chapter 1?

Ms. Singer: Can I --

Dr. Hann: Yes, go ahead.

Ms. Singer: This is again an issue we talked about in October, which was if we were going to have an entire chapter that was devoted to adults, which we all agreed was an oversight in Version 1.0, we didn't want the pendulum to swing back the other way and then have an oversight in that we were now under-representing the needs of children.

And so I think when we decided to have Chapter 6 that focused on adults, we had agreed that Chapter 1 would be -- its primary focus would be on children.

Dr. Hann: Any other discussion on that topic? Because I do think that's very important and it will set the tone, essentially, for the rest of this discussion that the Committee is comfortable with this chapter having a focus on childhood, particularly now that there is a chapter that

has a stronger focus on adults.

Dr. Johnson: Just one, I guess, need for clarification there. When we say childhood, oftentimes we do define that by an age range.

So, do we need to do that for this chapter, because childhood in some communities is considered up to age 18, other communities it could be up to age 22.

So, I think we need to be clear on what we're talking about, because again I think the original intention of this chapter was to really focus on those early years where you want to pick up children as early as possible.

So, that's why I ask the question.

Ms. Blackwell: Yes, I agree with you, Jennifer. I think it's very important to set the age parameters. And, in fact, we did add a correction in Chapter 6. We used age 21. And we did that because Medicaid's early - the EPSDT program, as you know, concludes at

the month of a child's 21st birthday.

And as I'm sure Gail would attest, most local education authorities terminate services at or around the end of a child's 21st year. Although, it does vary from state to state, so we did pick 21 as the break point.

Dr. Hirtz: That's a definitional issue which we come up against all the time in terms of the medical recommendations and things like that.

But I think in this case, the focus of this is really on the young child. And it's kind of weird to put in 18 or 21 when really what we're talking about is diagnosis in the toddler and early school age.

So, I would say for this purpose, we're better off just saying children or young children or something like that because we don't want to limit ourselves or, you know, really what happens in the adolescent and older child is a different question.

Dr. Hann: Okay. So, what I'm hearing is that the Committee is comfortable with this chapter focusing on young children.

Ms. Blackwell: And I hate to be specific, but young zero to five, zero to eight, zero to three?

Dr. Johnson: So given that now, I guess still, based on what the Panel was saying, that over time still could occur, that the different conditions or behaviors or co-occurring conditions may occur maybe when the child is three, and then again at five so that over time may still be a factor.

Ms. Singer: I think the idea behind this bullet was to try to capture the challenges inherent in diagnosis because of the heterogeneity and the variation in how the children present when they're young.

I don't think it was intended to focus on one person over his or her life span.

Dr. Trevathan: Correct.

Ms. Redwood: Could we actually

capture both by saying how much variation serves as symptom and severity associated with ASD within those with -- I've got this wrong -- within those with ASD and changes over time and what changes occur over time.

Because I know parents have heard that adolescence is a time when oftentimes children will develop seizures and there's a lot of changes that happen during adolescence in children with autism. So, I know that's an area where they're very concerned too.

So, I just think that if there would be a way to capture both maybe later on in the document, but parents are wanting to know how is this disease going to either progress or regress over time or will it stay the same.

So, I do think that's an important question that parents have. I just am not certain how we could capture that or if it has to be captured in this opening bullet, but just somewhere in the document.

Dr. Hann: Christine.

Ms. McKee: Do you think that goes into what does the future hold? I mean we talked about how with that chapter we weren't exclusively focusing on adults. We were looking at anyone's future, the transitions.

And so we put in very specific language so we weren't limiting ourselves there.

But I think what we're trying to get at is bringing the children into the systems of care, intervention --

Ms. Singer: Maybe we can restate this better is we say, how do variations in symptoms and severity create challenges for diagnosis so that it's clear that that's what we mean.

Dr. Johnson: I think that would help differentiate that very issue. Because again what we heard from various members of the Panel is that it's sometimes difficult to tease out when you're trying to make that

initial diagnosis.

Once a child has a diagnosis, the condition may change over time so that you may need to continually assess. And I think that's why the phrase over time got into that question. And again we just need to be clear are we talking about initial diagnosis.

And I think that's the general agreement that I'm hearing from the Committee, is that we're really talking about initial diagnosis.

