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SUBCOMMITTEE FOR
BASIC AND TRANSLATIONAL RESEARCH

WEBINAR AND CONFERENCE CALL

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The Strategic Plan Question 3 Planning Group convened via webinar and conference call, Lyn Redwood, *Chair*, IACC presiding.

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PROCEEDINGS:

Ms. Gemma Weiblinger: Hello, everyone. As the operator said my name is Gemma Weiblinger, and I am temporarily acting as the designated Federal official for Dr. Susan Daniels, who's currently on maternity leave.

Welcome to the IACC Basic and Translational Research Subcommittee's conference call to discuss a portion of the update to the Strategic Plan. This specific focus on Question Number 3, "What caused this to happen and can it be prevented?" I'll now turn the call over to Ms. Lyn Redwood who will lead the discussion. Lyn?

Ms. Lynn Redwood: Thank you, Gemma. I just want to let the participants know who are listening in, and I apologize for the delay. We're currently waiting for two members of our team to also join us, but we'll go ahead and get started.

We have a very short timeframe today. Our time for this call is actually scheduled for 30 minutes.

The purpose of this call is to discuss the documents that we've been preparing to date with

regard to the 2012 update, the Question 3 of the Strategic Plan.

We also -- I think a majority of the discussion today will also center around much of these documents but also how we will prepare for the actual presentations on the 30th.

The first item on the agenda I had was to discuss the documents today. We already have somewhat of a discussion. There are still edits being made to both documents: the science update and the gap initiatives.

So, Matt, we have a deadline of Monday. And, Elizabeth, from the call yesterday, you were saying that that was going to be 5 p.m. on Monday?

Dr. Elizabeth Baden: Yes. Eastern, please.

Ms. Redwood: Right -- to get those documents in. So, the ones that we've prepared so far that I sent around, several of those documents are supporting documents. One of the supporting documents was the information that Cindy had procured in terms of what progress was being made toward the initiative, specifically from like an NIEHS perspective.

As you know, it's impossible to really go through all the projects that have been funded at this particular time to be able to assess the type of progress that we've made. Hopefully, we'll be able to get into that the first part of 2013.

Also, by that time, maybe we'll have the new research portfolio with regard to what proposals have been funded for 2011, which we don't have yet; 2010 is the latest data.

The other supporting document that we have is the cumulative funding piece that I pulled together for 2008, '09, and '10. There was also a suggestion to add the number of projects to that document, which, Matt, I believe you did that.

And when I was looking back over the information this morning, I realized that some of those projects are actually ongoing projects from year to year. So it's a little bit misleading when you see, say, 2009 -- 11 projects and 2010 -- 14 projects for, say, the question short-term A. Several of those projects are continuations. So I think we're going to need to go back in and make those corrections.

Dr. Matthew Carey: Does that mean the funding levels are also ongoing? Those of ongoing projects?

Ms. Redwood: Right. If you look at those -- is this Matt Carey?

Dr. Carey: Yes, sorry. Matt Carey

Ms. Redwood: If you go into the reporter, you will see that several of those projects are identical from year to year. They're also in that question, and this was a question I had for NIH staff. Some of those projects all have the same title, but they're being conducted in different locations. So they're titled like 1/5, 2/5, 3/5. Is that one large funding initiative toward the same question?

Dr. Cindy Lawler: I think those would be sort of linked studies that were probably given separate awards but reflected maybe a multi-site trial.

Dr. Baden: Yes, Lyn – this is

Dr. Lawler: -- reporter as -- because the awards were made to separate institutions, but they would be -- it would be one of five sites,

two of five sites, I think.

Dr. Carey: Yes, like early or [Inaudible comment] they are multi-site.

Dr. Lawler: Well, that was a little different because those were --

Dr. Carey: That's different.

Dr. Lawler: Well, it was just -- I think that one only shows up once because it was a detail that isn't important but made through subcontracts. But I think it's just the one of five; the two of five is when a coordinated award included individual awards to the different participating sites.

Dr. Carey: Okay. But I mean, this is separate -- somebody could model. These are sort of independent projects; they're related, but they're separate projects going toward the same goal.

Dr. Baden: Yes, this is Elizabeth. That is correct. They have different grant numbers. The funding amounts are different for each site or each PI. They all have separate PIs, and so they are considered separate projects but, as Cindy explained, often linked. And you do often see it

for like clinical trials and things like that.

Ms. Redwood: I don't want to spend a whole lot of time on that. I just wanted to point out that several of those projects, like if you see the 11 projects those same 11 projects in 2009 are also funded in 2010. So, I just wanted to point that out.

In terms of the other two documents that we have, the science update, Matt will hopefully be getting the final product from the science experts on that.

And then on the gap document that I circulated, I saw a lot of comments Matt from you.

And I can try to go through and answer all of those. I don't know if we might want to set up a different call, because there's a lot of questions, and I just don't know if on this call we'll have time to really go through all of those.

If you want to toward the end of the call, if we have time -- we actually did schedule for an entire hour -- we can run through those. I'm afraid that that in itself would take up the majority of the call.

