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INTERAGENCY AUTISM COORDINATING COMMITTEE

SUBCOMMITTEE FOR
BASIC AND TRANSLATIONAL RESEARCH

STRATEGIC PLAN QUESTION 2 PLANNING GROUP

CONFERENCE CALL

FRIDAY, SEPTEMBER 28, 2012

The Strategic Plan Question 2 Planning Group convened via conference call, Walter Koroshetz, Chair, presiding

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PROCEEDINGS:

Dr. Roger Little: Good morning, everyone. Welcome to the conference call for the Planning Group to Update Question 2, "How can I understand what is happening?" of the IACC strategic plan for ASD research.

My name is Roger Little. I'm acting as the designated Federal official for today's call on behalf of Dr. Susan Daniels, who is currently out on maternity leave.

On today's call, please remember to identify yourself before you speak so that we know who is on the call. Thank you all for joining us, and I'll now turn the call over to the planning group leader Dr. Walter Koroshetz.

Dr. Walter Koroshetz: Great. Thanks very much, Roger, and thanks everyone for getting on the phone.

What I'd like to do now is just go around and do a roll call of the folks who are on the Subcommittee. So is Alison Singer here?

Ms. Alison Singer: I'm here.

Dr. Koroshetz: Great. Alison, do you want to

try to say a little bit about where you are and what you do?

Ms. Singer: Well, I am the founder and president of the Autism Science Foundation. I've been a member of the IACC since back in 2006, and I've worked on updating Section 2 of the Strategic Plan, now I think for the last four years.

Dr. Koroshetz: Thank you, Alice.

Ms. Singer: I can bring a little bit of historical perspective to the process.

Dr. Koroshetz: Absolutely more than that and you are up to date. David Amaral?

Dr. David Amaral: I'm in psychiatry and behavioral sciences at UC, Davis, also the research director of the MIND Institute, a neuroscientist doing work research on autism spectrum disorder. And I've participated periodically in the process of developing the initial matrix and then participated in [Inaudible comment] format of the Strategic Plan -- happy to participate.

Dr. Koroshetz: Thanks so much, Dave. And Kevin's on a train, but it sounds like pretty good

reception. Kevin Pelphrey?

Dr. Kevin Pelphrey: Yes, this is Kevin. I'll be a little slow if you ask me a question because I'll be on my cell. This is Kevin, and I'm from Yale University. I'm a faculty member in the Child Study Center. I also direct the Yale Office [Inaudible comment].

Dr. Koroshetz: Great, thank you and Carlos?

Dr. Carlos Pardo-Villamizar: Hi. I'm Carlos Pardo, Department of Neurology at Johns Hopkins University. I am a clinical neurologist and a neuroimmunologist. My laboratory work is in the studies of immunopathology of autism, assessment of biological markers in autism. I have participated in the IACC meeting a couple of years ago, and I'm coming back now.

Dr. Koroshetz: Thank you, Carlos. Good to have you. Dennis?

Dr. Dennis Choi: Hi, Walter. This is Choi. I'm recently back in academic neurology at Stonybrook University consultant to the Simons Foundation where I've recently served in.

Dr. Koroshetz: Great. Thanks. Kate? Kate?

Okay. So, I'm Walter Koroshetz. I'm the Deputy Director of NINDS, and I'm on the IACC and kind of been appointed kind of steer the ship in the process of updating the Strategic Plan.

And with me is the Assistant to the Deputy, Kate Saylor.

Ms. Kate Saylor: Hello, I'm Kate Saylor. And I recently started in NINDS working for Walter Koroshetz. And I have a background in neuroscience in ear development.

Dr. Koroshetz: Great. And she is responsible for all the hard work that went out on email. Did people or were people able to get the email that came out this morning? Let's see, anybody not get the email? Because that will help us in terms of explaining things as we go through. Okay, sounds like everybody got it. Okay, good.

Alright, so the agenda for today is basically to just kind of go over what our task is, and then we have a plan that Kate and I were thinking about that might be helpful but certainly is a draft and can be changed depending on the will of the group.

And so basically, our task is to update

Question 2 of the IACC Strategic Plan. And Question 2 deals with the biology or the biology -- or what we know about the biological basis of autism, particularly, what is happening early in development, are there known biological differences that help explain ASD symptoms, and can subgroups of people with ASD help us understand the etiology of ASD symptoms?

