U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

2ND IMPLEMENTATION WORKGROUP MEETING

WEDNESDAY, SEPTEMBER 10, 2008

The Workgroup convened at 11:00 a.m. in Wilson Hall, Building 1 of the Main Campus of the National Institutes of Health, Bethesda, Maryland, Thomas Insel, Chair, presiding.

PRESENT:

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

DUANE F. ALEXANDER, M.D., *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

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

PETER BELL, Autism Speaks

MARTA BENEDETTI, Simons Foundation (via telephone)

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

ALAN CRANE, Autism Consortium (via telephone)

WOLF DUNAWAY

PETER GERHARDT, Organization for Autism Research (via telephone)

LISA GILOTTY, National Institute of Mental Health

PRESENT (continued):

DOREEN GRANPEESHEH, Autism Research Institute (Via telephone)

LEE GROSSMAN, Autism Society of America

JAMES HANSON, National Institute of Child Health and Human Development

ALICE KAU, National Institute of Child Health and Human Development

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

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

LAURA MAMOUNAS, National Institute of Neurological Disorders and Stroke

CHRISTINE M. McKEE, J.D. (Via telephone)

RAUN MELMED, Southwest Autism Research and Resource Center (Via telephone)

ELIZABETH MUMPER, Autism Research Institute

LYN REDWOOD, R.N., M.S.N., Coalition for SafeMinds (Via telephone)

DENISE RESNICK, Southwest Autism Research & Resource Center and Denise Resnik & Associates (Via telephone)

ANDY SHIH, Autism Speaks (Via telephone)

PATRICIA TANSKI, Autism Consortium

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

ANN WAGNER, National Institute of Mental Health

DESIGNATED FEDERAL OFFICIAL: DELLA HANN, National Institute of Mental Health

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P-R-O-C-E-E-D-I-N-G-S

11:08 a.m.

Welcome and Introductions

CHAIRPERSON INSEL: Okay. We're good to go. Thanks, and sorry for the delay. I promise that our abilities to find biomarkers are better than to do technology here, and we will hear more about that in a few minutes.

Welcome to everybody to the second of the Implementation Workgroup meetings. The earlier meeting, the results of that you have in front of you, was really to set up some of the major issues around budgetary requirements.

Just to get everybody on the same page because there are some people at this meeting who weren't at the earlier one, this is all in reference to the Autism Research Strategic Plan. The plan is currently out for public comment until the end of this month.

It's probably just worth reminding

everybody that there were 35 initiatives that we'll be visiting today again and also I thought I would just mention that the plan is based on a set of core values which are worth reminding people about at the beginning of this meeting: sense of urgency, scientific excellence, the spirit of collaboration, which I think we'll hear much more about, consumer-focused partnerships in action, and this is the chance to hear about those as well, and accountability.

Many of those core values are really the reason for having this second meeting, to begin to explore more fully 35 initiatives and to look at questions around accountability, partnerships, scientific excellence, urgency, all of the things we've just talked about.

I want to remind people at the outset that what we're driving towards is the final version of the plan to be able to go to the IACC on the 21st of November. What we're

hoping is that the deliverables from this meeting, which will be around the budgetary requirements and a sense of accountability for each of the initiatives, will be transmitted to the IACC so they can put that together with all of the public comments that will be coming in by the end of this month and we'll have then a final document that will be up for further discussion and for voting at the meeting.

If the final document is accepted, that will go forward as an advisory document to the Office of the Secretary. So to think about this in context, we're advisory to the IACC and the IACC is advisory to the Office of the Secretary.

The meeting today is really to fill in that remaining piece that will go to the IACC for their November 21st meeting. I want to remind everybody this is a public meeting, so we have members of the public joining us as part of a webinar, and there are

also members of both this Implementation Workgroup and of the IACC who aren't here in the room with us but are finally now able to join us by phone as well.

So as you can see in this slide, and I'm hoping that the people who have joined us by webinar can actually visualize the slides, the purpose of this workgroup is to advise the IACC about budgetary requirements needed to complete and fulfill the research objectives described in the Strategic Plan.

The agencies and organizations that will be accountable for launching initiatives within the plan and for open competition and peer review are part of the workgroup. This is the list of both organizations and agencies involved, and I thought we would take this moment to go around the table and just make sure everyone has a chance to introduce themselves and we'll also get those people from both the workgroup and the IACC on the phone to introduce themselves

as well.

So Cindy, would you like to start at that end? Thanks.

MS. LAWLER: Hi. Cindy Lawler, Autism Representative, Program Representative from National Institute of Environmental Health Sciences.

MS. KAU: Alice Kau, Program Representative from NICHD.

MR. ALEXANDER: Duane Alexander, Director, NICHD.

MS. WAGNER: Ann Wagner, Program Representative for NIMH.

MS. GILOTTY: Lisa Gilotty, Program Representative from NIMH.

MS. TANSKI: Tish Tanski, Autism Consortium.

MR. TREVATHAN: Ed Trevathan, CDC.

MS. HANN: Della Hann, Acting Director of the Office of Autism Research Coordination.

CHAIRPERSON INSEL: Tom Insel,

Director of NIMH, and Chair of the IACC.

MR. BATTEY: Jim Battey, Director of the National Institute on Deafness and Other Communication Disorders.

MS. COOPER: Judith Cooper, Autism Program Representative from NIDCD.

MR. BELL: Peter Bell, Autism Speaks, and a parent of a child with autism.

MS. MAMOUNAS: Laura Mamounas, Program Representative at NINDS.

MR. DUNAWAY: Wolf Dunaway. I'm a person with autism.

CHAIRPERSON INSEL: Thank you. Maybe we can look at the next slide which has the list and while we do that, could we also just find out who's on the phone with us and we'll just begin to fill in this list hopefully from those who are not in the room.

MR. CRANE: This is Alan Crane from the Autism Consortium.

MR. GERHARDT: This is Peter Gerhardt from the Organization for Autism

Research.

MS. RESNICK: Denise Resnick, Southwest Autism Research and Resource Center and parent.

MR. MELMED: Raun Melmed, Co-Founder, Medical Director, of Southwest Autism Research and Resource Center.

MS. GRANPEESHEH: This is Doreen Granpeesheh from the ARI.

MS. YEARGIN-ALLSOP: This is Marshalyn Yeargin-Allsop, Program Representative from CDC.

MS. RICE: This is Cathy Rice, Program Representative from CDC, also.

MS. McKEE: Christine McKee, a member of the IACC, and a parent of a child with autism.

MS. SINGER: Allison Singer, Autism Speaks, and a Public Member of the IACC, and parent of a child with autism.

MS. REDWOOD: Lynn Redwood, Public Member, IACC, representing Faith Line.

CHAIRPERSON INSEL: Anyone else on the phone at this point?

(No response.)

CHAIRPERSON INSEL: Well, thanks to Christine, Allison and Lynn for joining from the IACC. We'll certainly make sure there's a chance for you to participate in this meeting as well. If you have questions, don't be shy about asking them as we go along.

MS. HANN: For those on the phone, I think several of you, I still need to receive your Conflict of Interest forms. So if you could please have those either faxed to my office or sent to me via e-mail as a PDF, I'd really appreciate it.

We really need to have those forms to have you fully participate in the meeting.

Thank you.

CHAIRPERSON INSEL: Okay. Let's go on and say a little bit about what we need to get done today and the next slide actually describes the main features of that.

First, we want to go back over the 35 initiatives and to look at the budgetary requirement estimates from the first meeting and again since not all of you were there, some of you may be wondering how were these developed. Where do these numbers come from?

The answer to that question is through discussion that we had a few weeks back in which people from all the different agencies and organizations who fund autism research or sometimes other kinds of research provided their best sense of what it would cost to do this, in some cases based on projects that are currently underway so they know precisely what it costs to do a particular kind of clinical trial which showed up in the Strategic Plan, so they could extrapolate from current experience, or in some cases it was based on experience with other disorders, knowing what it might cost to get a biomarker for Parkinson's and using that as a predictor for autism.

So it was bringing that kind of an experience to the table. The numbers are not perfect. The precision here is hard to even predict, but this was the best estimate that we could get from a discussion from all the people involved at the previous meeting.

What we thought we'd do today is to go back over some of those numbers. Some of them really were a very broad range, so they could be perhaps further refined. We want to look at questions around the number of years of funding. We again didn't spend a lot of time on that last time but get a sense of whether these look accurate or not, look at the start years that we have down so we can make sure that those actually match and we've already heard, we heard a little bit at the last meeting and we're hearing elsewhere, that some of the objectives are still not quite clear, and this came up last time because people were trying to understand what the costs were and realized as they began to drill

into this that some of the language wasn't right and we're not going to rewrite any of the objectives today. That's really for the IACC to do when they meet in November.

But it will be helpful if you see something that isn't clear for you through this committee to let the IACC know your concerns about that so these things can get ultimately changed.

The other piece that we hope to do today that we didn't do at the first meeting is getting into the issue of developing collaborations and developing the accountability part of what was meant to be in the plan.

So for each objective, we want to begin to identify who's going to take ownership of this and to think about who's doing it now, who's going to expand what they're doing or who's going to move into this area, and who will be partnering to make sure that it happens.

So it's not as if we're expecting a single group to do any of these. This is largely going to be a collaborative effort and that's part of why the IACC, I think, can be most successful in developing collaborations, reducing redundancy between funding agencies, and making sure that we're getting the biggest bang for our buck and leveraging what we're all doing.

Finally, as it says up here, we want to think about some initial milestones and what would be the appropriate measures of accountability and that may take some further discussion as we get into this.

So let me just underline a few things that we're not going to be doing today because I know this is always a question that will come up.

As I mentioned, we're not going to rewrite the objectives. They may not be perfect and there may be things that you want to say differently, but this is not the

meeting in which to do that.

We're not going to make any final decisions or commitments today because we are advisory. So what we can do is make our best guess of what we'd like the IACC to do, but it's up to the IACC to provide the final document that will go to the Secretary.

And finally, before we jump into this, let me remind you again that as we look at these budgetary requirements, these are cost estimates. They're not commitments for an investment. We're not making funding decisions here. This is really important.

So if the number goes up or down, it doesn't mean that we've decided to put more money or less money into something. What we're trying to provide here is guidance for the IACC about what we think any of these things would cost to get done. It's not in that sense a decision that something in particular will be funded by a particular group at a particular time, and again those

are all later decisions that will have to come out of the IACC process and what happens thereafter as groups work together.

But this will give us the guidance about what we think in our best estimate it will cost to actually accomplish the very things that the IACC says are the most important objectives to get done.

So with that as an introduction, let me see if there are any questions or further comments before we jump into the 35 objectives.

Peter?

MR. BELL: Just a question, Tom. It might be helpful for us to think beyond the Strategic Plan and how what we or what ultimately the IACC approves and then sends to the Secretary. Where do we go from there?

Just to kind of help us along the way so that we truly understand what the Strategic Plan is designed to do.

CHAIRPERSON INSEL: So a couple of

answers to that. One is that at the last IACC meeting, there was a recommendation that we have either a subcommittee or a workgroup, those are two different things that need to be developed, that will carry this along and will, after the submission of the plan, become involved in monitoring progress and thinking about revisions and that leads to the second answer, which is, I need to remind everybody this is Version 1.0, and if we have a final vote on this on November 21st, on November 22nd, we start working on Version 1.1 because we know there are things in here that are going to shift as the science moves forward. So this small workgroup or subcommittee will also be dealing with that.

I think, as I've listened to the conversations that have already begun, especially at the previous meeting, what I'm hearing is that one of the biggest things we can expect out of this is program officers from different organizations and agencies

beginning to work together in a new way and that could mean joint funding opportunities. It could mean that we start sharing data in a different way, and it could mean even a different kind of organization going forward, but I think that really needs to be developed and I think it's one of the real opportunities that we have here if we can do it in the right way.

