U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

FULL COMMITTEE MEETING

FRIDAY, DECEMBER 12, 2008

The meeting came to order at 9:00 a.m. in Conference Room A of 6001 Executive Boulevard, Rockville, Maryland. 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

DUANE F. ALEXANDER, M.D., National Institute of Child Health and Human Development

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

JUDITH COOPER, Ph.D., National Institute of Deafness and Other Communication Disorders (For James Battey M.D., Ph.D.)

LEE GROSSMAN, Autism Society of America

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

STORY C. LANDIS, Ph.D., National Institute of Neurological Disorders and Stroke

WALTER KOROSHETZ, M.D., National Institute of Neurological Disorders and Stroke (For Dr. Story Landis)

CINDY LAWLER, Ph.D., National Institute of Environmental Health Sciences

PRESENT (continued):

CHRISTINE M. McKEE, J.D.

PATRICIA A. MORRISSEY, Ph.D., Administration for Children and Families

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

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

STEPHEN M. SHORE, Ed.D., Autism Spectrum Consulting and Adelphi University

EDWIN TREVATHAN, M.D., M.P.H., Centers for Disease Control and Prevention

PETER VAN DYCK, M.D., M.P.H., Health Resources and Services Administration

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P R O C E E D I N G S

(8:59 a.m.)

WELCOME AND INTRODUCTIONS

DR. INSEL: Good morning, and welcome to the fourth meeting of the Interagency Autism Coordinating Committee.

We have this special meeting to try to complete the draft 1.0 of the strategic plan so we can get this ready quickly for sharing with the new administration as they come into Health and Human Services.

Let's start with a quick round of introductions, because some people will be joining us by phone. I want to make sure we all know who is here.

We'll start here. This is Tom Insel, who serves as chair.

DR. LANDIS: Story Landis, director, NINDS.

MR. GROSSMAN: Lee Grossman, president and CEO of the Autism Society of America, and the dad of a young man with

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autism.

MR. SHORE: Stephen Shore, my own autistic adult. And professor of education at Delphi University.

MS. REDWOOD: Lyn Redwood, Safe Minds.

DR. VAN DYCK: Morning, Peter Van Dyck, director, maternal and child health bureau at HRSA.

DR. COOPER: Judith Cooper, deputy director, NIDCD.

MS. SINGER: Alison Singer, Autism Speaks, and the mother of a beautiful 11-year-old daughter with autism, and legal guardian of my 44-year-old brother with autism.

MS. BLACKWELL: Ellen Blackwell, Centers for Medicare and Medicaid Services. I'm also the parent of a 21-year-old young man, Robert, with autism.

MS. HANN: Della Hann. I serve as the acting director for the Office of Autism Research Coordination here at NIMH, and today

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I'm acting as executive secretary for the committee.

DR. INSEL: And who is joining us by phone?

DR. MORRISSEY: This is Pat Morrissey, Tom. I'm the commissioner of Administration on Developmental Disabilities until January 2nd.

DR. INSEL: Anyone else on the phone from the committee?

(No response)

DR. INSEL: So we've been told that Duane and Christine will be here but late, and Ed should be here very soon.

So we've got a few other people who will hopefully be arriving very soon.

Let me just give you some quick updates about things before we get started. First of all this is the follow on to the meeting we had on November 21st, and we realized that we weren't going to make it all the way through in the 2-1/2 hours we had

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allotted for the strategic plan. So not surprisingly we made it through the first part of Chapter 3. We have quite a bit more to do today, and we'll take the entire day to get this completed.

Just to review from that meeting, we had 123 attendees at the Reagan Building for that meeting. There were 92 people who logged in Webinar, and 219 who joined us by phone. So large amount of interest, and I can't tell you how many of those people stayed through the whole meeting, but we know at least that many joined us at some part of the time.

Today as well we'll have people joining us by Webinar and by phone. We should be able to make sure that whatever we discuss here is as clear as possible to as many people who can join us if not in vivo at least by technology.

EDITING OF STRATEGY DOCUMENT

DR. INSEL: In your folders that

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you have in front of you, you have several things that I want to make sure you have a chance to look at. First, you will see this version of the first page of the introduction which included the language that people asked for last time about the complexity of autism symptoms, the idea that there are systemic manifestations of this syndrome, and we were trying to capture that in one place so we wouldn't have to complete each of the varieties of that all the way through the plan.

So we'll want to get back to that later in the day, but I want to make sure you look at it so you have it with you.

In addition you've got the comments from the plan that really now begin with the part we have to do today; that is the sheet here that contains the largest part of it, and these would be including comments from several members of the committee who wrote in.

There is also the comments on the

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introduction which we didn't get to in the first meeting. Then of course you have got your agenda. There is a letter from Lyn Redwood that reviews issues around the strategic plan and vaccine research. This was sent to you ahead of time, but if you haven't had a chance to look at it we have a copy here.

There is also a letter that came in very late last night signed by Autism Society of America, Autism Speaks, National Autism Association, Safe Minds, talk about curing autism, and unlocking autism, that also refers, and many of these had signed on to a letter from November 19th I believe, before the previous - I'm sorry, November 12th. So we have both of those letters which are fairly consistent with concerns about the plan and issues I think certainly need to be addressed in the plan.

There is also a note from Paula Durbin-Westby who spoke to us at the last

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meeting with her comments for consideration. And you will see there are a series of other supplemental notes which I'm not going to go through. But I would suggest that you look at each of these if you haven't seen them already. So if you have a chance to catch up with a lot of the things that have been coming in to the Autism Office of Research Coordination in reference to the plan. Clearly a lot of interest from the community that people want to make sure that we get this right.

And in reference to that let me just remind you of where we started last time, which was some discussion about what this is really all about, and that is, to come up with a document that we can provide as an advisory document to the secretary, to the Congress, and to the director of NIH, recognizing that there will be a new secretary and a new director of NIH and many of the members of Congress will be new as well. But that is why

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we feel this is particularly timely.

This may not be the perfect document that pleases everybody, but it does need to be a document that reflects the range of views, and gives the community including the secretary, the director of NIH and the Congress a sense of where the priorities are for research and what the needs are.

Before we get started, are there any other comments or issues that we want to begin to take on?

(No response)

DR. INSEL: Okay, I would recommend we do it much the way we did it last time, which is, we will get into the document, and I know this is tedious, but it essential that we get the document reading the way we want to. So this is essentially editing by committee.

And where we left off last time was on Chapter 3, and it will be up to page 4. We had a - I think we stopped at line 15,

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where we had a long discussion.

Lyn, I know you had written in saying you wanted to revisit the part that we had just completed, up to line 15.

What's the wish of the committee? Do you want to go back, or shall we move on and then take on that issue at the end of the day, that and any other issues that have come up with what we have already completed? People want to move forward, or do we want to start by backtracking on things we finished last time? Can I get a sense of the committee? Move forward?

Why don't we quickly just get a show of hands. That's not to say that we can't revisit things that we talked about last time. But we have so much to do today, I really need to get a sense of you about whether you want to start in the part we haven't been, or if we want to revisit where we've been.

So those of you who want to move

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forward from Chapter 3 on?

(Show of hands)

DR. INSEL: And those who want to go back and start over from places that we have already covered? Can I see a show of hands?

(Show of hands)

DR. INSEL: Okay, and Pat, you are on the phone. We need your vote?

DR. MORRISSEY: I agree with those who want to go forward.

DR. INSEL: Is there anybody else on the phone at this point?

(No response)

DR. INSEL: Okay, so we will -

MS. HANN: So it was six to four.

DR. INSEL: Six to four to move onwards. And again the hope would be that at the end of the day we can revisit any places that people think need to be looked at, so we get this to be reading the way everybody wants it to.

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But let's start to plow into the areas we haven't covered, and that takes us to page 4, line 15.

MS. HANN: We have Lyn's suggestions, beginning at line 15.

DR. INSEL: Okay. So let's start there. Everybody looking at the old version and potential new one. So we have three things. I want to make sure people are clear on what we've got in front of us.

Left-hand column - so Stephen, you weren't here last time, so it's worth going through this. Left-hand column was the original and what we'll call the default mode. So that is what we put out for public comment. Right-hand column are those comments that came in from the RFI, from the 140 or so comments, integrated into this document, and they are footnoted so you can go back to the comments in the RFI.

And then we have this additional list of comments that came from several

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members of the committee who wanted to make changes in both versions.

So what we are doing is looking at all of that at the same time, and deciding whether we want to stay with the original default mode; do we want to put in the changes that came from public comment; or do we want to include the comments that came from your colleagues on the committee. Okay?

And the first one up is on page 4, line 15, where Lyn has a comment about - well, do you want to go ahead and read it, Lyn, rather than my reading it.

MS. REDWOOD: Dr. Insel, having worked on the Combating Autism Act, there are several attachments to the bill. And the colloquy in the report where Congress was specifically requesting that the Combating Autism Act look into vaccine and vaccine preservatives. And that's why it was important for that to be included in the strategic plan since it wasn't being

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specifically addressed by Congress. And that's why I added in that additional line. It seemed like it was a good place for that to fit.

You can change wish to desire, but that was the reason for that proposed edit.

DR. LANDIS: So I was struggling with some of this this morning, and in thinking about it I recognize that there are huge tensions between going back and looking at factors that may have contributed or may not have contributed like thimerosol in vaccines. But if this is a research plan to go forward in your materials you pointed out that the only vaccine now which I think - I think you said this - currently contains thimerosol is actually flu vaccines. So the question is, if in fact vaccines, almost all vaccines don't contain thimerosol, to what extent is it worth it, is it appropriate for a forward looking research plan to focus on the past?

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MS. REDWOOD: I guess I could answer that that the flu vaccine does continue to contain thimerosol. Ninety percent of the product today contains 25 micrograms per dose. It's now being recommended for pregnant women during pregnancy, and also infants starting at six months of age with two doses.

The other thing I don't mean to imply is that thimerosol is the only concern with vaccines. There is also aluminum. There are many other antigens. We don't have any safety data on administering vaccines during pregnancy to pregnant women for a category C drug.

We also have the recent report that came out on mitochondrial disorders in children with autism. The authors of that report conclude that there may not be any difference between the stimulation of multiple vaccines to the immune system and the actual vaccines that they are there to prevent.

DR. LANDIS: I am not arguing

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about the vaccine piece. What I am concerned about is the emphasis on thimerosol and - so -

MS. REDWOOD: This is just saying vaccines, including mercury. I guess - I mean I think it's a wonderful thing that the amount was reduced. But for the children that were exposed, like my son to 125 times the EPA-allowable exposure, are you saying we are not going to go back and look to see whether or not there might have been harm that occurred?

DR. LANDIS: Well, so if we are trying to look forward to how we are going to understand multiple causes, for children looking forward, and if we are going to think about how we are going to develop better treatments, assigning blame in a retrospective fashion may not be the most effective use of the research monies that are available.

This is a philosophical issue. And I just wanted to bring that up.

DR. INSEL: One of the things that

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came out in the previous meeting - Ed has just arrived; he can bring us up to date on this - there is so much concern about this question of vaccine safety, and it's a concern that is not only around autism, and it's not only in this committee. But my understanding is that the department has taken this on as a fairly high priority issue.

But I thought you said something in the previous meeting about this being the focus of another workgroup or another project. And maybe it would be useful to understand if this isn't going to be in the plan, because it's not really specified in the default mode, who would be focusing on it.

DR. TREVATHAN: Well, there are a couple of - I'm not sure exactly what statement you are referring to, Tom, but there are other committees. Immunization safety committee and various committees at CDC, and then across the agency, that deal with immunization safety that certainly have seen

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these concerns.

And I know that going forward there is an interest in enhancing and expanding some of the immunization safety research in general, and not just about this. So I think that what you said is true.

And I actually think that that forum is the appropriate forum to have these discussions. I mean I guess the concern that I have with bringing this up at this time is that we did not address this issue specifically in the workshops and the work groups. We didn't have immunization research experts that were participating. That wasn't really the focus of what we were doing when we were developing the plan.

So if the focus is, there is a decision there needs to be a big focus on immunization safety, that's a different group of people, that's a different committee, different types of experts, that we don't necessarily have around the table here.

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And I know that we sent some information to Della, I think, about the meetings that were going to take place with that and so forth, and I'm sure that could be provided. But those are separate committees and separate issues.

DR. INSEL: Are those committees going to delve into the relationship to autism? Or is it looking at other aspects of vaccine safety?

DR. TREVATHAN: I'm not on the committee so I can't tell you exactly what their agenda is. But certainly I think in large part to some of the advocates that are sitting at the table here, you all have been at those meetings. That has been brought up before, so I assume that it will be in the future. And there - there still are some studies that have not been published that are either being completed, or analysis is being completed, and writeups are being done.

So certainly the investigations

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that are being done by those groups with the question of autism, vaccines, that work has not been all completed, and I don't think that all of us have all of those data at this time.

I think that that is the appropriate forum to bring this up.

MR. GROSSMAN: A couple of things that I'm a little bit confused about here is how we are going to take the suggested verbiage and incorporate it into the document. So I'm a little bit confused on that.

But some of the things I will specifically address are this - in this section we are talking about environmental risk factors. And I think to not address, or leave vaccines as a work product for the strategic plan to have incorporated in it would be a big mistake.

It has been identified by the Congress, I believe the new secretary when we present him with the strategic plan will have this on his radar screen, and to not have it

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in there is just going to delay the function for the strategic plan.

I think we should be somehow addressing the fact that this is ongoing research and it needs to be looked at, because Congress has asked for it and they will continue to ask for it, and it certainly needs to be in there.

How we incorporate the verbiage I'm not quite sure, and I'm still confused on that. But I would strongly advocate that it is part of our strategic plan.

DR. INSEL: Stephen.

MR. SHORE: I want to echo what Lee says. It seems like there is an awful lot of controversy about vaccines. And I don't know myself, I'm not qualified to say yes or no. But it seems like if we could come up with a study or some studies that we can all agree on, let's just finally put it to bed, and not so much to blame people but to say, this is what it is, and now we know how to work with

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it, or in the other direction, it's not vaccines, it's something else, so let's leave them alone.

MS. REDWOOD: And Tom, I want to follow up to what Dr. Trevathan said. I do think it is the responsibility of this committee. We are developing a strategic plan for autism. I think what the immunization safety review committee looks at are somewhat different issues, and I think it's something that is important to be in this plan. I think it's wonderful that the other agencies are looking at this as well; that's great. But we need a lot of people looking at it. We need a lot of independent researchers looking at this as well. So I think it's important for this committee to consider, and not to put that responsibility off on another agency, especially an agency that is responsible for vaccine promotion.

DR. LAWLER: Hi, this is Cindy Lawler. I'm going to chime in now. I need

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some clarification as well, because I think it's different if we are talking about describing for the state of knowledge vis-a-vis vaccines and autism and for the introductory aspect of this section to address question #3, but if we are talking about adding specific objectives, then I am going to have to agree with Dr. Trevathan that we really don't have the right expertise around the table to even sort of consider what kinds of studies would really be most appropriate in this area. So that would require a different kind of effort.

So I agree that I think we need to acknowledge that there are some open questions, but I'm very uncomfortable with, as we move forward, adding a sort of specific aim or objective that focused on vaccine without having some additional discussions with experts that can really help us address how that research should go forward.

DR. INSEL: So Cindy, just to

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clarify, you would want to see this described some place in the introductory comments but not to include specific short term or long term objectives?

DR. LAWLER: At this time. And I think - I joined late, and I was on mute for awhile, I had the wrong password - but from the webinar it sounds like we are still discussing the introductory part of question #3, is that right, or we have gone back to that?

DR. INSEL: No, we're at question #3, page 4, line 15. But we are really digging into this now because it comes up over and over again the next five pages of the document. So I think we need to come to some clarity about where the committee wants to go on this issue. And then I'm hoping the rest of it will be more wordsmithing.

But there is a fundamental question in front of us about how the committee wants to deal with vaccines under

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this issue of where the needs are. What do we know and what do we need? And I can remember with you that when we looked at the public comments we heard a whole range of comments including many people who said the word "vaccine" should not be anywhere in this document, and others who said that this is the most important and highest priority aim for research.

So this is a very charged issue, obviously.

Alison.

MS. SINGER: I think when you look at, when you read Section 3 overall, a lot of it is really jumbled together, particularly the sections what we know and what we need.

I think if we just look ahead - I know we are supposed to go in order - but if we look ahead at Section 3.4, it really repeats the fact of diversity of viewpoints that we also talk about in Section 3.2, which I know we just voted not to go back to

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revisit. But I think it might be worth going back to revisit, because I think some of the items that are listed in what we need are really what we know, so specifically in item 3.4, there are really only two items in what we need that are what we need. It's the idea of we need standards for identifying and claiming that environmental factors contribute to autism spectrum disorder. We definitely do need those standards in my opinion.

And then further down it specifies that what we need is the large scale study comparing vaccinated to unvaccinated groups. The rest of this paragraph is really what we know, and that is that there is this diversity of views. And I think that that is really repetitive of some of the language in Section 3.2.

So I think we should - the reason I thought we should reopen 3.2 is because I think we want to make sure that this document is very clear. If we are going to have these

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categories, we should focus on what we know and what we need. And then really in the short term objectives, Sections 3.14 and 3.15 really hone in on some of those short term objectives.

And I have to say in terms of what we need, I would support the idea of doing the vaccinated and nonvaccinated as a retrospective study. I think one thing we hear from families all the time is that we need to be able to answer the question, do individuals with autism - is there a difference.

So I would be supportive of keeping that in. But I would like us to focus - you know one of the issues we had last time when we go line by line is, we don't end up with a cohesive document. I think if we re-read what we did in Sections 1 and 2 a lot of it is also not very well organized.

So I would say let's look at really focusing on what we know, in the what-

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we-know section, and what we need, and then make sure that those are reflected in the objectives.

So for example again the idea of developing standards which is written as what we need is not listed in any objective. And I think that is a big omission.

DR. INSEL: So if I can just reflect on what you've said, I agree that there was a bit of this last time as well. We tended to spend a lot more time on these introductory, what do we know, what do we need, sections, and maybe not enough time on what we are actually going to propose as initiatives. What the team tried to do in taking in all the public comments was to preserve most of what was there in the original draft, but to use language that would reflect the diversity of views. And that is what you see in 3.4.

I think the sense that the group had was that the document would suffer from

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overspecification; that if we tried to make this document become highly prescriptive, especially in the what do we know, what do we need section, it would either be wrong, or it would not be helpful; that there was a need to be more specific in some of the initiatives, but in these sections really the intent was to reflect the state of where things are, including the great number of disagreements.

And there my own personal opinion is you do better if you stay general, you stay above the fray, and you simply say, this is the range of views that people have about this. The language that you see in 3.4 was meant to reflect that.

And it may be if we are trying to find some common ground here that that would be an approach to not get into the weeds on what do we know, what do we need, and try to stay descriptive about where the state is, where people are working, where they are disagreeing. And then for us to focus much

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more on the initiatives. But let's see how people feel about that general approach.

Stephen, did you have a comment? No, okay.

MS. REDWOOD: I just wanted to very quickly for the last time go back to this vaccine issue. Because there is a document that just came out last night as you mentioned that was signed by the Autism Society of America, Autism Speaks, the National Autism Association, Safe Minds, talk about curing autism, and unlocking autism, which were the largest national autism organizations.

And Section B of this specifically calls for this document to include research into vaccines. And I think when we go out and we ask for requests for information, and 48 out of the 148 that we received specifically want vaccines to be included, and all of the largest national organizations want them to be included, I really think we are being very unresponsive to the community if we don't do

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that, and I don't think it'll go over very well. So I just want to make that final point.

DR. INSEL: I think that is just where we are at. And that's really the struggle. We've got many people who feel very strongly as you just described. We also had plenty of comments from people who said, specifically, don't go there. There is no science. There is nothing to defend it. There is a piece in Science magazine about this, claiming that the science doesn't support continued investment in vaccine research related to autism. It's a split in opinion, and often that happens in areas where there is a lot of passion.

The bottom line is that you don't want to make this decision by counting the number of voices. It's not an election, and our job as a committee is to be a committee of experts, and we have to use our judgment here. And so we are likely to be split as well; it

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sounds like we are so far.

What I was proposing was to use the document to reflect that split; not to come down on either side to say we should or shouldn't do it, but to simply reflect the diversity of opinion here, particularly if what we are talking about is a document that is trying to capture the state of the field.

I don't think we are going to get unanimity about either side of this except to say that some people will feel that this is an area where we need to be - to perhaps have more research. Some would say you wouldn't. And we certainly need more information for the public, either about what has been done already, or how to interpret what's been done.

Alison.

MS. SINGER: I agree with what you've said with regard to the diversity of views that's expressed in the RFI responses. But I think if you look carefully at the responses from individuals who said no more

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research needs to be done, it's targeted more at the NMR and thimerosol, and not really - what hasn't been done is the retrospective studies on vaccinated versus nonvaccinated, and whether there is a difference in prevalence among individuals who are vaccinated, nonvaccinated, or vaccinated on a different schedule.

So I would say that when we talk about what we need in terms of studies that have not been done, that is certainly one that has not been done.

DR. INSEL: So you would support the language that is on page 6, under 3.4, that says others contend that definitive research has not been done such as a large scale study comparing vaccinated to unvaccinated groups?

MS. SINGER: I support that. I mean I would go back to saying that the - all of the other lines that talk about the diversity of views expressed in the RFI belong

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in the column, what do we know, instead of what do we need, and really the two items that should stay here in what do we need are the need for standardization and the vaccinated-nonvaccinated study.

DR. LANDIS: So it's as if the vaccination issue is a lightning rod for all of the concerns about environmental factors. And I am wondering the extent to which additional references to environmental factors should be included.

I know there were many things discussed at the IOM meeting, not to say that the vaccinated versus unvaccinated is not a reasonable study, particularly if the focus is more broadly on vaccination, but also to think about whether or not there are other environmental factors that we should be thinking about. And the issue of standards is an important piece of that.

DR. INSEL: Well, let's think about how best to go forward. Because we could

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spend the rest of the day on where we are right now. And clearly we are not going to come to a unanimous decision.

What I think we will need to do is to go back to where we started here, which is Chapter 3, line 15, and make a decision about the three versions in front of us. We've got the original version which you have in the left-hand column. You've got these comments about, recent studies suggest factors such as paternal age, maternal age, infections including those preventable by vaccines, maternal vaccination during pregnancy, hormones and pesticides have gotten added in.

Then we have a version from Lyn which she read to us about Congress' wish for studies on vaccines.

And we need to know what you want to do as a committee.

Are there any other comments on this before we take this to a -

DR. LANDIS: I would just say that

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I think it's important to follow up on Alison's point about taking out of the what do we need bits that are actually relevant to what do we know, and focusing the issue of the differences of view on vaccination in the what do we know, and say, we just don't know. I don't know if you were including that as one of the changes.

DR. INSEL: I wasn't, but if that - is that a recommendation? Because that would be the fourth option here, which would be to take most of discussion point 3.4, and to put it into this part under 3.2, which talks more about what do we know.

DR. LANDIS: I look at it, picking up on Alison's point, important for the field to develop sound standards for identifying potential environmental factors and establishing their contributions to ASD, that blue on page 6, that is one thing of what do we need. There is some stuff beneath that that goes into the what-do-we-know piece.

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So I would pull that out, and maybe you need a subgroup working on a solution.

DR. INSEL: Well, I wish we could, but you know what, we knew we were going to hit this, and this is going to be the big speed bump for this process. And I think we are just going to have to deal with it as a committee to get any closure on it.

But this is a fourth option, which is to - essentially this would take out some of the language we have now. It would, as I understand it, replace what Lyn is suggesting in terms of page 4 of line 15, and we'd take this whole section about public comments under 3.4 and include it in page 4 after line 15; is that right?

DR. LANDIS: So it is what do we know, what don't we know, and where is the largest - where are the most controversial issues in that distinction. And then I think it sets it up for the what do we need, and

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what we need is standards and potentially that study, assuming that if you had a group of people who were really knowledgeable about vaccination they would say that study could be designed in a reasonable fashion.

DR. TREVATHAN: I think - again I would just emphasize, a lot of the comments that I hear, too, are from people - I hear a lot of anger, and I think - I'm saying this, because I think it supports what you are saying, Tom. Parents that are angry - and we've heard that today. And when I hear scientists and physicians and some other people that are angry that feel like we are wasting money on vaccine research when we could be pursuing other areas that they believe are more fruitful in a time of very limited resources.

I mean I think the polarization on the views around the table, and the views that some of hear that are not sitting at the table are pretty extreme. So I think it is wise to

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acknowledge that those views are there, and without getting into the weeds of what the details are, because we can't do that justice. And there have been books written on these disagreements.

I guess along the lines of retrospective comparing vaccinated and unvaccinated children, of course the problem there is the selection bias, as to who is vaccinated, who is not. And before you even do a study like that, I think people would have to be very careful about the study design. Again I don't think the people at the table are here for that.

There has been discussion - and I know Duane is not here; I don't know if there is anybody from NICHD - but the National Childrens Study of course will be prospective observational, in spite of 100,000 women there is a question of whether or not that sample size is actually adequate enough for that.

And then I think there are very

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strong feelings that are prospective randomized vaccinated-unvaccinated study would be highly unethical, would never pass.

So it is a very complicated question, and in terms of how that question could even be addressed. And I would suggest to address that particular issue in this document at this state, when that wasn't part of a work group question and we didn't have the experts there, I don't think we can do that justice. I think it's an interesting and it's a very complicated question.

DR. LANDIS: So do you say what we need -

DR. INSEL: I'm supposed to be identifying or you are supposed to be identifying who you are so people on the phone know.

DR. LANDIS: Story Landis. Could we then put in the research plan the need for the assessment of whether or not one could conduct a either retrospective or prospective

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study, and would it be addressed in the National Childrens Study, instead of committing us to that at this point.

DR. INSEL: Lyn.

MS. REDWOOD: I talked - I wish Dr. Alexander was - but vaccine records will not be collected as part of the National Childrens Health study from what I've been told by Dr. Alexander.

DR. LANDIS: It could be recommended that they do be included, which would be a way of piggy backing on a major -

MS. REDWOOD: That would be great. I don't see us at the granular level of actually designing a study. I think if we say that a vaccinated-unvaccinated study needs to be done, we are not determining the design, whether it's retrospective, prospective, that just that it's a need. So that's what I'm asking.

DR. LANDIS: If scientifically feasible.

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DR. TREVATHAN: Some of this gets to - excuse me, I'm sorry, Ed Trevathan - some of this gets back to the recommendations that some specific standards be developed. I may not be using the terminology others have used, but some specific standards be developed regarding causality, and study design for causality in relationship to environmental exposures in autism.

That could be very useful, and I wonder if that is something the group can agree on that addresses Lyn and Story's and some of our concerns.

DR. INSEL: Right, thank you. So this is Tom. So that actually gets to what do we need, and we are still hung up on what do we know.

And I think the recommendation we have here, we have really four choices, and I want to push this because I want to move on. We have the original version, we have the version that you got in the second column from

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the coordinating committee, we have Lyn's recommendation which is on this sheet, and then the committee here has come up through Alison with the idea that we would take the section under 3.4 that begins, public comment to the committee reflected opposing views on vaccines as a potential environmental cause. And we could move that paragraph and insert it after the sentence on page 4, line 17, that says, in addition a number of environmental agents are being explored through research that are known or expected to influence early development of the brain and nervous system. So that could be inserted there.

One could even use that in place of the subsequent sentence that goes into several other factors. If the committee so wished.

MS. REDWOOD: Tom, I'm lost.

I don't see in here the reference that you are referring to. Can you give me the page again?

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DR. INSEL: Okay, let me walk you through option four. So we are stuck at line - on page 4, line 15 -

MS. REDWOOD: I've got that part. It was Alison's recommendation that I couldn't find.

DR. INSEL: Okay, that's on page six, and it's what falls under discussion point 3.4, and Alison's comment was that even though this is in the section, what do we need, it actually is much more logically connected to what do we know. And it begins with the sentence, public comment to the committee, this is on line 11, on page 6, or 12 -

MS. REDWOOD: Well, mine is not the same. Where is it? Okay, got it.

DR. INSEL: So there is about I don't know 12 lines that follow that talk about much more about what we know than what we need, and it was an attempt by the group to capture the diversity of opinions that were

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coming in through the RFI.

So a fourth recommendation would be to insert that section on to page four, and to move it from page six. It would end up - it wouldn't be at the end of the left column. It would go in after line 17, after we talk about the influence - I'm sorry.

MS. HANN: Actually in looking at the document -

DR. INSEL: This is Della.

MS. HANN: Sorry. In looking at the document, if we take the section that is on page six that we have just been talking about, which attempted to describe the diversity of comments that came in, that really does very much overlap with information that is currently on page four, beginning around line 8 or 9. Essentially there is a sentence that says, numerous epidemiological studies have found no relationship between ASD and vaccines. Concerning the mercury-based preservative thimerosol - then there is a

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reference to the immunization safety review committee in 2004.

If you stop right there, and then take the language from page six, that lays out the controversy.

DR. INSEL: But you are in the original column?

MS. HANN: No, I'm in the column in the blue with the changes, with the changes. That's the column I'm referring to. Thank you for pointing that out.

That is essentially - that is where the controversy in terms of laying out the controversy would fall right there, beginning on - my lines are a little bit mixed up, but I believe it's 8 or 9 on page 4. And it would replace that section and I'm not quite sure where the language would pick up again, but it's opposite the information on the CADDRE program, et cetera, is distinct information.

MS. SINGER: I would actually - you

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could move it to the end of what's currently there, as what do we know, the idea being that what's then left in what do we need are the two points that really reflect what we need, which is the importance for the field to develop sound standards for identifying and claiming that environmental factors contribute to autism spectrum disorder. And lower down, the need for vaccine research that has not been done, eg. A large-scale study comparing vaccinated to unvaccinated groups.

DR. LANDIS: Is scientifically feasible, if a compelling study can be designed that in fact will deal with Stephen's desire to put the matter to rest. I mean I think the worst thing we could do is to invest a lot of money in a design that doesn't satisfy the scientists or the parents and advocates, and you could imagine that there would have to be agreement that this study if conducted would be compelling, or maybe there will never be such a study.

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MS. SINGER: But to me I think that is something that maybe can go in the introduction as it applies to all of the studies that we are listing in the strategic plan.

DR. INSEL: So Alison, in the interest of moving this forward, why don't you lay out what you are recommending. We will make that option four, and then we can take this to a vote.

So can you just give me a sense of where that is going to sit and how that is going to read.

MS. SINGER: Okay, what I'm suggesting is that we take page 6, line 10, that starts, public comment to the committee reflected opposing views on vaccines as a potential environmental cause. Some contend that cumulative research on this topic indicates no role of vaccines - and all of this information about the second view and then the third view, concluding at the bottom

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of page 6, and then moving that into the section, what do we know. As I think what it's saying is that what we know is that there is a diversity of views.