The IACC plan was put together with a lot of hard work from people like Alison. In the last rendition, the Plan was not a rewrite for 2011, but basically it was adding addendums to the previous 2010 Plan.

Now, my understanding is that because the IACC, its existence, required congressional approval, the congressional approval did not come until fairly recently, but it did come. But the Plan is still due by the end of the year. So that means that we really have a very short time period. We don't have, you know, for instance, an entire year to do this. We have basically a couple of months to do this now.

And therefore, the decision at the IACC was

basically to do another addendum. So we have the Plan, we have the 2011 addendum, and then we will add on a 2012 addendum. That's the general -- but that actually makes it easier for us because it's not a total rewrite.

However, everyone around the table realizes that the Plan needs a total rewrite, and that will happen. Probably as soon as we do the addendum, we'll start working on the 2013, which will be a complete new write-up.

So therefore, what we're trying to do is put together an addendum to the sections -- basically what have been the major advances since last year, what gap areas have emerged since last year -- and then somehow incorporate into probably the first one is what progress was being made in fulfilling the objectives which are listed in the Plan.

So it's a fairly discrete task that we're up to. And the timeframe is short. The plan is to present our addendum at a meeting that is October 30th. So we need to get everything done ahead of that timeframe. Because of the fairly defined task, I think it's very doable.

So before we get into the actual nitty-gritty, can I ask if there are any general questions to what was just kind of presented?

[No response]

Dr. Koroshetz: So, sounds clear? So then the question is how to put the addendums together. And the first part is, I think, the essential part that will help us tie things together, and that is to try to understand what were the major advances that occurred in 2011 and so far in 2012 that we should highlight in our addendum that is related to what we've learned in the past year.

To that extent, Kate and NIH staff, Laura Mamounas, who have the NINDS portfolio on autism basically did a PubMed search and tried to then allocate the publications that looked relevant to this issue into certain categories.

And those categories were really taken from the previous Plan. So we went to the Plan, we pulled out what looked like relatively important categories, and then they went to the literature and assigned publications to each of these categories.

Now, this is just a beginning, but we thought it would be helpful if we got this started. And our process going forward really is to ask, are there categories that are missing, and if they are, we'll include them.

And then the next issue is for certain people on the Subcommittee to take charge of each of the categories and then look at what we did, add in what you think is important, and then condense it to a very short couple of sentences really for each of these categories.

Now, there may be some categories where you don't think it's important, where the research, for example, may not be significant enough to highlight in the addendum, and that's fine, too.

But that was the process we thought would be best, to put up the categories, assign them to people, have them look at what we assigned but also add things that they think are important and then to compile that also to the person who is assigned to each category to just write a short prose with the references.

And the idea then was, with those type of

inputs from the group, we would compile that into an addendum that reads well. Does that sound -- so how about comments on that process.

Dr. Amaral: That sounds reasonable, Walter.

Dr. Koroshetz: Okay, okay. Well then, let's look at the topics that we picked out from the previous Plan. And then -- yes, go ahead?

Dr. Choi: This is Dr. Choi. My question is I still don't understand the difference between Question 2 and Question 3.

Dr. Koroshetz: Okay.

Dr. Choi: I'm perfectly comfortable in looking at a category -- it makes sense looking at a category. But I can't answer the question is this the right list if I don't understand the boundary between them.

Dr. Koroshetz: Okay. So, good question. And there is -- That's actually not completely separate territory. Question 3 -- let's say this, that the categories we picked for Question 2, we did not generate new ones. We basically picked them from the previous.

So we feel that there's at least a precedent

for them. So the way that -- the convention that has driven the previous report is -- we haven't really changed that convention. So I think we're defensible there.

But what I understand the difference is Question 3 is what caused it to happen and how can it be prevented. So many of the -- they really overlap, particularly with regard to genetics. So the way I understand it is if the genetics is, you know, it's a pure genetics finding, that's Question 3.

If it's an environmental exposure that's being investigated, that's Question 3. If a gene has been discovered and then there's a study that shows the biological role of that gene in how it might interplay with autism or an autism-related disorder like tuberous sclerosis or Rett or fragile X, then that would be Question 2. So that's kind of how I see the overlap.