So I'm hoping, even as we talk about the individual initiatives today, we'll hear some examples of that.

MS. RESNICK: This is Denise. A comment and maybe just a perspective, too, while I was trying to interpret these numbers, and that is, how they speak in terms of our portfolio of investment and what they say in terms of their relationship and the amount of investment in any one of these areas.

So I'd just ask at some point, whether it's this group or the IACC, that we recognize what message we're conveying as it

relates to what the bottom lines are in terms of these respective areas of investment and how we prioritize, you know, what -- you know, in terms of what that means in terms of priorities, certainly what's called for, in terms of being able to achieve those goals, but I think it could be our message and I'd want to be mindful of that.

CHAIRPERSON INSEL: Thanks, Denise. You know, I think one of the things you'll see is the priorities come out a bit just based on how these different projects get staged in terms of what's short term and what's long term, but also it's probably important to recognize that there are a lot of things going on currently that are aligned with these 35 objectives.

These are not being done in an environment where there's no research and one of the things that we'll hear about, I hope, as we talk about the accountability piece and about how these will get accomplished and

implemented is the kinds of projects that are currently underway.

In some cases, actually I suspect that much of what is being proposed has actually already been launched by one organization or another and that's -- it's not to say we wouldn't count it. I think that's one thing that will help us to actually get a head start on some of these items.

MS. RESNICK: Great. Thank you.

CHAIRPERSON INSEL: Okay. Any other comments before we jump in? Can I ask you if you're on the phone, it would be helpful, I think, to mute, if you can, mute your line when you're not talking so that we don't get a lot of echo and sometimes we also hear things that you may not want us to hear, so that would also be useful.

Okay. With that as an intro, let's get started, and we'll -- I think the best way to do this is just to walk through it one by one and we'll -- we've got a schedule here,

so we will take a break part of the way through, so people can go off and get lunch, and then we'll finish up after lunch.

Question 1 - Costs, Organizations, and Milestones

CHAIRPERSON INSEL: So let's start with the first question of when should I be concerned and the first objective is to develop with existing tools at least one efficient diagnostic instrument that is valid in diverse populations for use in large-scale studies by 2011.

This was estimated to require about two years. It was one that was meant to begin quickly with about a $2.5 million price tag.

So can I get a sense from people about whether the cost sounds right, whether the time frame sounds right? Any revisions to this from the last meeting?

If not, who's going to do this?

MS. TANSKI: This is Tish from the

Autism Consortium. Last time we talked about some efforts are underway and we do have some things with the Autism Consortium in developing existing tools, both in terms of identification of those with autism spectrum disorders from a screening perspective and from a biological perspective, and Alan Crane, do you want to talk about that at all?

MR. CRANE: Well, you know, this is the first time I'm at the meeting, so I guess one of the questions is, is this more in the context of actual research?

CHAIRPERSON INSEL: Yes, so Alan, this is Tom again. It is, but the point of this is actually to not only develop but also to validate through a field trial or whatever that would take to show that the diagnostic instrument is effective and provides valid information and it has to be done within a diverse population.

So there's no question this is a scientific process.

MR. CRANE: So there's an initiative in Massachusetts that we're collaborating with called MAPSEA, MþA-P-S-E-A, that has a very brief validated instrument that they're using in diverse populations, but again it's more from a screening perspective.

It was developed at Children's Hospital and it's meant to, in the context of screening and bringing people into the research efforts, make it much more time efficient for pediatricians and it's actually being rolled out to very diverse populations, including the community health centers in Massachusetts.

CHAIRPERSON INSEL: So that sounds very much like what the second objective is. This one, the first one -- and so we'll come back to that in a moment. Thanks, Alan.

The first one is a little different and actually looking around, it's not clear to me who currently is invested in coming up with an efficient diagnostic

instrument. It's quite different than screening. So this would be something that we'll be able to have a much greater precision for the diagnosis.

Peter, is Autism Speaks involved?

MR. BELL: We are in what I would call very early planning stages of having discussions with Kathy Lord over how we can hopefully come up with a perhaps equally valid diagnostic instrument that does not take so long and doesn't require such an intensive battery of questions and so forth.

We're doing that in the context of our Autism Treatment Network and I'm sure a number of other areas, but it's in the very early planning stages. There's no specific commitment of any dollars of any kind. It's really discussion and conception of what it could be and what it would look like.

MS. GRANPEESHEH: This is Doreen from ARI. I just wanted to mention that we've been working on a project like this. We

stopped because of the DSM-V changes coming out.

So how does this play with that, the fact that some of the diagnostic criteria are going to be different?

CHAIRPERSON INSEL: So DSM-V is not going to be available, I think, very earliest until 2012. We are having a meeting on Tuesday with leaders of that effort to talk about whether even that date would be realistic. So we don't -- it's a great question, Doreen, but we want to go ahead and provide something.

Now that reminds me. I believe that Sue Swedo from NIH is actually the chair of the DSM-V --

MS. GRANPEESHEH: Yes.

CHAIRPERSON INSEL: -- Committee on the Autism Diagnosis. So it may make sense for -- in terms of accountability for this to put this in the NIMH spectrum or NIH anyway so that the person who's doing the DSM-V work

would be the person who we would expect to work with Autism Speaks and ARI or anybody else who is involved to come up with what this instrument might look like.

In fact, the meeting next week is specifically on coming up with diagnostic instruments for a whole range of disorders and figuring out how they would be validated.

MR. BELL: I know Andy's supposed to be on the phone.

Andy, are you able to talk yet?

MR. SHIH: Yes, can you hear me?

MR. BELL: There he is. Okay. Andy, you may want to also mention -- I understand, also, that we're working on the International Epidemiology Network as well in this area possibly or having some discussions.

MR. SHIH: That's right. My apologies to everybody. I was having a little bit of technical difficulty.

You know, in terms of activities right now relative to Objective 1, you know,

we're obviously exploring the possibility of producing a shorter, more efficient tool, diagnostic tool, and we're doing that in the context both in terms of our Autism Treatment Network as well as our international effort in epidemiology.

As part of the process of developing an autism screening and diagnostics -- I think that's something that will be less time-consuming and more efficient in the field.

CHAIRPERSON INSEL: So let me just check with you. I mean, is this something Autism Speaks wants to run with with our help or how would you like to --

MR. SHIH: Yes, I think what we would like to do today is to obviously listen to everybody, you know, what's the current activity or to give us a better sense in terms of where the opportunities might be, where our investment might make more sense, most sense.

I think one of the things that

we're very keen on understanding better today is obviously NIH's activities in these areas and certainly we're always willing and happy to partner and to work together with such an opportunity.

MR. MELMED: In terms of what you mentioned about collaboration, Andy, on thinking about your efforts in identifying biomarkers very early on in life, and we'll get to biomarkers later, but somehow linking the identification of biomarkers to the diagnostic testing and validating the two against the other might obviously be what is eventually going to be called for.

CHAIRPERSON INSEL: Right. This is Raun speaking.

MR. MELMED: Yes.

CHAIRPERSON INSEL: So right, exactly, and we'll get to that in just a moment, but I think you're right. It does influence this piece.

I think the hope here, as I

remember from the original discussion in the group that developed this as an initiative, was something that was more of a clinical tool, behavioral cognitive tool that could be used.

We were told that the average diagnostic work-up now is about a two-hour event at least and shrinking that down to something that would be more like the 10-to-20-minute event.

So what I'm -- I don't want to get stuck on this first item, but my sense is because of the potential connection to the DSM process, it might make sense for NIH to take this on, working very closely with Autism Speaks, potentially with Autism Consortium, ARI, and others, but it sounds like Kathy Lord has already been tasked by you.

So potentially getting Sue Swedo and Kathy together would be the next step and I can volunteer Sue since she's not here and I think she's not even in the city, so we'll

have a chance to surprise her when she comes back.

All right. I think we can -- unless there are any other issues about that, let's move on.

The validate and improve the sensitivity and specificity of screening tools and so this is what Alan was just talking about a moment ago through the MAPSEA project. This is really for looking at community populations.

Again, this was to be accomplished by 2012 with a cost estimate of $5 million, and can I get a sense from the group about whether that's realistic or not?

I'm assuming silence means either yes or we don't have a clue.

MS. GRANPEESHEH: Well, this is Doreen again. I guess we're -- here we're talking about, for instance, taking the ADOS or ADIR and expanding it? Is that what we're looking at as an example?

MS. WAGNER: This one is -- no. This one is talking about --

CHAIRPERSON INSEL: You should identify yourself. This is Ann Wagner.

MS. WAGNER: This is Ann Wagner. Sorry. I think this one is talking about screening tools which would not be the diagnostic tools of ADOS and ADI.

MS. TANSKI: Yes, this is Tish Tanski from the Autism Consortium, and I actually did not bring cost estimates for what is happening in Boston, and I did not participate in the -- in coming up with the five million number, but I think, just based on some of the early screening work we've done, it sounds reasonable, at least as a start.

CHAIRPERSON INSEL: But this is really -- it wouldn't make a lot of sense for us to move forward without at least exploring it and finding out what's going on there.

A question I have, Tish, is

whether this is something where the Autism Consortium wants to take the lead and figure out how to get this done working with, I think, lots of other partners here.

MS. TANSKI: Yes, we would.

CHAIRPERSON INSEL: This would be hugely important for the field.

MS. TANSKI: We'd like to do that.

CHAIRPERSON INSEL: Okay.

MR. MELMED: This is Raun again. Obviously including the ongoing validation of the MCHAT and their efforts. I mean, it might be, you know, -- it seems that there are numerous people going in different directions and it's -- I'd love to see it all coming together somehow through this process.

MS. KAU: This is Alice Kau from NICHD. We are funding Debra Fines' MCHAT effort, but you know, note that that's a parent checklist for 16-to-30-months-old infants. So it's not within the specifics of these objectives but which is very important

because if we can screen the younger ones well, we may not need to screen the -- we have to wait till they get older.

CHAIRPERSON INSEL: Right. Exactly. So why don't we get to NICHD and Autism Consortium together, and again in terms of the issues about budget requirements, it may be worth spending far more than this already with current efforts. It wouldn't surprise me to find that out, but I'd bet that they're not synergized at all.

MR. SHIH: Tom?

CHAIRPERSON INSEL: That's the purpose of this. Yes?

MR. SHIH: This is Andy. I just want to add that obviously similar to the last objectives, our current international epidemiology activity is considering some of these past objectives, and in addition, I think we're also exploring other opportunities. The funding depends on how these efforts develop.

I also just want to add that I think the price estimate is -- and I think it's fine and it's hard to tell. Certainly the way we're thinking about some of our international effort is through partnerships.

So we imagine that some of these explorations in different ethnic groups and populations might be done in partnership rather than having the costs being shouldered by any organization.

CHAIRPERSON INSEL: Right. We weren't worrying so much about the mechanism of getting to the five million so much as just getting the sense, a ballpark sense of what this would cost.

In the discussion we had last time, and Andy, I don't think -- I don't remember if you were with us, it was also pointed out that this may be one of those places where we could use supplements to get some of the work done, based on current efforts underway, and that would be true of

Autism Speaks as well.

I would imagine that there are some large-scale projects and some international projects that could be supplemented to help on the screening question.

MR. SHIH: Absolutely. For example, you know, we're exploring it for that reason and some of the international epi effort as well. We're thinking exactly, you know, in terms of supplemental mechanisms for some of these efforts.

CHAIRPERSON INSEL: So Tish, it sounds to me like you've got a small group of people who are going to help you to get this done and what we're talking about here in terms of accountability, we really want to have sort of an organization or an agency assigned to each one of these and what that means essentially to me is that you're the people we would come back to in six months or a year and say how's it going, where do you

need help, where are things not working, who's pulling their weight, who isn't, and how do we get this done?