MS. HANN: Where? Where would you put it in the what do you know? This is Della.

MS. SINGER: I would move it to the end of what is currently in Section 3.2.

DR. LANDIS: In the middle column?

MR. SHORE: In the middle column.

DR. INSEL: So just to be clear it would go then at the top of page 5, after the EPS?

MS. SINGER: Where we describe the CADDRE studies, yes. And then what that would leave in Section 3.4, what do we need, are the existing language here that talks specifically to the need to develop sound standards for identifying and claiming that environmental factors contribute to autism spectrum disorder, and the need to conduct vaccine

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research that has not been done, eg. A large scale study comparing vaccinated to unvaccinated groups.

But then at the bottom of page 6 -

DR. INSEL: Well we'll get there.

MS. SINGER: - there is additional language. I'm not saying to end before there.

DR. INSEL: We'll get there.

Peter.

DR. VAN DYCK: A question: The middle column where we just added the transposed piece to the end, did we vote on that as a committee last meeting as it exists?

DR. INSEL: We stopped at page 4, line 15. And for the last hour almost we've been working on line 16.

DR. VAN DYCK: So we've approved some of the parts in blue there.

DR. INSEL: Right.

So Lyn.

MS. REDWOOD: And also that was in the letter that I sent to the committee. I was

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wanting to go back if we have time today to go over that specific item, 3.2.

DR. INSEL: I know. It's looking less and less likely that we are going to get back - we still have the rest of the document. But we haven't gotten to the first line of the revision.

So let's go ahead and put this to a vote. We actually have four options in front of us. And we are talking about the last part of what's on page 4, Story?

DR. LANDIS: I'm thinking that it would be simplest just to vote first on transposing that paragraph; get that done. And then move on.

DR. INSEL: That's what we're about to do.

So the - what the motion that is on the floor is to take the section that was from page 6, move it under what do we know, at the end of this section, and that will finish off the section on what do we know, instead of

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what do we need.

Can I get a show of hands of who is in favor of that transposition?

(A show of hands)

MS. HANN: Okay, the vote is one, two, three, four, five, six, seven, eight, nine, ten.

MS. REDWOOD: Can I ask a clarifying point? Because previously you said that would be in place. You gave us three options to vote on. So now this is just the one option we are discussing.

DR. INSEL: We are going to get back to 16 through 20.

Those on the phone, if I could get a yes or no.

DR. MORRISSEY: Yes, this is Pat Morrissey.

DR. INSEL: And Cindy?

DR. LAWLER: I think yes if I can follow what you are doing. Let's go with yes.

DR. INSEL: Cindy, if it makes you

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feel any better, it is sometimes difficult in the room.

DR. LAWLER: I've got four different things going. So I think I understand what you are doing.

DR. INSEL: The question in hand is simply that paragraph six being moved to page four.

Now the other -

MS. HANN: One second. So were there any dissenting votes?

(A show of hands)

MS. HANN: Okay, thank you.

DR. INSEL: Now we still need to do the set of changes that begin with the sentence, recent studies suggest. So again this takes us back to where we started. We have the default language that doesn't include what's in blue, maternal age, maternal vaccinations. This is page four. This is lines 18, 19, 20. We have that language, and we have a recommendation by Lyn, which is in

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your accompanying document, that she started off the meeting with, talking about Congress has expressed a wish for studies on vaccines.

And before we go deeper into this, Cindy, you may be our expert on some of these studies on environmental factors. Are all of these ones in which the science would support them being included under what do we know, for instance, maternal age?

DR. LAWLER: Well, the one I have is, I'm not sure, I'm not real familiar with what evidence exists for the maternal vaccination during pregnancy as a risk factor, so I don't know if that comes from a rigorous study design. I think some of the others are probably reasonable as possible risk factors. The vaccination during pregnancy, I'm a little uncomfortable with that.

DR. INSEL: I thought the Reichenberg study showed it was only paternal age, and that's been replicated now twice, and not maternal age. But if someone knows of

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other evidence to the contrary that would be helpful to have.

MS. SINGER: I thought we talked about that at the last meeting and we had agreed to say, parental age.

DR. TREVATHAN: Yes, I think so too, yes.

DR. INSEL: Parental age would be a way to improve the language. And Cindy, you are saying that maternal vaccination during pregnancy -

DR. LAWLER: I am not familiar with that being a very definitive conclusion from a study, and I may not be familiar with what the reference to this is.

DR. INSEL: What about hormonal treatments or hormones, how good are the data for that?

DR. LAWLER: Well, hormones covers the waterfront. So I think it's under investigation. Again, a lot of it depends on -

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DR. INSEL: Would it be better to not specify and simply say, toxins, to try to capture a range of - and this - we do have data on pesticides that is actually quite compelling.

DR. LAWLER: On pesticides there is some suggestive data.

DR. INSEL: Again, I want to try not to overspecify if we can avoid it. So what is a better set of words that we could use here that would capture the broadest picture possible?

DR. LAWLER: Well, I mean I think a range of exposures are under study now. The ones that probably have the most support for, although it's still very preliminary, would be the paternal age and pesticides, so we could take out hormones and the maternal vaccination during pregnancy and substitute parental age for maternal and paternal age.

DR. INSEL: And then by leaving in other biological agents that may confirm

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environmental risk, you leave the door open?

DR. LAWLER: That would cover everything else.

DR. INSEL: Lyn.

MS. REDWOOD: Tom, I do want to point out that there have been several studies, the Palmer and also the Windham study that found associations between mercury. These were air studies. Also the one with pesticides, I think that was the Windham study, found heavy metals and mercury. So I would like to ask that mercury be included in there too as a study that has been supported as a potential risk factor.

MS. BLACKWELL: This is Ellen. I'm just looking at the original language. And we substituted parental age for paternal age, it looks like it's pretty broad, what we initially had in this document.

DR. INSEL: And if instead of saying, except that we don't capture such things as heavy metal exposure.

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DR. LANDIS: Which would be toxins, and that could include a variety of things.

DR. INSEL: So Story, could you give us - how would you - if you go back to the original to include heavy metals, what would the language be? So we use parental age?

DR. LANDIS: Parental age, exposure to infections, toxins, and other biological agents, because the hormones for which there seems to be the least evidence right now would be included in the other biological agents.

DR. INSEL: And pesticides could be under toxins - well, that would be a toxin for sure, right, along with heavy metals?

DR. LANDIS: Right.

DR. INSEL: Okay, so that is - again, we have three alternatives. So we have the original language. We have this modification which Story just read, and we'll ask Della to read it again before we vote. And the we have Lyn's language which you have

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in the accompanying document.

Is there any other comment about this before we take this to a vote?

So I'm going to take us through these. Della, will you be able to read option three for us?

MS. HANN: Sure.

DR. INSEL: So option one is what you have in the left-hand column. All in favor of going back to the default language?

MS. HANN: The vote is zero.

Anyone on the phone voting for the original language?

DR. MORRISSEY: I can't find the original language. Could you just read the original sentence?

MS. HANN: Sure. The original sentence read, recent studies suggest factors such as paternal age, exposure to infections, hormones and other biological agents may confer environmental risk.,That was the original sentence.

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DR. INSEL: Okay, so anyone on the phone voting for the original? It doesn't sound very popular.

Della, can you read us option two?

MS. HANN: Well, option two would be to keep the language as written in the right-hand column. That would be the second option, which is: Recent studies suggest factors such as paternal age and maternal age, exposure to infections, including those preventable by vaccines, maternal vaccination during pregnancy, hormones, pesticides and other biological agents may confer environmental risk. That is option two.

DR. INSEL: So actually we have four options here. Okay, all in favor of the right-hand column? Anyone on the phone voting for that?

MS. HANN: Zero.

DR. INSEL: Option three?

MS. HANN: The third option as I understood it, and Story you may have to

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correct me, is to a sentence that reads: Recent studies suggest factors such as parental age, exposure to infections, toxins, and other biological agents may confer environmental risk.

DR. INSEL: Does that sound right? And do you include in the parenthetical comment, including those preventable by vaccines, or are you deleting that?

MS. HANN: People are shaking their head no to include the parenthetical. Anyone on the phone wish to include the parenthetical?

DR. INSEL: I think it's dead.

Okay, all in favor of this new version, hands up?

MS. HANN: Okay, that's everyone in the room here. Those on the phone, how do you vote?

DR. LAWLER: Is that all the options? That was the last one?

DR. INSEL: No, we have another

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option coming up.

MS. HANN: We do?

DR. INSEL: Yes, there is Lyn's option still.

MS. HANN: Everyone in the room voted yes.

DR. INSEL: And on the phone we need a yes or no.

DR. LAWLER: Okay, I'll vote - that is probably the best of the four options.

DR. INSEL: Okay, so I think we are unanimous. So we are going to move on.

That takes us now to the top of page five. And we're now looking at discussion point 3.3. You see on the left the original language. This has been changed to say, although most scientists believe that risk factors for ASD are both genetic and environmental, there is considerable debate about whether potential environmental causes, genetic precursors or interactions between genes and environmental factors should be the

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highest priority for research aimed at identifying the causes of ASD.

And the only addition we have to that is a comment from Lyn. Would you like to read your recommendation?

MS. REDWOOD: Okay. Part of it is the same as before: Most scientists believe that risk factors for ASD are both genetic and environmental, and both should be priorities. Genetics has been funded to a greater degree than environmental factors, and there is need to support the latter as well as gene-environmental interaction so that this research achieves historical parity with genetics investigations.

DR. INSEL: Discussion here? Should we go ahead and take this to a vote? It's simple enough; we've got two options. So those who want - again - I'm sorry, three options. We've got the original version. We've got the amended version that you see in the middle or the right-hand column. And we

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have Lyn's recommendation.

So again, Della, let's take the group through this. All in favor of the original default, that is, making no changes; what you have in the left-hand column?

(A show of hands)

DR. INSEL: Those who accept the right-hand column -

MS. HANN: Wait.

DR. INSEL: There were no hands going up? What about on the phone, Pat or Cindy, speak up?

DR. LAWLER: We are voting for -

MS. HANN: The left hand column.

DR. LAWLER: What is added in blue?

DR. INSEL: No, no, this is the default version, the original August version, the beginning of what do we need on page five.

DR. LAWLER: Okay. No, I'm not voting for that.

DR. INSEL: Okay, and Pat?

DR. MORRISSEY: No, I'm not voting

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for that.

DR. INSEL: All right, the second option is the amended version which is in the blue. Which is the right-hand column. In favor?

MS. HANN: Eight.

DR. LAWLER: I'm in favor.

DR. MORRISSEY: Pat, I'm in favor.

DR. INSEL: So two more.

MS. HANN: Ten, 10 in favor.

DR. INSEL: And then we are looking at Lyn's language as a modification to that.

All in favor?

MS. HANN: Three.

DR. INSEL: Okay, thank you, we are moving on to now line 12 , which changes the term, however, to a statement of: to date, few studies have ruled in or ruled out specific environmental factors. And I think we'll just combine that with further discussion lower down, similar to other diverse areas, advancing research on the potential role of

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environmental factors requires resources and the attraction of scientific expertise. Bringing this to bear on autism will help to better define what environmental factors to study as well as the best approach for staging studies to examine environmental factors.

So all of that was added based on public comment.

We also have, let's see, yep, I don't see any additional comments, unless I'm missing something here, from the committee.

So can we take that language as a group. Do people feel that's an improvement, or do you just want to go back to the original version? Improvement?

So in this case we are just going to ask whether you want to make these amendments or not.

In favor of making the amendments - this is going from line 11 to line 22 - actually we can add in the four examples; so the rest of page five.

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All in favor?

DR. LAWLER: My hand is up.

DR. INSEL: Pat?

DR. MORRISSEY: I am for it.

DR. INSEL: Okay.

MS. HANN: Ten. And then the two on the phone, so that would be 12.

DR. INSEL: And then all opposed to these amendments? Can we see a show of hands?

MS. REDWOOD: Tom, I did have language there as well that was a suggested alternative. High priority for discussion, many studies have identified -

DR. INSEL: I think that is under 3.4, so that's the next page. We are just about to get to that.

MS. HANN: No, it is here. She is correct.

DR. INSEL: I have it listed under 3.4.

MS. HANN: I know. But it's a mistake on our part.

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DR. INSEL: Okay, so let's go back and show me where that would be inserted. Just flag the line that it would go into.

MS. HANN: It's 15 I believe. It's right before the sentence on, similar to other disease areas, is where I believe your language begins.

DR. INSEL: You are absolutely right. I now see it. So the part that is in black on your page is the part that is in blue on our page.

MS. HANN: Correct.

DR. INSEL: Okay, so let's - before we go forward, so we have an alternative, we had an addition to discuss, which is - and Lyn, why don't you take us through the language you are recommending. It looks to me like it would be inserted on page five before line 15.

MS. REDWOOD: It would be at line 10 where it says, to date, however, and then it starts with few studies that would start

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with the mini-studies.

DR. INSEL: Take us through that, and then we will have a chance to get reaction from the committee.

MS. REDWOOD: Many studies have identified a number of environmental factors which increase the risk, and these need to be replicated. There are reports of association of ASD with exposures to medications, toxins, infections, prenatally and postnatally, higher blood urine or hair levels of mercury than controls, and of biomarkers indicative of toxic exposures; and then it goes on to include the next sentence: similar to other disease areas, advancing research on the potential role of environmental factors require resources for larger scale studies and the attraction of scientific expertise. Bringing these items to bear on autism will help focus the environmental factors to study, as well as the best approach for staging studies to examine environmental factors,

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interaction between factors, and between individual susceptibility and various environmental factors.

DR. INSEL: Comments. Judith?

DR. COOPER: I was wondering if Cindy might weigh in on that. Because I don't know this area, and if one draft says few studies, and now Lyn is saying many studies, I guess I would just like Cindy's perspective.

DR. INSEL: Maybe even before we go there, just the large question. We are now into the section on what do we need, and it sounds like it's going to be an argument over what do we know. I'm not sure we need to take the time for that unless we want to go back to do the previous page again. I don't see a lot of enthusiasm for that.

So I do want to move us along staying focused on the structure of the document. This really is trying to ask the question, what's the next most important thing to do. So the question is whether we want to

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modify the language to include language about whether there have been many studies versus few studies, and the specifics of those studies.

DR. LANDIS: I mean I think the key factor in the few studies is, few studies have ruled in or ruled out, and that's probably an accurate statement consistent with identification of associations. Association doesn't rule in or rule out; it highlights things for study.

DR. LAWLER: This is Cindy Lawler. I'm also not in favor of the level of detail provided about these many studies and I think it is covered by the language earlier, and I agree with what Story said. WE have already talked about - in the document there are few definitive studies. Earlier than that we talked about there is kind of a range of exposure under study. And I'm uncomfortable with the granularity of this, the first two sentences.

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DR. INSEL: What about the last part of what Lyn is recommending? I want to read it, because it is different. It's a little more detailed, but it's also a little bit more conceptual than what's in here. It says, the focus of the environmental factors to study as well as the best approach for staging studies to study environmental factors interaction between factors, and between individual susceptibility and various environmental factors, which is not in the current version.

DR. LAWLER: I am surprised if it's not in the current version. But I would support including that. I mean I think it's the foundation of many of the objectives, the specific objectives that are laid out later in the document, looking at which exposures to look at, gene-environment interaction, attracting more scientists to the field. But I am fine with including this additional language here as a sort of way to reiterate or

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amplify how important it can be to bring new individuals into the field, and some of the things that they can do in terms of trying to identify the best approaches for tackling the vast array of exposures that could potentially be of import to autism.

DR. LANDIS: So Tom, maybe what you need to do is vote on the first replacement, and then the addition separately.

DR. INSEL: Can I have a motion to do that? Let's start there.

DR. LANDIS: I move to retain the second column language, and not replace it with the Redwood information, and I would also move, although maybe it should be a separate.

I move that we retain the column two information, and not replace it with the Redwood initial green, and that we add the second piece of green in the Redwood suggestion.

So there are two different things, but we could jumble - we could move it

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together.

DR. INSEL: I'm seeing a number of heads nod, including Lyn's. In the interests of time, why don't we make that the motion that we do both of those. So we are going to retain the first half, but we will alter the second half to include this comment about individual susceptibility.

And can I get a show of hands of who's in favor of that change?

DR. LAWLER: I am in favor.

MS. HANN: Twelve in the room.

DR. INSEL: We heard from Cindy.

Pat?

DR. MORRISSEY: Yes.

DR. INSEL: And anyone opposed?

(No response)

Okay, we are moving along, and that takes us to the last line of page 5, where again Lyn has a very small recommendation after, for example, instead of saying, some researchers believe, she has one

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approach is to study a large number of exposures, and then adds in, another approach is more tightly focused, and the next sentence. And it ends with a section that says, it would be important for the field to develop sound standards for identifying and claiming that environmental factors contribute as it would be for genetics.

And that would go into line 11. So those are almost semantic. I'm not sure that there is a lot of conceptual shift. But it does add this piece about putting in the kinds of criteria for environmental studies that we now use for genetics; at least the same standards.

Any discussion?

DR. LAWLER: I would support that. I mean I am a little bit disturbed with the idea that we need to develop sound standards, and we are just looking at that specific to environmental factors. You know there is a long history. If you look at lead research,

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I can imagine these kinds of comments being raised with some of the initial studies that suggests that there were effects at fairly low levels on cognitive outcomes in children. I think that sort of message, the kind of clues that can come, and really are all that can come from some of these studies, but they do provide us a way to start, and some hints about what to follow up, more mechanistically, maybe in animal models, is suggesting to me - it's just worrisome, because I think there is a great deal of the research into environmental risk factors, not just specific to autism, but sort of across the board, kind of the nature of the evidence that you can develop in humans.

DR. INSEL: So Cindy, just in the interests of time, do you want to change this?

DR. LAWLER: I think we do need to either put it on the same foundation as we would, how do we define evidence in the genetic arena or other arenas.

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DR. INSEL: Okay, so let's put this to a vote. We have the original - well, we have the language in the middle column, which is virtually the original language, with this for example add. Or we have the recommendation from Lyn to add this clause about making the standards, sound standards for environmental research as we have for genetics.

Can I get a show of hands for who wants to retain the original language as it shows in the middle column? Anyone on the phone?

Of those who want to change it with Lyn's recommendations?

MS. HANN: This is unanimous in the room.

DR. INSEL: It is unanimous in the room, and on the phone?

DR. MORRISSEY: Yes.

DR. INSEL: Okay, thank you, we are ready to move on.

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The next section is the one that we have already spent a huge amount of time talking about, and we moved it.

So Lyn, do we need to look at the paragraph you wanted to add here, or has that already been addressed by the modification that we made under, what do we know?

MS. REDWOOD: Has this paragraph then been voted on to be added to what do we know?

DR. INSEL: No, so the paragraph one - well, what you have in your addendum here is, one area that is important to address from a public health standpoint, and given a congressional mandate, is the role of vaccines in autism, including a large-scale study comparing vaccinated and unvaccinated groups; funding from CAA is sufficient to address this issue while still providing resources for other areas of research including the desperate for treatment studies.

So the question is whether you

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want to insert that language into the plan. And this area in - on page six.

Let's just put this to a vote. Those who want to insert this language, can I see a show of hands.

(A show of hands)

MS. HANN: Three.

DR. INSEL: On the phone?

Those who want to just retain the version we have, and we won't insert the language.

Hands.

(A show of hands)

DR. LAWLER: Retain.

MS. HANN: Nine, and then Cindy, that makes 10.

DR. INSEL: Okay, we are moving on to page 7. And you can see at the top of page 7, discussion 3.5, the language that came out of the public comment, and then Lyn has recommended some additional changes, and Ellen as well - well, I guess that is a little

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further down.

So Lyn, maybe you can take us through your recommendations on the top of page 7.

MS. REDWOOD: It starts with the original language of, research studies on risk factors can be pursued through several means. Smaller focused studies are needed for hypothesis testing, and to provide insight for replication studies.

And then it is all the original language. So it is basically, Tom, just wordsmithing. And then it goes down, if you look in green, other existing cohorts could be identified and used, and that is in relation to the CHARGE studies. And then the last sentence just adds on, another approach for studying risk factors for ASD requires large sample sizes to disentangle the many possible genetic and environmental factors that contribute to and help explain ASD. And then what I have proposed to add: and the

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frequently co-occurring gastrointestinal problems, sensory sensitivities and other common comorbidities.

DR. INSEL: Comments about this?

One issue that maybe we had decided not to put in, to list all the co-occurring comorbidities. So that might be something we can call, frequently occurring co-morbidities. I'm still not convinced that we know they are co-morbidities. So it may be - the language bothers me a little bit. I wonder if it's better to say, frequently occurring co-occurring medical symptoms, or something like that. We still don't know whether they are part of autism, some forms of autism, or whether they are truly additional disorders that are frequent travelers. It's just not clear.

MS. BLACKWELL: I would - this is Ellen - I would certainly support altering that language, and also deleting the word, problems, and crafting - because we use the

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same language actually in the introduction. So we need to come up with something that we can use throughout the document.

DR. INSEL: Medical symptoms?

MS. BLACKWELL: I think it's more than medical symptoms. Is it co-occurring symptoms? Co-occurring disorders? Is it always medical?

DR. INSEL: I think that is the scientific question. We actually don't know if they are co-occurring disorders or whether they are part of autism. That is the difficulty here.

MS. BLACKWELL: We need a word that is broad enough to cover all those things.

DR. INSEL: The problem with medical symptoms, what are you worried, that that won't include?

MS. BLACKWELL: For example is sensory sensitivity a medical symptom?

MS. REDWOOD: Tom, what if we addressed it with what you just said, in terms

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of the existence of other diseases, whether or not they are actually co-occurring conditions or a part of the actual disorder itself. Because that is really the question. I can't wordsmith language quickly.

MS. HANN: What if - this is Della - a possibility in listening to your discussion is frequently co-occurring conditions. And therefore one doesn't say if it's medical, if it's behavioral, if it's sensory or anything; it's just a condition.

MS. REDWOOD: But then do we want to add to that Tom's caveat of whether or not it's actually part of the disorder.

MS. HANN: You have that as the proposed language for the introduction when we introduce this idea.

DR. HOULE: This is Gail. Could you just end it at explain ASD. You may not have to start with examples because you are talking already about what it is you are trying to disentangle with the study.

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DR. INSEL: How do people feel about that? If you assume that ASD includes all this, do we need to specify? Okay, Lyn.

MS. REDWOOD: The reason I added that in there just to get some justification is because they are, I feel, overlooked in our children, and that a lot of these medical comorbidities if they are addressed and treated, the symptoms improve. So that's why I thought it was important to specify that in that area.

DR. INSEL: Story.

DR. LANDIS: I kind of liked the frequently occurring conditions. It separates those out in a sense from ASD, and if in the introduction there is a discussion of ASD plus or minus co-occurring conditions, then I think it addresses it.

DR. INSEL: Gail, can you live with that as long as we explain it earlier on in the document?

DR. HOULE: Yes.

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DR. INSEL: Okay, so here's what we have in front of us. We've got language that was originally in the document, so that's your left-hand column. We have the right-hand column. And we have this recommendation from Lyn to clarify what kinds of hypothesis testing studies would be needed, and adding in the information about the co-occurring conditions.

So we've got three options. Those who want to go back to the original version, a show of hands.

(A show of hands)

DR. INSEL: Anyone on the phone?

DR. MORRISSEY: No.

MS. HANN: That's zero.

DR. INSEL: Okay, the version in the right-hand column.

(A show of hands)

DR. INSEL: Anyone on the phone going for that? It's not a very popular one here either.

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And that leads us to the version suggested by Lyn, which is - we don't need to read it again but it's in the document next to you, and we'll just replace the final few words by saying co-occurring conditions instead of spelling them out.

In favor?

(A show of hands)

DR. LAWLER: Yes.

DR. MORRISSEY: Yes.

DR. INSEL: Anyone opposed?

(No response)

DR. INSEL: Okay.

MS. HANN: The vote was unanimous.

DR. INSEL: Thank you.

And we're moving on to further down the same page, okay, so it is to announce that Dr. Landis is leaving, and Dr. Koroshetz -

DR. LANDIS: Should occupy my seat in about 15 or 20 minutes. He was in another meeting, and I will be back in the afternoon.

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Tag team.

DR. INSEL: You are not replaceable, Story, but it will be good to have someone from NINDS. So we will see you later.

Moving down further on 3.5, there is additional language here.

MS. HANN: From Lyn.

DR. INSEL: From Lyn. Lyn, help me out to figure out where this is going, and which line. Similarly large birth cohort studies. Ah, here it is, line 17 in the middle column.

So before we get there, there are a few other changes I can see from what we have in the middle column.

MS. HANN: No. We took care of all those.

DR. INSEL: All right. So we are down to line 17, and there is simply a single addition in the parenthetical statement. It includes a comment here: immigrants with,

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higher autism prevalence. This is at the very bottom of the page. It would be the last line.

DR. LAWLER: I'm not aware of the data on that, so I'm a little uncomfortable with including it.

DR. INSEL: Again, we're in what we need, not what we know. So this is the recommendation here is that this is an opportunity, or potentially an opportunity for study.

MS. REDWOOD: Tom, this is Lyn. There has not been anything published, but just in the last month or two it has come to our awareness that Somali immigrants have a very high rate of autism, I think - help me out, somebody, I'm sure are aware of these reports that have been investigated - is it Wisconsin?

DR. TREVATHAN: Minnesota. I can - let me - there have been reports in the media about it, and the Minnesota Health Department

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is investigating that, and we are advising them. And actually this is just beginning. Actually it isn't documented that there is a higher prevalence. There is a question based on some educational data, reports from education. But the details, we haven't been able to get access to detailed records. So there is an investigation ongoing with the question - with that being a question.

DR. LAWLER: So why don't we say to do research on critical subpopulations that may be at higher risk.

DR. TREVATHAN: Right, I think that would be appropriate, because this is of extreme interest I think to all of us. But I think the question is if, not, it isn't definite that there is a higher prevalence. It's an important question that is being investigated.

MR. GROSSMAN: This is Lee. Our chapter in Minnesota with the Department of Health in Minnesota sponsored a conference

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with some others last month looking at this question. There were about 100 people there. And nothing was really addressed; it just opened up the door for more investigation, and many more questions to be answered. It's ongoing, and we have been monitoring it pretty closely.

So the Somali population is definitely very interesting, and one that will be involved - there is everything that Ed had brought up, or some of the questions that have been raised. But our people on the ground there definitely feel that there is an incredible prevalence among this population.

DR. INSEL: So we've also seen in unpublished data some geographic clusters that are not based on immigrant populations, but are based on area of residence; actually done by zipcode, where prevalence goes up about fivefold. So it would be - maybe it would be better then, instead of saying immigrants - what was the language the Cindy -

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MS. HANN: She said subpopulations that may be at higher risk.

DR. LAWLER: That may be at higher risk. Then all of those could be examples that would be important to pursue, but it's not an exhaustive list, and it doesn't indicate which ones there is really strong evidence for, versus one that is an interesting question and there might be some preliminary data that are suggestive.

DR. INSEL: So there is language, in the same parenthetical statement, it says, those with elevated exposure to specific environmental factors, older parents, but you would add in subpopulations that may have higher autism prevalence.

DR. LAWLER: Research on critical subpopulations that may be at higher risk. So that change is before the parenthetical example, and that would just allay any concern about whether there is strong evidence versus - for instance pregnancies in families with

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one child, I mean that is sort of a demonstrated high risk subpopulation. These other ones, it's important to investigate, but I don't necessarily think we can say they are high risk; they may be. They may be at higher risk.

The change I'm suggesting is, the phrase right before the parenthetical example, where now it states, research on critical high risk subpopulations, change that to research on critical subpopulations that may be at higher risk.

DR. TREVATHAN: So that would, under your statement, Cindy, a specific question for example of the Somalis could be subsumed in addition to other subpopulations, and what we're really talking about is potential clusters that would need further research and investigation, some of which of course we may not know now. I don't think we want to limit ourselves.

DR. INSEL: So would you do that in

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place of putting in a statement about immigrants?

DR. LAWLER: Well, immigrants is just one example. We could add another example. I'm not sure we need to be exhaustive.

DR. INSEL: I wonder if again it would be better not to overspecify, because once you start to list some and you don't list all. And as I think all of us know about emerging stories, but none of those are at this point published, or in the peer review literature.

So we've got two options. So and I'm going to ask Della to read the language that Cindy is recommending. We also have the one comment that is added by Lyn on including immigrants, or we could go back to the original version which includes neither of those.

So the wish of the group. Those who want to just retain the original language

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without any changes. In favor?

(A show of hands)

DR. INSEL: On the phone, anyone in favor?

(No response)

DR. INSEL: The second option is to include the language that Lyn has recommended, that immigrants with higher autism prevalence. In favor?

(A show of hands)

DR. INSEL: On the phone, in favor?

(No response)

DR. INSEL: All right. And then the final - Della, can you read us the language that we are talking about for the third option?

MS. HANN: Sure. As a complement to these large-scale studies, research on critical subpopulations that may be at higher risk. We still have the parenthetical then: eg. Subsequence pregnancies in families with ASD; those with elevated exposure to specific

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environmental factors; older parents; and immigrants. You're going to leave immigrants out? Okay, strike the immigrants.

DR. COOPER: This is Judith. Can't we just leave out the parentheses? Because the way Cindy has reworded it includes everybody, and then we don't have to worry about leaving somebody out.

MS. SINGER: I also think it's odd to say - I mean some of these examples, the first example sounds a little odd. So I'm in favor of taking out the parenthetical.

MS. HANN: That would now become the fourth or fifth option; I wasn't counting.

So now the option that is before us, the sentence would read, as a complement to these large-scale studies research on critical subpopulations that may be at higher risk, period. Could provide leverage in identifying genetic and environmental factors, with no parenthetical.

DR. INSEL: Who's in favor of that

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final language that we have?

(A show of hands)

MS. HANN: The vote is unanimous in the room. Those on the phone?

DR. MORRISSEY: Yes.

DR. INSEL: Okay, moving on, thank you everybody.

We are now - do people need to take a bio break for three minutes? Is this a good time to stretch? If I say three, I know it'll be five. So I don't want to say more than three, because we have so much to do. But let's take a quick stretch, and then we'll get back into it.

We're up to now page 7 line - oh we're up to research opportunities. We're on to page 9, okay.

(Whereupon, the above-entitled matter went off the record at 10:36 a.m. and resumed at 10:45 a.m.)

DR. INSEL: Now that we are going into Research Opportunities, we come right

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back to some of the issues that we've been talking about.

And you will see on page 9 that we really have to here address head on what we want to do about the statement about vaccines.

Before we get there there is one small change that was made from the public comments. So it's in line 12. It says, case control studies of unique subpopulations of people. And the unique subpopulations was struck from the original version.

Della, there was probably a rationale for that.

MS. HANN: There was. There were one or two public comments that felt that that was too restrictive.