Dennis, does that make sense?

Ms. Singer: This is Alison. I would also add that when we originally differentiated between Section 2 and Section 3, Section 2 really focused

on brain growth, brain structure, issues of connectivity, issues of tissue-based research, brain-based tissue research, so that would fall square within Question 2.

Dr. Koroshetz: Alright, but we had a problem. When we went through the literature, this was -- we didn't really have trouble with the other questions. We had questions about Question 2 and Question 3. So actually, in some of the articles that Kate put together, you'll see a little question mark, which is, is this really Question 3? So that's something that the people who take the topic should decide on.

Plus, the other thing is, we can put it together and then when the whole group comes together in late October, we're presenting Question 3, and the Question 2 people can talk and we can make deals there, too. So I wouldn't get too upset about it, except to say that I think we can leave the GI stuff, the pure genetics stuff, to Question 3.

Okay, any other kind of broad questions like that?

Ms. Singer: Well, again, it's Alison. I'll also just add that the issue of overlap is not unique to Questions 2 and 3. On other calls that I've been on for the Strategic Plan, there have been issues of overlap between Section 5 and Section 6, Section 5 and Section 7, Section 2 and Section 7. So I think we recognize, as we put together the entire Plan, that the sections are going to overlap.

Dr. Koroshetz: And we can take care of that when the general group gets together.

Okay, so let's then visit the discussion topics. And so I'll just throw out the name and I guess what I need is somebody to kind of take hold of one of the topics if you think it's relevant.

If you think it's not relevant, then just say so.

So the first one is biomarkers.

[Pause]

Is anybody interested in taking a look at biomarkers?

Dr. Pardo-Villamizar: Alright, this Carlos Pardo, I think it's because of the biomarkers,

particularly since that's one area where we did some work.

Dr. Koroshetz: Okay, so Carlos. Now, the next one unfortunately is a tricky one, so let me just explain what the problem is. The second one is called the molecular basis. That's really core to what we're doing.

Now, the big issue is that a lot of the molecular-basis papers come under the "understanding subtypes of autism," including syndromic autism. And that's because a lot of the biology comes from, as I mentioned, the Rett, the tuberous sclerosis, or the fragile X research. So I would say that the person who does molecular-basis should also do "understanding the subtypes" since they're so closely related.

And then remember, there's no reason to separate these in the report. You know, they're basically -- we can basically combine these two as we report them. So does anybody want to sign up for molecular basis with the addition of the subtypes?

Dr. Amaral: Walter, this is David. I don't

want to necessarily take that on, but I just wanted to say that I think there are other ways of defining subtypes of autism. So you know the issue of regression versus non-regression, the issue of developmental delay versus non-developmental delays, language versus non-language. So I guess I would say that -- I would recommend that -- we [Inaudible comment] the potential of broadening up the subtypes of autism section.

Dr. Koroshetz: Okay. So we actually -- you're right. And so maybe the thing is the subtypes -- the molecular basis person should do the molecular basis of the subtypes and the non-molecular stuff should go into a different bin.

Dr. Amaral: Right.

Dr. Koroshetz: Does that make sense? Okay, okay, so good, because I think that -- that's actually a good way of thinking about it.

So anybody want to jump into the molecular basis piece?

[No response]

Okay. Alright; I like molecules; I could do molecules. So I'll take that one.

Okay. Now, so let's see. While we're there -- so you mentioned a couple of things. You mentioned regression; you mentioned language, non-language. And we have regression listed. I thought we had language, but did it disappear? Okay. We didn't find it.

Ms. Saylor: [Inaudible comment] – we didn't create the category.

Dr. Koroshetz: So Dave, how would define that category then?

Dr. Pardo-Villamizar: I think that the issue of regression and the clinical subtypes is extremely important at the present. I would suggest that you keep that as a whole topic and that perhaps make the issue of the clinical characterization and the biological basis has been explored for those different subtypes.

Dr. Koroshetz: Okay.

Dr. Pardo-Villamizar: I think that is one of the approaches of that.

Dr. Koroshetz: Okay. So we would, say, call one topic then -- create a new topic called clinical subtypes, and in that we will include

studies of regression.

Dr. Pardo-Villamizar: Right.