So that's what we -- that's what you've just signed on to. I hope that's satisfactory.

MS. SINGER: This is Allison Singer. Can you expand on that? Because it's pretty clear that this is to be a strategic plan for the NIH and for HHS and so what exactly does it mean when another organization says it's going to take the lead with regard to accountability?

CHAIRPERSON INSEL: So I read the plan as talking a lot about public/private partnerships and the opportunity for everyone to work together to get this done.

I think that even if we were talking about the Autism Consortium, for instance, as leading in this effort, we need to remember that most of the people in the Autism Consortium, they have NIH funding, and

so it's not as if the money is coming from outer space here.

What we're really talking about, I think, is leadership and who's going to take the lead and it could be from any one of the many players to make sure that these things get done and as you've talked about before, Allison, what we want to be able to do is to revisit these over and over again and I think the IACC needs to know who to call and who are you going to ask if, in a year or two years, we don't have any progress on the screening tool, who do we go to to find out how to change that and get it done? Is that helpful at all?

MR. SHIH: This is Andy. I'd like to just follow up on that question. I guess for us it's important. We think that the leadership issue will probably emerge after additional discussions.

Like I mentioned earlier, at this point we don't have understanding in terms of

what NIH is planning to do and how some of the core activities speak to some of these objectives.

So I think once we are able to, you know, drill down a little deeper into more details about some of these activities, then I think we'll have an opportunity to identify leadership and so on.

I mean, I don't think today we are as an organization ready to sign on to take a leadership role with any objectives at this point because we don't feel we have all the information necessary to make that decision.

MS. TANSKI: This is Tish, and I think I should say what I thought I agreed to, which is to serve as the focal point and coordinator for coming up with a plan for how this might get done, that we would then bring back, so we look at what is being done, what still needs to be done, and then work with NIH and other agencies to figure out what role respective parties have.

I do not see it as having $5 million to spend.

CHAIRPERSON INSEL: So it goes back to the question about what -- the $5 million is not a funding decision. It's an estimate of what it would cost. What we're looking for are organizations and agencies who are going to take on the leadership for making sure these things get done, irrespective of where the funding comes from. It could come, for all I know, from an international source, but if you're the person who's accountable for this and it turns out that nobody wants to spend any money on it at all, then you need to come to the IACC and say shame on you. This is really -- this is what you said you wanted to do. You've told us this is a very high priority, and I need to know who's going to own up to get it done. Okay?

It's not meant that we're going to come to you in a week and ask where the $5 million sits. That's not what this is about.

Peter?

MR. BELL: Tom, if I could make a suggestion? This is Peter Bell from Autism Speaks.

I think as we're going through this, this is a great exercise for us to kind of do an inventory of who's doing what currently, and then I could also see another column being added of what parties are actively engaged in these different areas, but I think what you're probably hearing is a reluctance for any of us to sign up and say we'll take the lead, we're funding this, and the IACC is no longer responsible for carrying on that activity.

So I'm trying to be as straightforward and blunt as possible, but you know, I don't think anyone sees -- as you said at the beginning, what we're not doing to do is make any commitments or decisions today, but I think we -- the spirit of this is let's put everything out there, let's have a real

good sense of who's doing what, what kinds of things are happening today.

We know what the objective is, and then following up to that, it's okay, how are we going to make it happen, and I think many of us are coming to the table saying we want to be actively engaged in that, but I don't think anyone is, you know, kind of really ready to say, well, we'll take on the responsibility for spending $30 million in this area and you don't have to worry about that.

CHAIRPERSON INSEL: So is there -- is that clear? I thought that's what I was trying to say, but if I didn't say it right, it is ultimately the IACC that's going to have to weigh in here and say this is going to get done.

What I'm looking for here and what we want this conversation to be about is pulling all the parties together that have an investment here already or are planning to

make an investment because they really care about this issue and so they can take leadership around this.

I don't really think many of these are going to fall to a single institution or single agency. Some will but most of them are going to be spread, and what we're really trying to develop here is this partnership.

I just thought this was a great example where, in fact, the MAPSEA effort -- I don't know what that costs, but we didn't know about that, most of us here at the table. So there's already something underway that we need to build around.

We did have the grant that Alice mentioned in our list of things that we're currently going on and we've done a fairly careful analysis of what's in the NIH portfolio. So we have a pretty good idea of what we're currently funding, but what we don't know often is what's happening outside the NIH and so this is a chance to sort of

bring it all together, have the inventory much broader, actually make it very clear who's doing what.

Sometimes you'll find that we're funding the same people to do very much the same things and we can do better than that. I think as funding agencies, we can work together in a way that's much more efficient. Okay?

Any other questions?

MS. TANSKI: This is Tish. Part of it is identifying the gaps and strategies for putting --

CHAIRPERSON INSEL: So a lot of that has happened. So the -- so a lot of what you see here is the result of having done not a SWOT, we call it a SWOG, a strengths, weaknesses, opportunity and gaps analysis, and that's where -- so that a lot of time went into creating that before coming up with these initiatives.

Some of these we do have already a

lot happening in especially the next couple -- some don't and that's where we really want to make sure that we're all working together to fill in those gaps.

Let's move along, unless there's anything else on this --

MR. MELMED: Just one thing to clarify.

CHAIRPERSON INSEL: Is this Raun?

MR. MELMED: Yes, Raun. Sorry. The word "existing screening tools." Obviously the door is open for developing new screening tools as well as those which are existing.

CHAIRPERSON INSEL: So that's quite a helpful comment, and it reminds me that there are some areas of lack of clarity or sometimes lack of precision in the language which we can just underline.

As I said, we won't change the wording but some people have also been concerned about the word "validate" which has

a very specific meaning in science and a very different meaning in general parlance. So that's one we may want to look at.

MR. MELMED: We're working on developing a screening tool for autism spectrum disorders, specifically Asperger Disorder in the school-aged population, but that would be a new one rather than existing screening tool.

CHAIRPERSON INSEL: Right. So Della has taken note of this comment and it's one that we can then transmit through the process to the IACC to see whether they really feel it has to be only an existing tool or whether there's something that -- this is an opportunity to develop something new.

MS. HANN: If I could just -- this is Della. If I could just add to that, I think there was -- when this objective was being developed, the idea of taking what we already have and trying to validate it and improve upon it was discussed as well as the

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idea of developing brand-new tools and I think because of the sense of urgency and the need to try to get something into the hands of people who were doing this work quickly, the discussion leaned much more to taking what we already have and trying to make it useful.

It didn't mean that the development of other tools was not important by any means. It was just that for the plan itself trying to get this work done in a more efficient manner.

MR. MELMED: There might not be any great good existing screening tools for school-aged children.

CHAIRPERSON INSEL: Right. So duly noted. Good point.

Let's move on to the biomarkers item. Validate a panel of biomarkers that separately or in combination with behavioral measures accurately identified before age two one or more subtypes of children at risk, and this was one that was thought to require five

years, be funded apparently immediately, so that it could be completed by 2014, if I'm reading this right, at a cost of $30 million.

So comments about time frame and dollars.

MS. LAWLER: So the -- this is Cindy Lawler, NIEHS. The early study has a biomarker component. It -- you know, given the pace of enrollment and the need to follow the children for up to three years after birth, it wouldn't -- within the five-year time frame, it wouldn't fit well, but it certainly is a large existing investment that's targeted at this area that should be sort of included as part of this objective.

CHAIRPERSON INSEL: So Cindy, are you saying that you think that 2014 is unrealistic?

MS. LAWLER: For the early component. I mean, I'm sure there's a number of other studies that are looking at biomarkers that may have results before then,

but you know, the early is an opportunity to do it, but since they, you know, haven't yet started enrolling pregnant moms, you know, it's not going to happen, unlikely to happen in this time frame.

CHAIRPERSON INSEL: So one of the concerns that has been raised by others is that the word "validate" means that you would discover and then replicate it in an independent sample and that may be a real challenge to get that done in this time frame.

On the other hand, going back to the sense of urgency, many people in the original group felt that this is one of the most important things we could get done and that a lot has to go into this.

Tish?

MS. TANSKI: Yes, this is Tish Tanski. Within the Consortium, we do have several efforts that we believe could within this time period result in some biomarkers. We aren't limiting that to -- you had

mentioned the longitudinal studies.

We think that maybe we have some possibilities that could be done more quickly than tracking families from prebirth through three or four.

MR. SHIH: This is Andy Shih from Autism Speaks. We've worked with NIH over the past several years and made investments in projects and out of the activities, there are two networks that will speak to this particular objective and given that we have a bit of a head start already, I think we're optimistic about some of the more recent publications that we might be able to reach objectives at 2014.

CHAIRPERSON INSEL: Good. Thank you. That's helpful.

Any other comments about the time frame or the dollars?

MR. MELMED: I am -- this is Raun again from SARRC. We have been involved with efforts regarding proteomic biomarkers, but I

just think that without collaboration, really strong collaboration between all the players over here, 2014 is probably not going to be realistic.

But if there was going to be true collaboration and if there is insistence upon IACC that all the major players did work together in this context, then there's a possibility, but with everybody doing things piecemeal, it just -- you know, it hasn't been that helpful to date in my perspective.

MR. SHIH: This is Andy. I second that sentiment. I think that's an example. I certainly know that the Autism Consortium in Boston is now working with ATP, for instance, on some of these efforts and as well other researchers are coming together trying to make a major push, at least with regard to the genetically-based biomarkers.

MR. MELMED: Certainly SARRC would be very happy to participate as far as our collaboration with TJ and their capacity for

proteomics.

MS. RICE: This is Cathy Rice from CDC. Another resource to keep in mind are the large birth cohorts, the ARI bank blood spots, such as, I believe, Norway does but Denmark as well. It would certainly help when the infrastructure is already there and the materials are already there.

CHAIRPERSON INSEL: So there's a huge amount going on here. What I'd love to know is on the leadership question, who's going to help to pull all this together in a way that gets it done by 2014?

MS. MUMPER: Liz Mumper from ARI. I apologize for being late. I went to the wrong campus and I've been listening in by the audio feed on my phone.

This is an area that ARI is very, very interested in, biomarkers, especially with regards to how they affect chronic oxidative stress, chronic metabolic abnormalities, infection and inflammation.

So we're -- as we do not have a huge amount of resources financially, we do have a huge number of clinicians that are very interested in these issues and have lots of clinical patients. So I suspect that we would be able to take somewhat of a leadership role in this area because we feel it is so crucial.

CHAIRPERSON INSEL: So if I can just clarify, I think when the committee recommended this, the workgroup originally, this was not in children with autism. This was looking for predictive biomarkers. So this was looking for markers of risk in children under the age of two.

This really focuses on the Baby Sibs approach and that to me begs the question of who's supporting the Baby Sibs efforts, the collaborative efforts in that arena because that would be the group, I think, that would be able to drive this the best.

So who is that of the different organizations that are involved? Is this --

the A Centers have projects like this? Yes?

MR. ALEXANDER: The A Centers is a collaboration between Autism Speaks and NICHD to try and do some of this, but that's not all that's going on.

Tom, I just also want to take the opportunity to comment about the date here and the word "validate" because in discussions we've had, there's been concern about the idea that validating a panel by 2014 is really unrealistic. Identifying a panel to test and try to validate by 2014 is probably realistic, but to have the validation completed as well probably is not.

So I don't know if this is the time or place to deal with that or not, but I think we're talking about dates at least and that's something that we may want to think about.

CHAIRPERSON INSEL: We will transmit the idea that maybe the word "identify" would be better than validate, but

again that's going to be up to the committee to figure out. Since you're on the committee, Duane, you have a chance to make sure that that's --

MR. ALEXANDER: I will do it again, yes.