DR. INSEL: Any comments about that? Should we go ahead and strike that, or do people want to go back to the original version? This is page 9, line number 12, case controlled studies of unique subpopulations. And people felt unique subpopulations was too

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restrictive.

I see some questioning brows.

DR. TREVATHAN: If we strike it we are not prevented from doing case controlled studies of unique subpopulations; it just provides more flexibility. Is that the idea?

DR. INSEL: Well, again, I don't think you need to feel that the middle column in some ways has priority. This is just something that came out of public comment. We tried to put everything in, and some things may have improved it, and some may have made the document not as useful. So it's up to your judgment about this.

MS. REDWOOD: I think unique subpopulations gets back to what we were just discussing with regard to whether immigration or sunlight or living in a certain zipcode might increase your risk of developing autism. So I think it's important, unique subpopulations could provide us a lot of information.

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DR. INSEL: Okay. So just get a show of hands for those people who would go back to the original version which includes the unique subpopulations and let's see how many people -

MS. BLACKWELL: Tom?

DR. INSEL: Yes.

MS. BLACKWELL: I have one more suggestion for this particular sentence. I would prefer to just say people with ASD, and delete the word, living.

DR. INSEL: Okay, so give us what - how would it sound? Case controlled studies -

MS. BLACKWELL: I would propose that we just say, case control studies of people with ASD that identify novel risk factors.

DR. INSEL: Because if - you are not going to do it in people who are not living with ASD. Okay.

DR. MORRISSEY: This is Pat, Tom.

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I think the reason why living makes sense is because ASD affects a whole family, and you don't want to present the possibility that the studies be done about families, I mean impact of ASD on the family. And changes in other family members' behavior to help the person with ASD.

MS. BLACKWELL: Pat, this is Ellen. I hear what you are saying, but I'm not sure that that conveys in this sentence - although I do think we express it later on in the document when we talk more about services and supports to families.

DR. MORRISSEY: Okay, all right.

DR. INSEL: Della, can you give us the options here.

MS. HANN: Okay. One would be - one option would be to keep the very original, which appears on the left-hand side, which would be, case control studies of unique subpopulation of people living with ASD that identify novel risk factors. That's one

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option.

Can see who would be in favor of that option?

(A show of hands)

MS. HANN: There's no hands in the room. Anyone on the phone want that option?

(No response)

MS. HANN: I take that as a no.

So then the second option is, case control studies of people living with ASD, and identify novel risk factors, so dropping the unique subpops. Okay. That's the second option.

Anybody in favor of the second option?

(A show of hands)

MS. HANN: I see three - four.

Anyone on the phone?

(No response)

MS. HANN: So four.

The next option would be to retain the unique subpopulations and to also extract

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the word, living. So we would have: case control studies of unique subpopulations of people with ASD that identify novel risk factors.

(A show of hands)

MS. HANN: I see six. Anyone on the phone?

DR. MORRISSEY: Yes, this is Pat.

MS. HANN: Seven. Go ahead, Ellen.

MS. BLACKWELL: I'm sorry, I thought I was proposing saying, case control studies of people with ASD that identify novel risk factors.

MS. HANN: So that would be a last option to lose the unique subpopulations.

DR. LAWLER: That is what I'm voting for, option four.

MS. HANN: Okay, can I see a show of hands in the room who would go for that option, which is, please correct me if I'm wrong Ellen: Case-control studies of people - right, we're not having unique subpopulations

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anymore - so case control studies of people with ASD that identify novel risk factors.

(A show of hands)

MS. HANN: I see one, two, three, three hands.

DR. LAWLER: And Cindy.

MS. HANN: Four.

So the majority was for the one prior to that. Which was, case control studies of unique subpopulations of people with ASD that identify novel risk factors.

DR. INSEL: Okay, moving on.

We are now into the section on the bottom of page 9, and we have from the public comment we have two alternatives, one that says: focus scientific investigation on the role of vaccines in ASD. The other one says, make no mention of vaccine research science does not support.

So those - I don't think we are going to get a lot of people who want to put both of those things in. There is a question

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about whether to put either of them in or one of them in.

Any discussion? So we've got four options. We've got the possibility of including neither; including one; including the other one; or including both.

Am I missing any options? So the -

DR. LAWLER: I am confused. So there would be a bullet that said, focus scientific investigation on role of vaccines in ASD as a bullet under research opportunities?

DR. INSEL: That is right.

DR. LAWLER: Okay.

DR. INSEL: The original is on the table, the default. In fact we'll start there, for those who do not want to make either amendment to the original language. In favor of the original?

(A show of hands)

MS. HANN: I see 10 hands in favor

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of the original language.

And just to be clear, the original language is to monitor the scientific literature; okay, that is that bullet; that is still there. That's the one we're saying is the original, and it would therefore not include these two alternatives. That is the original language, just to be absolutely clear. And there was a vote of 10 people.

DR. MORRISSEY: I support that.

DR. LAWLER: I support it.

DR. INSEL: That's 12. Do we need to continue the vote, Della? Okay. So we accept neither of these comments, and we are moving on to - now there are a number of other comments here, again, from the IACC list, both from Lyn and from Ellen. Maybe we can dispense, Ellen, with your comment on page 10, line 5, including co-occurring conditions such as GI and sensory. We had decided last time we were going to incorporate all of that into language in the - so if it's okay with the

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group we won't even go there.

Then Lyn, you have a number of other suggestions here under research opportunities. How do you want to handle those? It looks like there are about five additions.

MS. REDWOOD: Do you want to just go through it and vote?

DR. INSEL: Right. So I guess what we can do is for each one we can see whether people want to add these in or retain the current language.

Want to take us through them? Maybe you could read them off.

MS. REDWOOD: The first was a suggestion for top candidates for genetic sequence variations in ASD and the symptom profiles associated with these variations.

DR. INSEL: Okay, so let me put my scientist hat on for a moment. In the many many months since this was first put together, and I'm sorry I missed this in the original

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version as well, we have come to understand that it's not just sequence variations that are important, but structural variations.

The word, sequence variation, now means something very different than it did nine months ago. And it's actually not where most of the action is. Most of the action these days in genomics is around copy number variations and changes not so much in sequence as in structure of the genome, at least for autism.

I wonder if it'd be better just to say genomic variations. It would certainly be better to say genomic rather than genetic, because some of these things are not in genes and yet they are important.

So just for precision's sake, to go back to Lyn's recommendation, it might read, top candidates for genomic variations in ASD, and the symptom profiles associated with these variations.

MS. HANN: This is to replace the

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very first research opportunity? Because the language is almost identical?

DR. INSEL: It just adds -

MS. HANN: Right, I just wanted to be sure that we didn't have a duplication unless you all wanted a duplication.

Okay, so then as I understand it, then, the proposal is to change the very first research opportunity, the wording of that, to read top candidates for genomic variations in ASD and the symptom profiles associated with these variations.

DR. VAN DYCK: What does top candidates mean?

MS. HANN: There is a question as to what top candidates mean?

MS. REDWOOD: The ones that we see in our research that seem to be the most common.

DR. INSEL: What about if we went back to the original language and just said genomic variations, and then nothing else

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would have to change if we just changed genetic sequence variations, to genomic variations.

MS. REDWOOD: I like that, but the original language doesn't say genomic.

DR. INSEL: That's what I'm saying. So we make that one change.

In favor of that change? Cindy and Pat are you clear what we're talking about?

DR. MORRISSEY: Yes, you are going back to the original and just doing genomics.

DR. INSEL: Yes, the number one research opportunity not in priority but just in the list.

DR. MORRISSEY: Yes, I support that.

DR. INSEL: So the final would read, genomic variations in ASD and the symptom profiles associated with these variations.

MS. HANN: And the vote was

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unanimous to accept that.

DR. INSEL: And then Lyn you've got a second bullet?

MS. REDWOOD: Yes, I do.

This again is candidates for environmental influences on ASD including the role of vaccines, pathogens, mercury, pesticides and other pollutants.

DR. INSEL: Can I make a recommendation if the group wants to go this direction that we make it parallel and just say, environmental influences on ASD and the symptom profiles associated with those influences? So it would be parallel to what we are talking about for genomics. In the case of genomics we didn't specify what genes we were thinking about. So maybe there is no reason to do that for the environmental factors either.

Lyn, do you think that misses the point? What is your sense?

MS. REDWOOD: I think it is the

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pleasure of the committee. I was just trying to point out specific - what seemed to be top priority in the research literature now that might be promising environmental factors to investigate.

DR. INSEL: Okay.

DR. VAN DYCK: Does that replace the last bullet before the alternatives?

DR. INSEL: This would be in addition. This is not - Lyn, you weren't recommending this as a replacement, were you?

MS. REDWOOD: No, and we voted against this as the alternative one, correct?

MS. HANN: Just the ones on page nine. We have additions that will occur on page 10 that we haven't gone through yet.

DR. INSEL: Okay, so let's look at what we've got here. So Lyn has put on the table an alternative that would say: top candidates for environmental influences on ASD with a listing of the possible ones.

I'm recommending a modification of

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that that would be parallel to the genomic sequence - genomic variation one, saying top candidates for environmental influence - or just say candidates for environmental influence on ASD, and the symptom profiles associated with these influences.

Are there any other alternatives or discussion?

So let's just go ahead and put that to a vote. Those who want to take the version that lists the vaccines, pathogens, mercury, pesticides and other pollutants. In favor?

(A show of hands)

MS. HANN: Three.

DR. INSEL: What about on the phone?

DR. LAWLER: That is for the alternative that Lyn has described?

DR. INSEL: Yes.

DR. LAWLER: No. I'm voting for your version.

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DR. INSEL: All right, so the second version would be, candidates for environmental influences and the symptom profiles associated with these.

In favor?

(A show of hands)

MS. HANN: Nine. Those on the phone?

DR. LAWLER: Yes.

DR. MORRISSEY: Yes.

MS. HANN: So that brings it to 11.

DR. INSEL: Okay, so we're going down the list here. Lyn, there is another one here on the - so this will be the second one on the original list. Family studies of the broader autism phenotype. You want to add, in the subgroup of families with inherited gene variance that increase autism risk.

MS. REDWOOD: I was just trying to define it more. But if we are not going that granular.

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DR. INSEL: Okay, so let's move on. What about these others? Should we dig into them? Or do you think they are too granular? What is your sense? Just tell us which ones will be important for the group to talk about?

MS. REDWOOD: I would say the next two, Tom, the one about studies in simplex families and inform and define de novo gene differences and the role of environment in inducing these differences. I think that is - maybe I'm wrong, if that is something that is currently being investigated.

DR. INSEL: It certainly is, but that doesn't mean it's not an important research opportunity. It's - if it is something that is likely to provide new insights, then we ought to list it as an opportunity.

MS. REDWOOD: The other thing I was trying to do, Tom, was specifically include more genetics research that incorporated a focus with environmental factors as well, so

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combining those two. So that's why I was adding this.

DR. INSEL: Okay. Can I get a show of hands for who would like to include that line, studies in simplex families. These are families with only a single individual with autism, that inform and define de novo gene differences. So these are sporadic or emergent gene differences, and the role of the environment in inducing these differences.

In favor?

(A show of hands)

MS. HANN: Actually it's all but one in the room.

DR. INSEL: And on the phone?

DR. MORRISSEY: Yes.

DR. INSEL: Okay, so this motion carries.

And then there are two other quick things. There is one on environmental and biological risk during pre and early post-natal development in at-risk samples.

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Comment on that? Who wants to include this? For those who think it should be included as a research opportunity, hands up.

(A show of hands)

MS. HANN: Eleven.

Anyone on the phone?

DR. LAWLER: Yes.

DR. INSEL: Okay. Pat?

DR. MORRISSEY: Yes.

DR. INSEL: Okay, we are moving on.

The last thing, Lyn, in your list, I think we have already taken care of with the comorbid conditions.

So we are now moving to the very end of the list of research opportunities, page 10. And there are several here, and the only question I think in front of us is do we want to include these or modify them in some way.

Again, going back to comments from the IACC, Lyn, I think you - these additions

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are from the public comment. Lyn, you had additional comments that are on the supplementary document.

MS. REDWOOD: I did?

DR. INSEL: Yes, so these are discussion points 3.7 and 3.8, that are open for comment. And 3.9.

MS. REDWOOD: Tom, I was just copying the recommended change. That wasn't really - I was just saying I was in support of it. Only the stuff in green were additions.

DR. INSEL: Okay, good, so we can just focus on - Ellen, you had a comment.

MS. BLACKWELL: It's the same comment.

DR. INSEL: Okay. So let's take a look at those additions at the bottom of page 10 and the top of page 11, and let us know if you want to just go ahead and vote on them or if you think they require some discussion.

The default mode is, we go back to the original version without these additions.

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Okay, I'm going to recommend that we put this to a vote so we can move on. Who wants to include discussion point 3.7 as it now is written in the final version of the plan versus the - so the first option would be to add this, the second option would be the default and not to add it.

Alison?

MS. SINGER: Can I just ask how this is different from the one that Lyn just added, biological and environmental risk factors during prenatal development? And this is study of environmental factors during prenatal and postnatal.

DR. INSEL: It's more specific and longer. But we already have language in here that we just agreed to that would say environmental factors and how they track with specific symptoms. So if you don't think we need this additional statement, you don't need to vote for it.

So who wants to add this in? Can

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I get a show of hands?

(A show of hands)

MS. HANN: One.

DR. INSEL: On the phone, anyone?

DR. MORRISSEY: Yes.

DR. INSEL: So there is one on the phone?

MS. HANN: So there is two in favor.

DR. INSEL: So I'm assuming the rest of us - let's just make sure by vote - want to exclude this comment and retain the language we had before.

(A show of hands)

MS. HANN: Nine.

MS. SINGER: The language that we had before is the language that we voted on?

DR. INSEL: Just a few moments ago, right.

DR. ALEXANDER: I'd just like to say that this is our kind of stuff. But I didn't vote to include it because I assume it

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was included in what we just agreed to before.

DR. INSEL: And the record will so show.

DR. LAWLER: Just a comment. I don't think it's included. The earlier bullet was for environmental and biological risk factors during pre and early development in at-risk samples. That's sort of a specific paradigm, looking at at-risk populations, not just sort of in general; looking at the role of environmental factors.

DR. INSEL: I'm sorry, Cindy, the language we are talking about is the one that we just added at the in research opportunities that says, environmental influences in ASD and the symptom profiles associated with these influences.

DR. LAWLER: Okay. Well, I mean I think there is probably some merit to indicating that we are interested in a wide variety.

DR. INSEL: All right, we are

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moving on to 3.8, include study of genetic, gene by environment, and environmental causes as inclusion of all reflects the viewpoints of various stakeholders. And again, your interest in including this additional language.

Those who want to add this, a show of hands?

(A show of hands)

MS. HANN: One.

DR. INSEL: Anyone on the phone - two -

MS. HANN: Two.

DR. INSEL: Anyone on the phone want to add?

(No response)

DR. INSEL: Those against adding this and just retaining the original language?

(A show of hands)

MS. HANN: Nine in the room.

DR. INSEL: And the final addition to the research opportunities: do not support

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research that explicitly or implicitly has a goal of eliminating people with ASD.

And Ellen, you had a comment about that which maybe you want to share here.

MS. BLACKWELL: I think we should return to the original language. It just seems to me that it would lend credence to the government engaging in such research.

DR. INSEL: Any discussion?

All in favor of - I'm sorry, Stephen?

MR. SHORE: Yes. I think what we are getting at - one, I don't quite understand it. And two, I think what we are getting at again is the idea of either eliminating people with autism, or are we focusing on ameliorating the more debilitating aspects of autism?

DR. INSEL: Yes, I think it's the later. So this is a negative sentence. It suddenly occurs to me, I wonder if we say, support research that focuses on what I just

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said, ameliorating the debilitating aspects.

MS. BLACKWELL: Stephen, I think we actually get to that in some of the services and supports pieces.

DR. INSEL: Yes, the question would be, since this is under causes, mostly environmental and genetic, whether we even need to go into this at this point, or whether we want to leave this where we can really unpack it in a much more comprehensive way.

I think what - if I recall the public comment about this was the concern that the genetics research would morph into eugenics and aborting anybody who had a risk gene for autism. And I think that is what was behind this language.

So if that is where we're coming from, let me see again if we can get a show of hands of people who want to add this particular language to the document. All in favor?

(A show of hands)

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MS. HANN: There are no votes at the table. Anyone on the phone in favor of including this?

DR. LAWLER: No.

DR. MORRISSEY: No.

DR. INSEL: Okay, we'll move on to short term objectives. So we are all on page 11, and we will start with the very first objective, which has several alternatives, as you can see. And they are really based on numbers. So the original objective was five environmental factors. Public comment has suggested 10, in one case, 20 in another. And we also have - okay, I think that - Lyn, as I see it from your comments that are sent in, it looks like if I'm reading this right are they the same as what is here?

MS. REDWOOD: Yes.

DR. INSEL: So we don't need to go through those specifically.

So what is the pleasure of the group? This is really a question of scale and

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scope. Do we want to stay with the original, which was at least five? Or do we need to set the floor at a higher - be a little more specific?

(No response)

DR. INSEL: If there is no discussion I'm happy to take this to a vote, just remembering that at least five could be 20; at least 20 couldn't be five. So in favor of the original language, can we get a show of hands?

(A show of hands)

MS. HANN: The vote for the original language is eight in the room. Anyone on the phone in favor of the original language?

(No response)

MS. HANN: Apparently not, so eight.

DR. INSEL: And those who want to go to the first modification, which is 10 environmental factors?

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(A show of hands)

MS. HANN: There is four in the room. Anyone on the phone?

DR. LAWLER: I would support going to 10.

DR. INSEL: Okay, and then we have the final one which is 20?

DR. MORRISSEY: This is Pat. I would too.

DR. INSEL: Okay, so you are going to 10?

DR. MORRISSEY: Yep.

DR. INSEL: And then at least 20?

(A show of hands)

MS. REDWOOD: I would go for at least 20, but if that is not going to pass I will vote for at least 10.

MS. HANN: All right.

DR. HOULE: This is Gail. Five large, 20 small studies. I mean it's a balancing act. It's not so much I think the number of studies as it is the size and the

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complexity of the offshoots of the studies. So I'm not really sure how you are going to give an accurate estimate.

DR. INSEL: What is the final vote? I think here we have such a split?

MS. HANN: What I have recorded is that there are eight people in favor of keeping the original language, which is at least five; and that there are now seven people who are in favor of the at least 10 which is the first alternative, and there would be no one now in favor of the 20. That is what I have written, and I'm getting some nods.

Eight to keep the original language; seven to go for the first alternative.

DR. INSEL: So in this case where there is - and looking around the table at the nature of the votes, it looked like in particular public members were those in favor of increasing the number of studies, I just

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wonder if there is a way to reflect that in the document, so that it doesn't come out with the sense that - this may be one of those places where we talked about how we are going to handle disagreement.

MS. SINGER: I think one way to reflect it in the document would be to increase the amount of money that is devoted to it. So that we would be able to be higher than five, given that it says at least five. I think the number would end up being determined by the dollars assigned. So that would be one way I think we would reflect that.

MS. BLACKWELL: This is Ellen. I think another way to address it might be to say at least five studies varying in size and scope, or indicate that there could be some what Gail suggested, diversity in the studies themselves, which is assumed but perhaps not stated here.

MS. REDWOOD: Della, what was the

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vote again? What were the numbers?

MS. HANN: It was eight to seven, and there are 15. There's two people on the phone.

DR. INSEL: And there are a couple of people at least who aren't attending. But we have a quorum.

MS. SINGER: So can I make the specific suggestion that if we are going to stick with at least five, that we at least move the estimated cost of doing 10 up to the at least five?

DR. INSEL: But the other point about that is, if I am looking at this right, it was 10 over five years, as opposed to five over two years.

DR. TREVATHAN: Not to muddy the waters further, but I think the comment that the question is not necessarily how many separate studies, but how much we can - how many gene-environmental interaction analyses can we really evaluate, regardless of whether

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you call it five studies or 10 or 20, and how good a job we can do.

I mean along these lines what we have figured out for example with the seed CADDRE study that given all the new susceptibility genes, and all the new - several environmental hypotheses we really need to increase our sample size with that to keep up with all the new hypotheses.

So I think that one approach could be - we need more funds, specifically on that probably about $17 million. So one approach would be to increase the budget for the at least five, then we can buy $15 million, $17 million, whatever we have here. Somebody made the suggestion of increasing it. But we could talk a little bit about the funding needed to try to take advantage of some of the new work we think needs to be done in gene-environmental interactions. I think some of us have some ideas on that. And that gets to maybe some of what Gail was saying and a lot

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of the concerns around the table.

DR. INSEL: Well, I'm going to suggest that we come back to this in terms of budget. It is a great suggestion that we may be able to have more of an impact by either increasing the size of the studies of the number.

We have set a floor. It doesn't have to limit anybody, but the budget might. So that may be the piece to revisiting. We will do that later in the process.

I want to move us through so we don't get lost in the rest of this. There is still an awful lot to discuss.

And that takes us up to page 12. There's again an alternative to the next short term objectives, which was to just delete the objective on the genomewide association studies, and the sequencing effort. And the recommendation from the public was to delete this objective because enough genetics research is ongoing. And I'm trying to see if

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there is anything here. It looks like comments from the group are not adding anything else.

Comments about this?

(No response)

DR. INSEL: Okay, who would be in favor of this addition which is now to delete this particular initiative on genetics. Can I see a show of hands for who wants to delete?

(A show of hands)

MS. HANN: There is a vote of three at the table.

DR. INSEL: And who wants to then go back to the original language - I'm sorry, we should make sure we get people from the phone. Anyone on the phone want to delete the objective?

DR. MORRISSEY: No.

DR. INSEL: Okay, and those in favor of retaining the original language, hands or voices?

(A show of hands)

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MS. HANN: Ten in the room.

DR. LAWLER: Yes.

DR. MORRISSEY: Yes.

MS. HANN: Plus two on the phone.

DR. INSEL: Okay, moving on to the next item, which is 3.13, the bottom of page 12, there is a recommendation to increase the number of biomarkers to 10, as opposed to at least three measures - well, we changed the word, validate, to identify. And then we - but we retained the original goal of three measures for identifying markers environmental exposure and biospecimens, and the recommendation is to increase the number of biomarkers to 10.

DR. LAWLER: This is Cindy. I think if we vote for that we need to push the timeline back a little bit or else think of a staged approach where we support biomarker development efforts in addition to more of a standardization of methods that are fairly well outlined at present. I don't think we

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can do 10 by 2011.

DR. INSEL: I think people thought about that at one point, but the concern was if we increased the number and we had to push the timeline back we wouldn't get this as a short term objective anymore. And in the original discussion there were a lot of people who felt that we really needed short term returns on the investment for this particular initiative.

But others either based on the original discussion -

DR. LAWLER: - having a long-term objective in development, and keeping this maybe more than three is reasonable, but I don't think 10 by 2011. I think that is a bigger effort.

DR. INSEL: Okay, but Cindy would you then take this one - are you recommending we take this out altogether and move it to long term? Or would you retain it as it currently sits?

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DR. LAWLER: I think we can do some work by 2011. Maybe three to five. But I think the alternative was 10 by 2011, and that may not be reasonable. I'd like to hear from Ed what he thinks.

DR. KOROSHETZ: This is Walter Koroshetz. I mean if you did this you would be really famous. This is really hard to do. Any disease people try to do it's hard to do once, let alone three times. So I would put this in the high risk category.

DR. LAWLER: Okay, but I think maybe the biomarker was used a little too loosely. What this objective is getting at is really methods for measuring markers of exposure, so not markers of disease so much, but just sort of standardizing the way people collect biosamples and measure organophosphate metabolites for example, to make sure that studies can be harmonized, and there can be some comparability.

DR. INSEL: Well, that is important

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to understand what we are talking about here. I had read this, Cindy, as surrogate markers, identify and standardize at least three measures for identifying markers of environmental exposure.

DR. LAWLER: Fine.

DR. INSEL: So they are not biomarkers in that sense.

DR. LAWLER: Correct. But I think what Walter, I think it was his comment, that it's just very difficult to do. And I thought he was thinking about biomarkers of the disease itself.

DR. INSEL: Okay, so who would like to include the addendum - or the alternative increasing the number of biomarkers to 10? Those in favor?

(A show of hands)

MS. HANN: The vote is four in the room in favor.

DR. INSEL: On the phone?

(No response)

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DR. INSEL: Those who want to retain the original language except to change the word, validate, to identify? Hands up.

(A show of hands)

MS. HANN: Eight. Anyone on the phone?

DR. LAWLER: Yes.

MS. HANN: So nine.

DR. INSEL: So the conclusion is that the final language is within the highest priority categories of exposures for ASD identify and standardize at least three measures for identifying markers of environmental exposure, and biospecimens by 2011.

We now have a whole series of additions -

MS. REDWOOD: Tom, was it three or five.

MS. HANN: At least.

DR. INSEL: At least, I'm sorry, at least three measures for identifying

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biomarkers.

MS. SINGER: So can we tag this one again for when we get back to the budget?

DR. INSEL: In terms of the budget.

MS. SINGER: Again, because it says, at least. The number will actually be determined by the budget.

DR. INSEL: This budget is not even close to what it costs to do what we are talking about. Yes, we will come back to it. Good point.

Page 13, we've got four potential additions to the short term objectives. What's the pleasure of the group here?

MS. SINGER: Can I suggest that we look at combining 3.14 and 3.15 and talk about initiating a large scale retrospective study to determine if the health outcomes including ASD among various populations with vaccinated, unvaccinated, and alternative vaccinated, and then include some of the language from 3.14 to specifically focus on cell populations.

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I'm reading from page 13, I'm reading discussion points 3.15 and 3.14, and I'm suggesting that they could be combined.

DR. INSEL: Alison, could you -

MS. SINGER: To specifically say a large scale. I mean I think this would have to be a very large group. And then if it were a large enough group we would be able to include in 3.15 a lot of the ideas expressed in 3.14.

MS. HANN: So if I might suggest that the language you are saying just to try to help be clear, so as I understand what you said - this is Della - to initiate a large scale study to determine if the health outcomes including ASD among various populations with vaccinated, unvaccinated, and alternative vaccinated groups, and understand whether and how certain subpopulations may be more susceptible to adverse effects of vaccine.

MS. SINGER: I would only - I would

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add the word, retrospective, large scale retrospective.

DR. INSEL: Duane?

DR. ALEXANDER: One of the problems with these is the unvaccinated groups. You really need to have a comparison sample you need - we are at 90 plus percent vaccination of these kids in the population. So you will have a very small number of unvaccinated or alternatively vaccinated kids to study. The National Childrens Study will have 100,000 kids to study, but we will only have for comparison unvaccinated 5,000 to 10,000. And that is barely enough, really not enough to give you a sample of sufficient size to make a determination of some of the issues.

DR. KOROSHETZ: This is Sandy. We talked about this a little bit earlier as well in line with some of Duane's comments. I think maybe what we need to do, we can assess the feasibility of conducting that sort of study. But I am uncomfortable with committing

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to initiating a study, because I think there are all these questions about can you come up with a study design that is going to be sufficiently powered and that you can deal with some of the biases of the different groups that will allow you to draw a reasonable conclusion.

So I would be in support of the short term objective of assessing the feasibility of that sort of approach, but not in actually including it as that we are going to initiate a study comparing these three groups.

DR. INSEL: Other thoughts?

MS. REDWOOD: I just, Duane's question, if you were to say, how many children did you say you might have in the National Children's study that hadn't been vaccinated?

DR. ALEXANDER: Five to 10,000.

MS. REDWOOD: So if you had 10,000 could you not look at total health outcomes in

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those 10,000 children compared to 10,000 age-matched controls that were completely vaccinated following the CDC schedule? I'm just curious. I'm just asking that question.

DR. ALEXANDER: You could do that. And in fact what we will have is essentially 90,000 age-matched controls. But the problem is for each one of those outcomes, the number gets small. And within the 10,000, the 5-10,000 cohort the numbers of any of those outcomes is going to be very small. And this is one of the things that has hampered vaccine studies all along is, the numbers of unvaccinated controls and the outcomes that are relatively rare demands a very large population.

We really seriously need to try and develop better methodologies to get the populations that we need for these kinds of studies. Because the studies that have been done all have suffered from the same problems of lack of numbers and so forth.

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Right now we don't have a very good way to do this. Within the National Children's Study, we can and we will address these issues, but it probably will not yield definitive answers on this kind of issue because of the unvaccinated sample that maybe quite different in composition in general from the vaccinated sample of kids.

So there is one example where this has worked pretty well in a different direction. If you take the case of post-vaccine encephalopathy, which has been around for quite awhile, people understand it, usually after DPT. And then in this case the syndrom resembles the severe myoclonic epilepsy of infancy. It resembles it so much that you would think it's the same disease.

And we know that the myoclonic epilepsy of infancy is caused by mutations in SCN1A. And those have been described and understood in the animal models. We know a lot about them. It turns out that there are

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other mutations of the same gene that explain about 80 percent of the kids with post-vaccine encephalopathy.

So there you don't need a big sample at all. You just need a target. You just need to know what you are studying. And then you can - there out of 14 children, because it's so rare, 14 in one sample, 11 of them had the SCN1A mutation.

So one might - the question in this case is whether you want to go after 100,000 children and do a huge fishing expedition to try to find something when you are not sure what you are looking for; or whether if you know this is happening in a subgroup you figure out what that target ought to be for the subgroup, and you chase them.

And really define you at-risk population. It's a different approach. And I'm not sure that this retrospective study of vaccinated versus unvaccinated - this is yet a third way to go at this as opposed to the

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prospective epidemiological effort.

And it's really - this is where you have to make judgment calls.

MS. REDWOOD: Tom, also, and I guess I would ask this question to Cindy regarding a report that came out of HHS that was headed up by NIEHS and CDC and Dr. Irva Hertz-Picciotto regarding the feasibility of doing these types of studies in the BSC data. And there were several recommendations in that study regarding how we could move forward to answer these types of questions. So I guess I sort of feel like maybe the feasibility of doing it has already been addressed in that particular report.

DR. LAWLER: I think those alternatives are separate kinds of study designs that really play to the strength of that database. So it's a little bit different from what we are talking about now.

DR. INSEL: Ed, you had mentioned before that there were other groups looking at

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the vaccine safety question. So again, I want to understand whether this even belongs in this discussion or not.

DR. TREVATHAN: Yes, I guess I would just reiterate that when we are talking about populations of children, vaccinated or unvaccinated, or you are just looking at outcomes of vaccines per se, that becomes more vaccine research as opposed to vaccine exposures that are looked at a component of autism research.

I mean there is a Venn diagram, I guess, and they overlap. But certainly I think that some of these issues that we are discussing, I do have concern that we don't have the makeup or expertise for the vaccine big population research on this committee to make these sorts or recommendations.