So, my question is whether the reoccurring assessment is covered elsewhere.

Ms. Blackwell: What if we said how much variation is there in symptoms and severity associated with ASD at diagnosis? Is that different? Does that not capture --

Ms. Singer: I think it was to try to capture the challenge of the heterogeneity in terms of making the diagnosis.

Dr. Trevathan: Early. In terms of making an early diagnosis.

Ms. Singer: Right.

Dr. Hann: So, what I heard you say, Alison, was how do variations in symptoms and severity create challenges in diagnosing --

Ms. Singer: In early diagnosis.

Dr. Trevathan: In early diagnosis.

Dr. Hann: An early -- okay. Diagnosis, I guess that is. Okay.

Any further discussion on that particular item? Okay.

I need some clarity too in terms of the other -- for the first one, what are the early warning signs. In the November version, it was what are the early indicators.

Dr. DeGraw: You might want to stick with signs, but delete warnings. Signs would be compatible with CDC's learn the signs?

Dr. Hann: All righty. Compromise. Way to go. Cross-agency collaboration is nice.

So, what are the early signs of ASD. Okay. And then we have really no changes to the second one. And then the third one, the changes that we just talked about in terms of the challenges to early diagnosis.

Ms. Singer: If I could just ask about the language suggestion that was made to, instead of use symptoms and severity, that characteristics and patterns of abilities and disabilities -- is that something that this committee wants to -- language that this committee wants to use?

Ms. Redwood: I just think it gets a little long. I don't know. I mean we're trying to keep short bullets, but I'm not -- I don't really care one way or another.

Dr. Hann: Any other discussion? We're going to have to vote on this as a cluster. Okay.

I'm not hearing enthusiasm for making that change. Okay. All right. I'm going to ask for a vote, and I'm going to read

to you what I understand is what is up for vote.

What are the early signs of ASD. The second one remains the same. The third one, how do variations in symptoms and severity create challenges in early diagnosis of ASD.

Okay. Do I have a motion for this, for these changes? Okay. I saw two hands.

Those in favor of the changes? Any opposition. No. Any abstentions? Motion carries.

Okay. Now, Jennifer, you started to walk us through in terms of the November versus the October.

Dr. Johnson: Sure. Well, actually one thing I'd like to have the Committee decide on is the comment on the October version, page 1, that starts on line 9.

There was mention at the scientific workshop about the revision to the

DSM criteria that are being considered. So, I just have a question there as to whether we need to change that sentence as a result or if we keep it the same.

Dr. Hann: Well, unless one of you know differently, I don't believe the new criteria have been published yet.

Dr. Trevathan: No.

Dr. Hann: I didn't think so.

Dr. Trevathan: Yes, I hate to say this, but I -- the impact of the change in the diagnostic criteria is something we don't really know yet. I mean we don't really know exactly what the Committee is going to do.

And at least it seems like the three of us here that are talking, we've all heard the same date, 2012. So, I would suggest we don't even go into that with this document at all.

We'll have enough time that we'll have to spend on this in 2012, I think.

Dr. Hann: Okay.

Dr. Johnson: So, I'd actually like to continue taking us through the October document and onto line 14.

I think with the decisions that we made about the bulleted questions, that I'm not sure if that change should be in there now.

Dr. Hann: Deb.

Dr. Hirtz: I just wanted to make a general comment related to this issue. This is the one question I've been paying the most attention to, because I've been worried.

It's so critical that we promote and continue to support campaigns for early diagnosis, and screening and diagnosis and research and so on.

On the other hand, I've had a number of families that I've taken care of where the parents have been so utterly guilt-ridden about not having made the diagnosis earlier. And it so destroys them that -- because of what's going on then, they feel

like it's my fault and if I had known, you know, these symptoms and, you know, if the child wasn't diagnosed until like four or five, you know, we've lost all this time.

I just want to be so careful that parents don't feel that it's their fault or that they should have somehow made this diagnosis earlier or pushed their pediatrician or whatever the circumstances were.

And I actually think we do a pretty good job and this is pretty good. I just want to be extra careful to not make parents feel like that.

Dr. Johnson: One of the reasons I ask the question is because it does appear in the What Do We Need section, this idea that individuals are getting the diagnosis when they're adults.

And I think it's now also in Chapter 6, correct?