CHAIRPERSON INSEL: But from your description, it sounds to me like it might make sense for NICHD and Autism Speaks and others who are in this arena to work together to really push this.

I know this is one of the places where we got the most enthusiasm from the workgroup. They really felt this could, maybe more than anything else, transform the picture here.

So is this a place where NICHD wants to take the lead?

MR. ALEXANDER: Yes, we can't do this alone, but we could take one of the leadership roles in it. Autism Speaks has partnered with us in the Baby Sibs Project and

so that partnership, I would hope, would be continued and will need some help and advice from others in terms of trying to identify this panel.

CHAIRPERSON INSEL: It sounds like you've got a lot of enthusiasm from SARRC/TGen since they've -- I think I've got it right. The proteomics effort includes a children at risk study, is that right?

MR. MELMED: It will.

CHAIRPERSON INSEL: So you would clearly be a part of the solution here and ought to be in the conversation.

Cindy?

MS. LAWLER: I think a key part of it, too, just echoing what Cathy Rice mentioned, is you really, part of it is the discovery aspect, but you also are going to need access to, you know, a fairly large population and there are, you know, some populations through -- we tap in through some of the CDC studies, that Norway and Denmark

are two cases where they've got prospectively collected samples on and this would not be a Baby Sibs paradigm. This would be a population-based.

So I think you're going to need the numbers of that type of study to really, you know, get beyond the discovery stage where you could, you know, get some good ideas from a Baby Sibs perspective. So maybe CDC would be -- or -- and I think NINDS has, you know, involved with the Norway.

CHAIRPERSON INSEL: Okay. Well, we'll keep that in the mix. That will kind of come up later. We've got another item that deals with that more directly but that's very helpful.

Moving on, the five measures of behavioral and/or biological heterogeneity. This was another huge issue that came up, which was essentially working out the phenome and trying to get a better understanding of the spectrum.

Here again, five years, 1.5 to -- I'm sorry. $40 million was the estimate. A point about the time frame or the dollars? Should we keep those numbers? Do they need to be revised?

MS. TANSKI: This is Tish Tanski from the Autism Consortium. We are involved in working on this in Boston and the numbers and the time look --

MR. MELMED: Could you speak up again, please?

MS. TANSKI: Tish Tanski, Autism Consortium. We're involved with doing this in Boston and I know many others are, and the number of years and the funding looks right.

MR. SHIH: This is Andy from Autism Speaks, and obviously involved with our Baby Sibs Consortium work and AGP speaks to this particular objective.

CHAIRPERSON INSEL: Okay. So is there -- I don't hear any interest in revising the estimates.

What about leadership and accountability? Who is going to be driving this?

MR. SHIH: From Autism Speaks perspective, I mean, this is an extension of some of the work that was mentioned published between the ASD and Autism Speaks and Baby Sibs Consortium and certainly some of the CDC efforts, you know, that we've been working together on, you know, could speak to this as well.

We would be happy to work with those agencies on this particular initiative.

CHAIRPERSON INSEL: And we have -- you know, there's a lot going on obviously with NIH funding, everything from our Intramural Program where we've got a big subtyping effort with the Mind Institute at UC Davis in this phenome effort, and there's additional funding, I know, that's coming into the phenome effort at UC Davis that's not from NIH and then we've got several grants that are

in this general area as well.

So I'm trying to get some clarity, though. I think for each of these, we need to have a single point person, and is that someone at NIH? Is it someone at Autism Speaks?

I'd love to assign David Amaral to this, but I really can't do that.

Ann, what's your sense?

MS. WAGNER: I think we could -- the NIH ACC could be the organizing force behind this one.

CHAIRPERSON INSEL: Is that okay with the group? NIH ACC. So that's the coordinating group at NIH that will take this on and make sure it gets done. Thanks, Ann.

MS. TANSKI: And I would ask that the Autism Consortium be part of that.

CHAIRPERSON INSEL: Moving right along, identify and develop measures to assess these three continuous dimensions of symptoms and severity that may be used to assess

response to intervention across the life span.

This has a 2016 due date on it, and here the costs span from $1.5 to $10 million. So it would be useful to get some less ambiguity around the costs and also to find out from you whether the time frame is realistic.

MR. BELL: Could I ask someone to help, maybe, define this in lay person's terms?

MR. MELMED: And also to include -- this is Raun -- whether these are predictive biomarkers or they're behavioral measures?

MS. WAGNER: I think these are behavioral or medical, I think. I think the idea here is that there are a lot of symptoms that are not well measured, particularly on a sort of continuous -- so they're not looking for you have it or you don't but how severe you have it in order to track how people are developing over time in a particular response

to treatment.

So I think it's looking at particular symptom dimensions and severity.

CHAIRPERSON INSEL: So this could -- just to clarify because I don't remember the discussion at the workgroup, but this could be an inflammatory marker as well as a cognitive marker or an imaging change or something like that, is that right?

MS. WAGNER: Yes, I think so.

CHAIRPERSON INSEL: How is this -- okay. So essentially, this is looking as a sort of surrogate marker for treatment response? Is that the way --

MS. WAGNER: Yes.

CHAIRPERSON INSEL: All right. So it feels like it's in the wrong category, but we can deal with that, I guess.

MS. HANN: Right. There was discussion on which category to put this particular one in, but it ended up here because it was more descriptive, essentially,

of the disorder over time essentially. So I felt it needed to be here with all the other descriptive pieces of it.

CHAIRPERSON INSEL: So in fact, isn't this really asking about supplements to ongoing intervention trials or new intervention trials, so building something into those so you have some continuous dimensions, some marker that you could follow to look at what predicts or what correlates best with response? Is that what we're talking about?

MS. WAGNER: I think that would be the idea.

CHAIRPERSON INSEL: So if it is really supplements, it's hard to believe that that would be a $10 million effort. It sounds to me like that's a much smaller -- a $1.5 million, along with maybe a $30 or $40 million intervention program might be the way to cost this out, but let me know what you think, those of you who are more involved in program.

Peter, what's your sense?

MR. BELL: I was just going to -- since we're in an advisory capacity -- provide some advice that we try to maybe clarify the language here and decide if this is in fact the right place for this because it just doesn't -- it doesn't feel like it is. I don't know. That's just my personal perspective.

CHAIRPERSON INSEL: Yes, if the question is when should I be concerned, it's -- and I think there was -- as Della said, we had considerable discussion, I'm not sure how it ended up here, but it's still something we want to get done. So wherever it ends up structurally, we still need to have the estimate.

MR. SHIH: It seems to me like the naturalistic treatment outcome objective.

CHAIRPERSON INSEL: Wolf?

MR. DUNAWAY: Okay. I remember, I do remember this and what -- you know, why it

came about, is that we were hoping is that people would see -- we want to find out or we were thinking about the fact that what things were consistent, you know, what elements of being on the spectrum are consistent and behaviorally, things that are pertinent, things that parents can look at and say, okay, if I see these things, maybe, you know, they should -- they would then say to me, you know, I should be concerned if I see these things, something that a lay person can, you know, -- the doctors can tell parents, people that are concerned, you know, what things can I look for, what things would I be able to see, you know, that would -- that should be a red flag for me to go to see, you know, whomever, the doctor, you know, and take some sort of intervention.

They were -- we were hoping that there would be one thing, you know, one or two or three things that you would be able to teach people to look for.

I mean, I think that's what I remember when I was a part of the other groups.

MR. BELL: Okay. That's actually really helpful for me to, kind of, wrap my arms around this. I mean, the way I see it is that, you know, when someone asks you as a parent, you know, well, how affected is your child, how do you respond to that?

I mean, you can use high-functioning and low-functioning and so forth, but then what does that mean? And I think what we're perhaps -- and I wasn't a part of this discussion, but, you know, what we're hoping is that there are some things that we can grab on to and say, you know, my child has this symptom and they're at a two versus and an eight or whatever and, gee, you know, we've applied this intervention over time and he or she has gone from a three and is now a six.

I think that's the kind of thing that, perhaps, we're trying to get at. Is

there something tangible, and in this case, there are three measures that we can develop where we have an easier time of describing our kids and how they have responded to different interventions and so forth?

MR. DUNAWAY: Well, he's right. The thing is, is that, I mean, the three things that you always hear, high-functioning, low-functioning, Asperger's, and there's not -- it's almost -- I mean, I have a person that's a friend of mine who's Asperger's or high-functioning at work and we sit there and have these endless conversations. Am I autistic? Am I high-functioning? Am I Asperger's? Am I this?

I mean, it would really be nice if we could have, you know, a way of measuring, you know, on a scale so that we can understand what -- you know, where they are on the spectrum so that they can, you know, identify the things that they need to work on, their strengths, you know, so that you can get a

really good picture. A person who has autism can focus their energies on the things that they need to fix rather than figure out, well, is it Asperger's or is it high-functioning? Am I this, am I that?

You know, it's -- you know, we're just asking for a clearer delineation of what being on the spectrum is and where each person is. Is there a way that we can, you know, like a football field, put hash marks so that we can measure and we can see where we are because right now, when you ask a parent, you know, well, he's high-functioning, well, what exactly is that, or he's low-functioning, what exactly is that, it's difficult.

CHAIRPERSON INSEL: Okay. Well, that, I think, provides a lot more clarity to what the task is. In terms of the time frame and the dollars, we need a little more clarity, especially on the dollars side.

We could leave this for the IACC to wrestle with but if the group has a feeling

about this range and wanting to narrow the range, this is a great chance to make a change.

MR. DUNAWAY: I'm more towards the higher end, and I'll tell you why. Because it's going to take -- I think that in order to do this right, it's going to take an interdisciplinary approach. It's going to be a whole lot of professionals with a whole lot of different insights and perhaps even a number of different organizations working together so that, you know, you can come together with all of the brain power that it would take so that we get, like I said, a really good picture, a really good measure of how we can break autism and the spectrum down in ways that regular lay people can understand where their child is, where they need to focus their energies, you know.

I just think it would take a lot of people and a lot of time to do this right.

CHAIRPERSON INSEL: Okay. Any

other comments about this? And in terms of leadership, it sounds to me like it should go with the groups that are doing the most in the way of interventions or developing diagnostic instruments, but --

MS. WAGNER: We can add that to our NIH ACC.

CHAIRPERSON INSEL: Okay. So this is an NIH ACC effort. Is that going to work for people?

MR. BELL: Yes, I think Autism Speaks would be involved both from an ATN Autism Treatment Network as well as our Toddler Treatment Network, too. So we'll be happy to be involved in that.

MR. SHIH: I agree with that.

CHAIRPERSON INSEL: As I recall from the original discussion, ATN was very much in the vision of this, so that would be an important collaboration.

Effectively disseminate at least one valid and efficient diagnostic instrument

in general clinical practice by 2016. So this is the long-range goal. It's thought to require five years to get accomplished, and again the figures are 5 million to 10 million, and we can accept that range and that time frame or we can change it.

What's your sense?

MR. SHIH: This is Andy, Autism Speaks. We think this is reasonable, both in terms of time frame and resource required.

CHAIRPERSON INSEL: Any other comments? Thanks, Andy. Hearing none, we'll go on. Yes?

MR. TREVATHAN: Sorry. Just before we go on to Question 2, just echo what Cindy Lawler and Kathy Rice both said. Going back to under the validate the panel biomarkers, understanding the limitation of the term "biomarkers," just one thing that I know we'll discuss later is, in the context, for example, of the Denmark, it's a really great place, our collaboration with Denmark,

to test potential biomarks and big samples of the general population before the age of two.

That particular resource is potentially terrific, but there isn't a clear distinction in some of these situations between, do we have existing resources, does this require new resources to do that, and this would be a situation in which new resources would be required but building upon an existing platform.