I thought Story's idea was a good one. Maybe there are questions we need to put forward to another committee and have them address. That's with the human studies.

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I guess the component that we haven't spent much time talking about, but it was under 3.14 that was added, looking at the cell in animal studies regarding vaccine components and multiple vaccine administration, that gets into some of the biomedical research related to vaccines. I don't know that we have expertise on that here either. I know some of that is being done at NIH, and some of you all know about that.

But I'm a little uncomfortable about that only because I don't know if we really have the expertise at the table on that science, on the cellular studies of vaccine safety. I know there are people that have expertise on that; I'm not sure that that's our group.

MS. REDWOOD: But again, if we are saying this is a high priority item that we want to see investigated, it would depend on the applications we get in as to how they design the study, and it would go through the

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scientific review process.

So I don't think again we are at that level of granularity, and I do think we have the capabilities now of doing primate studies and administering the full component of the CDC vaccine schedule to primates, and then not doing it in other infant primates, and looking at different cellular mechanisms, at different behavioral studies. We can do that research right now; it needs to be done.

So I guess I am just having a difficult time when I hear things like we can't really do this. We don't have the expertise. It's the National Institutes of Health for Pete's sake. I would think we could do this.

DR. INSEL: If I could just jump in here, because I don't want us to get overly hung up here. I think we have probably come to a place where we are not going to come to agreement, and it may be that it is your first statement about the priority of this, and I

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think that maybe - is this a short term objective that people want to see in the plan or not? I mean, bottom line, that is what we are going to have to decide. I mean we can play with the wording a little bit as Alison has recommended, but I think where the division is is whether people think this is a high priority to push out in the short term or not.

What we said under opportunities was that we wanted to at least look at the options and get a better handle on it. So this is in addition. We can put 3.14 and 3.15 together with language that Alison has recommended. I'm not so sure the language is what people will struggle with as the overall concept.

If it's okay with the group I'd like to do that. I'd like to merge 3.14 and 3.15, because they are, as I think Alison has said, conceptually linked, and it would be one initiative. And then we can decide whether

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people want to go forward with that or not.

MS. REDWOOD: Tom, I see that as two separate initiatives. Because I see one is an epidemiological study, and I see the other as being - using other approaches, cell lines, animal models, mechanisms. So I guess I would like to - personally I'd like to see them broken out because I do see them as separate initiatives.

DR. INSEL: Alison, microphone.

MS. SINGER: What if we said large scale studies to determine? And I was going to recommend, to your point, with regard to whether this is the purview of this committee or not, we could change health outcomes including ASD to prevalence, ASD, so that it's clear that it is the purview of this committee to make recommendations, instead of specifically focused on autism spectrum disorder.

MS. REDWOOD: I guess the only concern I have about that, Alison, is with

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regard to outcomes of - there are other things we have been talking about with regard to comorbidities, that I think whether it's mitochondrial dysfunction, whether it's gastrointestinal, immune, I think it'd be important to see whether or not those comorbidities also exist.

And that might help us also tease apart whether or not those comorbidities are a part of autism itself.

MS. SINGER: I agree. I am just suggesting that we put language in there that indicates that this is specific to autism, so that we address Tom's point, which is, is this the purview of this committee, or is this being handled elsewhere.

So I would be in favor of including what you are suggesting right now.

DR. INSEL: So give us the language that we are talking about. If we are going to modify any of these suggested additions, what would they say? Or do you want to keep them

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as is?

MS. SINGER: Well, I'm suggesting that we combine them to say, initiate large scale retrospective studies to determine - and this is where we have to change the language - if the prevalence and related conditions - what was the language that we used with regard to autism spectrum disorder among various populations of vaccinated, unvaccinated, and alternatively vaccinated groups, and understand whether and how certain subpopulations in humans may be more susceptible to the effects of vaccines. Co-occurring conditions is the language that Ellen is reminding me we selected earlier.

DR. INSEL: So would you be comfortable with a third alternative? When we put this to a vote we will have three choices? Am I getting that right?

MS. REDWOOD: But is that also including - because I hear retrospective, but I don't think that a retrospective type

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epidemiological study really gets at discussion point 3.14.

It's just that it's more broad. It includes animal studies, and not just human populations. And you can't really do a retrospective - well, I guess you could -

MS. SINGER: Well, you could say initiate studies including -

DR. INSEL: Why don't we do this? Go ahead.

DR. ALEXANDER: These are things that you are going to have to force together rather than things that go together naturally.

I'm also still concerned about the initiation of this study. This is - an alternative could be to design rather than initiate this study. Because this is not an easy thing to do. It's going to take a lot of expertise to put it together. And it's going to have some component of cost and population and numbers associated with it.

And this is something that is of

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concern not only in autism but in other conditions as well that children may or may not have in relation to vaccines. And this is something that has been under discussion at the Academy of Pediatrics with other vaccine interested organizations, within the department and elsewhere, just what - what approach could you use that hasn't been used to date, and would overcome the shortcomings of the studies that have been done to date, of doing a study that could answer these kinds of questions of reactions to vaccines - unintended reactions to vaccines, that go beyond just autism, but would address autism as a major component.

I don't think we are ready to initiate this kind of a study because of its complexity. We are ready to have a serious discussion about designing the kind of study that you would need to be able to do to answer these questions for autism as well as for other conditions.

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Now I could support a recommendation that said design this study, and do it quickly, so that we can then proceed to decide whether or not we have the resources and can implement it for autism and for other things.

I'm not sure I could support a recommendation to initiate it right now with the information that we have without a lot of work going into the design of it. And I think that epidemiologic study is sufficiently different from what is in 3.14, which is doing these studies in animals or cells to start with, which is quite different, particularly if you made it to design a study rather than to actually just start writing and carrying it out.

What are you saying, you would support 3.14, but 3.15 you would rather say to design the study, and have it a short, like one year, two year timeframe for designing?

DR. INSEL: Let's look at 3.14, and

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let's see if we can get some closure on this. So what is on the books here is a proposal to study the effects of vaccine, vaccine components and multiple vaccine administration and autism causation and severity through a variety of approaches: cell and animal studies; understand whether and how certain subpopulations may be more susceptible to adverse effects.

The alternative is none of that, and we haven't heard, other than the sense of moving this in together with 3.15, any alternative to this language.

Are we ready to vote on whether to include this or not?

Who would like to make this addition? Hands up.

(A show of hands)

MS. HANN: One, two, three, four, five, six -

DR. INSEL: This is initially, just separate, 3.14 separate.

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DR. LAWLER: I support including it.

MS. HANN: Wait a second. Since we've had this discussion, can I see the number of people who wish to have this included? Just 3.14, correct?

Six in the room. Anyone on the phone?

DR. LAWLER: I support it.

MS. HANN: So seven in favor. Pat?

DR. MORRISSEY: Nope.

DR. INSEL: And then those opposed to this addition?

(A show of hands)

MS. HANN: One, two, three, four five in the room.

Those on the phone?

DR. INSEL: Anyone opposed on the phone?

DR. MORRISSEY: I am confused.

MS. HANN: We are talking about –

DR. MORRISSEY: I do not want to

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include it.

MS. HANN: Okay. So that would be six. Seven in favor.

DR. INSEL: Did we lose some people?

MS. HANN: There are some people who haven't voted.

MS. SINGER: Is there an option to combine them together?

DR. INSEL: So then that would be a third option which would be to put 3.14 and 3.15 together in some form, as you suggested. But so Della, as you say the numbers, it sounds like the addition as we have it here has now passed; is that right?

MS. HANN: It has seven in favor, and there were six who voted to exclude, and then we had two who abstained.

DR. INSEL: Okay, we are moving on -

MS. SINGER: I just want to be clear. I don't want to abstain. I want to

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include them together. So that is not abstain.

DR. INSEL: But at this point the motion has passed to have 3.14. The only issue would be if you wanted to vote against it, in which case the motion would actually be locked.

MS. SINGER: We should clarify that the default is always to leave the document as it was rather than add or subtract.

DR. INSEL: Okay, and that we can use for the next discussion item which is 3.15, initiate - and here we have had some recommendations for change in language, but one of the alternatives is to change the word, initiate, to design an epidemiological study on health outcomes.

DR. TREVATHAN: I would just make one suggestion. We had - where we said we were going to determine the feasibility and design. I think some of the issues that Story

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raised before that I think are valid and consistent with some of Duane's concerns about sample size and bias we all share is the whole issue of the feasibility. I know that is within the question of design. But I think we need to make sure we address the question of, are these - can we design studies that can feasibly - that are feasible that can answer the question scientifically that we all may have.

So I would just add, determine the feasibility and design.

DR. INSEL: Okay, so we have now three options. One is the default, which is no addition. The second option is the language as you have it in front of you, which is to initiate the study, and the third would be to -

DR. ALEXANDER: Design and determine the feasibility.

DR. INSEL: Thank you.

Those in favor of the default

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option, hands up.

(A show of hands)

MS. HANN: There is a vote of one for the default.

DR. INSEL: On the phone.

(No response)

DR. INSEL: Those in favor of the language as we have it in front of us, to initiate an epidemiological study.

(A show of hands)

MS. HANN: The vote is four in favor. Anyone on the phone?

(No response)

DR. INSEL: And those who would say to design and -

MS. HANN: Determine the feasibility and design of epidemiological studies to determine - et cetera.

DR. INSEL: In favor?

(A show of hands)

MS. HANN: Six in the room.

DR. INSEL: On the phone?

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DR. LAWLER: Yes.

DR. MORRISSEY: Yes.

MS. HANN: So that is a total of eight.

DR. INSEL: So again, Della, can you read us the final language for the 3.15?

MS. HANN: To determine the feasibility and design, an epidemiological study to determine if the health outcomes, including ASD, among various populations of vaccinated, unvaccinated and alternatively vaccinated groups.

DR. ALEXANDER: "If" should come out; it doesn't make sense.

MS. HANN: Okay, fine.

DR. INSEL: Thank you.

Okay, 3.16, initiate efforts to expand existing large case control and other studies to enhance capabilities for targeted gene-environmental research.

Does anyone want to speak to that addition, short term addition?

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DR. LAWLER: This is covered under long term objectives, but this is in addition to do something more short term?

DR. INSEL: That is right. The only question is whether to move it into short term from long term.

All in favor of putting this addition in place as opposed to leaving it in long term?

(A show of hands)

MS. HANN: The vote is six in favor.

DR. INSEL: Actually one more.

MS. HANN: Seven in favor. Eight in favor, Ellen you had your hand up? Okay, eight in favor. So that is to add this to the short term, correct?

DR. INSEL: Yes, and I'm assuming, speaking on behalf of the team, I'm assuming that short term means by 2011.

MS. HANN: There is no assumption to that effect. It's up to this group to

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determine whatever the year date. When these additions were provided to us, people didn't provide dates.

DR. INSEL: So can we get some response from the committee for this one and for any of the ones that we are adding to short term, 2011 is the date we are talking about, or is it something else?

In favor of putting in 2011 for each of these short term objectives, can I see a show of hands?

(A show of hands)

MS. HANN: Thirteen in the room. Gail, I can't see you very well.

DR. HOULE: Well, that one I'm going to let you all determine.

DR. INSEL: The number, Della, does that pass?

MS. HANN: Yes, 13.

DR. INSEL: Then the last addition for short term -

DR. VAN DYCK: Did we finish the

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vote on that?

DR. INSEL: Sorry?

DR. VAN DYCK: Did we finish the vote on that?

DR. INSEL: On what?

DR. VAN DYCK: On 3.16?

MS. HANN: Yes, we did.

DR. VAN DYCK: Didn't we just take half the vote?

MS. HANN: Eight people wanted to have it added.

DR. INSEL: Then on 3.17, new and existing case control studies with enrollment of a broad ethnically diverse populations affected by ASD.

Comments?

DR. KOROSHETZ: I would just say that we should be doing that in all the studies we do as opposed to doing it separate. I mean you would like not to have some that are not broadly ethnic. So I think that should be a generalization in all studies.

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DR. INSEL: Rather than a short term objective.

DR. TREVATHAN: If it is short term, it obviously is going to be difficult to do new, big case control studies by 2011, because those things take time if that is the kind of time line we are talking about. So I don't known if this gets to the intent, but if you changed it to enhance existing case control studies, by increasing enrollment of ethnically diverse populations, there could be - because I know that is an interest that a lot of groups have. So I don't know if that gets at the intent. And then of course the cost would have to be determined.

DR. INSEL: I think there is language in the introduction that really goes after this issue that in all of the clinical efforts these have got to be inclusive and ethnically diverse. So the only question is whether we want to support some new and existing studies with this as a focus or

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whether it's something that we would expect of all the studies.

In favor of adding this language, see a show of hands?

(A show of hands)

MS. HANN: The vote is four in favor.

DR. INSEL: On the phone?

DR. LAWLER: This is the change that Ed has described?

MS. HANN: No, this is the language that is proposed. DR. LAWLER: I want to vote on Ed's revision, so no to the language.

DR. INSEL: Okay, then Ed's revision, which was -

DR. TREVATHAN: To enhance the funding of existing case control studies to enroll a broad ethnic and diverse population. So really just to scratch the new and just say we're enhancing existing case control studies, which is something we can do more as a short term.

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DR. INSEL: IN favor?

DR. KOROSHETZ: You mean this is like -

DR. INSEL: This is going to be a problem if we change the language.

DR. KOROSHETZ: No, but I'm just saying, I don't think he means what he's saying. Funding of existing, so if we did something in the future it wouldn't have to be - so it's existing in the future, right? To enhance the funding of existing and future studies to include.

DR. INSEL: Is that a short-term objective, or is that something that should just be in the - part of the mission statement, part of the set of values? Is this really - I guess I'm still struggling with - the fact that you say it means that somebody wouldn't do it. At least for my institute, you don't get funded unless you do this.

DR. TREVATHAN: This is sort of part of the fabric of what we are supposed to

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do. I think we all find it sometimes difficult.

I mean if you look at how easy is it to include for example Native Americans in studies. That's easy to say and difficult to do and sometimes requires additional resources. I don't know if that is what you all were thinking of when this was added. But if that is where we are going, then it does make sense to me to try to have some small emphasis and perhaps some additional funding.

But otherwise I agree with you. I think this is part of what we all try to do with all of our epidemiological studies.

DR. INSEL: Okay, so we're in the middle of a vote. We've kind of moved away to have a further discussion.

We've got some people who have voted for - I'm losing track here, Della.

MS. HANN: We had four people who voted to accept the new language as it is currently written.

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DR. INSEL: As is? Ed has recommended some additional change, and we need that language for the next part of this vote.

Enhance?

DR. TREVATHAN: Yes, enhance existing case control studies to enroll broad ethnically diverse populations.

DR. INSEL: In favor?

(A show of hands)

MS. HANN: Vote is eight.

DR. MORRISSEY: Yes.

MS. HANN: And nine from the phone. Anyone else on the phone in favor of that?

(No response)

DR. INSEL: And the final option is the default to go back to the original language in the left-hand column, which is none of this.

In favor?

(A show of hands)

MS. HANN: Four in favor of not

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adding at all. Anyone on the phone?

(No response)

DR. INSEL: Okay, we are going to finish this chapter before we break for lunch. I am determined to get through Chapter 3, which takes us to the long-term objectives. We are on page 14, and we are going to run through some of the same points - actually some of the same issues. On the top of page 14 the question is whether we move from 2012 to 2015 for the environmental factors. That was the recommendation that came out of public comment.

The other one is an alternative that we move to 20 environmental factors instead of 5 by 2012.

What is your pleasure?

(No response)

DR. INSEL: And lunch is not an alternative. So comments about these? Do you want to just go through and start voting? Okay, we can do that.

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So we have in front of us three options, the original language which is in the left-hand column, the paragraph at the top of page 14, or the alternative shown beneath that which goes from 5 to 20.

Can I see a show of hands for the original, the default option, which was five environmental factors by 2012?

In favor?

(A show of hands)

DR. INSEL: On the phone?

(No response)

DR. INSEL: The second option is five environmental factors by 2015.

In favor?

(A show of hands)

MS. HANN: Seven.

DR. INSEL: On the phone?

(No response)

DR. INSEL: And the alternative is 20 environmental factors by 2012. This includes the risk for subtypes and the pre and

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early post-natal period.

DR. LAWLER: Tom, what about the language at least five to eight over five years? That is not an alternative?

MS. HANN: That is part of the budget consideration, Cindy. That wasn't - because it says at least five, when we were computing the budget we thought, well, five is sort of the bottom, so we gave it a range.

DR. INSEL: So I need votes on the alternative of 20 by 2012.

In favor of - sorry, Stephen, we are midway through page 14 - in favor of this third option, hands up?

(A show of hands)

MS. HANN: We have a vote of five who are in the room who are in favor.

DR. INSEL: Anyone in favor of this on the phone?

(No response)

DR. INSEL: Della, give us the numbers again and tell us what we have

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decided.

MS. HANN: There were no votes for the original language. There were seven votes in favor of changing the date to 2015, but leaving the number of studies to at least five, which is the language that is proposed in the second column. And there were five votes in favor of making it up to at least 20 as well as some additional language.

DR. INSEL: Moving on to 3.19 -

MS. SINGER: Before we move on, can I ask that we again flag this one when we get to the budget?

DR. INSEL: Actually, that's why that language is in there about at least five to eight. The team had done that already. We'll need to come back to that on the budget.

MS. REDWOOD: Della, what were the votes on that again?

MS. HANN: There were seven in favor of moving it to 2015, and there were five who were in favor of moving it to 20. So

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not everybody is voting.

MS. REDWOOD: And the people on the vote got a chance to vote?

MS. HANN: Yes, they did. The people on the phone also had a chance to vote.

DR. INSEL: Number 3.19, we've got the original language which was a multi-site study of the subsequent pregnancies of 1,000 women versus the additional language to add monitor environmental toxins, to add the statement most relevant to the progression, pre-natal period and first three years of life, in parentheses, then to add: this study should include a control group or use methods comparable to the National Children's Study.

Comments?

MS. BLACKWELL: I think whichever one we adopt we need to clarify - and I'm not sure the best way to say this - that the child be a child of any age. If we really want to get a representative age here, it could be a child who is 25, and a mother who is 50 for

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example. Does that make sense?

DR. INSEL: So you'd be looking at her pregnancy - I mean it is possible that a 50 with a 25-year-old could be pregnant. But this is specifically to look at pregnancies.

MS. BLACKWELL: Okay, I hear you.

DR. INSEL: Other comments or issues?

I had a question here about - and maybe this is for Duane - it says using methods comparable to the National Children's Study. So I'm not sure what that means. Does that mean that it is prospective and longitudinal?

DR. ALEXANDER: Prospective, as well as the environmental exposures that would be assessed.

DR. INSEL: Okay.

DR. ALEXANDER: We will have included in this overall sample of 100,000 some women with previous child with autism, just by chance alone. There is no deliberate

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attempt to recruit to the study women with a previous child with autism. The numbers that we will obtain just as a - in the course of the study, I don't know what that number will be. It will be nowhere near 1,000. You will either have to do a separate study or modify the National Children's Study to oversample specifically or selectively sample an additional cohort of women with a previous child with autism.

DR. LAWLER: So there is a separate study, the early study, that will begin enrolling and plans to enroll up to 1,000 women.

DR. ALEXANDER: Yes, that starts in January. That is a pilot cohort.

DR. LAWLER: No, this is one of the A centers.

DR. ALEXANDER: Oh, I'm sorry.

DR. LAWLER: The study design. It's not - doesn't have the funds to enable it to do the sorts of sampling in terms of

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environmental exposure sampling that will take place in the National Children's Study.

DR. INSEL: So this was already in there. The intent has always been to do this as an objective. The only question is whether to add in the environmental toxins, and whether we need the additional sentence that says, this should include a control group or use methods comparable to the NCS.

And Cindy, in terms of design, does it need a control group, or can the unaffected sibs -

DR. LAWLER: The control group is siblings.

DR. INSEL: Okay.

DR. LAWLER: Probably the best control group.

DR. INSEL: So is it useful to have this sentence in there that this study should include a control group, or is that just understood?

DR. LAWLER: No. I'm in favor of -

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I think the original language was sufficient.

DR. INSEL: Okay.

All right, let's go to a vote and move this along.

Those who want to retain the original language, those in favor of the default?

(A show of hands)

MS. HANN: A vote of eight.

DR. INSEL: We are on 3.19, this is the left-hand column.

MS. HANN: Ten. So there were 10 people in the room with their hands up to accept and go for the original language which is in the left-hand column. Is there anyone on the phone?

DR. LAWLER: Yes, I want to keep it

DR. MORRISSEY: Yes Pat.

MS. HANN: Okay. So that’s a vote of 12.

DR. INSEL: Okay, we are moving on

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to 3.20. And here the original language is, risk factors in at least 50 percent of children by 2014. The alternative is just to drop this. And the second alternative is, 2014 does not seem realistic; should extend timeframe.

Comments?

MS. BLACKWELL: I had a comment about this. I was a little bit confused when I read the original language. Are we looking at genetic risk factors in just children or in everyone who has autism? I mean it was unclear to me.

DR. INSEL: That is a great point. Why does it say that? I have no idea. Does anyone have an explanation?

MS. BLACKWELL: I mean I think there would be more utility in looking at genetic risk factors in people with ASD.

DR. INSEL: That is an alternative.

Other comments about this?

(No response)

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DR. INSEL: So Ellen, you have just given us a fourth alternative. So the original one would be 50 percent of children by 2014. The second is, delete completely. The third is, extend the timeframe but not referred. And the fourth is, to change the language to take out children and say, in at least 50 percent of people with ASD by 2014.

In favor of the original language?

(A show of hands)

DR. INSEL: Anyone on the phone?

(No response)

DR. INSEL: The second alternative is to drop this. In favor?

(A show of hands)

DR. INSEL: Anyone on the phone.

(No response)

DR. INSEL: Third -

MS. HANN: Wait, wait, sorry.

DR. INSEL: Okay, we have two people who want to drop this objective.

MS. HANN: Okay.

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DR. INSEL: And then the third alternative is to extend the timeframe, and we will have to decide what that will be.

(A show of hands)

DR. INSEL: On the phone?

(No response)

DR. INSEL: Fourth alternative is Ellen's language, identify genetic risk factors in at least 50 percent of people with ASD by 2014.

(A show of hands)

MS. HANN: And the vote is nine in the room.

DR. INSEL: On the phone?

DR. LAWLER: Yes.

DR. MORRISSEY: Yes.

DR. INSEL: Okay, so we will change the language by replacing the word children with people. Children are people but this is more inclusive.

Okay, we have - towards the bottom of page 15 there is a line 18. There was an

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inclusion of U.S. populations. Population-based epidemiological studies including U.S. populations. Do we need to include that as an addition or not? This came from public comments.

MS. HANN: I think this came out from one of the work group meetings, and we were talking about adding on to some of the existing studies in other countries. And I thought it was important that there be studies here looking specifically at the United States, because our risk factors, our environment, may be a little bit different than other countries.

DR. INSEL: Other comments?

So in favor of including this specification? Oh, we do. But the alternative which actually does deal with this in part - okay. Why don't we do this? We can make that a third option, which includes even more than the U.S. population. But Lyn, do you think that we need both?

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MS. REDWOOD: Well, the alternative looks like it's including everything that was in the proposed language that included the U.S. populations. The main difference I see is the estimated cost is increased. Is that correct? Am I reading it right? So I see that as a difference between the two is that the funding has increased.

DR. INSEL: So why don't we do this? We can make this easy if we just include the language you talked about, which is including U.S. populations. We will have a choice between the original language, that addition, then we can deal with the budget issues separately.

Ed and then Ellen.

DR. TREVATHAN: So I think the - just to clarify I think this changes the intent. But technically it certainly, in some places like the CDC, epidemiologic studies and surveillance are different categories, and I think are subsumed here together. But it

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would be just helpful to clarify that if we have just have population based surveillance and epidemiological based studies, we'd have a bigger - it's just a bigger umbrella for this.

DR. INSEL: Do you think we need to specify that?

DR. TREVATHAN: Yes, because it's actually different in terms of some of the way some of the funding, the legislation is done, and actually some of the public health regulations and so forth for collecting the data are different. That was brought up by some of our policy folks that we needed to do that.

DR. INSEL: Any other comment about that? That would add the word, surveillance, it would be surveillance and epidemiological studies.

Ellen?

MS. BLACKWELL: I guess my question is, in adding those words, in including U.S.

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populations, does that imply that we did not include those populations in the original language?

DR. INSEL: Well, this came up in the discussion. There are some very large-scale studies underway in Norway and Denmark that we are very excited about for case control. And some people felt that is a great opportunity, but we should also think about what needs to be done within the U.S., because in terms of environmental factors they could be unique. So I think that is where this came from, although I suspect just the nature of this field that some of the initial studies will probably build on what has happened already in Norway or Denmark.

So let me read what I think is now the alternative to the original language, which is, support ancillary studies within one or more large-scale population surveillance and - it should be or - epidemiological studies including U.S. populations.

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DR. TREVATHAN: So if we could have that, it could be and.

DR. INSEL: Okay, surveillance and epidemiological studies, to collect nested case control data. And the alternative then is between the original language and this addition.

If people feel that we need to break those two things apart we can vote on them separately, but I don't see a lot of energy for that. So we will start with the default, the original language, in favor?

(A show of hands)

MS. HANN: There are no votes in the room.

DR. INSEL: Anyone on the phone?

(No response)

DR. INSEL: The changes in favor of this alternative language?

(A show of hands)

DR. INSEL: And on the phone?

(No response)

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MS. HANN: That was unanimous.

DR. INSEL: And then we have one more additional objective, which is at the very end of page 15, and this will finish off Chapter 3, maintain and increase sample sizes of existing comprehensive case control studies to ensure that they can effectively address GXE interactions from moderately common exposures, and genes with prevalence of 5 to 15 percent or vice versa, moderately common genes and exposures with slightly lower prevalence by 2015.

Do we want to go there, or is this something that we can deal with in version 2.0?

DR. LAWLER: I think it is too much detail.

DR. INSEL: It is a little granular?

In favor of the default, which is to not add this? People who want to maintain the status quo?

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(A show of hands)

MS. HANN: The vote is 10 in the room.

Any on the phone?

DR. LAWLER: This is to keep it?

MS. HANN: No, this is to not add it?

DR. LAWLER: Fine, yes, I want to do that, not add it.

MS. HANN: Okay.

DR. MORRISSEY: Pat, yes.

MS. HANN: And Pat does as well. Okay?

DR. INSEL: Actually, my own notes say - I actually thought this was a good thing to do, but I thought it was already in there. I think it is actually in - it is more specific than the language we already have. So I don't think it needs to be added.

Okay, that's it for Chapter 3; terrific. I knew this was going to be the hardest part of the whole thing.

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We have a little less than four hours left to do all the rest of this. I think we need a break to grab lunch. Can I ask you to bring your sandwich back here and we'll keep working. There is a cafeteria just at the end of the hall. You keep walking across the lobby and there is a cafeteria on the other end, and we will reconvene as soon as you can get your food and we can come back.

(Whereupon, the above-entitled matter went off the record at 12:15 p.m. and resumed at 12:34 p.m.)

DR. INSEL: All right. We have about three hours left to do a huge amount of work. And I really don't want to have another meeting. So while we eat, let's begin this piece on Chapter 4.

And let me make sure that members of the committee who are on the phone are with us. Pat and Cindy, are you still with us? Are you with us but you are on mute?

MS. HANN: I bet they are eating.

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DR. INSEL: Okay, well, so do we have a quorum?

MS. HANN: Seven, no we don't. So that's eight.

DR. TREVATHAN: Duane will be here in just a minute.

MS. HANN: No, Lyn's here.

DR. INSEL: Where is Lee?

MS. HANN: I don't know.

MS. HANN: Here comes Duane.

DR. INSEL: Walter, don't go to far.

MS. HANN: And here comes Judith. We are good.

DR. INSEL: We now have a quorum, and hopefully we will get Pat and Cindy to join quickly.

We are on page one of Chapter 4, and there is a recommendation at the bottom of that page, again, from public comments, on occupational therapy improved functioning - I think it should be can improve functioning in

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everyday activities such as eating, bathing and learning, as well as sensory integration, period.

So also there is a recommendation from Lyn that on page one, line eight, that we add in language that says - Lyn is with us, so do you want to read it to us, Lyn? I wanted to wait until you were chewing before I asked you to do that. I can help. Why don't I just to save time.

Although autism is defined and diagnosed by deficits in core behaviors, accumulating evidence suggests that the breadth of this disorder extends well beyond the behavioral diagnosis. There is increasing recognition that the multiple systemic issues in autistic children may influence vulnerability, onset and severity of symptoms and behaviors. Accordingly, the comprehensive care model of the Autism Treatment Network is based on the premise that treatment of systemic abnormalities in autistic children

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will improve joint attention and learning capacity so that maximum benefit from behavior therapies can be realized. The systemic component of autism supports the possibility that both the core behaviors and medical issues have a convergent mechanistic basis that if identified could provide new insights into treatment targets, candidate genes, and strategies for prevention.

So that would be additional language to add into line number eight under what we know. And actually Lyn I think you intended it as replacement language, so for that first paragraph.

Comments?

MS. REDWOOD: Tom, it sort of is basically what is there, but it is a little bit more exclusive.

DR. INSEL: Well, I think it's not just - it's more explicit. It is also conceptually a step beyond. It's saying, we can use this to understand something more

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fundamental about the disorder. We have to rethink what this disorder is. It is not simply the behavioral core symptoms, but there are many manifestations.

Judith or any other comments or questions?

DR. COOPER: Well, I was just wondering about the appropriateness of targeting or mentioning the Autism Treatment Network and maybe other models in this sort of introductory section. We haven't been specific I guess in our introductions - well, so that is my question.

MS. REDWOOD: I just sort of had that in there as support for looking at these other medical comorbidities. So if you are not mentioning that I think that would be fine. Just remove that sentence.

MS. HANN: So this is Della, just to help keep us moving, so we could I think Lyn just indicated that we could remove the sentence that begins with "accordingly," which

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mentions the ATN essentially, and just take that part off the table for consideration.

DR. INSEL: Okay, if we do that, can I get a show of hands for people who would replace the first paragraph, that is from lines 8 to 15, with that addition, Lyn's recommendation without the ATN sentence.

In favor?

(A show of hands)

MS. HANN: Thirteen; everybody in the room. Anybody on the phone?

(No response)

MS. HANN: There isn't anybody on the phone I don't think right now.

DR. INSEL: Okay, well, we have a quorum; we are going to keep moving.

We are moving down to the very bottom of the page where there is a line about occupational therapy can improve functioning in everyday activities, and as well as sensory integration. That is a modification of the original language. Are you in favor of that

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modification or should we go back to the original? This is at the bottom of page one, of the lines 21 and 22.

Original language, in favor?

(A show of hands)

MS. HANN: I see a show of one hand for the original language.

DR. INSEL: And the modification in favor?