Dr. Koroshetz: Language and developmental delay.

Dr. Pardo-Villamizar: Right. I think that that will make a better sense. Try to put those issues together. Because I think that there is a lot of -- if we try to do those separately, then it's going to be a lot of overlap between those different items.

Dr. Koroshetz: Okay, 0kay. That sounds good. Who would want to pick that topic?

Dr. Amaral: This is David. I'd be able to work with somebody on that or take it on.

Dr. Koroshetz: Okay, David, okay. Great. Okay, the next group is -- we termed this "sensory processing," so that would include things like -- that's a good question -- that might include -- that would include studies looking at some of the real problems in social interactions, auditory processing, visual/spatial skills.

Dr. Pardo-Villamizar: Again, I think that the sensory processing and neural system [Inaudible

comment] may be part of the same chapter.

Dr. Koroshetz: I actually --

Dr. Pardo-Villamizar: There is a lot of interaction in terms of sensory processing related with brain networks.

Dr. Koroshetz: Good.

Dr. Pelphrey: And I would second that. My sense of reading the articles under sensory processing and looking for others, it was the sense of being a bit underwhelmed by the progress in that area. So combining it as was just suggested is probably wise.

Dr. Koroshetz: Okay. So we'll do that. I think that makes a lot of sense as well. So, sensory processing, neural circuits will come together. And do we have a taker for that one?

[No response]

Dr. Pelphrey: What is the title again?

Dr. Koroshetz: So it will be the sensory processing differences in autism versus typically developing as well as neural systems and circuitry differences in autism versus typically developing.

Dr. Pelphrey: I would like to take that as

long as I can change the title. It's pretty cumbersome. Okay.

Dr. Koroshetz: Okay, so try that. Maybe this should be clearer. There are no titles --

Dr. Pelphrey: Okay.

Dr. Koroshetz: -- to the addendum. So the addendum is going to be closed. The titles are just for us to make sure we cover the waterfront. So the titles are -- it's -- we're going to just write, you know, what do you think the major advances are. They're not going to be subtitled.

Dr. Pelphrey: Okay. I like that idea, and since now we're sort of on the subject of the neural circuits, the two other areas that might fall under as general discussion of neural circuits would be the sort of unique Geswhin paper on brain [Inaudible comment] system. And then a paper coming out, there's a new *Nature* paper coming out using infused [Inaudible comment] stem cells in autism from Cora [Inaudible comment]. So those domains which are now separate, I think would nicely fall in as a sentence under neural circuitry.

Ms. Saylor: [Inaudible comment]

Dr. Koroshetz: Okay. Yes. Okay, if you want to take those, Kevin, that's fine.

Dr. Pelphrey: Okay.

Dr. Koroshetz: I mean, Kevin, I really want to emphasize that these categories are just for our benefit. They're not going to stand going forward at all. We're just going to write the advances, and we will order them in some fashion, but we're not going to belabor them.

Dr. Pelphrey: So I'm going to mute myself so you don't hear the background noise.

Dr. Koroshetz: Okay. So the next -- yes?

Dr. Choi: Can you hear me? There may be a need for clarification regarding the temporal horizons. Kevin just mentioned the paper that's about to come out. I am guessing captures the horizon.

Dr. Koroshetz: Okay. I have to get clarification on how long. When I did ask – I don't know if Roger is still on the phone -- I did ask Elizabeth yesterday, and it sounded like anything 2011 or 2012 was going to be okay.

Dr. Baden: Um-hmmm.

Dr. Choi: Anything published.

Dr. Koroshetz: Yes, it has to be published in 2012.

Ms. Singer: Usually though, we include ePub, so as long as it's ePubbed.

Dr. Koroshetz: You do.

Ms. Singer: I'm pretty sure.

Dr. Elizabeth Baden: No, that was Alison, but this is Elizabeth, and Alison is correct. Anything that's available online is definitely. I think the goal is to have this as up to date as possible. So any information that you can get your hands on is --

Dr. Choi: But it can't be on an individual basis. It has to be published.

Dr. Koroshetz: Got to be published, yes.

Dr. Baden: Yes.

Dr. Choi: If someone sends you a preprint, that doesn't count.

Dr. Baden: No.