Ms. Shurin: I suggest, based on what Deborah just said and Jennifer, that we

delete that suggestion, the many people, because it talks about missing critical opportunities. That's just got guilt written all over it to me.

Dr. Hann: Can we have a motion to not accept essentially the changes on lines 14 and 15?

I see those in favor of not accepting that. Those opposed. Abstentions. Okay. It's gone.

Jennifer, you had also mentioned earlier about the possibility of the sentences beginning on line 6 through 9 before the purple, whether or not those were something that you wanted to consider deleting.

Dr. Johnson: Right. And again I think that was because it, to me, falls in the What Do We Need section.

To me when I read it, and I think again based on the Panel discussions, it just seemed to kind of throw things off. It could be just a matter of preferences.

Dr. Hann: Discussion? I'm seeing a few heads nodding as to deleting of those sentences.

Alison.

Ms. Singer: I think it's fine. I mean I think it is what we know. We know that it is usually primary caregivers who are first to see the signs, that some children have issues from early on, and some children appear to regress. I don't know why --

Dr. Johnson: How would we be defining caregiver?

Dr. Trevathan: It's a broad --

Ms. Singer: I think it's broad enough to capture the people who first identify the early warning signs of ASD. What would you start with then?

You would just start right with diagnosis can reliably be made by age three, without describing the --

Dr. Johnson: What I'm thinking of is the cases where a child might be in an

early care and education setting in the care of somebody other than their -- the primary caregiver, to me, would be the child's parents. So, they may be in somebody else's care, and oftentimes those are the people who are identifying the early signs. And they may try to work with the parent who may not be ready to hear that their child has delays.

So, that's what I'm thinking about because they are an important source, too, of picking up on things that might be going on with young children.

Ms. Singer: Add in primary caregiver or early education providers.

Dr. Hann: Or take out the word primary. Just say a child's caregivers.

Ms. Blackwell: What is we said a child's family members or caregivers?

Ms. Singer: I think the idea there, again, was to imply, not the pediatrician. So, however we can state that, I mean no offense, but that's what it is.

The idea there was to say it's not usually the case that you go to the doctor and they're the first to tell you something is wrong.

Dr. Trevathan: I think you can get at it by just taking out the primary. That was the intent initially.

And whether it's grandparents, aunt, uncle, early education, Sunday School teacher, you know, there's somebody else, very often, that's the first to raise the red flag.

So, I think we're all aware of that, yes.

Dr. Johnson: The one caveat to that is in our panel we did discuss the idea that there are situations where nobody does notice, doesn't pick up on the early signs.

So, it almost seems contradictory to put that in there as an introduction to this sentence when we know that in some cases, nobody is noticing and the child is just going missed.

So, that was another reason why I was thinking maybe it would be --

Ms. Redwood: But isn't that addressed later?

Dr. Johnson: I'm just saying it's contradictory, that's all.

Dr. Hann: Parents are often the first, so I don't think we have to include every scenario here, just the typical one that it's not the pediatrician.

(Laughter.)

Mr. Grossman: Would it be more accurate to list what the average is for diagnosis, because the average is still four-plus years if you're white, and it's six-plus years if you're a minority. I think that says much more about the early identification.

Dr. Johnson: I think that may be in the What We Need section. But we'll look at that, I think, to --

Dr. Hann: So going back to these first two sentences, are there any changes

that the Committee is comfortable in making?

Dr. Johnson: I'm comfortable with taking out primary in front of caregivers.

Dr. Hann: Okay. Those in favor of removing primary. Okay. Those opposed. Any abstentions?

Okay. We are removing the word primary. We're moving on.

Dr. Johnson: Okay. So, moving on to line 15, again what our panel was getting at is this idea that there are co-occurring conditions.

I think, based on our discussion, that we would actually not agree to the part that's been added in terms of the co-occurring conditions emerging over time, however I think we should refine the sentence to reflect what's in the third bullet that these co-occurring conditions may make it difficult to make the early diagnosis.

Ms. Redwood: Which bullet are you referring to? I'm confused.

Dr. Johnson: The third bullet that's now going to read how -- I'm sorry. Page 1, line 15 that reads, some children at risk may also begin to experience co-occurring medical symptoms or co-occurring conditions that may emerge over time in children with ASD.