Dr. Lawler: I also had several questions, too, and I think probably merits sort of another call. Because I really -- we talked earlier about the very nice -- what is new in this research area that we asked our science experts to prepare. You know, there are a number of kind of gap areas that are embedded within those. And I would like our gap area document to really reflect primarily the gaps that are identified by these extramural scientists. And I don't know if that's the case, and if we've captured all of them or whether there's others in there that --

Dr. Carey: Yeah, they need to be, I would like to see that they're supported by the them --

Dr. Lawler: Exactly.

Dr. Carey: Yes. So I mean there may have to email -- some emails and maybe another call. But I think that there's a lot there to digest. It may take a while.

The other thing -- this is Matt Carey. If you just call me "Matthew," because we have two Matts on the call. Then we know who we're dealing with on each one.

Dr. Matthew State: I was going to suggest the same thing. So you're Matthew.

Dr. Carey: Sure. That's -- when I'm in trouble with my dad that's who I am.

Dr. Lawler: So that's Matthew Carey and Matt State, right?

Dr. State: Yes.

Dr. Lawler: I got it right? Okay.

Ms. Redwood: Well, one of the things that I did, and I sent around a document that was called "Research Opportunities." And I went through, and I was pulling out -- from what we had received from the science experts -- what appeared to be recommendations and gaps and was putting those into the research opportunities document.

And I saw that we added the one in there on advanced maternal age. I think that's important. I have that toward the top of the list of the research opportunities.

And I had asked everybody on the Committee to go through and make additions to those, so if there's things in there that you think are not reflected from what the science document has,

please feel free to put those in the research opportunities or embed them over into the gap initiatives.

I've been asking for people to do that, and I haven't got a whole lot of response back yet. So that would be really helpful because the things that are really fine detail like for specific projects really should go into the research opportunities section. And those are -- when we look at the Strategic Plan, you'll see how those are outlined. And unfortunately, that's not something that we're actually updating this year, but we'll start very first thing next year. So we'll actually be ahead of the game with those.

[Inaudible comment]

So that's why we're trying to sort of divide those up into broader categories of gaps for those blocks and then also the specific topics that would fall under those broader categories.

Dr. Lawler: I think maybe part of it is -- I mean I think there's some of the -- when we're looking at the research opportunities -- some of what's in italics, just kind of the bullet of the

idea is fine. But some of the sort of explanation or, you know, elaboration of how that can be accomplished, I think would merit some additional discussion.

In one case -- the bullet 3, I think -- there's so much combined in that that it's -- that we may want to sort of consider unpacking and which ones we really want to include. Is recalling how these research opportunities end up being included in the Strategic Plan, they really -- it's almost like a bulleted list. And while there's some specificity, there's not elaboration of how to sort of accomplish that. So I think this document we've got some of both and again maybe another call to talk about some of the specifics.

Ms. Redwood: Right. And they're different, Cindy, from chapter to chapter. So if you look, say, at Question 4 -- the research opportunities -- they have bullet points below them in terms of how they could actually be carried out. So, I mean, we can write those out however we want to.

They don't have to be just the bullet. We can include some details in terms of what our

recommendations would be for those as well. And also, I want to point out that we're going to get a lot of feedback at the in-person meeting from the other experts that will be around the table.

This is going to be a work in progress for at least a month, I can imagine. Elizabeth, what is the final deadline that Dr. Insel has on how -- for when this would be voted on by the IACC?

Dr. Baden: Well, first it would need to be approved by the whole Subcommittee, the Basic and Translational Research Subcommittee. And the date for that meeting is November 26th.

Ms. Redwood: Okay, great. So, my point is, at the actual in-person meeting on the 30th we'll have the afternoon for our team to meet together again in person and hammer a lot of this out. So please don't think that what you're seeing today will be our final product.

Dr. Craig Newschaffer: Lyn, real quick. This is Craig. I'm sorry to interrupt, but will the outside scientist we can comment on the gaps opportunity document as well?

Ms. Redwood: Yes. Oh, please.

Dr. Lawler: We really want you to.

Dr. Newschaffer: Yes, I just didn't have a chance yet. So it would be real helpful if you could just resend them because of all the emails. If you could just resend the latest versions -- like right now -- with gaps and opportunities in the message, I'll take a look at them over the weekend.

Ms. Redwood: Okay. Thanks so much Matt. And the other thing that I think is going to be really helpful is once we have this in-person meeting, we're going to be able to hear from the Question 2 team and the Question 7 team, because I do think that there are a lot of overlaps. So we may see things that, gosh, they're really not covering to the level of detail we would like them to be covered, and we'll add those in. And that specifically like your concerns about the epidemiological research or the ones with biobanking.

But if you get a chance, please look over especially that surveillance section in Chapter 7 in terms of what they're looking at. And then when

we're actually at the meeting, we'll be able to ask those types of granular questions. That's going to help a lot.

Dr. State: I just wanted to clarify. You said -- when you responded to Craig's comment -- you said "Matt." I just wanted -- it sounds like Craig's on the call, right?

Dr. Newschaffer: Yes, yes. That was me.

Dr. State: Yes that was Craig.

Ms. Redwood: Oh, I am sorry.

Dr. Newschaffer: You can call me Matt too if you want.

[Laughter]

Ms. Redwood: Thanks so much. Craig, thanks for joining us. What about Isaac? Did Isaac make it on?

Dr. Isaac Pessah: I did, yes. I'm here.

Ms. Redwood: Yay, wonderful. Thanks so much. Feel free to chime in here.