(A show of hands)

MS. HANN: I see eleven.

DR. INSEL: Okay, on page two there is also a recommendation for a change on line 16 and 17. It's actually in addition, it says for those who improve the resulting cost savings are significant, with a reference to that to support it.

MS. BLACKWELL: I'm actually not in favor of including this language. We don't know exactly what the cost savings are or if they are significant, or if they are even limited to those who improve. So I don't

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believe we should include this sentence.

DR. INSEL: Other comments?

MS. REDWOOD: My son has made dramatic improvement. He no longer has speech therapy, physical therapy, any therapy. He does grade level work. I can't imagine that that wouldn't be a cost savings just from what we were paying for out-of-pocket services that we don't pay for anymore. I mean that is my N of one, but -

DR. INSEL: Is there - has there been a good - there's an economic analysis of the cost of autism. Is there an economic analysis of the treatment? Treatment interventions?

MS. BLACKWELL: No.

DR. HOULE: To my knowledge there is not. I would be in favor of taking it out, because sometimes the misconception is that unless you can prove the cost savings to someone or another, that intervention is not worthwhile, or how much intervention is

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worthwhile and at what price.

So you start to say, well, this child made this much improvement at this much of a cost. Well, it's not enough of a cost savings to justify an expenditure. So I don't think there are figures, and I don't think there are data that you can tie that to, and I would not go there as a basis for looking for positive outcomes for treatment.

DR. TREVATHAN: So in other words we don't want to give the impression that we would think it has to save money or the treatment is not worthwhile?

DR. HOULE: Right, and we faced that generally in special education in the past. If you have a child with severe cognitive limitations or disabilities and you work very intensively with that child, it - and then you try to put a price tag on the measurement of what you have done, people have used that as kind of a fix-it model, if you can't fix it why spend money on the

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intervention. Eventually that could lead to that.

DR. INSEL: So are you suggesting - a counter-argument to that is that since this is a document that is going to be advisory to the new secretary, and the new secretary who was named yesterday at least as a nominee has made it very clear that comparative effectiveness and health care reform will largely depend on showing the cost efficacy or the comparative costs of the various treatments that are available.

They are very sensitive, for the first time in some ways, to the cost of the interventions that we have currently as opposed to ones that we are developing.

MR. SHORE: Possibly replacing that sentence with something to the effect of, for those who improve the resulting quality of life are significant, something of that nature. So talking about quality of life may be a better way to go about it, because that

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is what we are looking for anyway.

DR. INSEL: Right. Let's see if we can come up with some final language for that. So for those who improve the resulting benefits and quality of life may be very significant or something like that?

I'm also suggesting that there may be some value, excuse the pun, also suggesting that treatments may turn out to be - even if they are costly they may actually save money if they mean that you are getting people back to work or able to work or you are able to actually have an economic consequence. It's not the only reason to do it, but beyond even quality of life there is an economic argument to be made here for providing treatments.

MS. BLACKWELL: Then I would have to say, Tom, that it goes beyond treatment. It also goes to what sorts of services and supports. For example, health with employment. I mean I'm just not sure this is the place to put this sentence.

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DR. INSEL: I don't want to get bogged down in this.

MS. BLACKWELL: We have a whole other section on services later.

DR. INSEL: We have another section; we'll talk about that.

So one option is simply to leave it out and deal with it later. The other option is to have this revision as it's on the page. And the third would be to change to Stephen's language to talk about the quality of life impact for those who improve, even though that may in some cases be understood.

Hands in favor of those who want to just leave this out altogether and go back to the default?

(A show of hands)

MS. HANN: Ten.

DR. INSEL: On the phone?

(No response)

DR. INSEL: I think at 10 we are ready to move on.

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MS. HANN: So the vote was to not include.

DR. INSEL: Then we are on to page three, where there is language that is coming from public comment. Some therapists and parents question the effectiveness of ABA and emphasize the effectiveness of alternatives, and there are a few mentioned. Others look to the conclusions and recommendations of the 2001 NRC report, Educating Children With Autism, for insight regarding effective educational interventions for young children with ASD.

And Lyn, your comment was that we don't really need to put this in here; that it's probably - so any other comments?

MS. BLACKWELL: I agree with Lyn. I don't think the language is necessary.

DR. INSEL: Others?

MR. SHORE: If we put it in, I might even just insert, some therapists and parents question the effectiveness of ABA as

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the only intervention. That's if we vote to include that language.

MS. BLACKWELL: The only other comment I could add is that there - that it almost sounds as if we are endorsing one type of ABA when there are many treatments that fall under that umbrella. So I just think it's better not to include it at all.

DR. INSEL: Okay, those in favor of the original language which excludes this paragraph?

(A show of hands)

MS. HANN: Eleven.

DR. INSEL: And those - I guess we're done.

Moving on to page four, we have an addition from Lyn, line seven, and then there is - there were changes made from public comment which are shown in that middle box. So we actually have at least three alternatives here. We have the original, the public comment version, and we have Lyn's

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paragraph which is shown in your supplementary material.

Comments?

(No response)

DR. INSEL: You want to take this to a vote and just move on?

Those who are in favor of the original version?

(A show of hands)

MS. HANN: There are two votes - oh, I'm sorry, three in favor.

DR. INSEL: So this is the default; the left-hand column.

Those who are in favor of the - anyone on the phone voting for the left-hand column, the original?

(No response)

DR. INSEL: The right-hand column which is the piece from public comment, in favor?

(A show of hands)

MS. HANN: Eight.

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DR. INSEL: And then Lyn's version which is the longer and more specific. In favor?

(A show of hands)

MS. HANN: One.

DR. INSEL: All right, moving on.

There are two rather brief changes in the bottom paragraph on page four adding in issues of safety. So it's changes, efficacious interventions. Under what do we need, efficacious has been changed to safe and effective. Going forward, instead of saying attention is needed, it says, rigorous scientific studies are needed to develop and safely test. Those are two small changes at the bottom of page four.

Any comments about those?

(No response)

DR. INSEL: Okay, in favor of including those changes?

(A show of hands)

MS. HANN: Twelve.

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DR. INSEL: We are moving on to page five.

And here we have on line 11 a treatment that says - I'm sorry, a change that says, special attention is needed on treatment of co-occurring medical issues, which was the addition from public. Lyn has a - let's see, has some additional language here, on the same line, page five line 11, the identification of biomarkers in plasma, saliva, CSF or tissue is necessary to provide insights into targeted treatment strategies designed to improve or reverse autistic symptoms as well as insights into preventive measures. Further if biomarkers present in autistic children - present in autistic children are found to be present in infants and toddlers at high risk for developing autism, targeted intervention strategies to normalize these biomarkers could be tested for potential to arrest or reverse the symptoms and progression of autism.

Comments? This is actually not -

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this sort of preemptive idea, predictive preemptive, is not in other texts I don't think in this introductory section. We did mention it in the overall introduction, but since this about treatment, an argument can be made for including this here to really push the agenda for early diagnosis.

Alison?

MS. SINGER: I think this would be good to add. I would just say, for example, so that we are not limiting the biomarkers to the four listed.

DR. INSEL: Okay. So and this again this would not be instead of language that is in the current text, right? This is in addition, Lyn?

MS. REDWOOD: It would go at the very beginning.

DR. INSEL: It would go before special attention is needed, right?

So can I get a show of hands if we add, for instance - well, wait a second. If

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this would be beginning the paragraph, you wouldn't want to say for instance.

MS. REDWOOD: The identification of biomarkers, for instance, the plasma, serum, saliva -

DR. INSEL: Thank you. The identification of biomarkers for instance in blank blank blank. Okay.

In favor of including this additional language?

(A show of hands)

MS. HANN: Eleven.

DR. INSEL: Done. And the addition of the word treatment in front of co-occurring medical issues. In favor?

(A show of hands)

MS. HANN: Ten.

DR. INSEL: Right, we are moving on to page six. This is discussion point 4.3. And we have the addition of a line that says, not only marked improvement in their symptoms, or to fully recover from ASD. And that would

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be the one change to the text here.

Discussion? Stephen?

MR. SHORE: I haven't met everybody with ASD, or at least not yet anyway. But I have always seen - someone has been diagnosed with autism, I've always seen something. And saying, fully recover, seems to denote a cure to me, or an elimination of autism. There is always something there. Maybe it takes one to know one, but I do see it. So maybe we should fiddle with those words in there, or even not have them at all.

MS. BLACKWELL: I actually - I agree with Stephen, and I would even suggest that I think this makes it sound like autism is an illness. I mean as do the words and their symptoms. I would propose we just say, show marked improvement, with the comma after that.

DR. INSEL: Well, maybe this is a term of art, so maybe it's worth referring to what the word recovery means in this context,

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which is usually it means to be fully functional, to be able to work, to have a fully enriched life. And it's been an issue for other communities that have not wanted to use the word, cure, who have accepted the word, recovery in that context.

But if you think it's a loaded term, it's good for us to know that, because we don't want to send a different message than the term of art, recovery.

MR. SHORE: Yes, I think it's quite loaded, full of gunpowder.

DR. MORRISSEY: I support what Ellen and Stephen said. I would recommend that be not included.

DR. INSEL: Other discussion?

MS. SINGER: Can we also delete the words, and their symptoms?

DR. INSEL: So if you are going to say, marked improvement, what would that refer to if not symptoms?

MR. SHORE: Quality of life.

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DR. TREVATHAN: It would be improvement in functioning and participation in communities and so forth without necessarily an objective improvement in a symptom as measured by some professional, and we don't want to discount that.

DR. INSEL: So, Ellen, your motion would be to stop at marked improvement, and then comma, little is known about the characteristics of these individuals. So you would take out everything after improvement in both the original and the revised version?

MS. BLACKWELL: I think we could say quality of life, but marked improvement, doesn't that just sort of leave the door open?

DR. INSEL: Yes, I think it's the least specific and maybe the most useful.

So we have three options. The original option, which said marked improvement and their symptoms. The second option which says, marked improvement and their symptoms or to fully recover from ASD. And the third is

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just to stop at marked improvement.

So in favor of the original version?

(A show of hands)

MS. HANN: There are no votes in the room.

DR. INSEL: Anyone on the phone?

The revised version, fully recover from ASD?

(A show of hands)

MS. HANN: There are no votes in the room.

DR. INSEL: And the final suggestion, just marked improvement, and I think it looks unanimous.

(A show of hands)

MS. HANN: Pat, are you okay with that?

DR. MORRISSEY: I sure am.

DR. INSEL: And we are moving on to the next page, page seven, discussion point 4.4, whether to add in a bunch of examples.

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Do we want to go granular here in talking about clinical trials, of widely used interventions that have not been rigorously studied, and the alternative to adding in the specifics is to remove references to untested treatments, especially chelation, because studying these treatments grants them unearned legitimacy, which I guess actually goes back to the original version.

So really as I read this we have two options, the one is with and the other is without the specifics. How granular do you want this to be?

Discussion?

(No response)

DR. INSEL: All right, those in favor of adding in the specifics?

(A show of hands)

MS. HANN: There is one vote at the table.

DR. INSEL: And those who want to go back to the original version, which just

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says untested treatments or widely used interventions.

(A show of hands)

DR. INSEL: And the motion passes.

MS. HANN: Yes.

DR. INSEL: The next piece is some additional language, intervention and improved functioning and quality of life for people with ASD across the lifespan including older children, adolescents and adults with ASD, so getting around the language that said life for older children and adults, to include adolescents, and to say across the lifespan.

What is the sense of the group about that?

(No response)

DR. INSEL: In favor of these additions?

(A show of hands)

DR. INSEL: Opposed or want to go back to the original? Pat and Cindy?

DR. MORRISSEY: I'm fine with the

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language.

MS. HANN: Okay, so that is unanimous to accept.

DR. INSEL: And we are moving right along to the next page, we are on page eight, and we are at discussion point 4.5. And this gets to this issue about the co-existing medical conditions. We had decided already that we weren't going to list those each time, so we are just going to go past that, and we'll go back to the original.

The next one, 4.6, we changed early interventions to be interventions that may enhance neural plasticity and adaptive brain reorganization, and we've added children, adolescents and adults with ASD, to specify the different ages.

Discussion? Are these good changes? Not necessary changes? It does really shift the emphasis from early intervention to intervention at any point.

In favor?

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MS. BLACKWELL: Can I?

DR. INSEL: Yes, sorry.

MS. BLACKWELL: I would actually suggest that - I mean are we in here directly going for behavioral improvement or overall improvement in manifestations of ASD? What do you guys think? Isn't it more than behavioral improvement?

DR. INSEL: I think the focus being on neural plasticity and adaptive brain reorganization was expecting the outcomes to be cognitive, mostly, or behavioral.

MS. BLACKWELL: Can we say cognitive and behavioral?

DR. INSEL: Do we need to even specify? Should it just say significant improvement?

MS. BLACKWELL: That is kind of what I'm thinking.

DR. INSEL: Okay. So the language would be, as you see it, except thereby promoting significant improvement of ASD.

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In favor of these changes with that provision?

(A show of hands)

MS. HANN: Everybody in the room voted in favor.

DR. INSEL: And Pat or Cindy?

DR. MORRISSEY: I support it, this is Pat, yes.

DR. INSEL: Okay, now we are ready to look at some additional ideas. There are plenty of them here, so we are going to walk through them very quickly.

The first is outcome studies of the effectiveness of behavior therapies, and they are actually listed specifically. This is discussion point 4.8.

Sense of the group?

MR. SHORE: I wonder if -

DR. INSEL: This is Stephen.

MR. SHORE: Yes, this is Stephen. And I'm wondering if we should expand that to behavioral slash developmental, because if we

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say behavioral then that eliminates the Miller method, RDI, and Floortime, because those are developmental in nature. And it restricts us to ABA, and its variants.

DR. INSEL: Any other ideas about that? Judith?

DR. COOPER: And I think we could combine the second bullet with that, because if we've got communication therapy in the first one, we could add occupational therapy too.

MS. SINGER: I think some of these listed here are not actually therapies. Joint attention is not a therapy. I think we might in addition to adding developmental as you suggested, we might just add cognitive and then not include the list, and thereby leave it open for a wider variety of therapies to be tested.

DR. HOULE: This is Gail. I agree, some of them are strategies that are part of a program of therapy or part of therapy. So

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you are pulling out - you've got big broad areas in here like ABA, then you are pulling out techniques. So I would just go with the behavioral, the cognitive, the developmental progress.

DR. MORRISSEY: I'm fine with that.

MR. SHORE: Unless you wanted to say approaches in techniques, the approaches being such as ABA, Floortime, and the techniques such as peer mimicking, for example, sensory integration, joint attention seems more of a concept as opposed to a technique.

DR. INSEL: Walter.

DR. KOROSHETZ: So I just am questioning the wisdom of trying to get into details here, because you are basically dating yourself. You are putting names down that - you are equating things with each other. It starts out by saying that large scale studies that directly compare interventions and combinations of interventions to identify what

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works best for what individuals. That seems to me to be the statement you want. If you start to get into the details, then, it's I left something out, I put something I shouldn't have. I don't know that you want to go that far.

MS. SINGER: Could you just read that, Della, what Alison said?

MS. HANN: Well, this is Della, I've been trying to follow the discussion. I've heard outcome studies of the effectiveness of behavioral, developmental and/or cognitive therapies or approaches.

Do we want the parenthetical?

MR. SHORE: No.

DR. HOULE: No.

MS. HANN: Okay, so let's take a vote.

All those in favor of the change that I just read, which also includes the drop of the parenthetical, please raise your hand.

(A show of hands)

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MS. HANN: And it is everyone in the room.

Pat, are you in favor of that?

DR. MORRISSEY: Yes, I'm okay.

MS. HANN: Great, thank you.

DR. INSEL: All right, so that takes care of the first two at least. Let's see if there are any others that you just covered. The next one down here is studies that measure the physiological and performance effects to determine mechanisms through which sensory-based interventions influence behavior and performance outcomes. Do you want to go there? Is that too granular?

I see a lot of heads shaking. In favor of including this statement, hands up?

(A show of hands)

MS. HANN: There are none in favor.

DR. INSEL: The next one is methods for measuring changes in core symptoms of ASD from treatment including recovery. Is this a research opportunity, or is it worth

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including, or what is the sense?

MS. REDWOOD: I don't know if we really have a lot of good tools now for assessing these types of issues, and recovery, so I think it would be an important thing to address.

MR. SHORE: And I might add, we are going to use recovery, let's call it recovery of function.

DR. INSEL: So if we change this wording to say, methods for measuring changes in core symptoms of ASD from treatment -

DR. ALEXANDER: Period.

DR. INSEL: - period, without the recovery, would that be easier for everybody?

MS. SINGER: I guess I'm a little bit confused about what changes we are measuring. I don't understand core symptoms, changes in the core symptoms. And what treatment?

DR. INSEL: Yes, so this came up remember in the original discussions we had

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about screening and diagnosis and phenotyping, the issue, what we heard from some of the workgroups was the need to have measures sensitive to change so you could determine whether treatments were working.

So this is again just a research opportunity, but something that we need to focus on.

DR. HOULE: So are you talking about the metrics for measuring the change?

DR. INSEL: Yes.

DR. HOULE: Maybe you want to say that.

DR. INSEL: Well, it says methods, methods for measuring change.

DR. HOULE: Okay, so it's greater than - I know there are a dearth of tools out there that are really effective, and I didn't know if that was what you were trying to get at there, or whether you were trying to be conceptual.

DR. INSEL: As a research

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opportunity, it is the need to have methods that would be sensitive.

In favor?

(A show of hands)

MS. HANN: Okay, that's everyone in the room. Pat are you listening?

DR. MORRISSEY: Yes, I am.

MS. HANN: Are you okay with that?

DR. MORRISSEY: Yes, I am.

DR. INSEL: So Della, can you read the final language, because there were a couple of changes from what we have here.

MS. HANN: What I have as the final change is: methods for measuring changes in core symptoms of ASD from treatment, period.

DR. INSEL: That's accepted.

And the next item here is clinical trials of the efficacy of conventional anti-psychotic medications for improving behavioral symptoms in young children with ASD.

Interest in this? What is the sense? Obviously the FDA has already approved

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the use of Risperidone for this purpose, in both children and adults with ASD. Do we need an additional set of clinical trials. We have 60 so far in the document. Do we need another group?

In favor of including this? Hands?

(A show of hands)

DR. INSEL: Those who just want to move on and go back to the original?

(A show of hands)

MS. HANN: Everyone except for Gail?

DR. HOULE: Oh, I'm sorry.

MS. HANN: Okay, it's unanimous to drop. Okay.

DR. INSEL: And on the phone?

DR. MORRISSEY: I'm okay, this is Pat.

DR. INSEL: We know you are okay.

Studies of the effect of stress and stress hormones on the health of children

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and adults with ASD. Is this something we need to promote? Interest? All in favor of including this?

(A show of hands)

MS. HANN: There are no votes at the table?

DR. INSEL: Anyone want to include it on the phone?

(No response)

DR. INSEL: And the final one is clinical testing of children's blood, urine, hair, stool, et cetera, to detect mitochondrial dysfunction, toxic levels of heavy metals. I'm not sure how this is in the treatment section, but it is in here as an additional item, discussion point 4.12.

Comments?

DR. ALEXANDER: It doesn't belong here.

DR. INSEL: In favor of including it, hands?

(A show of hands)

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MS. HANN: No hands at the table.

DR. INSEL: We are moving on to short term objectives, so we are now in the middle of page nine, chapter four. The one change to the first bullet is to look not only at significant improvement, but also to add the words, or decline in ASD core symptoms across the lifespan.

MS. REDWOOD: I think it is important, because from time to time we'll hear parents say their children are doing well and for some reason there is a regression in behavior, so I think we need to look at those episodes as well.

DR. INSEL: Okay, in favor of including the words, or decline?

(A show of hands)

DR. MORRISSEY: This is Pat, I think the phrasing is a little bit confusing. Because you approve a course which means they become less of an issue, and if they decline, doesn't that mean the same thing?

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DR. INSEL: So maybe worsening would be easier?

DR. MORRISSEY: Yes.

DR. INSEL: Okay, thank you.

DR. HOULE: Or just changes. You are measuring significant changes. So you are measuring in all realms, positive, negative changes.

DR. INSEL: Okay with that? We are going to go to changes; everybody is nodding. Della, done.

MS. HANN: Okay.

DR. INSEL: Now there is an alternative here which is to quadruple the number of projects and the budget, so we go from four to 16 projects. And let me get your sense about that. This would be short term, so this would be over four years - I'm sorry, by 2010, to have 16 research projects that -

MS. HANN: To launch them.

DR. INSEL: Duane.

DR. ALEXANDER: I think just doing

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four is going to be a challenge, quadrupling that is virtually impossible.

DR. INSEL: So can I get a show of hands for who wants to bump it up to the fourfold increase?

DR. HOULE: Can I suggest another alternative? At least four. The other ones are a minimum of four. The other research you did minimums.

DR. INSEL: What does the group think? Okay, heads are shaking.

So the motion on the table would be to not accept the alternative of quadrupling, but to put in language that says at least four, launch at least four research projects.

In favor?

(A show of hands)

MS. HANN: Wait a minute. Eleven.

DR. INSEL: Opposed?

(A show of hands)

MS. HANN: Two.

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DR. INSEL: And on the phone, in favor or opposed?

DR. MORRISSEY: In favor.

DR. INSEL: Okay.

MS. SINGER: Can I ask that we flag this one again for the budget discussion.

DR. INSEL: Done. Done.

The same issue comes up on the next, where we support three randomized controlled trials that address co-occurring. And the alternative is to quadruple the number of projects and the budget.

Again, this is short term objectives. Sense of the group? Shall we go from three to 12, or the alternative would be to say support at least three.

MS. REDWOOD: I'd like to put in a plug for more than three, just because there are so many more things that we have not really addressed, seizures being a perfect example in our kids with autism. So I think there is a plethora of opportunity out there

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beyond three.

DR. INSEL: Other comments or thoughts about this?

So we've got two options. One would be the language that says, support at least three randomized controlled trials. The other would be to quadruple. Those in favor of at least, may I see your hands?

(A show of hands)

MS. HANN: The vote is eight here in the room.

DR. INSEL: On the phone?

DR. MORRISSEY: I'm okay.

DR. INSEL: So does that mean you are in favor of this language, or do you want to quadruple?

DR. MORRISSEY: No, I don't want quadruple.

DR. INSEL: And just for completeness those who want to quadruple the number of projects?

MS. HANN: Five.

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DR. INSEL: Okay.

DR. TREVATHAN: Della, could we flag that one to discuss at the budget as well.

MS. HANN: Yep.

DR. TREVATHAN: That looks like a very small amount of money for that task.

MS. HANN: So noted.

DR. INSEL: We are moving along here. I don't see anything else on page 10 until we get to the very bottom, which is discussion point 4.13. And that is the top of - it's the alternative on page 11. And this is the same issue about numbers. So the original plan says, three model systems, and the alternative is at least 20 robust model systems by 2012.

Model systems means here cellular models such as induced pluripotent stem cells, or an animal system such as a mouse with a knockout or a knock-in of a gene that has been implicated in autism.

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Reality is, there are probably over 20 right now in practice. But the question is how you want to pitch this.

There certainly are more than three. What is the sense of the group?

Walter, this is kind of NINDS turf.

DR. KOROSHETZ: I just have trouble with the numbers. I'm at a loss to say - I would like one really really really good one.

(Laughter)

DR. KOROSHETZ: As opposed to 20, not so good.

MS. SINGER: Twenty, and one really really good one.

(Laughter)

DR. KOROSHETZ: As opposed to 20.

DR. INSEL: My sense in looking at this is, three is not particularly ambitious, since I'm certain that we could point to many more than that today. Twenty by 2012 I'm not sure what that would be; I'm not sure if that

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is realistic or not.

I wonder if there is a number in between that is a little more realistic, that would also capture some of the budget issues that we have been talking about.

MS. SINGER: But if you are saying that there are more than 20, why would we not want to investigate as many as possible? We have already knocked down so many of these studies to be so low that if there is - if this is one you have identified as there are 20 - at least 20 available, then I think it behooves us to vote in favor of at least 20.

DR. INSEL: Yes, I guess it depends on just how you define it, if we are talking about candidate genes that have been knocked in or knocked out, or if we are talking about behavioral models. They are just - there is a lot going on in this arena. I'm just not sure how to put - how to define the number. I think I'm having the same problem that Walter is having. With everything that is

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going on, I don't think anyone has told us what we need it to tell us, so I'm not sure that numbers are the answer here as much as having one thing that really allows us to go from where we are now to understanding mechanisms which we don't have.

MS. BLACKWELL: What if the answer is some sort of descriptor before the words, model systems, like unique, or new, or ground-breaking.

DR. INSEL: So that's where the word, robust, came from, because we thought the word robust was - or at least someone though robust was a way of talking about its value. Oh, I see your point. You are right. It's not - that ended up with 20, and it doesn't say validate three robust model systems.

So what - I don't want to get hung up here. Does the group want to make some modification to either one of these? We could add Gail's recommendation to put at least, or

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Judith's recommendation to put at least in front of the three if that makes people feel better. What is your pleasure?

DR. MORRISSEY: This is Pat. Can I ask a question? This is clearly out of my realm of expertise. But couldn't it be possible that you would study more than one gene in one study? So talking about the number of studies doesn't really get you anywhere.

DR. INSEL: Well, I think the number of model systems is - doesn't get you very far. But I think where this came from was the sense from the workshops that we had that what was missing in this plan was the kind of molecular and cellular research which has paid off so handsomely in other areas of medicine. And this was I think the only item in the entire plan that actually speaks to that. And some people who have looked at the plan would say, what would move this field forward faster than anything else would be

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doing these kinds of studies. That has been what's made the big impact in hypertension, heart disease, diabetes, wherever you want to look.

And yet 98 percent of this plan doesn't go there, so there was a real interest from the workshops, or at least one workshop, on trying to get at mechanisms of disease, and it was thought this is the only place that is going to happen.

DR. MORRISSEY: Okay, so you have 20 studies going on now. So that represents in a way a baseline. So at least say 20 is okay, and the suggested addition, and then recognizing that the guide could set the criteria for what the studies are and evaluate the people who send in proposals will be the mechanism by which you get the robust studies. You know, it's like in the weeds, right?

DR. INSEL: Yep, one would hope that we would get some of these that will be in fact robust.

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DR. MORRISSEY: Right, so we don't have to solve that piece of it, because that will be done in the application review process or writing the request for proposal stuff.

DR. INSEL: Exactly. So we've got two alternatives in front of us. One we could say standardizes and validates at least three model systems if we add the "at least". That was basically the original language. And the revision is to bump this way up, and to validate and standardize at least 20 robust model systems.

And this isn't to replicate ASD, but only to look at features of ASD. So this could be much broader.

Is there any other comment, or are we ready to just take this to a vote?

(No response)

DR. INSEL: Okay. The original version, in favor of sticking with the "at least three."

(A show of hands)

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MS. HANN: There are no votes at the table.

DR. INSEL: And those who want to get ambitious and go to 20?

(A show of hands)

MS. HANN: Gail, what are you doing? So ten.

DR. INSEL: And we are moving on.

The middle of page 11, there are two very different recommendations. One is to delete the objective of five widely used interventions that have not been rigorously studied, and the other is to quadruple the number of projects. So this gives you a really good feel for what the public comment looked like.

Discussion?

(No response)

DR. INSEL: We've got three options. Are you ready to vote and move on? So those who would stick with the original language of five widely used interventions not

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rigorously studied?

MS. SINGER: Can we say at least 10?

DR. INSEL: I'm sorry, that's a good point. Test and the safety and efficacy of at least five.

(A show of hands)

MS. HANN: Okay, the vote is eight in favor of that option.

DR. INSEL: Those who want to delete this objective altogether - I'm sorry, we didn't get this on the phone. Anybody on the phone voting?

DR. MORRISSEY: I don't know what I'm voting for.

DR. INSEL: All right, let's back up. This is the middle of page 11.

DR. MORRISSEY: I know. That's where I am.

DR. INSEL: Okay, so the first option is the language that is shown in the box, which is, test the safety and efficacy of

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at least five widely used interventions that have not so far been rigorously studied.

DR. MORRISSEY: I'm voting for that.

DR. INSEL: Okay, so that's nine.

MS. HANN: That's nine.

DR. INSEL: And then delete this objective, I don't think we got any votes. And quadruple the number of projects, we've got?

MS. HANN: We've got four.

DR. INSEL: Okay. Moving on to page 12, there is an addition to the next item which is to establish a registry or consortium of registries to track seizure control medication use, adverse effects related to treatment.

Comments?

(No response)

DR. INSEL: Does this exist currently anywhere? ATN is not doing this?

DR. TREVATHAN: I would just - a

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note of caution, having established a few registries, they are always more expensive than you think, harder to maintain than you think, and usually people have a wide variety of different ideas as to what registries mean and what they are going to be used for.

We haven't done this to this point, but I wonder if there are some of these issues - this might be one - to flag and say this is something we really want to dive into when we meet in just a few months now I guess or less to start the next year.

This looks like potentially a big issue, and we don't want to short change it. I just don't know.

DR. KOROSHETZ: And one possibility would be to incorporate data fields on seizure control medication using adverse effects related to treatment and ongoing large cohort studies that have already been mentioned before. I think we should track it. The question is, the best way to track it is

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usually in concert with another study you are doing. We have that information plus a lot of other information.

DR. MORRISSEY: This is Pat. Are there other people that already have registries on this topic?

DR. INSEL: Not - I don't think in this population.

DR. MORRISSEY: No, I'm not talking about autism. The point is, if there is - I'm looking at cost and complexity and how fast you could do it. If there are registries out there dealing with seizure control medication and its effects, and so forth, in some ways, if somebody could find out what they are, then we could make an assessment of whether or not it makes sense to add ASD to that. Or for the people who are reporting to these registries, if the person they're reporting about happens to have ASD, that is included in the information base.

DR. INSEL: I think that's actually

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what Ed was suggesting is that we step back from this, maybe do it on the next round, get a sense of the feasibility and what else was available.

DR. TREVATHAN: I think too that this is an area of interest potentially - Walter may know more about this than I do - in the epilepsy community as well. So there may be some shared platforms and so forth coming up, but I don't know anything right now that would be applicable.

DR. INSEL: Okay, so who wants to add this in as a short term objective at this point? Can I see a show of hands for adding it now?

(A show of hands)

MS. HANN: I see a vote of three at the table.

DR. INSEL: And those who want to not add it here, but as you said, Ed, we could come back to it for a version 2.0?

(A show of hands)

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MS. HANN: And the vote is nine.

DR. INSEL: And Pat, do you want to add your vote here?

DR. MORRISSEY: Yes, I want to be in the second group, which means, don't do it now.

DR. INSEL: Okay, great, so we are going to move on to the long-term objectives. And we have a few comments here, though not many. First one is to add the term, scientifically rigorous, to the randomized controlled trials in humans. And instead of humans, to say people with ASD of all ages on three medications targeting core symptoms by 2014. We have alternatives, one of which was to delete this objective, and the other was to triple the number of projects in the budget.