At what point we get down to that level of detail so that we don't confuse new and existing resources would be nice. That's probably beyond the scope of today.

CHAIRPERSON INSEL: Yes, I think it is, although on this particular one, there is actually an item which says specifically to support ancillary studies within one or more large-scale population-based epi projects in nested case control data and it actually was meant to build on the Denmark and SEED studies. So we'll get to that in a few

minutes.

So to finish this out, Question 1, are we okay with the numbers, the time frame, the dollars, for an efficient diagnostic instrument? This is obviously based on the first item, which would be a more short-term solution. This is looking at the longer-term version of that.

On the short-term one, the NIH had taken the lead. Is that going to be workable for the group, again, that we will do the long-term, because I think they really are sequential? Unless I hear anything else, we'll keep moving.

Ann, other thoughts?

MS. WAGNER: No. You know, this one, there was confusion about what is meant by dissemination. That's --

CHAIRPERSON INSEL: I couldn't hear you.

MS. WAGNER: On this one, I think there was confusion about what is meant by

dissemination. So is this dissemination research? I mean, I think NIH can do -- help do the research but isn't usually the disseminator, I guess, is my point.

MS. HANN: Right. My recollection -- this is Della. My recollection in terms of developing this objective is that it was beyond just developing the research kind of ideas of how to disseminate it but truly was the dissemination component on it.

So how do we -- once we have this wonderful tool, which hopefully we will, how we really get it into the hands of those in the practice community.

CHAIRPERSON INSEL: So this is where the Department of Education, CDC, this really ought to be a -- if that's what this is about, -- it's interesting how the verbs are really hanging us up here on most of these, is trying to understand what the actual action is going to be, but if it is dissemination, I think you're right. That's not what NIH does.

We ought to get clear about that.

MR. TREVATHAN: Ed Treveathan at CDC. If the emphasis is on dissemination, then this really does fit within at least the platform that we've used in our -- the collaboration at CDC to do the Learn the Signs, Act Early campaign that really works with the AEP and other organizations that can really get down to the community level to implement these instruments. So that would be a platform that could be built upon for this.

CHAIRPERSON INSEL: So maybe, Ed, this is one where you and Marshalyn, CDC, ought to take ownership --

MR. TREVATHAN: Right.

CHAIRPERSON INSEL: -- and then we'll do the hand-off with the short-term. Once there's a diagnostic instrument we can look to you for the dissemination. Okay.

MS. MUMPER: And Tom, Liz Mumper from ARI. I have a conference call with the leadership of the AEP next week. I'd like to

get early ownership from them on this because I think they would be good collaborators.

I want to caution us, also, not to forget the American Academy of Family Physicians because a huge portion of children get their care through family physicians.

MR. TREVATHAN: Right. I agree, Elizabeth, and we do work with them.

I think the others are the nurse practitioners, too, that we want to make sure children that see nurse practitioners for primary care have access to these instruments as well.

MR. SHIH: Tom, this is Andy from Autism Speaks. We will be interested in working with CDC and others on this particular objective as well.

MS. RICE: This is Kathy Rice. I would add that we should certainly have HRSA involved in their million.

CHAIRPERSON INSEL: Peter?

MR. BELL: I have just a point of

clarification. So we're, I think, still talking about the validating the diagnostic instrument and differentiating between diagnostic instrument and a screening instrument. And screening is, you know, how you filter through and get the kids that seem to perhaps be at risk and might ultimately get a diagnosis and so forth, whereas the diagnostic instrument is really what is used to eventually help make sure that the people that are actually in research studies and so forth qualify for that diagnosis.

So to me, there's a little bit of a differentiation here. I think absolutely, it makes sense to work with the AEP and AAFP and nurse practitioners and so forth on the screening side of things, maybe less so on the diagnostic instruments which really are probably more geared towards research or that you need both in those kinds of --

MR. TREVATHAN: Well, we want to have at least the understanding, I would

think, of the diagnostic instruments, you know, at the primary care level, not that they would be implementing them, because, of course, one of the problems with the early diagnosis is the long wait to get into these rather prolonged diagnostic events that occur in specialty clinics.

So we somehow obviously need to work across between screening and diagnosis and have all those groups work together, I think would be -- and this was a conversation we had with folks at the BAP just very recently.

MR. DUNAWAY: The other thing is, is that -- it says here that they want it to be briefer and less time-intensive. So, I mean, this does address the fact that not only do they want to have a diagnostic instrument but they also want the diagnostic instrument to take less time because a lot of times in the case where you have the nurse practitioners and people who receive care that

may be on the lower end of the insurance spectrum, they don't have a whole lot of time to invest in, you know, a long-term instrument to do the diagnosis.

So the word "briefer" is really important here. I just don't want it to get lost.

MS. YEARGIN-ALSOP: This is Marshalynn. I'm sensitive to the time, and I think the CDC should take the lead, but I echo Peter's comment. We're not talking about diagnostic instruments in general pediatric practices. So I think we need to explore this a little bit more and work with those organizations that are actually doing the diagnosis on these children, not screening but diagnosis, as I understand the way this is written.

MR. MELMED: And also, this is Raun, I think it's important to emphasize that a diagnostic instrument is not the same as making a diagnosis. A child passing or

failing one particular instrument should not make the child have autism or not. It's a clinical diagnosis, based on a measure but not entirely so and therefore not appropriate in a primary office.

CHAIRPERSON INSEL: So maybe in 2016, we'll think about this differently, but the item here really does say to disseminate in general clinical practice, and if the group does feel that that's in some way not realistic or is not the right target, again, I think it would be helpful to have that language to -- that we can communicate on to the IACC.

MS. WAGNER: Tom, this is Ann. Not to go on and on forever with this conversation, but I think maybe the wording didn't mean specifically a general pediatrician's practice, it meant general clinical.

Right now, most diagnoses are happening in clinical settings of various

kinds and I think that's what I meant by general clinical practices, out there for use clinically.

MS. YEARGIN-ALSOP: Right. We're talking about neurologists, developmental pediatricians, and others with expertise in this area that are developmental psychologists that are making a diagnosis.

CHAIRPERSON INSEL: So the word "general" may have been --

MS. YEARGIN-ALSOP: Yes, it's kind of confusing.

CHAIRPERSON INSEL: -- the confusing word.

MS. YEARGIN-ALSOP: So I think we need to clarify the language here.

CHAIRPERSON INSEL: Got it. Okay. Are we ready to move on? Good. We're going to do the second question at this point. Question 2 - Costs, Organizations, and Milestones

CHAIRPERSON INSEL: What can I

understand -- how can I understand what is happening, and we have -- we're so fortunate that lunch is in front of us, so it will keep us moving along. I'm hoping that will provide some time pressure.

Short-term objectives. Establish an international network of brain and other tissue acquisition sites with standardized protocols for phenotyping collection and distribution of tissue by 2010. This is a two-year $5 million proposal initiative. Sense about time and costs?

MR. SHIH: This is Andy from Autism Speaks. We think this is realistic, and obviously we have a partnership with NIH at this point relative to Autism Tissue Program, and we're looking forward to working with NIH on this particular objective.

CHAIRPERSON INSEL: So NICHD has a big repository. Is this -- does this look realistic to you in terms of time and costs?

MR. ALEXANDER: Yes. So far, that

repository is just domestic, it's not international. What we'd have to do to meet this is clearly to add the international component to it. We've been in discussions with Autism Speaks on doing that, and we think it's doable.

We'll shoot for 2010, can't guarantee it.

CHAIRPERSON INSEL: So I can't help but go back to Raun's comment before about the importance of everybody playing in the same sandbox here, and if there are other repositories developing, this would be a great time to know about that so we can try to unify the effort.

I don't know what else is out there. I know that Autism Speaks and NIH have been in discussions about this for some time, and the other piece of it is that most of the discussion here is focused on brain tissue, but huge interest right now in also bringing skin fibroblasts and cell lines, IPS cells

made from them into some form of repository.

MS. TANSKI: This is Tish Tanski from the Autism Consortium. We are not, as a consortium, funding skin fibroblasts but I believe Simons is funding some work in that area, so you may want to --

MS. BENEDETTI: Hi, this is Marta Benedetti from the Simons Foundation. I just joined.

CHAIRPERSON INSEL: Good timing. Welcome.

MS. BENEDETTI: Good timing. I just logged in.

So we are not really funding a lot of work in that area if we're talking about the IPS. We have a grant that does an arm to fund some of that work and we are looking as everybody else is at, you know, potentially being involved in more work about it and just to clarify, we're also involved with Autism Speaks and NIH in working on financing the Brain Bank and Brain Tissue Bank.

CHAIRPERSON INSEL: Okay. But this does sound like a child health initiative, and I know NIMH is also involved with you around the distribution, Autism Speaks is involved, NINDS is involved. There's a lot of people doing this, and it's going to happen rather quickly.

This might be a nice flagship project actually for the IACC to point to because it's coming together for many partners.

I just want to -- the last point about this is, if there are others, whether it's Simons or SARRC or others who ought to be in this project, this is going to be really important to get everybody to play together so we get the largest and the most diverse sample possible.

We have an idea about increasing the number of at least brain tissue samples very quickly, and that's going to take a much broader effort than what we've had so far.

Let's keep moving to four research projects to identify mechanisms of metabolic and/or immune system interactions with the CNS that may underlie the development of ASD during prenatal/postnatal life.

This was meant to be by -- in four years, by 2010, as the date on here. So I think it's four years of funding but that they would be supported by 2010 and $6 million was the number that was proposed to support four such projects.

Comments about the time frame and the dollars? Okay. I'll assume that that's reasonable.

In terms of leadership on this, Cindy, is this a place where NIEHS would be an important player?

MS. LAWLER: We'd be interested in participating because we have some existing investments in this area, probably wouldn't be comfortable leading the objective.

MR. SHIH: Autism Speaks is in a

position of exploring the topic of our high risk/high-impact mechanism. It's also through the Baby Sibs gene-environment interaction study. So we'd be happy to participate in this as well.

CHAIRPERSON INSEL: And we have some interest. We're doing -- this is from NIMHS's side. We have a workshop coming up in about a month, Ann, isn't that right, to begin to look at this question, and we've got some funding in this arena, and I know NINDS has been in discussions about it as well as we think about some of the metabolic sides of this.

I think what we need here is the leadership piece. So who's going to be stepping forward to make sure we get this done? Is this one where Autism Speaks has the biggest investment? Is that possible currently?

MR. SHIH: We're in the exploratory stage at this point. We haven't

made a funding commitment yet.

MS. WAGNER: Well, NIH ACC can have -- take the lead in pulling in all the people who expressed interest in helping and figure out how to get going on this.

CHAIRPERSON INSEL: Yes, and I think we have more than half of this currently funded, currently invested. So Ann, if that makes sense, between what the different NIH institutes are doing, we'll pull it together, but I do know from other conversations that Autism Speaks has got some plans here. We really again need to make sure that we synergize well with them.

Anyone else who should be in this discussion, we need to sign them up now and we'll pursue that together.

Moving on, three studies --

MS. REDWOOD: Hey, Tom?

CHAIRPERSON INSEL: Yes?

MS. REDWOOD: Hey, Tom. This is Lynn Redwood. I just wanted to comment on

that in that I think that's just such an area that deserves more funding and more initiative. It's a very promising area for our kids in terms of investigations and finding possible treatments.

So I would really like to see four each in metabolic and immune versus together and actually more budget like 10 million. So I don't know if it's an appropriate time to bring that up, but I just think this is a very promising area of research that's been underfunded and under-investigated.

CHAIRPERSON INSEL: Okay. Other comments? Peter?

MR. BELL: I assume that would be an IACC decision?

CHAIRPERSON INSEL: Yes, that's something that will come up at the IACC meeting, and we'll have to -- as you know, we have a public comment process as well.