What I'm suggesting is that we do not accept what's in blue there that's being a suggested addition to that sentence, because what we agreed to is that we're just focusing on that initial diagnosis and we're not concerned about what happens after a child receives the diagnosis.

Dr. Hann: You're suggesting essentially the phrase, suggesting that assessments may need to be conducted more regularly, be stricken?

Dr. Johnson: No. I'm suggesting that we keep in the sentence, some children at risk may also begin to experience co-occurring medical symptoms. And I'm suggesting that we

add a phrase so that it reads, some children at risk may also begin to experience co-occurring medical symptoms that create challenges to early diagnosis.

Ms. Singer: I don't know that it's the co-occurring medical conditions that create the challenges in diagnosis. It's the heterogeneity of the children that creates the challenges.

I think this change is fine. I think it makes sense. There's a typo. It should be over, space, time. But other than that I think it's fine as is with the change.

Dr. Johnson: Our panel didn't agree, but that's okay.

Dr. Hann: Those in favor of --

Dr. Guttmacher: My question is the more regularly. More regularly than what? Should we just --

Ms. Singer: We'll take out more regularly.

Dr. Hann: So, they need to be

conducted regularly?

Dr. Guttmacher: Yes.

Dr. Hann: Okay. So, what I'm hearing is to accept this change, but to strike the end of it or where it says -- to strike the word more.

Okay. Those in favor. Opposed. Okay. Thank you very much.

Jennifer?

Dr. Johnson: Okay. So, the next addition would be on page 1, line 21. The addition of the sentence, and this is what you brought up earlier, Lyn, about there being language in there about the children losing explicit symptoms.

And as I said in our panel, the whole notion of losing explicit symptoms was one that not everyone agreed to. And we did come up with language that everybody could agree to, to describe this idea of losing the symptoms of ASD.

Dr. Houle: Does that have a

citation to go with it?

Ms. Shurin: If there's no peer-reviewed evidence there, then it's not evidence. It's just case reports or suggestions or opinions or a single parent report.

But if we've got documentation just in the sentence before of an example, then it seems like if we add this, we need to have a peer review document there.

Ms. Redwood: There is one that went out just this past year, and I'm trying to remember the name of the author.

Wasn't it presented at IMFAR. Who was on one of the panels?

Dr. Johnson: Oh, Robin Hanson?

Ms. Redwood: Yes. Didn't Robin just talk about a recovery -- maybe Deborah Fine.

Dr. Johnson: Yes, Deborah Fine was on our panel. And so, she's the one who talked from the research perspective about

that.

She initially was using the terminology, lose. But as we discussed it more, she was suggesting some other language to talk about this idea, but not describe it again using the terms, lose.

Ms. Redwood: But there is research on children that recover.

Dr. Houle: I would recommend that the citation be added. We're talking about what we know, and we're talking about a research plan, a research document.

I mean, just even for the, you know, we've got the same citation, the Landa one from 2007, with the baby sibs project, but in line 13 it says most children with ASD exhibit signs of abnormal development well before the age of two.

Ms. Redwood: Alison is saying that's in our summary of advances.

Also the National Children's Health Survey just came out where they found -

- they asked the question about how many children have been diagnosed with autism and how many still have the diagnosis. And it was like 33 percent that no longer have the diagnosis.

Dr. Trevathan: Let me --

Ms. Singer: That was the HRSA data.

Ms. Redwood: Yes.

Dr. Trevathan: I was involved with that study. That was HRSA and CDC together. That's really not a reference for use for this point.

You can't distinguish -- it is a telephone survey and it's obviously got some limits, there are some advantages, but you can't distinguish in that in those data between someone who, a nurse or pediatrician said, you know, I think you might have autism. And then they go to a specialist, and the specialist says, no, your child doesn't meet diagnostic criteria.

So, you can't -- those people that have that happen to them are also subsumed under that 30 percent, so you can't -- we really -- we don't have data from that study to say that children lose symptoms of autism. You can just say whether someone ever told you your child had or might have autism.

So, I think Dr. Fine's reference would be better for this purpose.

Dr. Hann: In looking at the November version, there is a sentence that I think the Panel felt captured that. If I could, it's on page 3 of the November version at the top.

Some children may no longer exhibit characteristics of ASD that meet diagnostic criteria, whereas in others it may worsen.