Comments?

(No response)

DR. INSEL: I think this group is getting tired.

MS. REDWOOD: Tom, before we get to

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the discussion about adding scientifically rigorous - and I think we decided it would be addressed in the introduction, and all of our research would be scientifically rigorous. So I don't know that it is necessary.

DR. INSEL: Okay, are there comments about people with ASD of all ages, as opposed to saying humans?

(No response)

DR. INSEL: Okay, so the other issue then has to do with whether to triple versus delete. And I'm going to suggest we just take this to a vote.

So we are going to drop out scientifically rigorous, because everybody's head was nodding when Lyn made that recommendation.

The language will say, for the revised version, complete randomized control trials in people with ASD of all ages on three medications targeting core symptoms.

MS. SINGER: In at least three?

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DR. INSEL: I'm sorry, that is even better, on at least three. So again we have the original language, which is in the left-hand column, which is one option, which says as you can see it. We have the modified language. The third possibility is to get rid of this altogether. And the fourth possibility is to triple the number of projects in the budget.

MS. REDWOOD: Tom, I have a question with the wording, medications. Because there are things out there, and I don't if you would consider, say, CoQ10 or carnitine or these mitochondrial cocktails as really being medications. So is medication somewhat limiting?

DR. INSEL: Walter?

DR. KOROSHETZ: I wouldn't think so, at least not from our point of view. I mean, CoQ10, carnitine, we consider them treatment medications.

MS. REDWOOD: Okay, that was my

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point. I just didn't want to have - because I view those more as supplements than medications. So I didn't want it to have to be something that was - okay, if you think it covers those kind of things, that's great.

DR. INSEL: Okay, so those who would endorse the original language, three medications in humans? I don't see a lot of hands going up. On the phone? I don't hear any voices.

The next column, I'll read it to you, now says complete randomized control trials in people with ASD of all ages on at least three medications targeting core symptoms by 2014.

In favor?

(A show of hands)

MS. HANN: There is eight votes at the table.

DR. MORRISSEY: I'm okay.

DR. INSEL: So nine. To delete this objective.

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And then the final is to triple the number of projects.

(A show of hands)

MS. HANN: Five.

MS. REDWOOD: Can I just say something? It's interesting that when we take a lot of these votes that the advocates here at the table are all voting for many more numbers of items to research, and I think that we are being fairly consistent, but they are just not moving forward. And I think that maybe that will get to the introduction, because this is such an urgent issue, and it seems just somewhat apathetic to say, we are going to look at three. I just have to go on the record that it's disappointing as a parent, and to other parents too who are really struggling with this disease that that's where we set our bar.

DR. KOROSHETZ: I think I'd go on the record. I agree with you, and I think from my point of view, I think the numbers are

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- I'd like to do as many good ones as we can do. Having done these, I know kind of what the numbers mean in terms of how many you can pull off. And if you try to do too many you end up with slop. So I think that is the other - so I think we are all in the same boat, so the numbers should be as many as we can do. That should be what we are going to. I think if you put a number down, you are running into feasibility, quality, versus what you want to do. I don't disagree with you.

DR. TREVATHAN: I would just like to go on the record, too, agreeing with Walter. CDC does not do clinical trials, but having run quite a few clinical trials in my career in similar populations, that is the issue. I mean there are only so many investigators out there who can do these. There are only so many sites that can pull them off. And there are only so many hypotheses. And if you try to do too many, very often they don't get completed. I mean

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unfortunately I think many of us have seen clinical trials that get initiated, don't get completed, people don't have the resources. So that really is a balance between not taking it seriously enough and then overcommitting and then coming up with, as Walter says, slop.

So I think that is where we are coming from.

DR. INSEL: But I think this is a really important point to make. And you would see this if we were having a discussion about any form of cancer as well or any form of heart disease, that what you tend to have when you bring the public and scientists together is exactly this tension. The public wants as much as possible to go into interventions, and the scientists are saying, but we don't have the targets. We wouldn't know what do. What would be a novel intervention, when we don't even know what we are targeting?

Now fortunately we do, increasingly we know that for leukemia,

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lymphoma, breast cancer. But here, I think, what the scientists are telling us is, we are not ready yet to develop the next set of interventions until we have molecular targets, and we don't know those.

And I can tell you, I have now hit most of the major pharmaceutical companies in this country, asking them to work with us on autism, most recently Genentech, and they all say the same thing: that we will do this when you show us where the targets are. You show us the enzyme, you show us the protein, and we'll be right there. But until you get that we are going to work on something else.

So I think that is part of the tension, but I think your point is really well taken, we've got to see this as the brass ring, and we really do have to find a way to up the commitment to move quickly to get something that is useful.

MS. BLACKWELL: I think it is also important to remember, and Ed alluded to this

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a few minutes ago, that this is only our first strategic plan. We have to do this again. So if we don't get it perfect this time, we are going to kind of have a better sense of where we are when we start working on the second version.

DR. MORRISSEY: This is Pat. My motivation was simple. When I say the phrase, randomized control trials, I was thinking, they are going to be big, so three didn't bother me because they are going to be big; not that I don't care.

MR. GROSSMAN: And from my standpoint, I see everybody around this table as being an advocate for the community. It's just a reflection of some people, including certainly myself, really really trying to push the envelope. And to me that is not a judgmental thing. I think we all come at this from our own different perspectives and realities, and with that I - just the fact that we are moving this forward I think is a

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major, major accomplishment for the IACC and for everything that we are all trying to achieve.

DR. INSEL: Duane, you're getting the last comment, and then we are going to complete Chapter 4.

DR. ALEXANDER: Just a point that first of all we have added "at least" before almost everyone of these. So there is a commitment to go at least that far. But also with regard to that, the wording in this one needs to be fixed. Because right now everyone in the clinical trial has to be taking three medications.

(Laughter)

DR. INSEL: We will take that under advisement. Well, they have to be on at least three medications.

(Laughter)

DR. INSEL: Which brings us to the very final item on Chapter 4, we have a suggested addition to support prospective

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trials for commonly used anti-epileptic medications in well defined groups of people with ASD.

Do you want to add this or is this something that is a little, again, rather granular. Now we do have a piece earlier on on doing trials on a whole range of aspects in addition to core symptoms, I believe.

So comments, questions? Add it? Leave it?

(No response)

DR. INSEL: In favor of adding this piece on anti-epileptics? Hands for those who want to add this?

(A show of hands)

DR. INSEL: On the phone is there anybody who wants to add it?

(No response)

DR. INSEL: Okay, it's not going in, and we are moving on to Chapter 5.

The good news is that this will go a little quicker I think at this point. And

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Ellen, you are going to be in the hot seat. You can just keep your microphone on, and you can walk us through this. You have lots of great ideas about how to make some changes.

But let's go to page one on Chapter 5, and eliminating barriers to service was added in, as well as adding in at the end of that paragraph, families identify which services will work best for them.

And Ellen, you had a comment there about strike which will work best for them and replace with, are necessary or are needed.

MS. BLACKWELL: It just seems to leave more room.

DR. INSEL: So could you read that? So we'll use that as a motion if you could read us how you would like this to read, and then we can decide whether to stick with the original or to make the change.

MS. BLACKWELL: Disseminating research findings in the community, eliminating barriers to service, and helping -

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I would actually say people and families identify which services are needed.

DR. INSEL: Is "people" better than "individuals."

MS. BLACKWELL: Yes, we always like people at CMS.

DR. INSEL: Okay. Okay. Comments?

(No response)

DR. INSEL: In favor of that new language, hands up?

(A show of hands)

MS. HANN: Twelve at the table.

DR. INSEL: Okay, moving on, the very next line, communities vary tremendously in how they define ASD and determine eligibility for services. Again, Ellen, you had issues about that. You said it needs clarification.

MS. BLACKWELL: I think the original one makes more sense than what was substituted here.

DR. INSEL: Okay. Who wants to

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make the change, or we can go back to the original language.

Those who would be in favor of the change?

(A show of hands)

DR. INSEL: And those who want to retain the original language?

(A show of hands)

DR. INSEL: And on the phone?

DR. MORRISSEY: I like the original language.

DR. INSEL: I'm sorry, we need hands up for those who want to retain the original language.

MS. HANN: This is for the communities one?

DR. INSEL: Yes.

MS. HANN: To retain the original language.

DR. INSEL: Which is what Pat has voted for as well.

MS. HANN: Twelve and Pat, that'd

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be 13.

DR. INSEL: And the next line, Ellen again, help us with this. It says, and are very diverse in how they use and apply state and federal - so that is part of the same issue, so we'll go back to the original language there.

And then the next potential change is on lines 10 and 11 on page 2 where it says, the professional infrastructure, and it specifies health care workers, educators, law enforcement, or capacities often inadequate to provide timely diagnosis, appropriate care and assurance of safety.

Issues with that? Or what is the perspective on the language? Because this is a change from what we had before?

DR. MORRISSEY: Well one I have, I don't know whether people in law enforcement would be in the business of diagnosing. So in some cases, the question is, detect, or have a sense that someone has a disability in kind

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of a general sense, not in a specific sense. So probably from a standpoint of clarity, timely diagnosis doesn't work for the three populations that are listed there.

DR. INSEL: So Pat, we could go back to the original language, which doesn't get into - it doesn't specify. It just says, provide timely diagnosis and appropriate care.

DR. MORRISSEY: But you know what, I think mentioning assurance and safety is a really big deal, because especially when you are dealing with the law enforcement and criminal justice system. So I think we have to include some reference to that, including assurance and safety or something.

MS. BLACKWELL: Pat, this is Ellen, what if we put, provide timely diagnosis, comma, appropriate care, comma, and health and safety, period?

DR. MORRISSEY: Yes, in the original right?

MS. BLACKWELL: Yes.

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DR. MORRISSEY: Yes, that would work.

DR. INSEL: So we're going to drop out the parenthetical that was added, and you will add just one piece to the very end, it'll say, provide timely diagnosis, comma, appropriate care, and - Ellen?

MS. BLACKWELL: And -

DR. INSEL: How about assurance of safety, that doesn't ring for you.

MS. BLACKWELL: Assurance of health and safety.

In favor of that new language? Lee.

MR. GROSSMAN: Yes, I have a change. I don't know of any jurisdiction with general policies to support ASD interventions.

MS. BLACKWELL: I thought we were working on the original language.

MR. GROSSMAN: Well, that's in the original. So if we could change - I just don't know any place like that on earth. So

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could we change it to something like within virtually every local and state jurisdiction -

DR. INSEL: Why don't we just start at the professional infrastructure and just leave out that first piece? Why would you qualify it?

MR. GROSSMAN: That's fine.

DR. INSEL: Okay, so the language now would say the professional infrastructure or capacity is often inadequate to provide timely diagnosis, appropriate care and assurance of health and safety.

In favor?

(A show of hands)

MS. HANN: Everyone at the table has raised their hands.

DR. INSEL: And Pat, you okay with that?

DR. MORRISSEY: Yes.

DR. INSEL: Moving on to the next section, availability of appropriate lifespan

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transition opportunities has been added in as well as the associated financial costs, instead of saying burden, to families.

Stephen, do you have a comment? Okay, so the word burden tended to sound pejorative.

Any issues about this? Is this an improvement?

Okay, in favor of the additional working?

(A show of hands)

DR. INSEL: Moving on to - actually was there anybody we didn't capture? I think it is unanimous.

And Pat, are you okay with that?

DR. MORRISSEY: Yes. Unless I say something, you don't have to worry.

DR. INSEL: Okay, move to page three, adding in adults with ASD.

MS. BLACKWELL: Wait, you missed one.

DR. INSEL: Okay, Ellen.

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MS. BLACKWELL: Bottom of page two. I'm just not convinced that children with ASD always have a much more difficult time than other children with special health care needs. And I thought we should insert the word, may, or are likely to. But it just seems like it's making a judgment about children with autism versus children with other health care needs.

DR. INSEL: So it does say, in general. Does that help you at all? It doesn't say, always?

MS. BLACKWELL: I don't know, how do you feel about it, Lee? Okay. Okay.

DR. INSEL: Okay.

DR. KOROSHETZ: I would object to that too. Knowing some other pediatric neurology populations. I mean they are all - I'm not saying one is worse than the other, but I think comparing them - there are some really terrible things that can't get any care at all.

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DR. INSEL: There is a reference here from the literature, so it's not really an opinion - well, the hope is that it's justified through the literature.

So the question about adding adults with ASD to the next page where we talk about the effects on outcomes for children and families. And this was again something we got a lot from public comment. They felt the document was far to child focused.

Okay with that? Those in favor of adding adults with ASD, if I can see a show of hands?

(A show of hands)

MS. HANN: Everybody in the room.

DR. INSEL: Okay, and Pat?

DR. MORRISSEY: Okay.

DR. INSEL: All right, so that is unanimous.

We are moving now to what do we need, the second part of page three. And there is an additional comment from the

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public. As it is, families who must know how to find and access services finding - finding ways to assist them in navigating such a diverse and complex set of systems is critically needed.

MS. BLACKWELL: I just thought this sentence was rather confusing. It's not just the families; it's a whole constellation of people involved. It could be the person with autism. So this sentence is confusing.

DR. MORRISSEY: I think what that person is trying to say is that the family and/or the person and the people around the person may need to access help or services from a variety of places, and that process of finding out what they are, and scheduling them, and all that sort of thing is complicated, and not easy and time consuming, and so that's what they are after there.

MS. HANN: So my - this is Della - to help with the confusion in trying to clarify what you just said, Pat, if we started

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with the word, finding, so drop the initial phrasing. So finding ways to assist families and people with ASD and assisting them in navigating and go on that way.

DR. MORRISSEY: Yes, the key thing is the navigation.

MS. HANN: Right.

MS. BLACKWELL: I actually had a suggested wording for this, which was: People with ASD and their families need assistance navigating complex service systems.

DR. INSEL: All right, people like that. That will be the third alternative. Let's vote on that first. Can we put that language in? Can you say it again, and we'll make that a motion?

MS. BLACKWELL: It's on page 7 of the draft. It's, people with ASD and their families need assistance navigating complex service systems.

DR. INSEL: And that would replace the addition at the beginning of what do we

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need. In favor?

(A show of hands)

DR. MORRISSEY: I'm okay.

MS. HANN: Okay, everyone but Gail voted yes.

DR. HOULE: No.

MS. HANN: Okay.

DR. INSEL: Okay, we are moving on to the next page, on page 4 Ellen has pointed out that when we talk about a participatory action model, we mentioned families, communities, and somehow people with autism were left out. So if we are talking about - this is on line 10 or 11, on page 4. You see that, using participatory action model, families and communities can become empowered to become partners in research that can in turn inform policy.

I don't know how that happened, but I think that the framers of this constitution wanted it to say - did not want to exclude people with ASD. So Ellen, you

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were recommending in your comments here that people with ASD be added to the list of those who can be empowered.

In favor?

(A show of hands)

DR. INSEL: That looks like it's unanimous. And we are moving now to the bottom of page four, where it says, annual state of the state review of policies, and this will provide a national database for families to search regarding services and supports. And then it goes into the specifics of what this would include.

MS. BLACKWELL: I think it should say it's a national resource for stakeholders. It's not a database, and it's for everyone, not just families.

DR. MORRISSEY: This is Pat. This may be a footnote that could be put here somewhere. We funded a congressionally mandated national clearinghouse and technical assistance center on family support. It

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doesn't deal specifically with autism, but obviously kids with autism or adults with autism would be - information about how to help them would be part of that.

So it may make sense just to recognize that there may be clearinghouses out there that could help in this process. And I'm not sure, but does the Combating Autism Act have a clearinghouse function in it?

DR. INSEL: No, not specifically. This came up at the workshops, Pat, and there was - people were aware of the report that is out there, the clearinghouse. There was a request to do this specifically for autism. And it has been done in a very focal way for autism, but a request to have a comparison across all the states, and I guess one - I'd be interested in Lee's response to this, but the public comment that came back was the need to be a little more specific here, to say what would actually be in it, so at the end of the day people had what they most wanted out of

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this, and not just a document that would sit on the shelf.

But Lee, can you speak to this? Is this actually the kind of thing that we want?

MR. GROSSMAN: I think there are two separate issues here. The original language is specific enough, and when the proposed changes are submitted you are looking at something entirely different. That's the way that I look at it.

And I don't see how the two connect.

DR. INSEL: I think we were initially, and this is conversations we had with the first IACC services subcommittee when we talked about getting the government accounting office or national research council or somebody else that would be involved in funding this type of review of what states are doing.

DR. MORRISSEY: ABB has the state

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of the state report for individuals with developmental disabilities, and that focuses on in a large measure how much Medicaid money is going to any state for different things, and then looking at specific categories of other demonstration project monies that come in to help people with developmental disabilities.

So it's all established activities that can be tracked back to some stable funding source or a federal funding source. So you know I think Lee is right that the laundry list beginning on page four is a different kind of thing.

MS. BLACKWELL: I agree, Pat. I think what we were trying to do is to get a state of the state for people with ASD very similar to the state of states for people with developmental disabilities. And I think Lee's suggestion to return to the original language would probably be okay.

The only thing I would add is,

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perhaps after families we could put, and other stakeholders.

DR. INSEL: So the motion here, Ellen, would be not to accept the revision but to go back to the original language and add, individuals with ASD and their families and other stakeholders.

Yes, Gail?

DR. HOULE: Well, there are two different ways to read it depending on where you put the emphasis. But if you look at the annual state of the state review of policy, service and supports for individuals with ASD and their families, it is a review of the supports for individuals with ASD and their family. You don't want to include the stakeholders because they are not the targets of the services. So I think it's fine. I did not read it that other way.

DR. INSEL: So that would retain the original language.

Okay, so this makes it easy. We

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can either have the original language, or we can put in the revision.

All in favor of the original language?

(A show of hands)

MS. HANN: Okay, everyone at the table.

DR. MORRISSEY: I am too.

DR. INSEL: Okay, we are moving on. We are now in the middle of page five on Chapter 5. Cost effectiveness study of ASD interventions and services to provide individuals, families, schools and service providers with effective economical options.

And that is a revision by adding in the effective economical options.

Comments?

(No response)

DR. INSEL: In favor - so we can go back to the original language, which was a little less specific. It still says cost effectiveness studies, and it stresses across

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the lifespan. It just doesn't add in the additional clause.

IN favor of the original language?

(A show of hands)

MS. HANN: The vote is everyone at the table has agreed to that.

DR. INSEL: Okay, and Pat?

DR. MORRISSEY: Me too.

DR. INSEL: Okay, right. And then the one other thing further down, line 16 and 17, we are talking about adding in, evaluate services and intervention outcomes in the studies that characterize diagnostic and service utilization.

Comments about that?

DR. MORRISSEY: I think it's important to include outcomes here. Because that's a big deal, across government. What has the money bought?

DR. INSEL: Right. Okay, so those who want to take in this new addition, hands up?

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(A show of hands)

DR. INSEL: It looks unanimous in the room. And Pat, you just said you endorse it.

We are moving to the bottom of the page. There is an additional recommendation for a short term - I'm sorry, for an opportunity, training for health care professionals, service providers, emergency responders and educators. And some have asked whether this is actually research and should be in a research plan or not. It's the training function, particularly for providers.

What's the sense of the group? Is this a research plan, not appropriate? Those who want to add this additional item, can I see a show of hands?

DR. MORRISSEY: Well, I don't think the training is a subset of research. It's really a distinct function in and of itself. And since we don't have a training chapter -

DR. HOULE: You could turn it into

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research by - rather than adding training as part of this research agenda, you could add identifying best practices for training health care professionals, and that might give you a services research project.

DR. MORRISSEY: That will work.

DR. INSEL: So just an opinion here, because this is a huge issue. It's incredibly important, building the capacity for providers. But if you want to put a chunk of the research budget into that, you are not going to have that budget available to do the science. And you have to make a decision up front I think about whether that belongs in a research strategic plan, or whether you want to put that into your services effort to make sure it gets done.

DR. HOULE: Well, I wasn't talking about using research money for training. I was talking about using research money to identify effective training outcomes in communities.

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DR. INSEL: So do research on the best way to train?

DR. HOULE: Yes, what works when you are bringing all these people together, training them and have an impact; what is the best. Not the direct training. We are not funding the training. Funding a look at some of the principles.

DR. INSEL: Okay, got it. So that would be one way to modify this.

DR. MORRISSEY: You could even add, law enforcement too in this.

DR. INSEL: So Gail, do you want to provide some language for that, and we can make that a motion, and then we can take it to a vote. And Pat was saying to add law enforcement along with emergency responders.

MR. GROSSMAN: May I have a comment? I think the list can go on forever. We could add about five more things to this as well. So unless we are going to start listing things, maybe if there was a broad - just a

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broad comment that could be made to include just training. Because I think minority outreach is an area; criminal justice system are things that come to mind.

DR. MORRISSEY: Lee, I don't mean to disagree with you. But I think two things that I know a lot about at this point in my life are emergency responders and the criminal justice system. And I think if you put professionals as a general term to cover everybody, people won't naturally think those, or include them in any type of research effort to find out what they need to know to operate appropriately.

MR. GROSSMAN: I could go either way, either make it a longer list, or - once you put a list here you are going to start - you have limited yourself.

DR. INSEL: Before we get into wordsmithing this, maybe we should get a sense of the group, do you even want to go there. Because I'm not sure from the first comments

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that people even want to have this in this part of the plan.

So can I get a - and we can then change how we want to word it - but just initially how many people want to include this item which will become an item about research on training in this part of the plan? Who wants to include it?

(A show of hands)

MS. HANN: Five.

DR. INSEL: Pat?

DR. MORRISSEY: Well, since it's less than eight, I'm up a creek.

(Laughter)

DR. INSEL: But you are in good company.

DR. MORRISSEY: Maybe that raises a broader issue. Clearly if we are going to have an impact on how people with autism are treated, training is a central part of that. And if this is the only place in the whole document that training is even mentioned in

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any context, I think we have to save it. If you don't want a laundry list, I don't care; I can live without a laundry list. But I clearly think that we definitely need to mention training or develop best practices related to training somewhere. And if you don't like a laundry list, say such as.

DR. INSEL: Well, let's get a show of hands of the number of people who do not want to go there at all as an item. And again, I can refer back to the Trevathan approach which is to say that - that doesn't mean it wouldn't be in document 2.0, but it wouldn't be in this document at this point.

So those who don't want to have this item in the report?

(A show of hands)

MS. HANN: Okay, the vote at the table is seven.

DR. LANDIS: Is Cindy still here?

DR. INSEL: No, Cindy is not - if she's here she's been on long term mute. We

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haven't heard from her.

DR. TREVATHAN: Cindy has emailed me, and we are actually working - there is an effort to correct a problem. She is on the line - hello, Cindy - but she is not able to be heard. So there is a technical issue. But she emailed me saying that she seems to consistently agree with the minority, so we haven't lost anything perhaps. But they are working on trying to get Cindy back on.

DR. INSEL: Well, if we assume then that she agreed with the minority then the vote was tied in this last one, wasn't it?

MS. HANN: No, it's actually six to seven. That's what it is. I counted six that wanted a statement with regard to training, and seven who do not want to have a statement.

DR. INSEL: Ed, I thought you said that she was consistently agreeing with you.

DR. TREVATHAN: I don't know if she agrees with me. She doesn't see what I'm voting for. But she said she tends to agree

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with the majority, so she's not too stressed.

DR. INSEL: Oh, the majority.

DR. TREVATHAN: The majority, so maybe I misspoke. So we are now talking about you, Cindy. If you send me your phone number, then they can give you a call.

MS. HANN: Actually, we have, and we are waiting for her response.

DR. INSEL: We are ready to move on to longer term objectives. I don't think I see anything else until page six, and we are moving through now - even on six, so we are down to the final part of Chapter 5. There is an alternative and an addition. ON the alternative - this is now at the top of page seven - increase the number of services to at least four, and increase the cost - that is increasing it from three to four - that is the first one. And then you can see the addition, which was an RCT, of long-term effects of the intervention methods.

So let's take the first one on,

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going from testing the efficacy and cost effectiveness of three evidence-based services for people, changing that to four, or at least four. And the other alternative, to go back to Gail's comment, it could be at least three.

DR. HOULE: Well, that was not my comment on this one.

DR. INSEL: Okay, but that was the canonical Gail -

DR. HOULE: The at least is in there in the modification. So yes, it could be at least three or at least four.

DR. INSEL: I don't know how long you want to debate this. Certainly we could talk about it for awhile. But why don't we just decide.

Those who want to have the language say at least three, if I could see hands.

(A show of hands)

MS. HANN: The vote is five for at least three.

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DR. INSEL: And those who would move it to be at least four.

(A show of hands)

MS. HANN: Eight.

DR. INSEL: And I'm assuming that you won't actually say increased cost but that will go into the determination. So it would be just changing the language from at least three to at least four in the nomination, and then the addition here is to complete RCTs of long-term effects of intervention methods. We don't have a cost estimate for that.

Discussion about that? I assume this would have a due date of some time in 2020 or something like that.

Do we want to add this in, or is this something for Trevathan's version 2.0? What do you think?

MS. BLACKWELL: I do think it goes to what you were saying earlier, Tom, about cost effectiveness of services and supports, and how important that is going to be in the

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coming years. So although it's easy to say, let's table it, that's just one more year that we lose in terms of trying to figure out whether or not something had efficacy. I mean maybe this needs to be reworded. How many studies? At least one.

DR. INSEL: The other thing that - Ellen, just, if you look at the language we have tried to adhere to, rather than saying complete we usually say initiate or launch or something like that, because it is hard to know, especially for a long term - that is a 10-plus year study. If you want to say when it's going to be completed, you are probably closer to 2030 rather than 2020 in this case.

But do we even need to go there? What is the sense of the group?

I think the sense of the group is that everybody is really tired of this. Come on guys, we have to hang in here a little bit longer. We're getting close to the end of at least the chapters. We still have to do the

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intro, but we do need to get this done.

What is your sense? Shall we put this one off, or do you want to deal with it now?

Lee?

MR. GROSSMAN: I guess I would want a clarification on what completion means. Does that mean that all of these studies are going to be done, whatever number it is, that they will be completed in 10 years. Is that possible?

DR. INSEL: So this goes back to what we were talking about before for some of the EPI work. We may really need to have a better sense of the feasibility. I'm not sure we have that. I don't know that anybody has vetted this idea well enough the way we did for the other ideas that went through workgroups and came out of discussions and very careful consideration.

This may be one of those that we have from public comment that we want to throw

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into the next workgroup to decide whether this is something that ought to be in the next version of the plan.

MR. GROSSMAN: I mean I would want us to pursue the idea of these control - randomized control studies obviously, as the data presents itself it'll be made available so that we can utilize it. I don't know if that is addressed in the rest of the research plan; if not, this might be a place to put that in there. So that we are pushing to have these studies done, and that we have access to the information.

DR. INSEL: Duane?

DR. ALEXANDER: It's my impression that these interventions are in such a fluid state right now, and with even lack of much short term evidence of effectiveness that committing to a long term randomized control trial of something like this doesn't seem a wise way to go until you have at least some evidence of short term effectiveness. I just

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don't see making that commitment to a 10-year investment.

DR. INSEL: Okay, so let's see how the rest of the group feels. Those who want to add this in as a new initiative; we'd do some budget estimates on it later. But who wants to include this?

MR. GROSSMAN: I have another area of clarification here. Are we talking specifically here, I'm assuming this is referring to services.

DR. INSEL: I'm not clear. I don't know what it is.

MR. GROSSMAN: Okay, it's in the services section.

DR. INSEL: Yes, but it's really not clear what they are talking about.

MS. BLACKWELL: It's intervention.

DR. INSEL: It's interventions, broadly. So I think that is part of where the sense was that this should be remanded to further consideration and maybe thought about

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for the next version of the plan.

MR. GROSSMAN: I mean if there is no agreement that it does mean services then I'd say take it out. If we are going to talk about services, I think that is something - it's going to take a decade or more to approve any system change in service model. And again if it draws support to that occurring I'd say keep it in, but if it's not directed specifically to services -

DR. INSEL: So what about if we take this and refine it. Because I agree with you. I think we do need to have some long term efforts, something very ambitious, something that has comparative effectiveness component to it. But it just doesn't sound like it's ready. Unless anybody is feeling strongly that this is something we want to push forward. Okay?

Is there any - in favor of going back to the original language not including this - hands?

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(A show of hands)

MS. HANN: Okay, the vote is unanimous at the table.

DR. INSEL: Chapter 6, and I promise you a break when we get finished with Chapter 6.

We are in the section about what does the future hold, initially what do we know. And there is a sentence that has been added in at the very beginning of that. Given the increase in prevalence of ASD over the past few decades, we know that the number of adolescents, adults and seniors with ASD is also on the rise.

The term, seniors, has given some people some heartburn, and we should talk about what would be better language.

Ellen? Help us with that.

MS. BLACKWELL: I always like older adults. I'd rather be an older adult than a senior.

Of course that begs the question,

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do I want to be a junior.

We usually use older adults.

DR. ALEXANDER: But it is inconsistent. We saw it's risen over the last two decades. Nobody has had time to get to be a senior yet.

DR. TREVATHAN: I think it also presumes that we have baseline rates for ASD prevalence in adults, and we don't. So we could presume that it's right, but we don't have the data. So to say this technically, we don't know - we can't prove this is true. We can have an hypothesis that it's true based on available evidence.

MS. BLACKWELL: I would actually recommend that we strike this sentence. I mean I agree 100 percent with Ed and Duane. We in our Medicaid home and community base waivers, and in the Medicaid and Medicare programs, we know that we have many many adults with autism spectrum disorders who were diagnosed decades ago with mental - and still

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carry a diagnosis of mental retardation. States report that they know that these people have autism, and quite frankly it probably would not make much of a difference in the services they receive, having a different diagnosis.

So this is an important discussion that we will probably get to later, but it starts right here.

DR. INSEL: Other comments?

So alternatives are to go back to the original language, or to put in this addition. Those who want to retain the original language, show of hands?

(A show of hands)

MS. HANN: Nine.

DR. INSEL: And Pat? And Cindy?

DR. MORRISSEY: I'm fine.

DR. INSEL: Cindy, are you with us yet?

The vote on the addition, that is those who would put in the alternative?

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(A show of hands)

MS. HANN: Three.

DR. INSEL: Okay, we are moving to the bottom of the page. It looks to me like, Ellen, you had a comment on the word, neighbors, so they can receive support from their neighbors and communities to help them lead productive and fulfilling lives. And you were concerned about -

MS. BLACKWELL: I think people could receive support from many different places in the community. It's not just - it's well beyond neighbors.

DR. MORRISSEY: I think the phrase to use is natural support. Which will cover everything under the sun.

DR. INSEL: I'm sorry, Pat, could you just say that again?