Dr. Newschaffer: This is Craig again. I'm going to chime in one more time because in the surveillance section Chapter 7 is that something you sent around? I'm just having trouble

navigating all the documents. Is that something you sent around?

Ms. Redwood: I'm sorry, Craig. No, I didn't actually send that chapter around, but if you go to www.iacc.hhs.gov --

Dr. Newschaffer: That's the existing Chapter 7.

Ms. Redwood: It's the existing Chapter 7 -- 2011.

Dr. Newschaffer: Okay. Okay.

Ms. Redwood: So, they have -- and that was a chapter that we added after the first year, but it goes through a lot of the infrastructure needs. It has sections on biobanking, surveillance, data sharing -- research

Dr. Newschaffer: Got it.

Dr. Lawler: I guess the more important point is what we don't have access to, because other working groups are working toward this same collection of documents in respect to through the biology of autism, Question 2, and resources and infrastructure needs, which includes surveillance prevalence in Question 7.

So I think, at this point, while we can look at what has happened with those questions in previous years, we are just in a position of having to anticipate -- rightly so -- that I think some of what's been covered in this Question 3 document are going to be well covered in -- when we get to the meeting and hear what the Question 7 workshop or group is proposing. And the same for the biology of autism in terms of some of the biomarker --

Ms. Redwood: Exactly.

Dr. Lawler: So I think we do need to be cognizant of that and, to the extent possible, really sort of focus our efforts on what really is kind of the core aspects of what this group is being asked to do, because we won't get another opportunity for these experts to come together this year around these genetic, environmental risks.

Ms. Redwood: Exactly. And I've asked Elizabeth previously if she had any documents yet from the other committees, and she did not. So as soon as those are available, I'm sure she'll be

circulating those out to us.

Elizabeth, will we actually get those before the meeting, or will they be there waiting on us when we arrive?

Dr. Baden: You will get those before the meeting. So we'll send all of the documents that are sent to us by hopefully next Monday, and we'll turn those around as quickly as we can. And so, hopefully, by the middle of next week, you would have those in hand to start reviewing. And we'll make sure those go out to all of the IACC members and also all of the external experts to take a look at.

Dr. Carey: This is Matthew. One thing is there's limited time, even though the workshop is two days. It's going to be a lot easier to jettison entire sections than to build one up. Look, you guys have covered this, so we, you know [Inaudible comment] before we start talking. That's easy.

But if you say, why don't we fill this in, it'll take up all of our time to maybe do one, to add one thing in. So I think we should go for

broad rather than narrow.

Ms. Redwood: Okay. The thing that -- in terms of the actual write-up, though, we are limited in terms of the number of words we can use. So we've got to keep that in mind, too.

If it's okay -- since I think this is critical and this is -- we only have a few minutes left for the call. I'd really like to go over the actual 20 minutes that we have for presenting all of this data.

I sent an email out a few minutes ago that sort of outlines just throwing together sort of ideas to just share with the Committee and to get feedback in terms of how we best utilize that 20 minutes and those five slides to present the data that we have.

Dr. Lawler: So, Lyn, this is Cindy. Let me start off here because I think my thought for this is that we really need to lead with the new science findings, our external experts, what they've sort of identified in terms of what's new.

And it doesn't make sense to me to really devote much of any time in our 20 minutes talking

about current and ongoing initiatives. It may be that we could ask Matt, Craig, or Isaac if one of the findings has emerged as a result of initiative X or this sort of new way of conducting research. That can be part of what they're describing.

But I just -- to me it doesn't make sense to lead off with any kind of discussion of the current and ongoing initiatives. Because, one, we really don't have time to get the information about the whole breadth of the initiatives and really fairly represent them in two minutes. So while I think it's fair game for the discussion, but so I'd want to start with what's new in this area.

Ms. Redwood: Okay. I agree with that, but the reason I put that in there, Cindy, is that there are going to be a lot of members in the audience that aren't privy to a lot of this additional information in terms of what are some of the ongoing projects.

So I'm wondering, from Elizabeth or Gemma, is there a way for us to actually have those available in paper or maybe even to just give them

a quick reference if anybody would like a copy?

Dr. Baden: Sorry. Are you referring to the update drafts or like the Strategic Plan?

Dr. Lawler: So Lyn, let me just chime in here, because the real issue is we don't have that information across funders and at the most recent.

And what we have and what I included in some pieces of progress are ones that are particularly -- I happen to be well-informed about because they're ones that this institute, NIEHS, has a role in. But in no way does that sort of describe what's going on, the breadth of activities at Simons or Autism Speaks or even the other NIH institutes. So we just don't even have a way to in a short period of time to collect that information and sort of present it in a way that would -- you know, it needs to be credible, not just, these are the things that one program person happens to be aware of. So that's another reason.

In 20 minutes, again, I just, I don't -- you know, again, and it's not that there's information that we could -- comprehensive information we could make available. We just haven't collected

that information to make it available either by me describing it or by providing something to people at the meeting.

Ms. Redwood: Okay. Well, we will scratch that one off. Jumping down to number 3, the research portfolio analysis that was another sort of ancillary document that we created as part of this review. But I think it's important and that would be something that we could have copies of and share and not actually include it as part of the presentation.