And so if we wanted to adopt something like this where, finally evidence is emerging that some children may no longer exhibit characteristics, et cetera, et cetera,

and then we can also look for the citation.

Okay. I'm seeing heads nod. Does that sound agreeable to the Committee? Does anybody disagree? Okay. We're going to do that.

Dr. Johnson: Okay. And if we could stay with the November document for just one minute and do a little cross-walk between the November and October documents. In the November document on page 3 starting on line 9, the sentence that starts, recent studies of children at high risk because of a presence of a sibling with ASD. So, that was an addition that was recommended by our panel.

And the original sentence read because of family history of ASD. So, the recommendation was just to be a little bit more specific about why a child might be at high risk.

And those are the studies that tell us that autism can be detected by 12 months of age.

Dr. Hann: So, on the October version that would be line 18?

Dr. Johnson: On page 1, yes.

Dr. Hann: On page 1. Recent studies of children at high risk because of the presence of a sibling with ASD --

Dr. Johnson: Right.

Dr. Hann: -- suggest that, then it would continue as it currently appears.

Dr. Johnson: Yes.

Dr. Hann: Okay. I'm seeing heads nod for that change to swap out family history to be a little bit more precise.

Anyone disagree? Thank you.

Dr. Johnson: I believe it was intended to be an older sibling, yes.

Dr. Hann: Okay. Go ahead, Jennifer.

Dr. Johnson: We're now onto page 2 of the October document. And I just want to -- I think the only changes that were suggested here on line 2, instead of saying, different

levels of clinical severity, it would read different levels of clinical variability?

Ms. Singer: Variability is redundant.

Dr. Johnson: Yes. Okay. And then continuing on, a video glossary of early red flags would read a video glossary of early indicators.

Dr. Hann: Or signs.

Dr. Johnson: Yes.

Dr. Hirtz: I actually know of another glossary like that. It's not the only one. So, maybe we should just say there are -- there exist some -- it's not just -- there's a whole program to show examples to parents.

I'm not sure I would call it a glossary.

Dr. Hann: But this has reference that's hanging off of it.

Dr. Hirtz: Right, but this is -- what I mean is this is not the only one. There are tools available for a parent. I

just wonder if we could make it more general.

Dr. Hann: Okay, Alison, would you say your suggestion again, please? Do you have the microphone on?

Ms. Singer: I'm sorry. So, on line 2 we would change it to, there are tools available for parents and caregivers, comma, including a video glossary of early red flags.

And then continue on the sentence with the citation from --

Dr. Hann: Do we want to say early red flags or signs to tie back to your statements at the beginning?

Ms. Singer: I mean you can say --

Dr. Hirtz: They are red flags. That's what they are.

Ms. Singer: In that particular glossary she uses the term, red flags. She says typical behavior and red flag behavior. She didn't want to say atypical behavior.

Dr. Hann: I was hearing lack of enthusiasm for changing it other than the part

that Alison just said.

So, that sentence would be changed to there are tools available for parents and caregivers, including a video glossary of early red flags.

Ms. Redwood: I like Susan's suggestion of putting quotes around red flags.

Dr. Hann: Is that all right? Anyone opposed? Okay. Go, Jennifer.

Dr. Johnson: Okay. So, now that takes us into the What Do We Need section. And what you see there, I think we would -- the Panel agreed that those were appropriate changes to this section.

Ms. Shurin: Could I make a comment about line 10? I don't like the verb and I can't come up with a better one, but it almost implies that the kids are at fault for not accessing -- they're not accessing assessment services.

First of all, the kids don't access it. The parents get it for them. But

also it's either that they don't have access for it or they don't have a means to get to them.

I don't know. It just doesn't seem quite right.

Ms. Singer: So, the suggestion is to change, not accessing assessment services to, not benefitting from assessment services.

Dr. Johnson: Well, I guess let me clarify here. I think the point that's at issue here is what Lee brought up earlier. And that is what we're seeing is children who come from different ethnic and racial populations are typically getting diagnosed at a later age.

I don't have a reference for that. I don't know the research on that. So, I don't know specifically how that should be stated, but that's the general notion that's trying to be addressed there.

Ms. Blackwell: What if we said they may have difficulty accessing

assessments?