DR. MORRISSEY: Natural supports. It's a term of art.

DR. INSEL: Can you read - I'm lost. So can you read what that would read

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like, Ellen?

MS. BLACKWELL: Okay, so I think what Pat is saying, also it is important to improve public understanding of ASD in adults, including older adults, so that they may receive natural supports to help them lead fulfilling and productive lives.

DR. LANDIS: As opposed to unnatural?

DR. MORRISSEY: Natural supports from people in their community.

MS. BLACKWELL: How about community support?

DR. INSEL: So they may receive support from their communities to help them lead productive and fulfilling lives. So we are just going to drop out the term, from their neighbors.

Okay? Stephen, does that make sense? Okay, moving on, efforts to improve public awareness and community supports that help reduce stigma by emphasizing the positive

aspects of ASD. That's an addition. That came from public comment. Do you want to include that or not?

I think there was a mix of views on that. I think some people - let's see here - yes, so Ellen you had some concerns about the use of the term, stigma, and positive aspects.

MS. BLACKWELL: I think it's certainly good to improve community awareness, but isn't that what we might want to say?

MR. SHORE: I think we want to move beyond just community awareness that autistic people exist.

DR. MORRISSEY: I think the issue is acceptance and inclusion. They want to educate communities to understand, accept and include people with ASD in community activities.

DR. INSEL: What about the language that we have here? That is the addition, do we need to alter that, or would you feel

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comfortable voting on it as it is?

MR. SHORE: I think it is fine the way it is.

DR. INSEL: Duane?

DR. ALEXANDER: I would suggest we might accomplish the objective by saying, public awareness and community support could help foster acceptance. I think that is what we are talking about.

DR. INSEL: I thought Stephen was saying something more than that.

MR. SHORE: Yes, it's one thing to accept or tolerate, and it's another thing to appreciate and welcome.

MS. HANN: So just to help us move along, so the sentence could read, efforts to improve public awareness and community support could help foster acceptance and inclusion.

MR. SHORE: And appreciation by emphasizing the positive aspects of ASD.

MS. BLACKWELL: I've got one.

DR. INSEL: Ellen is going to have

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the solution.

MS. BLACKWELL: How about efforts to improve public awareness may improve community inclusion.

DR. INSEL: Stephen is talking about something else. If I hear you right, it's trying to also - it's more than acceptance or inclusion, but appreciation, that people with ASD can bring something to the community that is important and useful.

I have to say, the language that is here it seems to me does that. But if it doesn't for other people, we need to figure out how to make it work.

Efforts to improve public awareness and community supports could help reduce stigma by emphasizing the positive aspects of ASD. You don't like the term stigma?

MS. BLACKWELL: No, I don't like it at all.

MR. SHORE: We could get rid of

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that. Community supports. And then remove "could help reduce stigma", just by emphasizing that it is to improve - I can live with it too.

DR. INSEL: So Stephen, give us the language that you think would work.

MR. SHORE: Efforts to improve public awareness and community supports by emphasizing the positive aspects of ASD. That's if the word, stigma, is getting in the way.

DR. INSEL: You need a verb. Efforts to improve public awareness and community supports -

DR. LANDIS: Could help foster acceptance, inclusion and appreciation by emphasizing -

DR. INSEL: All in favor? You got it. Did you get that language, Della?

MS. HANN: What I have is -

DR. LANDIS: Could help foster acceptance, inclusion and appreciation, so

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it's taking out reduce stigma which is negative, and have positive, foster acceptance, inclusion and appreciation.

MS. HANN: By emphasizing the positive aspects of ASD, right?

DR. INSEL: And all hands went up. So Pat, you are okay with that?

DR. MORRISSEY: I didn't hear what it was, because somebody didn't have their microphone on, but I agree.

DR. LANDIS: Oh, okay, what it was, was, could help foster acceptance, inclusion and appreciation by emphasizing the positive aspects of ASD. So we got rid of - we replaced "reduce stigma" with foster acceptance, inclusion and appreciation.

DR. MORRISSEY: That means people won't accept the negative aspects of ASD. I think that phrase is kind of weird. The issue is to accept somebody as they are with all the good things, all the interesting things, all the things that might drive you crazy. You

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see that, Stephen? It's like the communities can accept the positive aspects of somebody with ASD, but they sure as hell are not going to accept the negative aspects.

MS. BLACKWELL: Maybe Della could read the sentence back without the positive aspects.

DR. MORRISSEY: Yes, take out that phrase.

MS. HANN: Okay, so now what I hear is efforts to improve public awareness and community supports could help foster acceptance, inclusion and appreciation of people with ASD.

DR. MORRISSEY: That's perfect.

DR. INSEL: Moving on. Top of page three, Ellen you had a line that you wanted to change. You were concerned about, with more narrowly defined autistic disorder.

MS. BLACKWELL: I don't know what that means.

DR. TREVATHAN: It is right at the

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top of page three. I have no idea what that sentence means.

DR. INSEL: I think it means Kannerian Autism. That's a term that is fairly commonly used in medical circles anyway.

DR. TREVATHAN: So it's the more core syndrome of the ASD spectrum.

DR. INSEL: Right, as opposed to the full spectrum. So narrowly defined it's classical autism.

Okay with that? Can you live with that?

All right, page four. We are moving now into research opportunities. There is an addition of strengths and weaknesses, following the term, trajectories, and -

MR. SHORE: What about - comment. I wonder about replacing strengths and weaknesses with characteristics.

DR. INSEL: Because strengths and weaknesses again has a value judgment.

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MR. SHORE: They have value judgments, and what might seem like a strength could be a weakness and vice versa. You might now know until later.

DR. INSEL: Do you need anything in there, or could you just say to follow the trajectories as it was originally stated that account for clinical, psychosocial and biological heterogeneity. Maybe you don't need the change. What do you think?

MR. SHORE: Well, the characteristics helps us focus on different aspects.

DR. INSEL: But I thought that's actually what the rest of the sentence did by saying you can focus on clinical, psychosocial and biological complexity.

Well, we can again put this to a vote. We've got three options here. One is to go back to the original. The other is to add strengths and weaknesses. And the third is characteristics.

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Who wants to just retain the original?

(A show of hands)

MS. HANN: Okay, the vote is six people at the table.

DR. INSEL: Strengths and weaknesses?

(A show of hands)

MS. HANN: Zero.

DR. INSEL: And Pat, the third is to say trajectories of characteristics that account for clinical psychosocial -

(A show of hands)

MS. HANN: Six.

DR. MORRISSEY: I like the first one.

MS. HANN: So that would make it seven.

DR. INSEL: And Cindy, are you anywhere in the ether? She's still not available. Ed, can she email you, since we are really at a virtual tie. She's not

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responding?

Okay, so what's the -

MS. HANN: So the vote with Pat's vote is seven to go back to the original language, and six to adopt the word, characteristics.

DR. INSEL: So we are now at the end of the section on research opportunities, and we have two additions that have been put in. One is on improving safety, and the other is models of financing to pay for services.

And what is the sense of the committee about those?

(Comment off-mike)

DR. MORRISSEY: I have a comment on the first one. I don't think we really need to single out people as ASD. There is a lot of work going on in communities to develop functional ways to identify people in an emergency, and to also deal with them prior to an emergency hitting. So I don't think we need to spend research money here on that

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topic.

DR. INSEL: So is there a research question about how to do this? There is a comment here from Lyn about using amber alert or GPS systems.

DR. MORRISSEY: They are dealing with that generally, Tom, for people with disabilities and the elderly now, and there are all kinds of issues connected to registries, Amber Alert, how you do it, how you keep things updated and current. But the topic is on the table and people are dealing with it, and if they do deal with it people with autism will also benefit.

DR. INSEL: Sense of the group? Should it be here, not be here? It wasn't in the original, but is this an improvement if we include it?

Again, remembering this is a research plan, so what do you think?

(No response)

DR. INSEL: All right, those who

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want to include this addition of improving safety, that is, which is locating ASD individuals when lost or during local emergencies. Those in favor of the addition? Lyn?

MS. REDWOOD: Tom, I guess I'm a little confused by it. Because I think it is important. Almost on a weekly basis there is an article in the paper about a child who is missing that they can't locate, and they are gone for several days, and usually the outcome is very tragic. And so I guess I don't know how you make a research question about that. Is it the service that we need better ways of tracking these children, or are methods to protect their safety more? It's a huge issue, but I just don't know how to approach it the best way.

DR. INSEL: Yes, we are at that end of the spectrum where it is a little difficult to know whether things will end up in a research plan or a services plan, or whether

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there are some things that just need to be done as opposed to being studied, and that's really the question here. Is this an article for study, or an article for now, implementation.

Lee, what is your sense about this?

MR. GROSSMAN: Well, that it needs to be done.

DR. INSEL: But is this a scientific question? Do we actually need to do science around this issue, around safety?

MR. GROSSMAN: No, I think we know what we need to do.

DR. MORRISSEY: I think there are three issues. One is what Lyn raised, you know, when a kid gets lost. The second is when an emergency hits an area in general. And the third is whether it's a research question or a service issue.

And this gets back to my point about training being kind of lost in the

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plans. So maybe you need to decide whether one of these three things is worth mentioning here and say it. Could be a safety issue, could be an emergency issue, or preparing people at the local level to be more attuned to how to find somebody with autism in either a safety situation or an emergency.

MR. GROSSMAN: Well, under the general umbrella of preparedness as we say at CDC, there is an area of research on just how do you implement certain types of relief for safety purposes, for example, in various disasters.

And we certainly all saw in Katrina how some of that didn't work very well. So that is a whole category of preparedness research. Now if that is thought to be an area of need, which I suspect that we aren't doing a good enough job, and we may not know all the things we need to do, then that may be an issue to consider.

I also wonder, not to keep

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repeating myself, this could be bigger than we think, and may be something to take up in another year.

DR. INSEL: Right, but Ed, remember, we are still in research opportunities, so we are not making any recommendations for initiatives. This is really just putting on the table what things might be ripe for development.

I'm struck by the fact that people sense this is a really important issue. Personally I'm not convinced that we know everything we need to know about it.

MR. GROSSMAN: Well, we're not close to it. But I mean I worked with Jose quite a bit after Katrina and Rita, where we were looking at - because the entire disability community was kind of in shock after that, how the treatment, and autism specifically was just - I mean we went down to town hall meetings in Louisiana, and the stuff these families were telling us were just - it

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was unimaginable. So we tried to develop a plan out of that to kind of do a research and outcome on what it would mean to set up disability safe houses within driving distances of every place in the U.S. in case of bioterrorism or hurricanes or tornadoes, et cetera. And it became clear out of that that we didn't need research; we just needed to do it. And that's why I made that statement earlier.

DR. INSEL: Let's take this to a vote. I think this is actually a tough one. But who wants to add this at this point?

The alternatives are to add the line that says, improving safety such as locating ASD individuals when lost or during local emergencies. The alternative would be to leave this out at this point; we can come back to it next year. But we need to make a decision.

So who wants to add this in at this point?

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(A show of hands)

MS. HANN: There are no votes at the table.

DR. INSEL: Lyn - I'm sorry, Pat.

DR. MORRISSEY: That's okay.

DR. INSEL: so we are going to move on to the next bullet, which is models of financing to pay for services and provide for long term care when family is no longer available, another piece of what was though to be a research opportunity from public comment.

MS. BLACKWELL: I don't see this as a research opportunity. This is more of a policy discussion.

DR. INSEL: But there is not a scientific agenda around figuring out the best way to finance this?

MS. BLACKWELL: Well, we know how our present services system is set up. I don't think it's models of - it may not even be models of financing. It might be models of services and long term care for people with

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autism. This is extremely confusing.

DR. INSEL: Okay, who wants to include it at this point? Anyone? Hands up?

(A show of hands)

DR. INSEL: There is no one raising their hand. Pat?

DR. MORRISSEY: No.

DR. INSEL: Okay, we are moving on to the objectives. We have only a few here, but there are some suggestions for alternatives.

The first one is at the bottom of page five. It just says that we should increase the amount as the number of incoming data sets that could be utilized if the funding were available. In addition to NDAR, the ARI, Dan's data set should be linked.

So it's calling for the harmonization and the integration of databases. And the recommendation as I read it, the alternative, is simply to push the

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budget up.

So I'm not sure we need to actually vote on this. It could come into the budget discussion.

All right. Moving right along, the next one is - adds the terms, residence and employment, following the word, functioning in the second bullet. So this is two studies to assess and characterize variations in adults living with ASD, and it's in the parenthetical part where it says, such as social and daily functioning, residence, employment.

MS. BLACKWELL: I think these are the wrong measures. I gave Della a copy this morning of a national core indicators sub-domains. And we don't have to reinvent the wheel here. But when you look at things like work, community inclusion, choice and decision making, self determination, relationships, satisfaction, service coordination - I mean there are endless suggested changes up there.

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But maybe we should just come up with a couple of umbrella words here to cover all of those.

DR. INSEL: The other thing that we have heard earlier in the day is that people were just leaving out the parentheticals because they over-specify. And would that - in this arena would that be helpful or not? What is your sense?

DR. TREVATHAN: Can you subsume - actually most of these under functioning, just social and daily functioning?

DR. INSEL: So that would go back to the original language? Just leave it out?

MS. HANN: And also, it sounds like you are also suggesting leaving out demographic, medical and legal status. So just have it to be social and daily functioning.

DR. INSEL: Without the parentheses?

DR. TREVATHAN: Yes.

DR. INSEL: Lee?

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MR. GROSSMAN: Well, there is a suggestion just to strike everything in parentheses, and after living with ASD just say and quality of life.

DR. TREVATHAN: Sure, that gets it.

DR. INSEL: So read us the proposal, launch at least two studies -

MR. GROSSMAN: To assess and characterize variations in adults living with ASD, and their quality of life.

DR. INSEL: By 2011. In favor of that language?

(A show of hands)

DR. INSEL: I don't see anyone opposed. Pat are you okay with that?

DR. MORRISSEY: Yes.

DR. INSEL: Moving along to the - towards the bottom of this page, at the bottom there is an alternative for the number of trials that should be increased because only two trials across three age groups, and all these aspects of functioning seem too few.

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So there is a wish to bump up the commitment to look at the efficacy and cost effectiveness of intervention, services and supports.

And Ellen, you had a comment on this as well, around the list of aspects of daily functioning. You wanted to use the NCI subdomains.

MS. BLACKWELL: I'm sorry, which line are we on?

DR. INSEL: We are on page six, and we are looking at - well, no we are already down to line 13, or we are also looking at the alternative language.

DR. LANDIS: So it was actually line three.

MS. HANN: Mic, Story.

DR. LANDIS: Sorry. I was doing real well this morning. Instead of - in line three, instead of "at least two" it would be -

DR. INSEL: No, we are further

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down.

DR. LANDIS: You are down on the alternative, right?

DR. INSEL: No, we are down to lines 13 and 14 on page 6. It says, where it says, conduct at least two clinical trials to test the efficacy, and the comment in this supplement here from Ellen was that under the last bullet, for examples, use some of the NCI subdomains, and there is a whole long list of those.

So what you are saying, Ellen, if I understand you, instead of using educational, vocational, recreational and social experiences, you want these other items?

MS. BLACKWELL: Again, do we need to include - can we just take out the parenthetical?

DR. INSEL: Yes, I think that's what the group wants to do. Okay? We could do that. So that is one option.

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The other is that we are still left with this alternative about increasing the number of trials, and what's the group sense about that? Again, these are short term objectives, so if we are talking about by 2012, and in this case it says to conduct, so there may - whether you think it's feasible to actually bump this significantly.

Duane, what is your sense?

DR. ALEXANDER: I think that in the timeframe available getting two of these started and well underway is probably not unreasonable. Two doesn't seem like a whole lot, but in this area with these complexities it's probably not bad.

DR. INSEL: Okay, so let's look at this. We've got three options here. The first is the original language. The second would be to put in the - to take out the parenthetical statement. And the third would be to bump up the number of trials, and we haven't specified, but it would be

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significantly more than at least two.

Can I get a sense for who wants to stick with the original language?

(A show of hands)

DR. INSEL: There are no hands going up.

MS. HANN: No votes.

DR. INSEL: Who wants to bump out the parenthetical and keep the public comment option?

(A show of hands)

MS. HANN: Seven.

DR. INSEL: And who wants to go to the third alternative, which is to bump up the number of trials, and we will have to look at what that would mean? And bump out the parenthetical?

(A show of hands)

DR. INSEL: We've got four, and Pat?

DR. MORRISSEY: I'm on the second one.

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DR. INSEL: Which is to conduct at least two trials or to increase?

DR. MORRISSEY: The second one we voted on.

MS. HANN: The second one was to conduct at least two, and then it dropped the parenthetical.

DR. MORRISSEY: Right, that's it.

DR. INSEL: So we will stick with that language and bump out the parenthetical. And we'll move on to the long term objectives. And we are really in the home stretch here for Chapter 6. We've got one more page.

There are no comments in the first one, but on the second one we've got two alternatives - or one alternative and one addition. The alternative is to conduct a needs assessment to determine how to merge or link administrative databases, and the addition is to conduct a cost-benefit analysis on the provision of early services and interventions with regard to long-term cost-

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benefits regarding employment, productivity and federal-state assistance.

DR. MORRISSEY: Did you change the page?

DR. INSEL: Sorry?

DR. MORRISSEY: Did you change the page? I'm still on page six on the computer.

DR. INSEL: We are now on page seven, so on the computer we are now on page seven, thank you. You can see it much better than we can; that's probably why.

So this is discussion point 6.6. There are some comments from the committee. Cindy Lawler says this is an important addition. Lyn as you can see has comments, and I won't bother to read them. But she has got - I'm not sure actually what's changed here, Lyn, it's the same language, I think, but you've added in under the cost-benefit analysis to take out early services and put in over the lifespan.

All right, sense of the committee,

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what do you want to do with this?

DR. TREVATHAN: Just one point, Tom, and I don't know that we need to change the wording to include this. But one of the things that has come up recently at CDC, and this is - could potentially be some low-hanging fruit for us is that the ability to potentially link some administrative data sets with surveillance data, which previously we thought we couldn't do very well but it looks like there may be some opportunities there.

We could assume that administrative includes surveillance data, but it really technically doesn't. So that would be nice; that would give us the opportunity to really have an idea of what is going on in populations and compare that with some of the administrative data we've got, some of the CMS data for example.

DR. INSEL: So I should be clear about what we're talking about here. Because the original provision was a long term

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objective that said by 2018 we will do this. Then the addition or the alternative is to do the needs assessment right now, and it actually has a timeline of 2009, so you'd have to start it yesterday.

And it says that within a year we want to actually know how to get this done. That is a very different proposal, and it would it of course to a short term objective. And I think actually this is consistent with some of the things that the services group has been talking about as well, trying to get our hands on these big administrative databases and figure out how to use them to do some research, particularly the CMS database.

Duane?

DR. ALEXANDER: I prefer Lyn's alternative. It's a thing that is a necessary first step, has a reasonable timeframe, and something we could do very quickly.

MS. BLACKWELL: I think I'm a little bit - initially I reacted to Lyn's

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taking out the word, early, and said okay. But I think there is some benefit to leaving it in, because most of the controversy seems to surround what are in fact early intervention services, and whether or not the -

DR. INSEL: I'm sorry, Ellen, but that is actually the - that's the addition. So I want to make sure we get this alternative done.

MS. BLACKWELL: Okay, we are still on -

DR. INSEL: Yes, on the needs assessment.

MS. BLACKWELL: Yes, I agree with that.

DR. INSEL: So this would actually go then in the short term.

So in favor of putting in this additional language? We could actually take this as not instead of but in addition to what we are talking about, so rather than an

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alternative it is an additional short term.

In favor?

(A show of hands)

DR. INSEL: It looks unanimous except for Judith.

DR. COOPER: Are we keeping the 2009 date?

DR. INSEL: Yes. So this would be done, we would be doing a needs assessment now, and actually figuring out how to do this. We actually have people who do this kind of thing, so I'm comfortable that's realistic. I don't know how to do it, but they know how to do it.

MS. HANN: So it was unanimous. Just for clarity purposes, so we are agreeing to say, conduct a needs assessment to determine how to merge or link administrative and/or surveillance databases. Because Ed wanted the word, surveillance, to be added to the databases as I recall.

DR. INSEL: Right, is that okay

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with everybody?

MS. BLACKWELL: We need to revisit the cost on this one, too, correct?

DR. INSEL: Yes, we have to revisit the cost.

So people are okay with retaining the original language for the long term goal. That takes us to the addition, then, which is the cost-benefit analysis.

And Ellen, we can go back to your comment.

MS. SINGER: My apologies. Yes, I think we - I mean this is actually an important piece, because we really don't have data on the impact of various early intervention strategies. But I think the way it's worded is poor, because these first two - the first two items inside the parentheses refer to the person, him or herself, and the other relates to federal programs, which are not the same thing.

So I'm not sure what the person

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was looking for, or the entity who wanted this added in.

DR. MORRISSEY: Ellen, I have no idea who sent this in. But the way I read it was, they wanted to know if you had intervention A, if you looked at that person later in life, do they have a good job, do they live independently, those kind of things. So the parentheses were trying to get at some outcomes later in life by identifying who had an early intervention program at the beginning of their life. So it's kind of like a longitudinal study.

MS. REDWOOD: The other thing about early, I think by not having early, it doesn't mean we couldn't still look at early services, but yet some people don't get services early. They are diagnosed later in life, or they began therapies maybe as teenagers.

So I think that we need to look at whether or not even starting services later can be beneficial.

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DR. MORRISSEY: I think if we changed this whole thing, Lyn, to a longitudinal study, you then have information throughout a person's life. Because if it focused only on early intervention, and a person had successful employment outcome later, you really wouldn't know whether that was associated with early intervention or something else had happened.

So I think this should be rephrased to be a longitudinal study, and I think Gail you are better at this, but the longitudinal studies out of the U.S. Department of Education with regard to kids or facilities have been very very informative.

DR. INSEL: But this wouldn't preclude that. This would simply say, look at a whole range of different times, and the lifespan, to figure out what the cost-effectiveness of interventions would be.

DR. HOULE: I agree, because early intervention really is a small slice of the

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interventions across - your population in early intervention is going to be out of early intervention very quickly, and they are going to be receiving other interventions. So we do need the long term, I feel.

DR. INSEL: Okay, so let's go ahead and vote on this. We've got a couple of possibilities. One option is not to put any language in at all, so we go back to the original.

The second would be to put in the language that we had from the public version.

And the third option is what we have from Lyn, which is striking out the word, early, and putting in, across the lifespan, or over the lifespan, after interventions.

MS. BLACKWELL: And Tom, the only other thing I would add is again I think that the federal-state assistance part needs to come out, and that the parenthetical needs to come out, and that the parenthetical needs to be focused on the characteristics of the

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person, not whether or not they received federal and state assistance. Does that make sense?

DR. HOULE: We don't have that, Judith and I. You are talking about the parenthetical part. Which document are you looking at? We don't have anything like that. We can't find public -

DR. INSEL: So this is on page eight. It's - well, it ends - the addition is actually on page eight. So it's to conduct a cost-benefit analysis on provision of early services and interventions with regard to long term cost-benefits regarding employment, productivity and federal-state assistance.

MS. BLACKWELL: Then I think we should strike the words, federal-state assistance, and just focus on the characteristics of the person. They are employed, they are productive, they are engaged in their community. But it's not tied to federal and state assistance.

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DR. INSEL: Wouldn't you want to know what the value of federal and state assistance would be in the long run? Whether that has been a good investment or not?

MS. BLACKWELL: If we are tracking their employment, wouldn't we know their - all right, so it could be -

MS. SINGER: You are looking at federal-state assistance as an input, and we are looking at employment and productivity as an output, and that's I think why it's confusing.

MS. HANN: And I think some people are also thinking of federal-state assistance as an output as well.

MS. SINGER: Is that right?

DR. INSEL: Does that help?

MS. BLACKWELL: Maybe it should say, and the need for federal-state assistance. Because that is how it's attached to the individual.

DR. INSEL: All right. Okay.

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So the language - so the alternatives are, nothing, versus conduct a cost-benefit analysis on provision of services and interventions over the lifespan with regard to long term cost benefits - it's a little bit wordy here - I'm not sure you need the long term cost benefits - regarding employment, productivity and the need for federal-state assistance.

So with your permission we may wordsmith out the cost benefit - one of those.

DR. LANDIS: If you just took out the cost it would be okay.

DR. INSEL: With regard to the long term benefits.

DR. LANDIS: Benefits regarding employment, productivity and the need for federal-state assistance.

DR. INSEL: Got that, Della?

MS. HANN: Yes.

DR. INSEL: In favor?

(A show of hands)

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DR. INSEL: Anyone want to go to the default, which is nothing at all?

(A show of hands)

DR. INSEL: I don't see any hands.

Pat, where are you with this?

DR. MORRISSEY: I want the first option.

DR. INSEL: Okay, so Della, that is another unanimous one.

We are finished with Chapter 6. You have earned a break, but it will be short, because we still have to do the introduction.

So let's reconvene in about five minutes.

(Whereupon, the above-entitled matter went off the record at 2:56 p.m. and resumed at 3:07 p.m.)

DR. INSEL: Okay. We are going to have a 15-minute public comment period at 3:45, because the meeting is scheduled to adjourn at 4:00. So that means we have 35 minutes to do this introduction.

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We have a lot of comments about the introduction. Remember, this is just to set the stage, and to try to both inspire and also command the sense of urgency.

One of the first things we should look at is left over from the previous meeting where you said that you wanted to have some language that would deal with the associated symptoms for autism. And the team has tried to craft something like that.

It's in your folders. It's a single page that looks like this; it says draft on it. And that's - yes, it'll just say page one, and it's discussion point intro one, and what that language says is, some children with autism also have a range of medical symptoms including but not limited to motor and sensory impairment; seizures; immunological and metabolic abnormalities; and gastrointestinal symptoms. The existence of medical symptoms in greater than predicted numbers raises the question of whether they

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are secondary comorbidities or rather systemic manifestations of some underlying mechanism also implicated in autism pathogenesis.

That's a proposal.

MS. BLACKWELL: Are they all children with autism?

DR. INSEL: So if we said some people with autism, that would be better.

Okay, any other comments about this?

Okay, can we get a show of hands who wants to include this language at this point right at the beginning of the introduction.

All in favor?

(A show of hands)

MS. HANN: It's unanimous in the room.

DR. INSEL: And what about on the phone? Pat, are you still with us?

DR. MORRISSEY: Yes, I'm still here.

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DR. INSEL: Is this okay with you?

DR. MORRISSEY: Yes.

DR. INSEL: All right. Anybody else on the phone at this point?

(No response)

DR. INSEL: Okay, so we can go to the rest of the introduction where we've got lots of discussion points. We've also got comments from many of you. And I think probably the best way to manage this is just to begin walking through it.

Now Lyn you have very substantial recommendations for revisions, and I think the only way we are going to be able to do this is just to go through it in order. And we will just start with the discussion points that we have here, in the document.

The next one is listed as discussion point intro two, and it says, the prevalence rate is substantially higher than two decades ago, leaving many parents, families, health care providers and

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policymakers asking, what has changed? Why are there so many people with ASD? Is this an epidemic?

So that's an addition that was no in the original draft.

And Lyn, you have got some very extensive language. Do you want to share that with us?

MS. REDWOOD: I will. Tom, outside of reading the whole thing, I don't know if people have had an opportunity to look over this prior to the meeting. But it is just adding more meat to what's in there now.

It tries to set the stage more for a tone of urgency, and develop this plan. So if you want I can read through this whole thing, but it's fairly extensive. So I'm asking for your suggestion.

DR. INSEL: So the first question would be, where would this be inserted? Tell us where - it begins with the prevalence of autism spectrum disorders, but what is the

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lead in to that?

MS. REDWOOD: It would be right where the introduction starts. And instead of having the autism spectrum disorder share a diverse combination of core clinical characteristics, and going into a definition of autism, it starts more with, we are somewhat at a crisis now with regard to the prevalence rates of autism.

DR. INSEL: Okay, what is the wish of the committee? We sent this out ahead of time to make sure you have a chance to look at it.

MS. REDWOOD: The other things are still in there, the Center for Disease Control rates is in there, but it also goes into a little more detail by saying that most adults with ASD struggle with ongoing and mostly unmet needs for employment, housing, social supports. Compounding these stressors, families with a child with autism typically lose income. And then it cites references for

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these. The cost to society of ASD is currently estimated at $35-90 billion annually, the higher estimate being comparable to Alzheimer's disease. Despite expansion of research on ASD over the past decade the effort has been inadequate, while the known urgency increases daily.

MS. BLACKWELL: I think, although I certainly wouldn't dispute that we want to deliver a plan that has a sense of urgency, I am going to again register our concerns that we are talking about prevalence rates when we really don't know how many adults have autism. So I'm comfortable with saying that there is greater diagnosis, greater precision in diagnosis, but this seems like a giant leap to me.

It also is sort of dismissive of the adults that we know have autism now that aren't diagnosed with it. And to make a statement like most adults with ASD - I mean there could be many many adults that aren't

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diagnosed with ASD.

DR. INSEL: Other thoughts or comments about this? Judith?

DR. COOPER: I might like to suggest a revision to that last sentence, Lyn, about despite expansion of research on ASD over the past decade, perhaps rather than saying effort has been inadequate, something like there is a critical need for continuing research or something like that.

MS. REDWOOD: That is fine. You know we are sending this report back to Congress. And I want them to really feel like this is an important issue that deserves their attention, and that we needed a little more up front to catch their attention with regard to what's happening in our country today.

And from what I've heard, and Ed, maybe you can speak to this, the rates are going to be even higher in a new report that is going to be released by CDC, one in 150. Is that just rumor?

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DR. TREVATHAN: Well, that is a rumor. The data aren't out yet. So I can't really comment on it. I think it is the case, that many of us think - we are pushing very hard for better recognition, to better address some of the needs Ellen has mentioned. So I think we and our European colleagues don't think that our estimates are complete necessarily in spite of our best efforts. So I think that we will have more complete ascertainment, and there is a good chance - I'm not saying it will be - but there is a chance the numbers will be higher later, but we'll have to see.

DR. INSEL: So what is in front of us as a choice? Because we have language we had dealt with before, and we have crafted a bit more extensively just now. And I think Lyn what you are suggesting is replacing it with this introductory paragraph, right?

So we can change the last sentence of what Lyn is recommending. What the

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committee needs to decide is whether they are going to go that direction, or go back to what you have from the document that we looked at a minute ago. What is your sense? What to vote? Are we ready to do that?

So the vote would be between the modified language with the public comment, and with the comments from the team that has dealt with the physical medical aspects, so we already did that. So it's that versus putting in this new paragraph, and we would strike the last sentence, despite expansion of research on ASD over the past decade.

So all in favor of the language that is in there now? The original language is in the middle, and would include the statement that the prevalence rate is substantially higher than two decades ago leaving many parents to ask.