What do people think about that? Because that was the -- that was another 2 minutes out of the 20 minutes.

Dr. Lawler: Did you send that around also in the latest batch, Lyn?

Ms. Redwood: Yes, it was attached last night. I think -- I can't remember -- I think it was the very first email that sort of had the ancillary documents, and the second email was the science.

It's the one that -- the first call that we had several weeks ago, Cindy, that I sent around. It actually breaks out each of the questions that

we have now in the Strategic Plan for Question 3 by year with the total overall IACC-recommended budget, the timeframe, and then what progress we've made to date -- 2008, '09, and '10. That was the one that was sort of useful in looking at the genetic spending and the environmental spending.

Dr. Lawler: So we have 2010 data?

Ms. Redwood: Right. We don't have 2011 data. But one of the things that I did that's unique that isn't on the IACC Web-site is combining those initiatives for the past three years of data that we have. So that makes it a little bit more comprehensive.

[Pause]

So. Everybody still here?

Dr. Carey: Yes.

Dr. State: Yes.

Ms. Redwood: Okay. It just got very, very, very quiet.

Dr. Lawler: I think I'm talking too much, so I'm going to let other people weigh in.

Dr. State: This is Matt State. I'm terribly sorry, but I have a dissertation defense; my

student's graduating, so I have to run right at two o'clock. Just quickly, I know that our first task is -- Craig and Isaac and I think are probably very close to having a revised draft of the science update. Unless Isaac and Craig feel differently, I think we should be able to do one quick round of email exchange on that and have that ready to go over the weekend. Does that sound right to you guys?

Dr. Pessah: Sounds correct to me.

Dr. Newschaffer: Yes.

Dr. State: Great. And then I think Craig also said -- and I'd be happy to be cc'd on that as well -- that if you re-forward those documents that Craig and I will chime in. We'll have an opportunity to take a more specific look at the research opportunities document and provide edits as well by Monday.

Ms. Redwood: Great.

Dr. State: Okay? Thanks. I'm sorry I have to run but I've got to go introduce him.

Dr. Carey: Bye.

Ms. Redwood: Okay, thank you.

Dr. Lawler: Bye, Matt.

Ms. Redwood: Okay. So, Cindy, your recommendation is to open with the new science findings.

Dr. Lawler: Right. And then maybe -- again, just given that the data are old, 2010 is old, you know, and we're really -- by the time this is published, we're talking 2013. So while I think it makes sense to maybe preface the discussion of gap areas, roadblocks with some information about funding levels or the most recent information we have, which is not very recent, but I wouldn't spend, you know, I'd maybe make a point, one point, but I wouldn't spend much time at all really. And it would be, to me I think it would just preface the discussion of gap areas and roadblocks to progress. I don't know. Matthew, what do you think?

Dr. Carey: That sounds about right to me – because I mean, even 2010 data. I remember I tried to put together a spreadsheet afterward trying to go question by question, and it doesn't match up. It actually doesn't match up. So we've got old

data. We've got some idea. Right now we're talking even how do we include ongoing versus non-ongoing projects, number of projects versus funding levels? So we have a lot of stuff there.

I think it's old, it's not. I think you can make the statement that you need to make actually fairly quickly right in one slide it's actually pretty significant and then we can go on. But yes, if we don't know what's happened in the past two or three years, we're --

Ms. Redwood: Well, one of the things -- let me interject here though. One of the things that you see in this document are trends over time. So oftentimes you can see that the trends are following about the same. So if you look, say, at the genetics funding for one particular project: 2008 -- $37 million, 2009 -- $49 million, 2010 -- $34 million. So these do tend to sort of track over time.

And it's the same with several of the categories that we see here. When you look at what are the environmental or subsequent pregnancies, it's running around $2 to $3 million per year.

So even though we don't have data for 2011, I do think it's important and that it definitely highlights the areas where there's gap. So I agree we can refer to it in just one slide or at the beginning of the gaps,

Dr. Lawler: Yes, exactly.

Ms. Redwood: but I do think it's critical because we're relying on -- identify some of those gap areas.

Dr. Carey: Yes. But I mean, I remember looking through it and like 2009-2010 also -- I mean it's got kind of a weird compound rate. Like right now, the ARA funding.

Dr. Lawler: Yes.

Dr. Carey: You had some things go way up and some things go way down. And if you look at it from one trajectory, this is going way down. Some things may have stayed flat while others actually -- we can total up by questions.

Genetics actually go up a lot. But you could say well, you know, there's a time trend there if you added up all the questions, but it's not really a trend. And we don't know -- and if we're

trying to figure out what is that trend, you know, what has happened in the past couple of years, especially given kind of increased emphasis from the IACC to request a higher level of funding in certain areas. So part of it's being met. That's the important question.

Dr. Lawler: We don't have the data to really address in a robust way. So that's why I, again, I think you can make some points in two or three sentences and then sort of move onto the gap areas.

And you know, Lyn, these are really critical questions that I think the whole Committee intends to figure out a way to kind of assess progress beginning with next year's Plan.

So it's not that I don't think it's really important that we kind of understand what the distribution are in a more sort of real-time manner and be able to maybe make some statements about possible trends. But I just, you know, with the limitations of the data we have and the limited time here, I just, you know, I wouldn't want to --

Ms. Redwood: Right. So right now, Cindy, it's two minutes. So we can just use that and maybe present it at the very beginning of the gap area discussion. Yes.