Lynn has the advantage of being on the IACC, so she can have some direct

influence about making sure this comes up.

MS. REDWOOD: I'm trying to plant the seeds now, Tom.

MR. BELL: In the spirit of advice, you know, I think that's wise. I mean, I think this is an emerging area. It's something that's getting a lot more attention. I think there's still some question as to how rich it's going to be and so, you know, that's one of the reasons why it's one of the three areas that we've identified within our high-risk/high-impact and so, you know, there is some risk to it because it's probably not as well developed and understood, but we also believe that it has the potential for high impact and so I think it's something that should seriously be further explored, and the IACC should decide whether or not they want to make a bigger investment.

CHAIRPERSON INSEL: Yes, this is also a place, as you say, Peter, where I think we're going to be informed a lot by what

happens in other areas of science.

So for those of us who have begun to think about adult onset macular degeneration as an immune disease for the first time, based on the recent discoveries, you can see how it shifts an entire field when you have a discovery that's relevant, and I'm not sure right now that we have the people in this field to really push it, but one would hope that a couple of really seminal discoveries could make a big thing happen here.

Okay. Anything else on this before we move forward?

Launch three studies that specifically focus on the neurodevelopment of females with ASD by 2011. That was considered to require five years of funding and an estimate of $8 million over that period of time.

MR. BELL: I was not a part of the discussion, but that seems like a lot to me.

So I don't know. That's just my naive opinion.

CHAIRPERSON INSEL: Right. Other comments about this?

I know people have wondered whether this really is a separate initiative or whether this could be embedded in the phenome project or other projects that are here where you could enrich the sample for females with autism, and there was a question raised about whether this needs to stand alone or whether it could be added, and I throw that out there.

I think that will be transmitted to the IACC, but in any case, I think the $8 million came from a recognition that if there were three studies involved, it would -- and they were longitudinal or at least they could be longitudinal, it may require that kind of an investment, but I would turn to some of the program people to give us a better sense of that.

Anybody want to represent the discussion from the last meeting about this?

MR. ALEXANDER: Yes, this is Duane Alexander. I think that the general tenor of the discussion was that in the prioritization of things, this would not be particularly high and that probably it ought to be folded in with something else rather than even a stand-alone effort.

We're as interested in gender differences as anybody, and I would have difficulty singling out this one for particular focus and attention.

CHAIRPERSON INSEL: I think one of the concerns raised, Duane, was that this sounded like a descriptive study that wasn't going to take us much further, rather than a mechanistic study that could really respond to what the IACC wanted, which was to transform the diagnosis and treatment and outcomes for people with autism.

MR. ALEXANDER: Right.

CHAIRPERSON INSEL: Well, I don't see a lot of enthusiasm for this in any form here at the table. Maybe there's more enthusiasm from those on the phone.

Let me ask you, beyond Peter's concern about the cost, is there anything else we want to transmit to the IACC about this? What about on this one, the leadership? Is this a case in which we want to -- rather than assigning leadership assign that it be moved in some fashion? What's your pleasure? What do you think would be the best way to handle this?

MS. WAGNER: I think subsuming it under the goals that are talking about phenotyping would be a reasonable thing to do, so that whoever's taking the lead there would be consider this aspect as well.

CHAIRPERSON INSEL: Still not clear, Ann. Say that again. Subsuming it under which part of this?

MS. WAGNER: It would be which

one? Number -- under Long-Term Objectives, so the characterization, the very next one.

CHAIRPERSON INSEL: Got it. Okay. Well, again, we're not going to rewrite these but that could be something that we can transmit to the IACC to consider, and you can see how they would fit together pretty logically.

Is there someone who wants to take leadership of this if it remains as an independent item? Heads are only shaking around the table. Anyone on the phone feel strongly about this and want to make sure that this gets done? I think we have an orphan. If that's the case, we -- let's flag it, and we'll -- that may be informative to the IACC, that nobody here wants to actually be on the hook for this one.

Let's move on. Complete a large-scale multi disciplinary collaborative project that longitudinally and comprehensively examines the biological-clinical developmental

profiles of children, youth, and adults with ASD change over time as compared to typically developing in individuals.

This has a 2020 time frame, so 12 years of funding would be needed, and the range here, this is one where there's a broad range, $50 million to $100 million.

Comments about the time frame and the costs?

MR. DUNAWAY: The only thing I remember about it is that I remember the joke, sort of somebody said it was like -- it was supposed to be sort of the Framingham for Autism. So, I mean, that's where I think -- I think that was the reason why it's so big and why the money was -- why there's so much money with it because that's what they were saying. So, I mean, that's what I remember from it.

CHAIRPERSON INSEL: Right. I think that's what I remember as well. It was the Framingham for Autism, except in this case

all of the subjects were affected. So it was -- well, although they're typically developing individuals as well. So it is in that sense even more, but it would be enriched certainly for children with and adults with a diagnosis.

But it is very much a longitudinal, descriptive, population-based study.

Ann?

MS. WAGNER: Yes, I was just going to say that I think some of the difference -- the range of estimates came from the type of design people were thinking could be used to accomplish this. So it might depend a little bit on sort of who steps up to the plate to actually do it and which design they're, you know, preferring.

MR. ALEXANDER: This is Duane. Much of this fits in with the characteristics of the National Children's Study, where the planning is underway. We hope to be in the field with recruiting by 2010.

We will have, obviously, recruitment at birth or during pregnancy by 2020, 10 years of experience with part of the cohort. We're not going to have any adults in this study, but clearly it has the characteristics of doing this, and we estimate that in the hundred thousand children that will be recruited, there will be about 800, probably, with autism.

So we will have a large population of kids with autism and a substantial control group for all kinds of comparisons and all kinds of capabilities of longitudinal follow-up, including neurodevelopmental studies of females, along with the males.

So that this would be a home for that orphan, but we will not have adults, at least not by 2020. So if there is a desire for adults to be included here, something else would have to be added. By 2020, many kids who were originally recruited for the Norway or Denmark studies will be close to adulthood,

and so that is a possibility.

So a majority of the objectives here could be met by the National Children's Study, which is going ahead and the costs, they are very difficult to predict. The infrastructure will be there, but adding on some of the studies of particular extra interest in autism will go beyond that.

CHAIRPERSON INSEL: Good. Thanks, Duane. Now, in terms of the adults, I know that there are some large networks that are already developed for treatment of people with autism, maybe mostly children, like the ATN, there are something like 18 sites now, and the CTN.

Either Peter or Andy, can you tell us, do they involve adults as well or is that really focused on children?

MR. BELL: It's all children at this point.

CHAIRPERSON INSEL: Is there a network out there anywhere for adults with

autism?

MR. SHIH: Not that I'm aware of, but I do want to add that, you know, this is an objective that we're interested in getting involved in as well, in addition to the exploratory work that we're doing with the Baby Sibs on a gene-environment interaction project.

We're also exploring opportunity, trying to provide supplement to bring some of the A studies together into a larger sample set and address some of the gaps there, and certainly, I think, what was mentioned earlier about the opportunities for children's studies, we're interested in exploring that as well.

MS. RICE: Tom, this is Kathy Rice, and you're question about is there an adult treatment network, the only one I'm aware of is the -- there's an adult residential programs organization, NARPA, that may be of some use here, and just another

resource comment here.

In addition to the National Children's Study, although it's not part of the current protocol, the SEED Study also has children with autism and population controls and having a follow-up component would be something that would help with this objective, also.

MR. TREVATHAN: Yes, this is Ed Trevathan. So just building on that, so this -- what you would be talking about, Kathy Rice, and we've discussed it, is just adding to the SEED platform to follow the children that are currently being just enrolled for case control, for case cohort studies, right?

CHAIRPERSON INSEL: Let me also invite Lee Grossman from the IACC who's here who has a comment about this as well.

MR. GROSSMAN: Yes, this is Lee Grossman of the Autism Society of America. We work very closely with NARPA and actually are organizing them and expanding that

organization. It's a group that represents primarily residential facilities for adults with autism, but they've expanded that.

Their primary purpose is to provide a place for these individuals to go but to help them to the point where they can return back to the community, and this is part of a number of initiatives that we're going to be launching next year in adult services and which is going to be one of our highest priorities next year.

We will have a database that we're going -- that we hope to launch shortly after the beginning of the year that will be able to capture data on adults and, I mean, obviously we'd love to participate in this initiative.

MR. DUNAWAY: This is Wolf. That's -- I guess of all the things that I hear when I come here, the most depressing thing that I hear is the fact that there's no infrastructure for dealing with people who are autistic and adults and, of course, because

I'm an adult and I'm autistic and the fact that I know so many other people that are on the spectrum and that are having a difficult time because there is no medical, there is no psychological infrastructure for people that are adults that are on the spectrum, I mean, it's like you all are having a difficult time even sounding like you can find a group of people that, you know, are adults that you can fit into the studies, and the thing is we're out here, you know, but there's no infrastructure for us to, you know, come together and to, you know, unite you in a way -- I guess become available for your studies because, I mean, I would suggest you need to perhaps put flyers out or do something to reach out to the community because we are out here. We're not invisible.

You know, most of us with autism, we know we have it. It's hard enough to be diagnosed, you know, when you're an adult. It's hard enough to find a doctor that can

diagnose you.

So like I'm saying, it's important that we develop, we come up with something here so that we can try and find autistic adults so that we can reach out and help them.

MR. GROSSMAN: Again, this is Lee Grossman. You're absolutely correct and that's part of our initiative, is to begin to provide a face for the adults that are on the spectrum to identify. We believe the numbers are dramatically unrepresented in terms of what's being reported and certainly in terms of the amount of services that are happening.

On this coming Monday, the Services Subcommittee of the IACC will be having a conference call and we're in the stages now of planning the activities for that group and a heavy emphasis of that will be around adult services and activities.

CHAIRPERSON INSEL: So I'm a little befuddled here. I think what we're hearing as I've listened to this conversation

is that there is -- the most robust effort is with children, and it seems obvious that with the National Children's Study being launched, if that could in some ways intersect with all the things that are going on, I think we have a figure of 1,800 kids per year are coming through the ATN, so that could very quickly build up a very serious database.

So if you had the right data coordinating center, you could bring together several thousand children with autism in some period of time.

What I'm befuddled about is how you bring the adult piece into this and who would do that. So on this item, for instance, who would take the lead for pulling this together in such a way that there is a data coordinating center, there's a full network?

Go ahead. Yes, someone on the phone?

MR. DUNAWAY: Can I ask a -- one thing. Whoever it is that decides they want

to do this, I will be at your total disposal. All you have to do is call, I'll fly, go wherever it is, you know, wherever I can help. This is one that is so near and dear to my heart, I will invest whatever I have to to help. Like I said, that's -- it's just that important to me.

CHAIRPERSON INSEL: It also seems like one where NDAR would be really vital because a lot of what we'd be talking about is the data coordination, and we think about what Framingham was, a lot of that was depositing, sorting, and being able to share this huge database.

Peter?

MR. BELL: I think Lee is absolutely correct in the sense that 2009 is going to be the year of the adult for autism. The face of autism is changing. Those of us who have kids who are starting to become adolescents and soon to be adults are starting to realize, you know, what the implications of

that are.

I, to a certain extent, feel like we are where we were 15 years ago with autism, with respect to adults, is we don't really know, you know, what needs -- we're starting to get a better sense of what needs to be done but this is clearly a segment of the population that has been underrepresented, underserved, and I think I'm glad to hear that ASA is going to be working on some initiatives. We are. We need to be talking obviously and -- but, you know, I think that the discussion a year from now will be much richer here because we're just starting to really figure out what exactly needs to be done, both from a service perspective as well as from a research perspective, and it's important to kind of differentiate between those two.