Dr. Koroshetz: No. Just like NIH. Okay. All right, so the next group that really goes together well would be brain structure and neuropathology.

Dr. Choi: That has David Amaral's name on it.

Dr. Amaral: Yes.

Ms. Singer: Yes.

Dr. Koroshetz: Alright.

Dr. Amaral: That's fine.

Dr. Koroshetz: Good. And then regression we'll put into the clinical subtypes. Circuitry would -- we'll combine with sensory processing. Subtypes we dealt with, so the next one that has somebody else's name on it, immune and autoimmune basis of autism -- so, Carlos?

Dr. Pardo-Villamizar: Okay.

Dr. Koroshetz: Can you take that one?

Dr. Pardo-Villamizar: Yes.

Dr. Koroshetz: Okay. Now, the next ones may not be complete, but they're -- so we'll refer to them as "epilepsy and gastrointestinal." Certainly around the IACC table there's been a lot of interest in these two, you know; I call them manifestations of autism. Some people call them co-morbidity. I don't agree with that. But -- And there may be more. But do people get the gist of what we're looking for there?

Dr. Choi: Walter, I'll take that on.

Dr. Koroshetz: Okay, great. So you don't have to refine yourself to epilepsy and GI, but that's where most of the reaction has been.

Dr. Choi: I'll call it comorbidities.

Dr. Koroshetz: Okay. And then, so gender and sex relates to the -- in the preponderance in males, what's the biology of that. I'm not sure that has to be a specific topic or not or whether it could be included in some of the other things.

Anybody have any thoughts on whether somebody wants to take that on or whether we can just assume that the other groups will also be considering that one as relevant?

[Several speakers]

Dr. Pelphrey: I'm sorry, Alison, go ahead.

Ms. Singer: I was going to say if Kevin's not going to speak, one thing we have to acknowledge is that there's now an ACE award specifically looking at gender differences. So that's something that's clearly emerged for the good.

Dr. Koroshetz: Yes. So, Alison?

Dr. Pelphrey: This is Kevin. I'm happy to

write about that.

Dr. Koroshetz: Kevin. Okay. The last one on our list is use of bio-specimens in IPS cells. Again, does that stand by itself, or does somebody want to just take a look at that when they start talking about molecular basis and biomarkers?

Dr. Amaral: Walter, this is David. I think that can stand by itself. That still may be one of the gap areas.

Dr. Koroshetz: That's where it came from, yes.

Dr. Amaral: Yes.

Dr. Pelphrey: I agree.

Dr. Amaral: So I'd be happy to do that or do that with somebody.

Ms. Singer: I'm happy to work on that. I also want to point out that in the call for Chapter 7 we identified the need for tissue as the primary gap in infrastructure. So it will be part of the Chapter 7 gap area. So we should just coordinate between the two chapters there.

Dr. Amaral: Okay.

Dr. Koroshetz: Okay.

Dr. Pelphrey: That sounds great.

Dr. Koroshetz: Okay. So, and Alison, anything we missed here? Areas that we need people to think about?

Now, of course, if anybody thinks of anything, they can include it. So don't feel yourself confined. If there's something you see you think maybe somebody else might have missed, feel free to put that in your report, and then we can all kind of get back together again on it.

Alison, can you think of anything that we should?

Ms. Singer: No, no. I would just remind everyone to try to be as concise as possible in their writing that we're not looking for pages on each one of these areas. The entire update including all of these sections should be between 1,000 and 1,200 words. So that's not very much.

Dr. Koroshetz: Right.

Ms. Singer: That has been really the biggest challenge in doing these.

Dr. Pardo-Villamizar: For each topic, what do you suggest in order to how extensive? One thousand words?

Ms. Singer: I would say write what you need to write, and then we'll pare it down. But we have six sections now, and the entire update is supposed to be about 1,200 words. So that's really 200 to 250 words apiece. So you really have to home in on the key successes and the key gaps.

Dr. Koroshetz: Right. So you don't want to write about individual papers, you want to say something like in this area there has been considered, you know, there's been a new discovery, you know, that this molecule is affecting synaptic function. There's been a link to GS, something like that. And then you just give three references.

Ms. Singer: Right.

Dr. Koroshetz: You know, so that -- it's really a sentence that's going to make it out of anything you think is important. We'll try and make it flow in the sense that it's not just choppy but it has a theme to it.