But then we also have another -- What is it? -- 25 minutes for question and answer. So I'm sure that during that discussion period it will be brought up, too. So --

Okay, so then key points, findings. I guess sort of my question -- and I'm sorry we've lost Matt -- but for Craig and Isaac, how do you guys want to divide that up? Do you want just one of you to present that section? Do all three of you want to sort of present the part that you contributed to?

Dr. Pessah: Well -- this is Isaac. I think that we're going to converge on a document we all feel comfortable about. But I think there are quite disparate views on what that document means.

In other words, what's the relationship of thousands of genetic variants relative to environmental susceptibility? I think that both of those sort of mindsets need to be presented as

opposed to one or the other.

Ms. Redwood: Okay. Well, I agree with that. I'm just wondering though -- whether or not if each of you are presenting individually during that time -- would you also want to include the gap discussion? So when you're actually talking, you can say, well, this is the -- these are the findings that are key and then these are the areas that we see as gaps.

Dr. Lawler: I think --

Ms. Redwood: Ten minutes for the science findings and 10 minutes for the gaps.

Dr. Lawler: When I read that document, they've already embedded those gaps in that, which is nice in their -- you know, it's pretty easy to pull out those gap areas.

Dr. Newschaffer: Although I think, Cindy, there might be additional gap areas just because the length of that document is pretty short. So the implied gaps are a potentially limited set of things that might want to be highlighted.

Dr. Lawler: Okay.

Dr. Newschaffer: There could be a few more.

Dr. Pessah: Could those be embedded in the discussion of the new science?

Dr. Lawler: Yes.

Ms. Redwood: That's what I'm thinking. We have a total of -- Elizabeth, is there any way to at least get maybe six slides so each -- if Isaac, Craig, and Matt each have two slides, one maybe for the new findings and one for gaps? Do you think that would be allowed?

[Pause]

Dr. Baden: Yes. Lyn, you can have as many slides as you want as long as you can present them within 20 minutes.

Ms. Redwood: Oh, okay. The way I read the email last night it was that you get 5 slides in 20 minutes.

Dr. Baden: Yes, 5 slides -- the main goal is just to impress upon everyone to keep this, you know, keep the presentation short. We're hoping that people will read things ahead of time. And mostly to allow time for discussion because, as your group has already noted, it's really -- you really need to learn about what the other groups

are doing too to make this all cohesive.

Ms. Redwood: Right, okay. Isaac and Craig, does that sound okay?

Dr. Pessah: It sounds fine to me.

Dr. Newschaffer: Yes, I think it will be fine.

Dr. Lawler: So then, let me make sure that I understand it. So then you guys will do the new scientific findings. Part of those, or embedded within those, would be some gap areas because there's just -- that's the natural progression.

But when, you know -- the end slide when we enumerate the specific research opportunities -- there would be, you know -- some of the gaps that had been described in the science findings would sort of be listed, but there would be some other kind of research opportunities as well.

Dr. Pessah: I think it would be good to reaffirm what the gap areas are. And then if we don't cover any of them in the new science section, you could highlight them as well.

Dr. Lawler: I think I'm fine with sort of there being some repetition because the other option would be cutting up your science advances

to take out anything that looked like an opportunity, and that doesn't make sense to me. So we'll just plan to have the research opportunities more of a bulleted list that will reinforce in many cases what's being presented in what's new science.

But then we'll anticipate there will be more as well, that you guys will help supply us with some of those. And I'm sure we'll get more ideas at the meeting.

Ms. Redwood: Well, let me just comment on that, Cindy, because the research opportunities section we have not been tasked with updating.

Dr. Lawler: We have not?

Ms. Redwood: No. We've been tasked with updating the new science and the gaps. On the call that we had with Dr. Insel, toward the end of the call I specifically asked him about the research updates or research opportunities is what they're actually called.

And he said that it would be a good idea to take advantage of the fact that we have the experts at the table to get the feedback on what

these research opportunities would be, but we will not be making any additions to that list until next year.

Dr. Lawler: Okay. Well, then that's -- I knew we weren't putting new objectives into the Plan, but I didn't realize we weren't adding or – But that's fine. I mean, those will still be useful. We'll have a useful list of updates.

Ms. Redwood: Exactly. So I really think we should sort of stick to the broader categories of the new science and the gap areas moving forward and then have a list that we've generated.

We could actually, I mean, we could make a slide of that and list that, but that's going to be a more detailed project if that makes sense.

[Pause]

So if that could be included with the presentations from the science experts, those gap areas that would be ideal.

Dr. Newschaffer: Well, again, if we're limited on time, we may not be able to cover all of them. So it may be a good thing to maybe make sure we cover some of those that are important that we may

not have covered. But that's --

Ms. Redwood: Right.

Dr. Newschaffer: I don't think we can be comprehensive in the amount of time.

[Laughter]

Ms. Redwood: No, and we also can't be comprehensive when we're limited to, what, 4,000 words or something. I mean, we have two pages, and there's just so much more to do.

Dr. Lawler: And Lyn, I'm also -- as I'm looking over this latest version of the gap document, it seems like much of it was covered in last year's. So really we need to make sure we're focusing just on the gap areas that are new.