MS. HANN: It's this one, the one with the blue at the top. That is the one that you all just voted on.

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MS. BLACKWELL: Did we discuss the use of the word, ailments, in this middle paragraph?

MS. HANN: I thought that had been deleted.

DR. INSEL: You lost me. Where is ailments? Yes, that's gone.

So the first choice is the language that is on the board now. So what's on the screen.

The second choice would be the language that Lyn has provided minus the final sentence, which does a little bit of a slam at the research.

MS. HANN: Judith, could you say your edit to that sentence, please.

DR. COOPER: Clearly additional research - something like, despite expansion of research, there are critical research needs - I don't know. Something about research needs continue.

DR. INSEL: Something like, the

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urgency commands the need for continuing and increased research support.

DR. COOPER: Right.

DR. INSEL: Okay. A show of hands for the original - that is, for what's on the screen currently?

MS. HANN: No, that's not right.

DR. INSEL: I'm sorry.

MS. HANN: That's not right. It's the blue sheet. The one with the blue header is the one that you voted on a little bit ago. So the question is to retain this one, or to take that away and adopt Lyn's suggested language with the change in the last sentence.

DR. INSEL: So with one addition, Della, which is that if you accept this one there is the additional part in blue, which includes the statement that the prevalence rate is substantially higher leading many to ask what has changed, and is this an epidemic.

Are you with us?

MS. BLACKWELL: Can we say that the

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diagnosis rate is higher? Or are we all okay with prevalence? I think that is the question.

DR. INSEL: Prevalence means -

DR. TREVATHAN: Technically it'd be better to say prevalence estimates. That might be a way to be as accurate as possible, and address your concern.

DR. INSEL: Lyn.

MS. REDWOOD: I hate to add in another edit, but Stephen just pointed out, instead of saying most adults, it would be better to say, a great majority of adults with ASD struggle. That's down toward the bottom. Instead of most adults, it'd be a great majority.

DR. INSEL: Okay, I need a show of hands. Those who want to go back - or want to use the original version with the addition of prevalence rate is substantially higher.

MS. HANN: Prevalence estimate.

DR. INSEL: Prevalence estimate.

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So it's this page, that is with the language you have already agreed to, and the piece on the prevalence estimate is substantially higher than two decades ago.

Can we see hands up for the people who want to do that?

DR. HOULE: I have a question. This blue page first column or middle column?

DR. INSEL: Middle column. You have already agreed to that. So the only addition is what you see on the screen in blue towards the bottom of that box.

In favor of that language?

DR. TREVATHAN: With the prevalence estimate.

DR. INSEL: Prevalence estimate. All in favor?

(A show of hands)

MS. HANN: Five.

DR. INSEL: Actually, I'm going to abstain on this. So make it four.

MS. HANN: All right, four.

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DR. INSEL: So we're moving now to the option which is language provided by Lyn in blue, which you have in front of you, but we are changing the last sentence to say despite expansion of - I'm sorry, we are going to have to wordsmith this a little bit. Della, do you have language that we already came up with?

MS. HANN: No, I did have it beginning with despite. Despite expansion of research in ASD over the past decade there is a continuing need for this research to address the urgent needs of families and people with ASD.

DR. INSEL: Wouldn't it be growing need? Growing need.

Can you read it again and make sure we get this right?

MS. HANN: Despite expansion of research in ASD over the past decade, there is a continuing need for research to address the urgent and growing needs of people and

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families with ASD.

DR. LANDIS: That's unbelievably awkward.

MS. HANN: I didn't say it was beautiful.

DR. LANDIS: I mean I think if we just - I mean why should anyone if the research effort has been inadequate, why would you give anyone more money to do more inadequate research.

DR. TREVATHAN: But that's out.

DR. LANDIS: I know. So that's all I care about is that that be out.

MS. HANN: It's out.

MS. REDWOOD: Also the small edit that Stephen had suggested which would change most to a great majority.

MS. BLACKWELL: I'm really uncomfortable with the cost - with this sentence about cost estimates in here. I mean the cost to society. I think that entire sentence should be struck.

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DR. LANDIS: So maybe we could vote on - see how many people are - support some version of Lyn's, and if it's a majority then we can deal with issues like that, given your concerns about cost estimate.

DR. INSEL: Can I just respond? I think the data are really pretty well done. The Gann study dug into this with some care. I think there is - and I haven't seen anybody refute the numbers that we've got in hand. So unless somebody knows something different, the numbers that are cited here are all in the peer reviewed literature, and are pretty well accepted at this point. They may be wrong, but they are accepted. And they made it through into the best peer reviewed journals.

Am I - is there something more recent that would modify any of those? Okay.

DR. ALEXANDER: Tom, could we also agree that in that first sentence of this version that it would be prevalence estimates like we did in the other one.

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DR. INSEL: So Lyn, this is your version, you are okay with that?

Okay, so Story's recommendation is that we take a look at this in concept, whether we want to go to this somewhat more compelling language, and a little more detailed.

Those in favor?

(A show of hands)

MS. HANN: The vote is seven.

DR. INSEL: Great. So we've got - the motion carries to switch out the introduction, the first paragraph, to include this language, which has more detail. There are some changes in the specific wording, particularly on the last sentence, and maybe rather than trying to wordsmith in the last 20 minutes, if you are okay with this we will come back to you with what the final sentence will say. I think we need to move on, there are so many other things.

Della, can you live with that? I

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think we are close, but clearly we have to say something that makes sense.

Moving on, we are still on the first page of the introduction. We haven't got to the vision, the mission, all the wonderful stuff that is still to come.

MS. REDWOOD: One question of clarification. This sentence that deals with the additional medical symptoms, do we want to adopt some of the language that we had talked about earlier there, so we lose the word, ailment, and all that? Okay.

DR. INSEL: Is that understood? I want to see heads nodding? Lyn? So we are switching back - what we voted to before in terms of the physical symptoms, we will switch out this language.

MS. REDWOOD: The only one that wasn't in there was sleep.

DR. INSEL: And could be included - everyone okay with including sleep as another aspect? Great, that was a conspicuous

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absence.

The next block involves the second piece of this, so it's the bottom of page one. And Lyn, you have changed the language a little bit. Congress passed the CAA. Throughout this act the intent is to rapidly increase, accelerate the pace, and improve coordination.

MS. REDWOOD: I just added a sentence in front of it, and respond to the heightened societal concern. Congress passed the -

DR. INSEL: People all right with that addition? All in favor?

MS. SINGER: Can I just ask one question about the last sentence here? Oh, sorry.

DR. INSEL: Go ahead.

MS. SINGER: It says the strategic plan covers all activities of federal agencies. At the bottom of the paragraph.

MS. McKEE: Wasn't that what it was

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supposed to do.

MS. SINGER: Well, they have budgets outside of this budget too.

DR. LANDIS: We have no control over CMS, or AHRQ, or Medicare or Medicaid. I mean all of those are federal agencies. So research-related federal agencies, federal agencies that can contribute.

DR. INSEL: Could we leave this out? Does it add that much to mention this? Or could we stop the sentence with ASD research?

MS. HANN: And recommended research.

DR. TREVATHAN: If you just cut that phrase that says, covers all activities of federal agencies, and still left the end which includes a recommended research budget, that would -

DR. INSEL: Well, but again I think it's a little bit semantics. It doesn't actually say research budget. It says

budgetary requirements. So what the law says is, includes a strategic plan for ASD research with budgetary requirements.

MS. REDWOOD: If we could just go back to what the actual law says and insert that there, that would work.

DR. INSEL: Okay, the term is budgetary requirements.

So we were in the middle of a vote. This is votus interruptus.

(Laughter)

DR. INSEL: So what Lyn has recommended is, in response to the heightened societal concern over ASD be added in the next sentence, and we will add the language from the CAA that specifies what the IACC is supposed to do.

In favor?

(A show of hands)

MS. HANN: It's unanimous at the table.

DR. INSEL: Anyone opposed?

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(No response)

DR. INSEL: Okay, moving right along, we are up to page two, and I don't see -

MS. HANN: Just to clarify, that part that we just did, that we just agreed to, that you just agreed to, excuse me, that is in addition to the language proposed at the bottom of page one, or is that instead of. I just need to know.

DR. INSEL: That is instead of.

So moving on to the next page, the - I see one additional comment, again I think this is from Lyn, on page two, lines 10 through 22, where it says, convene four scientific workshops with broad public participation to identify research opportunities. There the language was changed to be, convene four scientific workshops and solicit input from the public and non-government research sponsors to identify research opportunities.

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Is that more precise?

DR. TREVATHAN: Yes.

DR. INSEL: In favor?

(A show of hands)

DR. INSEL: No opposed. We're moving on to page three, to the vision statement. There is a change that now includes the term, seek understanding of the increased prevalence of ASD. It could be prevalence estimate or whatever it was, Ed, that you had suggested.

Identify ethical ways to prevent disability and improve. That was the comment that came from the public. I see that Lyn has a recommendation for a bit of a modification here which you should have in front of you which says, the scientific research of the U.S. government accelerated in response to the strategic plan will seek understanding of the increased prevalence, blah blah blah, prevent future disability from autism acquired through environmental factors, and functional recovery

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of every individual on the autism spectrum.

MS. BLACKWELL: I had a comment on the comment that was added in the second column. I don't think we should add this language about ethical ways to prevent disability, because it implies that there are unethical ways to prevent disability. I'm just not sure that it is necessary.

MR. SHORE: But they exist, so maybe that's why we have to have it.

MS. BLACKWELL: Is there another way to say that, Stephen?

MR. SHORE: I don't know. I thought it was pretty good the way it was.

DR. INSEL: Other discussion about this? We've got now three options: the original vision statement; modified vision statement; and a further modified vision statement.

MS. BLACKWELL: I guess I don't understand about the scientific research of the U.S. government. I mean one of the things

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about this plan was it was going to include input and participation from other than federal agencies here. That seems a little awkward to me. But maybe I don't understand, Lyn, what you were aiming for there.

MS. REDWOOD: That's fine. Even though this is coordinated, we are not making recommendations about what the private sector should do, so it is really sort of the U.S. government based research agenda. I guess that was my point. But if that's redundant or not necessary, that's fine. I'm not 100 percent wedded to that language.

DR. ALEXANDER: Hopefully the plan will inspire and accelerate research in the private sector as well. I think you would accomplish what you want by saying the scientific research accelerated, and just leave out the U.S. government.

DR. INSEL: So the original language was to accelerate and inspire research that will profoundly improve the

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health and well being of every individual on the autism spectrum across the lifespan.

DR. LANDIS: I actually like that better.

DR. INSEL: All right, let's put it to the vote. We have three flavors: original, modified and modified by Lyn.

Those who want to do the original?

(A show of hands)

MS. HANN: Nine.

DR. INSEL: And do we need to go further?

MS. HANN: Apparently not.

DR. INSEL: Okay, we're talking now about the mission statement. We've got the same issues there. We've got the original. We've got a modified from public comment, and Lyn also has some suggestions there for us as well.

So open for discussion.

DR. LANDIS: I like the original mission statement. It's short and sweet and

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to the point. And I think that's what we're all working for, and kind of the more things that got added on, it kind of got kludgey.

DR. INSEL: Kludgey is good.

(Laughter)

DR. INSEL: Other comments?

All right, so we've got original, we've got modified kludgey, and we've got modified Lyn.

All in favor of original?

(A show of hands)

MS. HANN: Nine.

DR. MORRISSEY: Ten.

MS. HANN: Ten.

DR. INSEL: All right. Moving right along to core values, here again we've got some discussion points. The first one is under sense of urgency.

DR. LANDIS: Lyn has now - we now have this elegant, urgent thing that starts this off. I'm wondering if we need to repeat that here. Given the punch of the first

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paragraph. But -

DR. TREVATHAN: Well, I think -

MS. BLACKWELL: If you look at the second - I'm sorry, Ed. I was going to say if you look at this modified second version, there is a paragraph in here.

DR. TREVATHAN: I was going to say, looking at I guess it's the middle column here, I mean I certainly understand why people are trying to say, when they are talking about urgent response, similar to SARS or bird flu. But if you really dig below the surface, bird flu is a threat, not a reality. And autism is a reality. I mean there are some - I don't know that we want to give examples of responses, because those responses really aren't the same. I mean I don't think we really want a response that is theoretical, for example, a primary prevention response of something that doesn't exist, as we have with say SARS and bird flu. So for that option, if you just put the period after response. It's

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an urgent response people are looking for I think.

DR. INSEL: What about addition of the term, national emergency? It'S interesting wording here, because it says it leads some but not all to demand the ASD be treated as a national emergency. So you are putting in here that apparently there are many people or some people who feel that this should not be treated as a national emergency. Is that what you want?

Judith?

DR. COOPER: I would say since we modified the introduction we kind of captured the prevalence issue, and I think Story's comment about keeping things sort of sharp and focused and succinct, I mean these are the core values. We just need to sort of list them. So I think I would support keeping it the way it was to start with.

DR. TREVATHAN: I agree. I know we are getting in a lot of detail before someone

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reading this document, the first thing that hits them is that sense of urgency is bolded, and it's number one. So that might be a pretty effective - I think short and sweet and to the point.

DR. INSEL: So the options here are the original language or the modified language.

Those in favor of the original?

MS. HANN: Or Lyn's modified.

DR. INSEL: I'm sorry, there are three, right. So A, B and C. Those in favor of A, which is the original?

(A show of hands)

MS. HANN: Okay, the vote is seven.

DR. MORRISSEY: Eight.

MS. HANN: Eight, thank you.

DR. INSEL: Do we need to go on, or is that enough?

Those in favor of version B, which is the one on the screen currently?

(A show of hands)

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DR. INSEL: And in favor of Lyn's modifications?

(A show of hands)

DR. INSEL: Okay, we got three.

I'm moving to excellence. So here we've got again three options. We've got the original. We've got the addition of urgency while important should not trump scientific rigor nor expose individuals to greater than minimal risk. And we've got comments from Lyn which change that last sentence to say, urgency is compatible with scientific rigor. Safety and efficacy standards should be applied to ASD as much as any other population.

Comments?

MS. REDWOOD: And again, Tom, that was in response to the proposed edits. If the proposed edits aren't accepted, then that would be deleted.

DR. INSEL: All right. Yes, I think looking around the room, I think there

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are others that aren't excited about the proposed edits. So it's not kludgey, but it's yucky.

(Laughter)

DR. INSEL: So, Lyn, are you okay with the original version if we go back to that?

MS. REDWOOD: Yes.

DR. INSEL: Okay, in favor of the original?

(A show of hands)

MS. HANN: The vote seems to be unanimous. How about you, Pat?

DR. MORRISSEY: Yes.

DR. INSEL: Spirit of collaboration, there is one addition from the public comment. It's, so we will treat others with respect, listen to diverse views, dah dah dah, discuss submitted public comments and foster discussions where appropriate.

I don't see - so that is the only recommended change. In favor or not, I think,

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unless there is anything to discuss here.

Well, we certainly are discussing submitted public comments. It'd be a wonderful irony to actually strike that out.

(Laughter)

DR. INSEL: All in favor of the original version which does not include that statement?

(A show of hands)

MS. HANN: Three.

DR. INSEL: And those who want to include this addition, which says discuss submitted public comments?

(A show of hands)

MS. HANN: Eight, it carries.

DR. MORRISSEY: Nine.

MS. HANN: Nine; thank you, Pat.

DR. INSEL: Okay, consumer focused. There is again an addition from the public comment pool. It is important to consider the impact of research on ASD individuals' human rights, dignity and quality of life from

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prenatal development forward.

Comments? Does that - is that - so again let's just put this to a vote. Who wants to retain the original language?

(A show of hands)

MS. HANN: Okay, the vote is four for the original language.

DR. INSEL: And those who would take on the addition which is shown in blue.

(A show of hands)

MS. HANN: Six, Pat?

DR. MORRISSEY: Yes.

MS. HANN: Okay, seven to include the language.

MS. REDWOOD: If you are going to include that language, can I make a suggestion, that instead of saying ASD individuals, you say a person with ASD, please.

DR. INSEL: Okay, everybody's head is nodding. Pat, you are okay with that?

DR. MORRISSEY: Sure.

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DR. INSEL: Okay. Then we've got one additional comment for - under accountability there is an addition of the term, assessing impact, which has come from public comment. In favor of that addition under accountability, can I see a show of hands?

(A show of hands)

MS. HANN: Eight to include.

DR. INSEL: And those against, to retain the original version, show of hands?

(A show of hands)

MS. HANN: There aren't any. And Pat?

DR. MORRISSEY: Mine would be accepting the change.

DR. INSEL: Yes, the change passes.

We are now at 3:45 almost, 3:44. We have still got about 10 pages of this to do, or a little less than that.

MS. HANN: And the budget.

DR. INSEL: And the budget, so we

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have - we are not going to make it. We are required to have a period for public comment. We have many people who have written in and want to have a chance to talk to us, and we are going to have to shift to public comment mode. Della assures me that we can use December 26th for all of us to get together again to finish this. There is always the 25th, as Lee suggests.

DR. MORRISSEY: The president just gave everybody the 26th off.

DR. INSEL: I understand that.

DR. LANDIS: It was a joke. We do get the 26th off.

DR. INSEL: We will work with you to figure out the way to get this completed. We still have some work to do. Obviously the budgets need to be discussed, and some of them you haven't even seen because there are some new proposals that need to have a professional judgment budget added.

We have got another seven or eight

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pages of the introduction to work through. One possibility is that we meet electronically. We will find a way to do this. I really want to have something to hand over before January 20th - I should say January 21st to be most accurate. The new secretary needs to be able to get something from this coordinating committee that he can take forward.

Now thanks for hanging in there with us. We have now got six people who have asked to speak to the committee for public comment. Since we have exactly 15 minutes I'm going to have to ask each of you to limit your comments to about 2-1/2 minutes. And I will do the timing. I'm sorry I will have to interrupt you - oh you are right in the middle - but let me begin by introducing Karen Driscoll.

MS. DRISCOLL: Good afternoon. My name is Karen Driscoll. I am a Marine Corps wife, and parent of a child with autism. My

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husband is an active duty Marine, helicopter pilot and veteran of two combat tours.

I come today to you in an effort to obviously raise awareness of the issues impacting our military children, as well as ask for the advocacy of this group to focus on this - and I know you guys mentioned this earlier - a critical subpopulation at risk.

In my advocacy efforts within the Pentagon and on Capitol Hill, we have been gathering data through the Freedom of Information Act on the number of our military children with an ADS diagnosis currently.

Based on the total population of our military dependents under the age of 21, that puts autism prevalence of our military children at one out of every 88.

This is an alarming figure, because this is an at-least picture. These are the diagnoses that we know of today as well as, it does not include data on children that might use alternate insurance via an

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employed spouse in the civilian sector.

So this is an at-least picture that puts autism prevalence in the military at one in every 88. And I highlight this to you because in my efforts I've been advocating for the treatment needs of our military children, and how the unique military lifestyle impacts the quality of life of the individual child itself, his future for - future in terms of developing functioning and able to succeed in life. But this also has an impact on the family unit, the mental and physical health of the parents and siblings. But we have a unique aspect of the impact on combat readiness. Because when we don't take care of our children and families here at home it impacts the war fighter overseas.

And I want to highlight that picture to you in my personal story. My husband is a helicopter pilot, and while in Iraq, his squadron was responsible for casualty evacuations in support of 1 MEF,

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which is 1st Marines. You want the helicopter pilot focused on his mission and in support of his Marines. You don't want that helicopter pilot worried about the $4,000 therapy bill that it's taking to pay for his child's treatment. Or more importantly, how his wife is going to survive this deployment without him, and take care of perhaps more than one child with an autism diagnosis.

So this is a unique subset of our population that is obviously critical to the health of our country, and I want to highlight that unique aspect and ask for your support. Obviously, the treatment needs, but to research why our military children are at higher risk.

And if I could just wrap up, obviously I want to talk about - and I know there are some wonderful advocates in the room - on the vaccination safety, that this is a unique population that obviously has a higher compliance in vaccination, as well as a unique

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population that might be exposed to additional environmental toxins based on the military lifestyle, the nature of military installations.

So I ask just to raise that awareness, that there is a unique population out there, obviously critical to the success of our country, but also has a unique lifestyle that could be measured immediately and identified and tracked with an already diverse societal population in and of itself.

DR. INSEL: Great, thank you very much for joining us.

MS. DRISCOLL: Thank you for your support.

DR. INSEL: Thank you. I wish we had more time. And maybe we will find a way to do that once we have an additional meeting after the strategic plan is finished.

Paula Durbin-Westby has also asked to speak to the group.

DR. TREVATHAN: Tom, we have

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written copies of these comments, don't we, in circulation? The ones we have, can we be sure we circulate?

DR. INSEL: Right. I think that would be extremely useful.

MS. DURBIN-WESTBY: Since I only have 2-1/2 minutes I kind of rewrote most of it.

I'm Paula Durbin-Westby. Public Law 109.416 is not just about scientific research. The Inter-Agency Autism Coordinating Committee has among its duties to develop and annually update a summary of advances related to among other things access to services and supports for individuals with ASD.

Under committee composition it lists a number of non-scientific agency members including the Department of Education, the presence of these representatives indicates that the mandate of the law is broader than scientific research, especially

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as it has been more narrowly defined several times during the past two IACC meetings where different things have been tabled, because they said well this is not research, or not scientific research. So I would suggest going back and adding in the services objectives that were talked about, such as training, safety improvement and others.

Another thing, a person on the autism spectrum is needed to stand in for Stephen Shore when he is not here. Hopefully that can be remedied immediately. Again, I always ask to increase the number of individuals who are direct representatives on the IACC and the subcommittees.

I recommend making at least one additional change in the composition of the committee, and that is to include another agency with a focus on actual research across the lifespan, for example, something like the National Institute on Disability and Rehabilitation Research, because it has as its

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goal a focus on rehabilitative research that impacts individuals throughout their lives.

Remove language that urges cost savings as a goal of research. There is a danger that a focus on cost effectiveness will preclude those who do not improve or are in need of more substantial services throughout the lifespan.

In general the IACC should move away from language of cost to society.

The strategic plan should recommend - I just completely lost that. That might be the end of what I'm going to say. Am I up anyway?

DR. INSEL: Well, you are right at 2-1/2 minutes.

MR. DURBIN-WESTBY: Okay, and you have my written comments so you can see what else I said.

DR. INSEL: Thank you very much.

MR. DURBIN-WESTBY: Thank you.

DR. INSEL: Thanks for joining us.

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Theresa Wrangham.

MS. WRANGHAM: Good afternoon. My name is Theresa Wrangham. I'm the parent of an 18-year-old daughter with autism, as well as president of Safe Minds.

I want to thank the committee for the opportunity to speak, and the wonderful work that has taken place here today. I think a lot was accomplished.

I would however want to draw attention to the concerns that remain that have been forwarded to IACC with regard to concerns on vaccine language within the plan. And I would respectfully like to remind the committee that our community supported the Combating Autism Act due to our understanding of the urgency that is facing our nation, and the intent of this act with regard to vaccine research is very clear.

Senator Enzi in his Senate colloquy stated, however, I want to be clear that for the purposes of biomedical research,

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no research avenue should be eliminated, including biomedical research examining potential links between vaccines, vaccine components and autism spectrum disorder.

Rep. Smith added, I believe that we do not yet have the answers we need regarding the biological effects of thimerosol, and I am hopeful that research on environmental factors will include further study to find these important answers.

This issue continues to be scientifically debated and requires additional study, and the intent of the act is clear and this committee should assign research priorities as it pertains to autism and vaccines.

The committee has Safe Minds science summary in this regard, and it's clear that it requires your action.

We also ask that the strategic plan be a thoughtful process in which the committee is allowed the time necessary to put

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forward a plan that the community can enthusiastically embrace; that the budget not be constrained, but be bold in pursuing answers; that the research priorities focus on the environment, gene-environment interaction and treatment that continues to be underrepresented.

We ask that adoption of an oversight review and evaluation mechanism such as an autism advisory board and Department of Defense grant review model be considered.

We respectfully request that a workgroup be convened, January of 2009, to focus on these additional enhancements to the strategic plan.

Thank you.

DR. INSEL: Thank you. And I will just call the committee's attention to the letter that was sent in I think last night which is in your folders as well.

Ari Ne'eman?

(No response)

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DR. INSEL: All right, Jim Moody?

(Comment off-mike)

DR. INSEL: Okay, and the last name I have here is Ann-Mari Pierotti.

MS. PIEROTTI: Good afternoon. I'm Ann-Mari Pierotti, associate director of clinical issues in speech language pathology at the American Speech, Language and Hearing Association.

On behalf of Catherine Gottfred, president of ASHA, I'm pleased to have the opportunity to provide comments to the IACC today. ASHA is the professional scientific and credentialing association representing more than 130,000 speech-language pathologists, audiologists, and speech and hearing scientists in the United States and internationally.

We are all aware of the devastating toll that autism spectrum disorders, or ASD, can have on individuals and their families and caregivers, and we also

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know that difficulties with language and social interaction are among the hallmark characteristics of individuals with ASD.

Therefore we wanted to take this opportunity to speak to you today about the critical and central role that the speech-language pathologists play in providing programs and services for individuals with autism.

We also want to make sure you are aware of the resources that ASHA has that may be helpful to you as you finalize your strategic plan.

SLPs are often the first professionals to see a young child with language and social problems, and are often the first to recognize ASD. SLPs are involved in a wide range of roles addressing the needs of individuals with ASD, including screening, identification, diagnosis, program planning and intervention.

SLPs need to be integrally

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involved in all aspects of care. They collaborate with families and other professionals, conduct research, and are involved in advocacy to support greater independence for individuals with ASD in home, work, school and other community environments.

ASHA convened a committee on autism to create resources delineating the roles of SLPs in the diagnosis, assessment and treatment of communication disorders associated with ASD across the age span. And the ASHA documents are available to you and the public on ASHA's website.

These documents involve the systematic review of research on interventions designed to improve the language and social interaction skills of individuals with ASD, and we believe that these documents and other information that ASHA has related to ASD can be useful to this committee.

ASHA commends the significant accomplishments of the IACC, and we very much

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appreciated the chance to respond to the RFI. We highly recommend that the strategic plan for autism spectrum disorder research put more emphasis on intervention research. We look forward to working with you as you develop and implement your strategic plan.

DR. INSEL: Thank you. Exactly 2-1/2 minutes, remarkable.

MS. PIEROTTI: I thought about taking out the pronouns.

(Laughter)

DR. INSEL: Well, only a speech and language pathologist would come up with that line. That's terrific.

We are nearing the end, and I need your input on how best to proceed. We've got the cross-cutting themes to still do, and the budgets to still work on. Obviously some of the budget issues we are not ready to do, because we need to get some input about what those numbers might look like before we can get your sense of what they should be at the

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end of the day.

There are a couple of options. One non-option is, we can't stay here because my understanding is that by FACA rules if the meeting is scheduled until 4:00 we have to end at 4:00. Is that right?

So as much as we might like to actually just take another 45 minutes and get this done, the rules don't permit it. We have to go by what the published agenda and schedule was, and that's what we are going to do.

Now what we can do is think about yet another additional meeting that doesn't need to be here. It could be done by Webinar or phone conference. It would again have to be listed in the Federal Register, so it wouldn't be - we couldn't do it in the next 10 days, or 15 days, Della, what is the actual time frame?

MS. HANN: Where is Kate? Okay, it has to be announced in the Federal Register 15

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days prior to the event, and it takes us about five to six days to process it here at the NIH. So we are talking a couple of weeks.

DR. INSEL: So we are into January? No matter how we cut this. That may be a much briefer discussion, and we will have some additional information before that meeting because of the budget issues.

But what remains really is not a huge chunk. It's the cross-cutting themes. I think we could do that fairly quickly. I think we could do it by phone, and we would have to take time on the phone to go around and get everybody's vote. We would also have to have that open to the public so that everybody who wants to listen in will have a chance to do that.

But we will have to get back to you about a particular day to do it. I think we are talking about something closer to a two-hour rather than an eight-hour meeting.

Story?

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DR. LANDIS: Now, I haven't sat through all of both of these meetings, but my sense is that I think it would be very hard to run a Webinar or a phone-based meeting that would leave everybody with a sense of endorsement and comfort with what we are producing, so I think it should be a face-to-face meeting. But you could get a vote on this.

DR. INSEL: That's why I'm bringing it up. I really do need your input about how you want to do this for the next round. I don't think it needs to be a full day. It may not even need to be a half a day. But we should probably think about something two to three hours, so it's close.

What is your pleasure? How do you want to proceed? I have to tell you I am non-negotiable on the end time. We have to have something to deliver on the 21st of January. So it's got to be before then.

What is the sense of the group?

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DR. ALEXANDER: I think we will do well to get the majority of the group together without the travel complications involved, and Story, I prefer face-to-face meetings too, but I'm not sure we can have the luxury of doing it in this case.

I'm okay with going with the Webinar videoconference, telephone conference format for this, with the understanding, that most of what we've done we have at least seen twice before, and we should be in pretty good shape to come to grips with finalizing these and getting this wrapped up within two or three hours. So I'm okay with doing it the way you originally suggested which is a Webinar, telephone conference, whatever.

DR. INSEL: Without sounding contrarian, the only thing I'd want to also remind anybody of, anybody who has ever built a house knows it's the last 2 percent that takes the longest and is the most difficult, and that may turn out to be the case here,

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that there may be the final pieces of this that are still going to take some wrestling.

So I'm mindful that - Lyn had begun today with wanting to go back to a piece that we haven't - that some people still feel needs to be worked on.

So those pieces that still are unresolved are likely to be the most complicated. So we may need to take some extra time. But I hear your interest in getting this done by an efficient way.

Any other thoughts or comments about this?

Della, is there anything else we need to do in terms of input at this point?

MS. HANN: No, not that I can think of. We will do our best to identify a half day - what I'm going to drive for is for a half day, and we'll either do it just totally by Webinar, or it'll be optional, just like this meeting was, that people could tune in by Webinar, but if they could make it to

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Bethesda, that's great too.

I do remind you, all of our meetings always have to be done in a public venue, and we also have to allow for public comment. It is a requirement.

So that will have to happen at that meeting as well.

DR. INSEL: If I can take the prerogative of the chair and make a last comment here. I really want to commend everybody on hanging in here today. I thought we had a lot of healthy disagreement, and there were a lot of votes that were split.

I too share some concern that a lot of the splits seem to go between public and federal, and I worry what that means. I think we do need to have a further discussion about this.

But what struck me today was how well we were able to discuss the areas of disagreement, and how in going into many of them it was never clear how the votes were

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going to come out, and I saw people switch their positions as the discussions went on.

I just think this has really been a terrific exercise, and a really healthy conversation. So I want to thank all of you for participating in this, and staying the course.

And with that, we are adjourned. Thank you.

(Whereupon the above-entitled matter was adjourned at 4:05 p.m.)

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