Dr. Hann: Okay. So moreover, many children culturally, linguistically and other diverse groups may have difficulties accessing --

Dr. Johnson: I just was concerned about stating something where --

Ms. Singer: Well, David Mandell has a citation. We can find David Mandell's paper where he looked at age of diagnosis in inner cities versus in suburban populations.

Mr. Grossman: And --

Dr. Johnson: I don't think it's that the services aren't there, I think it's that they have difficulty accessing those services.

Dr. Hann: Okay. We'll find then a citation for that, but can I please get the correct wording that you would like?

Dr. Johnson: Well, I think if we can get a citation, it would, be many children from culturally, linguistically and other

diverse groups are more often identified at a later age? Diagnosed with ASD at a later age.

Ms. Singer: Because of lack of access to assessment services.

Dr. DeGraw: How about moreover, many children from culturally, linguistic and other diverse groups may have limited access to assessment services leading to delays in diagnosis.

Dr. Johnson: Okay. Moving on to line 14, this is what I brought up earlier where we're now contradicting what was in the What Do We Know section. Because the discussion on the Panel is that if somebody does recognize that there are some delays, they may just tell the parents just wait and see what happens, we'll see if things improve in the next year, thinking that children may if they're showing delays, those may change over time.

So, that's why -- and actually based on the conversation, that sentence would

change. And let me find it in the November document. I think it's going to be on page 1 in the November document.

Starting on line 13, pediatricians and other early childhood professionals often recommend, in quotations, a wait-and-see approach for children who are slow to gesture or talk thinking they will catch up in the second year and therefore, delaying access to assessment services.

Dr. Trevathan: I think the November document is better for that sentence in part, because depending upon what universe of children you're discussing who are slow to walk or talk, the statement in the October may or may not be accurate.

So, I think as soon as you say, most, people will interpret that as being greater than 50 percent. That may or may not be true depending on what you're actually looking at, so I think you're better off with the later version.

Dr. Hirtz: I might add second or third year. For walking, it would be the second year. But for talking, many pediatricians don't get alarmed until three.

Dr. Guttmacher: the implication there, of course, it seems to me, is the pediatricians are wrong to do this. Delaying seems to me -- I mean it's a statement of fact, but it's also a weighted statement of fact and I'm not sure that there really are data to say that pediatricians as a whole are really wrong to -- there would be lots of needless assessments, et cetera, et cetera, if every child who was, et cetera, et cetera.

Dr. Hirtz: Well, you're right in the sense that if a child walks at 14 months and not at 12 months, there is generally no cause for alarm given other things are normal.

So, it does depend on the whole picture and when exactly the child is being evaluated and how much exactly is not going on particularly with language.

So, maybe we need to soften that a little bit.

Dr. Guttmacher: Yes, I would.

Ms. Shurin: Well, Ellen's point too is it's not all pediatricians. And I certainly think that even speech language pathologists, for example, some might and some might not.

So, I think we could say many or there's some pediatricians that do the wait-and-see, and others send them right on for diagnosis. So, I don't think we should lump them all.

Ms. Blackwell: And I think maybe we should add a period after second or third year, period.

Dr. Trevathan: I hate to bring this up after we've worked so hard on this sentence, but is this sentence necessary?

I mean it seems like no matter how we tweak this sentence, we look at it and we say, you know, that's not exactly true, may

not be right.

It's also possible that there's no way we can make this sentence completely accurate in this setting, and these are impressions that we all have based on our own experience and anecdotes.

I'm not sure we have practice guidelines, which Deborah certainly has worked on more than I have, or other documents that say that this is an actual -- can we just take this sentence out and --

Dr. Hirtz: I agree with Ed. And I think as I read it, it seems like the point that's being made is we need additional tools because right now it is so difficult to interpret delays in language or walking or so on.

It's not the point to sort of point the blame that they need to immediately get referred to services, the point is we need more than just these signs that we have right now, biomarkers or other ways.

Dr. Johnson: I agree with what everyone is saying. I'm just going to point out two things. One of which is this was a discussion in the Panel, and they felt pretty strongly that pediatricians and other early childhood professionals are not listening to them and taking them seriously if they come to them and say, you know, I have these concerns.

So, that's why it's in there, but it was also originally in the Strategic Plan in a different -- the sentence read pediatricians recognize that most children who are slow to walk or talk will catch up in the second year.