Ms. Redwood: Right. But some of the gap areas though are continuing; even though they may have been mentioned last year, they've not been fulfilled.

Dr. Lawler: But I think that's a different question. If we're going to have an appendix that says you have the current gap areas for 2011, and then the appendix is what new gap areas. So I don't think not including it in the new gap area

means that the 2011 ones weren't met. Or you know, either were met or no longer important.

Ms. Redwood: Which one are you specifically referring to?

Dr. Lawler: I think just sort of in general the, you know, the idea, the sort of convergence of environmental and genetic risks. The sort of the combined, you know, interdisciplinary findings that sort of combine different kinds of data sets and so on, I think was part of what was mentioned in 2011.

Ms. Redwood: So I sent around previously -- I pulled out the actual gaps from 2011 and categorized those. I can send those around again. One was suitable model systems that they had. Expansion and integration of epidemiological studies using different designs and --

Dr. Lawler: Right.

Ms. Redwood: -- data. A lack of adequate post mortem brain tissue, which continues to be a gap; further development and application of sensitive assays for DNA methylation, those types of things; system modification, epigenetic markers, greater

collaboration between genetic and environmental science investigators.

Dr. Lawler: Right.

Ms. Redwood: Those were the main, and I think there are actually about six of them that I sent around previously. And I was asking if we know if there's some progress made in these areas. So if you're saying that they're already included, I just took a brief look through what's there for what's already included.

Dr. Lawler: Well, I just think, just stepping back, sort of the strategy at the beginning of this section -- Do we want to sort of indicate that there is sort of continuation of these gap areas remain in sort of a new light, a few of them? But then really focus most on new gaps that weren't gaps last year because we didn't really sort of understand enough to know that it's a big gap.

Ms. Redwood: Can you give me an example?

Dr. Lawler: I think, you know, kind of more understanding of maternal/paternal age and whether that's related to sort of mutation rates and the

whole copy number, it just, it wasn't --

Ms. Redwood: That one's in there.

Dr. Lawler: -- a compelling case last year. And I think now there's sort of enough that we really need to understand on many different levels how those kinds of risks play out at a molecular level, sort of the maternal/paternal age thing and the whole sort of de novo mutations of these copy-number variants.

Ms. Redwood: Right.

Dr. Lawler: Just as one example. And I think we didn't really know enough a year ago. It was interesting, but now it's really a gap because we don't know the extent to which the maternal/paternal age may reflect these sort of mutations induced by potentially preventable environmental exposures. And that's just one example, I guess.

Ms. Redwood: That one's in there, Cindy.

Dr. Lawler: That was in?

Ms. Redwood: Yes.

Dr. Lawler: The gap area from 2011?

Ms. Redwood: No, no; it's from the document

that's circulating.

Dr. Lawler: Okay. I'm just -- maybe I don't have the very first one, the very latest one. Because --

Ms. Redwood: There's one that Matt added that I had just like the first three or four. And that's why I've been asking for people to put things in the other research opportunities document to move over into the gaps. So that is [Inaudible comment] Matt sent this one around. It's the one we've all been sort of making comments on, or maybe just Matt and I have been making comments on, from this morning.

Dr. Carey: Cindy, actually, can I ask a question? This is Matthew. One thing I'm drawn to as well is when we're looking at gaps, you know, a gap in 2011 is not going to be closed in 2012. We're going to start making progress toward it.

Dr. Lawler: Right.

Dr. Carey: Right? And if we run into the same problem we've identified before, we don't really have that information to say completely for all areas what progress has been made toward those. I

mean, we can kind of -- so I mean at some point I think we kind of assume those gaps are still going.

It's just whether they're, you know, what are we doing to move toward them. At some point, we've got to kind of flow that in front of the rest of the Committee and hope that if somebody says there's something going on, you know, they can say. But it may not be -- I don't think we can determine it -- very much determine

Dr. Lawler: Right.

Dr. Carey: what gaps have even been tried to be closed.

Dr. Lawler: Another tack is -- are there gaps -- yes, the gap areas probably all remain. Are there ones that have risen in import based on data over the past year?

Dr. Carey: Yes.

Dr. Lawler: Or are there -- you could potentially make a case that this is a gap area.

There's some progress, but we now know that it's -- or we need much more to make further progress.

I guess I'm coming back –

Dr. Carey: Yes.

Dr. Lawler: to I'm just not -- it's kind of unsatisfying as it's kind of laid out now. And I'm trying to understand why. And I think part of it is knowing which of these gap areas kind of I want them to tie back to the science experts and their opinions. Two, I want them to understand which ones we've -- are continuations or maybe increased priorities from the year before.

Ms. Redwood: Well Cindy, one of the things when you look at what the science people have included, and specifically Isaac, was this lack of support for environmental studies. And when we had the call this past Monday that was one of the biggest gap areas we discussed.

And that's what the gap area document that I circulated in the first draft leads off with, because that's been a continuation of a problem that was identified back in 2006 with the very first IACC that was developed under the Combating Autism Act.

When they reviewed their matrix, they said

this whole area of the environment really hasn't received enough attention and enough funding. And I think we continue to lag behind in that funding because that infrastructure with regard to focus and support and funding has not been there to look at environmental factors.