CHAIRPERSON INSEL: This sounds to me like the kind of thing that, again I don't want to put Ann on the spot, but the NIH ACC

probably ought to be in the center of this in some way, that this is one of these cross-cutting very large-scale efforts that is going to need to involve all the NIH institutes. If it is really going to develop like a Framingham study for autism, then I can't imagine that the NIH wouldn't be at the center of it in some way, if for nothing else at least for the data coordinating and the database itself.

So is that where we are going to go in the leadership of this? You can hear the enthusiasm for it. I think there's no question that this is going to be a big part of what the IACC will be doing and looking at in the future.

Ann?

MS. WAGNER: Yes, I think that's right, and other people who are interested can sort of figure out if there are ways to leverage what's already happening out there.

CHAIRPERSON INSEL: Yes. So I

think part of what this is about is, we have so many networks and some of them are treatment networks, some of them are the ACE networks, and this is trying to figure out a way, and that's where I think NDAR can come into play, to pull it all together into one structured, longitudinal survey and thinking about what the common measures ought to be and how this could be done and then expanding it.

I think the other thing, Kathy Lord's effort with adults, I think everybody's right, this is a gap for us that needs to be addressed.

MS. WAGNER: The efforts on the Intramural and MIND, I think, at least Sue told me those were intended to be longitudinal as well. So there might be ways to pull that in.

CHAIRPERSON INSEL: Right. So you're going to -- you'll have your hands full.

MR. BELL: I would also add --

CHAIRPERSON INSEL: It sounds like an important effort.

MR. BELL: I would add to the list IOM, I know, is starting to move into the adult arena as well.

CHAIRPERSON INSEL: Okay. So this would -- this is probably going to be the basis of many, many more conversations, and we're talking here about scale and scope. So this is going to be very, very broad and large.

MS. MUMPER: Tom, Liz Mumper. Duane, is it too late to add in new biomarkers to the National Child Health Study or have they already been all determined?

MR. ALEXANDER: No, they are going to be included. It's a process of determining what's going to be looked at and how much resources we have to look at a whole variety of things.

MS. MUMPER: So that's still in a --

MR. ALEXANDER: We're still defining what we'll be collecting and looking at.

MS. MUMPER: Great.

CHAIRPERSON INSEL: I'm going to recommend that we take a break now for lunch. It's exactly one question behind, but we will catch up. Maybe what we can do is make the lunch break a little bit shorter. So if I can ask people to come back, to bring it back here in about 15 minutes. You can eat at the table. This is Wolfson Hall and we're pretty easy about that stuff here at NIH. So there's a cafeteria just down the hall. Those of you on the phone, we'll plan to be back here again about 1 o'clock, maybe a couple minutes thereafter, I have 12:48 on my watch, and we'll get started on Question 3 at that point.

See everybody then.

(Whereupon, the above-entitled matter went off the record at 12:48 p.m. and resumed at 1:05 p.m.)

AFTERNOON SESSION

1:05 p.m.

CHAIRPERSON INSEL: All right. People are just coming back into the room, so we'll take just a moment while they find their seats.

Question 3 - Costs, Organizations, and Milestones

CHAIRPERSON INSEL: All right. Initiate studies on at least five environmental factors identified in the recommendations from the IOM Report as potential causes by 2010, two years, and the dollar amount is $14 million.

Questions about the time frame and the money?

MR. TREVATHAN: This is Ed Trevathan at CDC. I know Cindy Lawler and I've talked about this and there's been a lot of discussion.

I guess if it's "initiate using currently existing platforms" was sort of, I

think, the discussion we had initially and I see some people nodding their head. The time frame could be reasonable, at least from our point of view, if we maybe -- it may be slightly optimistic, you know, using some existing platforms, like the CADDRE sites.

Again, the funding, however, would be using platforms but funding would -- currently funding wouldn't support this at this point and then the question -- I don't know really how you all feel about that in environmental sciences.

CHAIRPERSON INSEL: Cindy, comment on this?

MS. LAWLER: So, first, I just want to point out that the recommendations from the IOM report are very broad and cover, you know, a large number of environmental factors. I think it's really important to not constrain ourselves to think about, you know, nasty chemicals as being the only kinds of environmental factors that are of interest

here and it's important that the -- you know, if we think instead of non-genetic factors, I think it's important to see involvement, you know, wide involvement across, you know, the NIH and also the advocacy groups to really be able to address this issue.

So I'm very reluctant to just have NIEHS and, you know, CDC charged with, you know, doing this because I think that really misses some potential opportunities to add exposure components to other kinds of studies outside of, you know, epidemiology studies that we may have going now.

MS. MUMPER: I think this is an area of huge interest for ARI, so I know that we would love to be involved in clinical projects, Cindy. We would welcome that opportunity.

MR. SHIH: This is also a major priority of Autism Speaks, where we're currently exploring some of the opportunities in this area with our Baby Sibs Consortium as

well as with some of the ACE Programs and certainly with our epi and environmental sciences programs. We're actively pursuing opportunities as well.

CHAIRPERSON INSEL: So tell us, can we do five such -- identify five such factors or initiate studies in five factors within two years and would the cost be in the range of $14 million? Are those accurate numbers?

MS. LAWLER: It's impossible to say. I mean, conceivably, it could be one study. If it's an epidemiology study, it's unlikely that it's going to be looking at a single factor as one example.

CHAIRPERSON INSEL: So I know it's impossible, but we don't have any -- we have to come up with a budgetary requirement. What we need to know here from those of you who do this, are we in the ballpark or is that number -- should that number be four million or 40 million or is this pretty close?

MR. SHIH: I think this is probably a good start. I mean, certainly the first thing we're looking at obviously is doing add-ons to the existing platforms.

CHAIRPERSON INSEL: Okay. Any other thoughts about dollars or time frame? This can be done within two years? Yes? No?

MS. LAWLER: I think the key word is "initiate" studies and not "complete" but, you know, identify and, you know, start a study or leverage an existing study that begins collecting, you know, other kinds of data that could address it. So that is potentially doable within two or three years.

CHAIRPERSON INSEL: Got it. Okay. So I hear the time frame is okay. The dollars, while people don't know how really to pin the number down, that this could be a workable number. It's within at least an order of magnitude of being correct, and the question is leadership. Who's going to take -- if I say take charge, that would be probably

considered -- so -- but who wants to take the leadership on this to make sure that it gets done in the right way?

MR. TREVATHAN: Well, there's so many components potentially of this. I mean, this -- I wonder if this is one of those where, sort of, it's a joint NIH maybe across different institutes and CDC because, as Cindy said, when we talk about environmental, we're not just talking about toxins. I mean, it could be infectious exposures and all sorts of things and so we may have one of the platforms that could be used, but we're going to -- there's a lot of expertise that's required.

CHAIRPERSON INSEL: Andy, how much is Autism Speaks invested here? Is this some place that you want to take the lead?

MR. SHIH: Again, I think we're starting to explore this area and I think, you know, to echo Cindy's comments, I think initiating is probably reasonable. Certainly, I think, as we mentioned, the possibility of,

you know, trying to supplement some of the existing ACE studies to add additional components to it and certainly with the Baby Sibs initiative, with the gene-environment interaction study that's being planned right now, but I don't think we have a significant investment at this point. Maybe a year from now we would.

So I think we're uncomfortable in taking the lead on this particular objective at this point.

CHAIRPERSON INSEL: So I got that. Now who -- so who wants to take the lead?

MS. WAGNER: Well, it sounds like maybe this is another NIH ACC coordinating sort of role with CDC and AS and anybody else, unless somebody else wants to do that.

CHAIRPERSON INSEL: What's the sense of the group? Is that appropriate or is there --

MS. LANDIS: You know, I hate to volunteer other people, but it seems to me

that if taking the lead doesn't mean coming up with all the dollars but assuming responsibility for making sure that it -- that the projects go forward, it seems to me like CDC and NIEHS and NIH, since this is really in your bailiwick and ACC would be a good steering committee for this.

I think it's going to be very hard to come up with a single person for each of these when it's very broad and responsibility is split.

MS. LAWLER: But we have other examples where ACC has taken the lead for very cross-cutting issues and I think this is another case, given the, you know, the history in this area. It's very important that this not be, you know, marginalized and just, you know, put in the corner of NIEHS or, you know, CDC and they'll figure it out and the rest of us will keep, you know, doing autism research.

I really -- I think it's important to make sure that that coordination and

integration happens from the beginning, you know, and doing that through the ACC will make that, you know, with CDC and the volunteers, will make that, you know, easier to have occur.

CHAIRPERSON INSEL: Maybe. I guess I'd want to take issue with that characterization because I think in those cases where people have stepped forward, I hope it's not with the assumption that they're going to be marginalized and isolated.

This really is taking the leadership for creating the coordination function and so if it's around environmental factors, you know, you'd want to have whoever has the most expertise in that area being the group to take the lead.

I hear your reluctance to do this and understood and maybe if that's the case, we'll have the ACC do it, but I suspect that most of the expertise for -- at NIH amongst -- for environmental science is going to be at

NIEHS.

So I'm willing to go with the ACC, if that's what Ann wants to do, but I wonder if we're missing an opportunity.

Ed?

MR. TREVATHAN: CDC will be happy to partner with whatever component of NIH seems most reasonable to lead on this.

MS. MUMPER: And ARI has had wonderful experiences with NIEHS in the past. I would like to see them be very much involved.

CHAIRPERSON INSEL: All right. So Cindy, I hear what you want to do is have the ACC do it. Have I got that clear?

Moving on, coordinate and implement the inclusion of 20,000 subjects for genome-wide association studies as well as sample of 1,204 sequencing to examine more than 50 candidate genes by 2011. In this case, it was thought that four years of funding would be needed and again the verbs

here are "coordinate" and "implement," and $40 million was the estimate of costs.

In terms of time frame and dollar amounts, again this is a place where, as some people around the table will know, the costs for doing genotyping fall by about 50 percent every year or every other year. It's very hard to estimate what the costs will be in 2011, but based on current costs, I think that's where the 40 million comes from.

Jim?

MR. BATTEY: Yes, I think in today's market, 40 million's reasonable, but I think it's also very likely that that number will turn out to be high to get this work done in the fullness of time because those costs for doing sequencing have a long and colorful history of declining and sometimes declining extremely rapidly as the technology emerges.

MS. TANSKI: This is Tish Tanski from the Autism Consortium. Many of us are involved in efforts underway now, if combined,

will help get us along on this goal and we would be happy to either lead or participate in this effort.

We are working with Broad Institute and would be happy to be part of this.

CHAIRPERSON INSEL: I know Simons has also -- I don't know if Marta is still on the phone, but Simons Foundation has been involved and I think their goal is 2,000 by the end of this year.

MR. HANSON: Tom, Jim Hanson, NICHD. The only caveat I would issue is I wonder what's going to happen when we start doing more epigenetic studies, and I think the costs may get reinflated. We'll go from sequencing to looking at the other modifiers.

CHAIRPERSON INSEL: Well, that will be a separate initiative because this is really about, on the one hand, genotyping for GWASS and then sequencing.

MR. BATTEY: There is, as part of

the roadmap, there is an epigenomics initiative that's just being launched and one component of that is the technology development component whose goal is to be able to do genome-wide epigenetic analysis and do it at a cost that's more reasonable than the cost is today.

MR. HANSON: I think it will be a while before we're there, though. That's my own assessment.

CHAIRPERSON INSEL: This is a place where NIMH has already worked very hard to pull together this kind of a sample. The aim is to have 20,000 well before 2011. So I'm going to nominate the institute to take the lead on this and we'll coordinate the efforts.

I know there's already a lot of discussion underway with Autism Speaks, with Simons Foundation, and others about using the repository that we support at Rutgers.