But I agree with you. I think it's somewhat of a pejorative statement that is making some assumptions about what's occurring.

Dr. Hann: All right. So, I've heard that we can tweak the sentence to include the idea of some and potentially adding the third year also, and then dropping

the last phrase which is, therefore, delaying access to assessment and services.

So, we have one version as a tweak, the other version -- the other suggestion on the table is to drop the sentence altogether.

So, may I see a show of hands of those who wish to have the sentence tweaked?

Therefore, do I see a show of hands of those who wish to have it dropped?

Thank you very much. It's unanimous. Goodbye to that sentence.

Dr. Johnson: If we could stay with the November document, this is the issue we brought up earlier about the biomarkers. It's on page 1, line 18.

The sentence that was recommended is the discovery or reliable biomarkers could potentially identify people with ASD or infants who will subsequently develop or are already -- Lee can read it. I'll let you do the reading.

Dr. DeGraw: Wouldn't that be more of a what we need to know?

Dr. Hann: So, just to help clarify, she's taking elements out of the November document from page 1, and transplanting it over to the October document which is on page 2 in the What Do We Need section.

Ms. Singer: How is that different than what's in the October -- oh, it just says the discovery of reliable instead of just biomarkers?

Dr. Johnson: And I guess it could potentially --

Dr. Hirtz: I would take out the second half of that so that providers can initiate --

Dr. Hann: Deb, your microphone, please.

Dr. Hirtz: I would suggest we take out the second half of that so that providers can initiate intensive early intervention

strategies to address or possibly preempt developmental delay.

First of all it's not necessarily developmental delay. It might be, but it might be autistic symptoms.

Secondly, I'm not sure it adds anything at all. We've already -- we're talking about -- we talk elsewhere about early intervention, and here we're talking about making a diagnosis.

Ms. Blackwell: I'll second that.

Dr. Hann: Okay. So, what I hear is essentially to -- if you look at the October version, line 18, there's a sentence that begins with word biomarkers. Instead, it would now begin with the discovery of reliable biomarkers could potentially identify people with ASD or infants who will subsequently develop or are already developing subtle signs of ASD, period.

Ms. Blackwell: Yes.

Dr. Hann: I see head nods.

Everyone in agreement? Oh, come on. You can do it. Thanks. Anybody disagree? Okay.

Dr. Johnson: Okay. Now, I'm going to take you back to the October document. We're done with the November document. To look at the recommended edits that start on page 3, line 1, 2, 3, 4 and 5.

I don't know if you want to take those one sentence at a time or just, you know.

Dr. Hirtz: Well, I just want to comment that I'm really glad that we -- it wasn't in the November version, but in the October version is where to refer for services, because I think that's a key obstacle to pediatricians making a diagnosis. So, it's good to have that in.

Ms. Singer: Parents don't refer for services.

Dr. Hirtz: Okay. You're right. It should be --

Ms. Singer: Parent access

services. Or it should say pediatricians and caregivers.

Dr. Hirtz: Yes, you're right. It should be changed a little bit.

Ms. Singer: To access. Where to access services.

Dr. Hirtz: Yes.

Dr. Johnson: So, to keep it as parents and caregivers, but where to access services?

Dr. Hirtz: Yes.

Ms. Blackwell: I'm also wondering if in line 1 and 2, because we have early intervention, it should say early intervention providers.

Dr. Hann: So, take out care and education and have intervention?

Ms. Singer: By the time you go to early intervention, you're diagnosed. So, I think this is referring to early care in preschool prior to diagnosis. They're the ones who might not have received training in

recognizing the early warning signs.

Ms. Shurin: In the original version, we call them health care and other service providers may not have received training.

Dr. Hann: So, to say health care and other early service providers?

Dr. Johnson: I mean it's not a service. Early care and education is a generally accepted term to cover the wide array of situations the child may be in at an early age if they're not cared for by the parent.

One thing in line 4 just to make this consistent with the What Do We Know section, the sentence that starts, fifth, parents and caregivers may be unaware of the early warning signs. So again, that's where that we have that inconsistency.

So, I think we just need to revise that to make sure that's consistent with what we said in the What Do We Know section.