So I feel strongly that's one of the biggest gaps that we have. And if we don't address that, we're going to continue to lag behind in important findings.

Dr. Lawler: So I think what part of my discomfort is it's almost like mixing what the science gap is with the reason for the gap or how to fix the gap. And so I think maybe at the beginning, at the highest level, the major mega-gap is really we have very little understanding of how the environment influences autism risk alone or interacting with genetic susceptibility.

Dr. Pessah: Well, there's another way to look at this, Cindy.

Dr. Lawler: Yes.

Dr. Pessah: You know, there is another way to look at this -- is that the genetic findings, this

really amazing amount of information that's emerged over the last two to three years regarding de novo copy-number changes in terms of copy-number burden -- in terms of highly penetrant mutations that have been identified -- these all point toward environmental factors being a major role.

And I know geneticists don't look at it that way, but to us toxicologists it's extremely clearer that the environment is playing a major role here.

Dr. Lawler: So how could you, you know, it's almost like we have these genetic findings --

Dr. Pessah: We can't wait until all 1,200 or 1,800 or possibly more genetic variants are identified because, at the end of that day, we're really going to be so far behind. It's one thing to identify genes. It's another to begin to do something about what we know.

Dr. Lawler: Okay, so I think that is a science gap. I mean, you know, lagging behind our ability to --

Dr. Pessah: Exactly.

Dr. Lawler: -- make use of these genetic findings that are emerging in terms of understanding functional significance and really how that plays out with respect to environmental.

I mean that is a huge gap.

Ms. Redwood: That I think is the biggest gap we're facing. You can identify these other studies, like paternal age,

Dr. Lawler: Mm-hmmm.

Ms. Redwood: the importance of the report. But unless we really have the investment in doing the environmental research, we're not going to be able to move those types of studies forward. That's sort of my point.

We can keep saying what needs to be done, but when you look at the research portfolio, there's several topics we have in there now that have no funding. And those topics have been on the books for a couple of years. So that's why I'm feeling this level of frustration with continuing to sort of identify these gap areas and these specific projects when they're not getting fulfilled, so that's why that was the number-one gap areas when

I created the draft.

And you know, again, this is a document that everybody has input on, but I do feel strongly that that's what's really holding us back right now and that it needs to be identified in the gap.

Even though it may not be a specific scientific research question, it's a huge roadblock to us moving forward.

[Pause]

So how do we want to move forward from here with regard to this gap document?

Dr. Pessah: One, I think that that major gap that we discussed can be presented within the context of the new science. We're not trying to belittle the amazing amount of genetic information that's been unfolding. I think what we need to do is put it in context of how we can help the kids that are influenced by gene-by-environment interaction.

Those of us that have worked with highly penetrant single gene mutations, and this is not just my opinion, this is actually fact. I mean, just read the literature, that even though we know

exactly which gene is causing which disorder, we've been unable to do much about most of these disorders from a genetic perspective.

And so the idea is, if we identify environmental modifiers, these are strategies that actually can be prevented and could in fact contribute to better outcomes. So I think that we can address this in context of the new science. But the perspective has to be given from Craig's view, from my view, and from Matt's view.

Dr. Newschaffer: I think that there's no doubt, and I think, Cindy, maybe your comments are -- was that, you know -- this particular gap is one that sort of flows obviously from the summary document as we've prepared it so far.

Now I haven't reviewed the gaps document, so I'm at a disadvantage. I don't know what it looks like and I'll look at it over the weekend. But it sounds to me like we're not that far apart here.

So I think maybe, Lyn, if – Isaac I don't know have you looked at, Matt said he was going to look at the gaps document over the weekend. I was going to look at it. Have you had a chance to look at

the gaps document yet?

Dr. Pessah: I have. And in fact it kind of sort of put in my mind how to address that, and that's what I've just sort of spoken about. So I can go back and offer some suggestions of how to craft it. I just haven't seen any feedback.

Ms. Redwood: It would be wonderful to have Isaac, Craig, and Matt, all three, look over the gap document and make -- that would be great. But again, we are -- I know how incredibly busy your schedules are, how precious your time is, so is this something that you think you could work on and get done by Monday and make edits to collaboratively to?

Dr. Pessah: So when was the latest draft sent out? Was that last night?

Ms. Redwood: Right, there was one last night that I sent out in the emails, and then there's one this morning that Matthew's made a lot of edits and comments on.

Dr. Pessah: This was the science document or the gaps document? Because there are two different --

Ms. Redwood: Gaps document. Yes, let me -- I can pull it up, Isaac, and tell you exactly which email it was on.

Dr. Lawler: Didn't Matt State already made some comments on the gap document?

Ms. Redwood: No, I don't believe so.

Dr. Lawler: Or the research opportunities document?

Ms. Redwood: Matt Carey?

Dr. Lawler: No, Matt State.

Ms. Redwood: Yes, no. Matt had looked over -- he had three sort of recommendations at the end of the very first draft that was circulated for the what's new. And I had sent those out in the previous email sort of saying, you know, are these already being covered in other areas of genetic research? That's what I was referring to in terms of the gaps, Cindy. Does that make sense?

Dr. Lawler: No.

[Laughter]

Dr. Pessah: Maybe it would clarify things if you sent it again and labeled it just latest draft of gap document, even if it -- I'm trying to find

it here, and I can't.