Dr. Pelphrey: Yes.

Okay, so then --

Ms. Singer: And I would just also add we

talked about this on another call, that if the progress in a particular area has been slow or disappointing, then it's perfectly fine to put that in as well.

Dr. Koroshetz: And that might go into the gap area section. So, timeframes are short. We want to have the thing written by October, that last week in October. So if we can push people to try to just take their sections with what they've done and send us what you think are advances with a short sentence in the next -- Kate's trying to ask that we get this in by October 10, the advances piece.

It's a short timeframe, but you know, I think it's doable. And then I'll take a look at it, and we'll compile things and send it out for review. Then we'll try and get a teleconference the week of October 15 to 17. I'm not here then -- maybe the next week.

And then we'll try and write it up and submit by October 22. Then on October 30, we'll have an in-person workshop where we can discuss the draft together and the write-up together.

[Pause]

If it's a gap area, again, certainly if your area, you go through them and then we read the gap area section, and if you can think of new gap areas or, as Alison was saying, if in your area research has been stagnant, to highlight that, how can that be improved, and put that in the gap areas suggestion. Then we can use those to compile the gap areas.

Ms. Saylor: And the same thing for objectives. The short-term and long-term objectives if something in your section relates to one of the objectives and if you have a suggestion about updating an objective, something like that, also include that.

[Pause]

Dr. Baden: Hi, this is Elizabeth with OARC. And I just want to clarify for the objectives, if it's informative to look at those to help identify some of the ongoing gaps or to see where we've -- to kind of gauge where we've made progress -- that's great.

But just to clarify, as Walter has mentioned,

this is an addendum. So we're not going to specifically revise the objectives. But do look at those if it's helpful for your process.

Dr. Koroshetz: Okay. Yes, so I guess just so it is useful -- if it doesn't quite fit right down the alley, then not necessarily tying in advance to an objective.

Like one of them was understand the mechanism of metabolic, immune system interaction with the central nervous system that could influence ASD during prenatal/postnatal life. Then it may -- something you add to your advances could potentially link to the short-term objective. And maybe just star it as you do that. That might be helpful as we kind of tie the advances into the objectives.

So that was the general gist of the call we wanted to get through today. So the plan would be that we would send out the assignments to the revised kind of topic areas and then if you could look through the papers that we sent and also things that you know about.

And then just pick and choose which ones you

think are important to incorporate in a report back to us on what you think the advances are that we should highlight, as well as then in your areas if there are gap areas that you think are worth highlighting in the addendum to the gap areas, then also include that.

And so it's a fairly defined task. Does anybody have any questions or any suggestions going forward?

[No response]

Roger or Elizabeth, did we forget any major things that the group needs to be aware of?

Dr. Baden: I think you covered everything.

Dr. Little: Yes, I think so.

Dr. Koroshetz: Okay, alright, so Alison, any further thoughts?

Ms. Singer: No, I think we're good.

Dr. Koroshetz: Okay, okay, so we'll try and get the emails out. And if there's any question with the email on anything we said on the phone, please email us back right away and we'll clarify that.

If anybody has any questions, feel free to

email me and or we get on the phone. We really appreciate everyone's help in trying to move this forward. I apologize, a little bit, for the short timeframe. But I think the people on the phone have a really good grasp of the area, so we're hoping it's not going to be too onerous to just kind of pick out the really big things that have occurred in the last two years since the last report.

Alright, well any other questions before we close?

Dr. Baden: Walter, this is Elizabeth again. One more thing, we do ask that on all email correspondence if you could copy both myself and Gemma Weiblinger in the Office, and I'll send an email note around to everyone so that -- to be sure -- you all have our email addresses.

Dr. Koroshetz: Got it. Okay. So thanks everyone for getting on. Kevin, I hope you get to where you're going.

Dr. Pelphrey: Okay, thanks. Thanks for including me.

Dr. Koroshetz: David and Alison, thanks for

coming -- and Dennis.

Dr. Choi: You are welcome.

Dr. Koroshetz: Alright; take care now everyone.

Ms. Singer: Thank you -- bye.

(Whereupon, the Strategic Plan for Question 2 was adjourned at 1:05 p.m.)