So fifth, I would suggest that it's just caregivers. I think that's what we agreed to, correct? Yes. Some caregivers may be unaware.

Good to go?

Dr. Hann: I think so. So, here's how I'm hearing it. It will be fourth, health and other early care and education providers may not have received training in recognizing the early warning signs of ASD and pediatricians may not have received training on using existing screening tools at well check-ups as recommended by the American Academy of Pediatrics. Fifth, some caregivers may be unaware of the early warning signs of ASD and where to access services, leading to delays in diagnosis.

You want the word warning out of that sentence?

Dr. Johnson: Yes.

Dr. Hann: So, just early signs?

Dr. Johnson: Yes.

Dr. Hann: Okay. Does anyone disagree with that change? Okay.

Dr. Johnson: Moving quickly on page 3, October document, line 20, the aspirational goal -- actually, no. I'm sorry. I need to take you back into the November document.

So in the November document page 5, line 1, the aspirational goal. So, that is where the Panel ended up.

Given our conversation, I would suggest that the second sentence be removed and that we just have children at risk for ASD will be identified through reliable methods before ASD behavioral characteristics fully manifest.

Dr. Hann: Does anyone disagree with that change?

Dr. Johnson: We got it. I'm just trying to do my own cross-walk here.

If we can stay with the November document for the research opportunities, first

bullet on line 7, the issue that came up at the October 23 meeting was the use of the term, broad-band developmental screening instruments. So, we changed that to say, including general developmental screening instruments. And then the rest reads the same as what you saw on October 23.

Dr. Hann: Okay. Let's move on. We'll do this en bloc then.

Dr. Johnson: Second bullet, it reads the same as it did on October 23, that addition.

On the third bullet, the word symptoms was changed to characteristics in that recommendation in how we use the terminology.

Again on the next bullet, the detailed criteria for specific ASD sub-types, just changes in terminology based on the recommendation that we don't use symptoms and severity.

Dr. Hann: Here it's a little

awkward because we have variations and variability.

Dr. Johnson: Yes. On the next one, the ASD subpopulations, the addition there of appropriate early intervention. I mentioned that earlier as a change that was recommended.

Ms. Singer: In line 1, so that we don't say variations in variability, can we make that variations in characteristics and severity?

Dr. Johnson: One line 10, page 6 of the November document, the change there was just a minor change with the inclusion of bioethical and other ethical considerations.

Dr. Trevathan: Why don't you just say ethical?

Dr. Johnson: Okay. I don't quite honestly remember where --

Dr. Hann: Also going back up, and I don't mean to belabor this at all, but on line 5, it implies that there are

inappropriate early interventions.

Is that what we wish to communicate?

Dr. Johnson: That's what --

Dr. Hann: Is that what you all wish to communicate?

Dr. Johnson: And on line 12, page 6 of the November document, one of the things that the Panel talked about is the need for training programs and the use of screening and diagnostic tools. So, that's why it was added in there.

Dr. Hann: Our committee is leaving us. I'm trying to see. We've got ten. So, I think what we're going to have to do is move this to the next meeting to finish Chapter 1.

In terms of Chapter 7, all of you have had a chance to look at what -- I know we very much thank Alison and Cathy Rice for putting together that. There have been numbers of bullets along the way that people suggested moving to Chapter 7.

I think OARC can try to take a crack at moving that into that section so that when we meet again in December, we can discuss it.

Are people feeling comfortable with having a Chapter 7? Anybody disagree? Okay.

Ms. Blackwell: Would it be helpful if people sent comments to Alison and Cathy Rice in addition to the short discussions we have had today.

Dr. Hann: Why don't you send them to OARC? We'll give them a little break.

Ms. Blackwell: Okay.

Dr. Hann: Since they very kindly put it together and provided wonderful prose already for it.

So if you do have some comments, please send them. We'll do our best to do incorporations or do our lovely comments on the side as we've been known now to do to bring it to your attention.

The next meeting will be at some point on the 11th. I've heard strong sentiment to be able to do that vis-a-vis a teleconference to help cut down on travel for people, which we can do.

We can also have a gathering here, do it sort of like both ways if people want to have like a gathering here, and then have the other people on the phone or whatever kind of stuff.

We are adjourned. Thank you all very much.

(Whereupon, at 4:59 p.m. the above-entitled matter was concluded.)