Dr. Newschaffer: Yes. We have asked that earlier in the call, and Lyn was going to just send out the latest version.

Dr. Pessah: Okay, great.

Dr. Newschaffer: And I think -- I don't know that -- so I can definitely look at it over the weekend. I don't know that Isaac, Matt, and I will be able to like harmonize like we did with the science document.

So I think maybe what we should do is, we should just each send back to you guys our comments on the gaps document, and then you guys can sort of try to put it together. I mean I'd be comfortable with that.

Ms. Redwood: Okay, can you be real specific? So what I want to say, like instead of saying sort of the criticism "I don't like this, this doesn't belong here."

Dr. Newschaffer: Edit it, you're saying.

Ms. Redwood: Yes. If you can just say, hey, you know, what about inserting this instead?

Dr. Newschaffer: Yes, yes.

Dr. Pessah: That's what I intend to do, Lyn. And then which -- how you integrate that, really I'm fine with.

Dr. Newschaffer: Yes, me too. And I totally get it. I know the frustration when you send a group document for comments and you just get a bunch of different like criticisms and no helpful wording.

[Laughter]

So we'll -- and put that in the email, too, because Matt's not on now. I'm sure he'll take the same tack, but just say, you know, go ahead and edit this text as you would want it to read and then we'll just each send in our own. And then you guys can work on the integration.

And then on the science document, we're pretty much close, so I think we'll have the agreed-upon consensus version of that ready, too.

Dr. Lawler: And for the gap document, too, if I think we've had some discussion about sort of just the framing of the document. But I'd be really sort of interested in if there are gaps that are not reflected we need to know, you know,

so we can include those. And then also if there are gaps that just are not necessarily you would choose to highlight or you feel to be priorities, please identify those, too.

Dr. Newschaffer: Right. So I know I'm going to include some that I think my guess is --

Dr. Lawler: Probably on there.

Dr. Newschaffer: No, right. But I also feel that there might be a decision -- so, I'll make it a little concrete, and I've got to run too. It's right at the end of time.

But like, for example, when we want to try to translate the gene-environment interaction to additional epidemiological approaches, we run into sort of limitations around the analytic approaches that are available to address gene-environment interaction.

So, autism isn't the only field that hits up against this. I mean, cancer does; lots of others do. But I think we're getting to the point where autism probably has a stake in wanting to emphasize the development of more statistically efficient methods for detecting gene-environment

interaction – so this is my opinion now -- as a priority. Because we're going to eventually want to come back to population data and try to test for gene-environment interactions.

Whether we get a clue that they exist because toxicological evidence suggests that this chemical induces de novo mutations, whatever it is, at some point we're going to want to see in the population-level data. And, as many of you guys well know, you know, with the tools we have now, we need huge studies that combine very rich environmental and genetic information, which would probably also be an aspirational goal.

But I think that our field probably also wants to promote methodologic work in that area. But whether that rises to the top of the gap list, I don't know. But I think we need to start paying attention to those things. And I've got other similar issues in terms of more efficient ways to think about biomarkers of exposures, et cetera. So I'll add some of that in, throw it into the mix, and you guys can figure out where it belongs.

Ms. Redwood: Hey, Craig? Actually, there's the

second paragraph and the third paragraph -- I tried to address that in terms of what types of new computational approaches you could do to be able to integrate some of these findings.

Dr. Newschaffer: Okay.

Ms. Redwood: But not being a scientist, I struggled with writing that up.

Dr. Newschaffer: Yes; well, I'll give it a shot.

Ms. Redwood: Paragraph 2 and paragraph 3 -- that's exactly what I was trying to address. But, yes, please look over that.

And also I want you to know when you read this that, when I started this document, I didn't have your final science document yet.

Dr. Newschaffer: Got it.

Ms. Redwood: So I was sort of shooting at a black box with coming up with these things. So, that's probably another reason why it doesn't segue as closely with the science document.

Dr. Newschaffer: Okay. Alright, well, I'm sorry. I think I've got the weekend homework. I've got to go now, too, so --

Ms. Redwood: Okay. Well, thank you so much. And we've probably -- I know we've gone over time.

So are there any other questions? We'll hopefully get these documents back this weekend. Cindy and Matt Carey, the three of us will put our heads together on Monday and hammer out this final gap document to submit to Elizabeth by five o'clock. Does that all sound doable?

Dr. Carey: Yes.

Dr. Pessah: Yes.

Ms. Redwood: Okay, any other questions?

Dr. Lawler: Lyn, I just want to take this opportunity to really kind of thank you. I know you've done most of the work here to give us a strawman that we can poke holes in and that's, you know -- I really do sort of appreciate the effort that it's taken to do most of this de novo. And I think you've really given us a lot to think about. I know it represents a tremendous amount of work on your part.

Dr. Newschaffer: Definitely.

Dr. Pessah: Yes, thank you, Lyn.

Ms. Redwood: Okay. Well, listen, thanks

everyone. Have a wonderful weekend. And we'll communicate by email on Monday.

Dr. Pessah: Yes. Bye-bye.

Ms. Redwood: Okay, take care everyone. Bye-bye.

(Whereupon, the conference call of the Strategic Plan Question 3 Planning Group was adjourned at 1:24 p.m.)