MR. SHIH: Tom, this is Andy. I

just want to add that obviously we'll be happy to help. One of the ways we're thinking about this is to help, you know, pool samples from other studies to contribute to this overall objective. So we're exploring the possibility of pooling samples not only from the AGP but also from Baby Sibs, the Autism Treatment Network and so on.

CHAIRPERSON INSEL: Great. Okay. Moving right along now: highest-priority categories of exposures for ASD, validate and standardize at least three measures for identifying markers of environmental exposure, biospecimens by 2011.

This could go to Jim's comment about epigenetics. It could go in many other directions. Questions have been raised about the choice of verbs again, about the validating and standardizing, but that's what we've got.

The number of years needed, three. Costs are -- here's a huge range, between

600,000 and nine million.

So help us on the refinement of the costs and tell us what you think about the time frame.

MS. LAWLER: So I think the higher cost estimate is associated with what you mean by validation. If we really -- to really validate, nine million's probably not going to be enough.

There are some ongoing studies through Exposure Biology Program of Gene-Environment Health Initiative that NIEHS could use to show some progress in this area. There are, you know, some exposures that would be good candidates for application to studies with ASD.

So I think we're, you know, interested, we'd like to involve the CDC labs as well. I know they have a pretty active program in developing, you know, innovative biomarkers of exposure and so on.

CHAIRPERSON INSEL: Does the -- so

in terms of the cost estimate, how do you want to refine that, or should we?

MS. LAWLER: I mean, I think we need to go back to the IACC with a message that, you know, validation is probably not going to be possible within a three-year time frame within -- you know, even with $9 million, that, you know, you can certainly do some discovery work and standardization and so on and begin validation studies, but "validate" is going to be problematic.

CHAIRPERSON INSEL: So if the verb were "identify," what would the cost estimate be in that case, just roughly?

MS. LAWLER: Well, I mean, if you started with some exposures, you know, where there was already some assay development and you were looking at a more modest effort to try to standardize, do some round robin studies to make sure that you would get reproducibility in different settings and sort of harmonize protocols and, you know, share

some samples, those kinds of activities are doable within three years for 600,000, you know.

What's not doable is more the kind of high-risk, more the discovery science, within that time frame because then there would be, you know, no real opportunity to validate. So, you know, in three years, we can maybe take some of the products from the exposure biology and try to, you know, field test, begin field testing or, you know, take some of the CDC efforts, maybe I think they have some efforts looking at, you know, trying to get more out of the newborn blood spots, you know, as an example, so there could probably be some other, you know, development efforts and, you know, testing that in other settings.

CHAIRPERSON INSEL: So if I hear you right, you would be taking this to a somewhat more modest goal of identifying over three years and then it would be about a

$600,000 effort, or in that range, to provide the standardization and to have three measures done.

Other thoughts or comments about this?

MS. MUMPER: Tom, Liz Mumper from ARI. I would like to offer as one measure that's already been worked on a lot by James Wood in Seattle which is urinary porphyrins. He's far along on that pathway.

I'd like to see us take a ball we already have in play and run with it. I think with about $2 million, he could amplify his work and we would have a marker that at least those of us involved in assessing these kids clinically have found helpful and we wouldn't be starting from scratch.

CHAIRPERSON INSEL: And the exposure question there is what? What's the exposure there?

MS. MUMPER: Number of exposures, arsenic, lead, mercury, zenobiotics, depending

on the particular porphyrin marker. There are about six or eight environmental exposures that can be captured, depending on where the enzymes are disabled in that pathway.

CHAIRPERSON INSEL: So if the question is number of years of funding and cost estimates, aside from what that particular study would be, what's the best estimate that we would have for this? I hear three years. I'm trying to get a sense, because of the range, whether you're saying $2 million for one, Cindy's saying over $9 million for validation but 600,000 is reasonable, if we are just looking to standardize.

Can we get any other sense of -- what's the opinion of ACC about this? Yes?

MS. REDWOOD: Tom, this is Lynn Redwood. I would really hate to lose the goal of validation just because we have a short time interval, and I'm wondering whether or not it might be feasible to separate this out

into two initiatives, one that would be more short-term with the three-year goal but then also maybe a long-term that would go to out to five years, expanding the budget beyond nine million and also trying to validate whatever markers we come up with.

I just don't want to lose that initiative to be able to validate these biomarkers.

Anyone else?

MS. LANDIS: I thought this was not a biomarker per se but --

MS. REDWOOD: Exposures, biomarkers for environmental exposures, I guess, is the way I viewed it.

MS. LAWLER: This is a little bit problematic because it's not necessarily specific to autism and certainly, you know, what would be specific is taking, you know, reliable exposure biomarkers and applying them in the National Children's Study which is going to measure, you know, ASD as one of the

outcomes.

So the application of existing biomarkers, you know, that makes sense, but, you know, I think that's what Story was getting at. It's a little iffy to think about validating environmental exposures because, you know, I don't think we know enough at this point to identify some that, you know, are going to be particularly germane to autism relative to, you know, lots of other kinds of disorders.

So, you know, how do we put this objective in the Autism Strategic Plan?

CHAIRPERSON INSEL: What is this? Does anybody know what this is about? What was in mind when the group put it on the list? What kind of -- were they thinking about epigenetic tags? Were they thinking about changes in sort of neural imaging marker or some kind of a urinary measure? What did they have in mind?

MS. LAWLER: So my sense, this

came from one of the big challenges in trying to link environmental factors to, you know, any disease. You know, the lack of precision surrounding the exposure, certainly the exposures that would be in the most ideologically-relevant time periods which is, you know, likely to be very early in life.

So, you know, from that, that's a challenge. That's an obstacle, and I think, you know, there was, you know, the desire to have the Strategic Plan reflect movement towards that, but in reality, this obstacle is not specific to autism. I mean, it really just, you know, sort of reflects the state of the science in, you know, environmental health, which is why the Exposure Biology Program will provide, you know, sort of an input that is relevant here, although it's not going to be autism-specific.

So I think there was -- you know, that was the genesis of this, recognizing that that's, you know, a roadblock and wanting

something in the plan that could, you know, show progress toward an important roadblock.

CHAIRPERSON INSEL: Okay. That's very helpful. So if that's true, so then this is kind of a way of focusing the Exposure Biology Program on the needs of people with ASD and could feed into the questions about risk and diagnosis and all of those issues.

MS. LANDIS: I mean, one strategy might be just to add those two numbers together and divide them by two and anticipate the possibility that there would be very good clues, like the porphyrin marker we've heard about, there may be others that we don't have an understanding of yet and that we would pursue the most promising markers with the resources that were required and since we don't know how many they are and what they're going to be, it's hard to put a specific figure on it, although I thought that figure of two million to validate the porphyrin markers was an interesting -- you could almost

use that as an argument to say that four million or four and a half million is not a crazy number.

CHAIRPERSON INSEL: So, Story, that really argues for what Lynn was suggesting. So that you might want to have a short-term goal of identifying some candidates and then as a longer-term goal -- and again we're going to have to have the IACC do this because we're not going to rewrite this, but a longer-term goal would be to begin to validate those, recognizing that that's a much greater expense, but we don't know what those would be and we don't know how long it would take and you can't validate something until you know what you're looking at.

MS. LANDIS: But to get to Lynn's point, we wouldn't -- we would only be interested in pursuing marker exposure -- evidences of exposures for which there was a strong correlation or preliminary evidence that it would be relevant. You wouldn't want

us to be tearing off after some very interesting and promising for Parkinson's exposure risk. You'd want to make sure that whatever you picked up on, you had good evidence was potentially a marker for autism.

CHAIRPERSON INSEL: So this seems like a good way forward. If we were to keep the budget on the lower side of this estimate, let's say it's around a million dollars to do the identification as part of the Exposure Biology Program, and then recommend to the IACC ultimately that they'll have to come back and create an additional category for the validation which would be a longer-term objective when we have something for -- something that can be validated but we're just not there yet.

This really kind of breakthrough science. We -- this is a place where we need a lot of additional discovery work.

MS. LANDIS: So in fact, what you could be arguing is that the first piece would

be to standardize-- identify and standardize-- three markers, three measures, working towards validation, so that there would be kind of a preliminary validation in the choice or reason to think it would be validated in the choice.

CHAIRPERSON INSEL: Right. So we're not -- we promised at the beginning that we wouldn't rewrite any of this but we will make recommendations and that would be one.

In terms of taking leadership on this, the Exposure Biology Program is part of -- where does that sit? Is that roadmap?

MS. LAWLER: NIEHS.

CHAIRPERSON INSEL: NIEHS?

MS. LAWLER: NIEHS has lead. We'll be happy to take the lead for this objective.

CHAIRPERSON INSEL: Great. Okay. Moving on, --

MS. REDWOOD: Tom, this is Lynn again. I think if the final number was one million for sort of the short-term objective,

I think that's too low. And, you know, in the past matrix, we identified environmental factors as an area that was highly under-funded and under-investigated.

So I really would like to see that number higher than one million, if that was your final number.

CHAIRPERSON INSEL: What's the group feel about that? I turn to Cindy here who knows the field best of all in terms of -- because I thought -- I think what we're talking about is a huge investment in exposure biology, but it's not all autism-specific and so what I heard her saying was that we could use small amount of additional funds-- small is relative-- to be able to focus that on ASD questions, is that right?

So what's your sense? What's the right ballpark number?

MS. LAWLER: 600,000 is probably a little too modest.

CHAIRPERSON INSEL: So give us a

sense of what -- what do you think would be necessary to take the big Exposure Biology Program and deliver at least the standardization and identification of three measures?

MS. LAWLER: I mean, I don't think that would happen all through the exposure biology. That's, you know, sort of -- so they're developing sensors for, you know, components of air pollution and there's, you know, sort of some suggestive evidence that that may be something to pursue for etiologically-relevant to autism. So that would just be one example of something that's being developed anyway that could be deployed in the context of prospective autism study if it's a sensor.

The porphyrin example, that would be more of an example of some, you know, existing information about a biomarker that's really a response to a class of exposures. So again that could be done, you know, probably,

you know, relatively, you know, with a modest budget to try to, you know, see if that holds true in a larger population.

So, you know, I guess a mix of using, you know, leveraging additional efforts or using kind of existing clues. The porphyrin would be one example.

CHAIRPERSON INSEL: So just what we need is a number. If we were to do this asthma or autism or any single disorder, I mean if you wanted to do this, thinking about this as an example, but let's say we were talking about asthma and the same question came up, what's the sense of what it would cost to get it done? Again, we're talking about order of magnitude now.

MS. LAWLER: I mean, I think you captured that with the "600,000 is not out of the ballpark." It could go somewhat higher to get started on using existing clues.

CHAIRPERSON INSEL: Should we take this to $2 million? Is $2 million going to be

-- to get three of these measures identified?

MS. MUMPER: I would really like to see it be at two or three million, Tom. This is so important.

CHAIRPERSON INSEL: Okay. I think it's $2 million, and again we're talking order of magnitude. So that's a very broad range.

Moving on, determine the effect of at least five environmental factors on the risk for subtypes of ASD in the pre- and early postnatal period of development by 2012.

This was a five-year initiative with a $10 million cost estimate. Your sense of time and cost? I'm assuming everybody thinks this is about right since there are no comments.

Duane?

MR. ALEXANDER: I think the time frame is probably a little short. If you consider using the National Children's Study for at least part of this, by 2012 we'll only have two years of experience and a whole

cohort won't have been recruited, so that's probably too soon.

But there may be other ways to approach it, above and beyond NCS. But that would be -- if we participate in this, that would be our contribution, what we could learn from the kids diagnosed with autism at NCS, but that's not going to happen by 2012.

CHAIRPERSON INSEL: What would be the better year to put in there? Is 2014 more reasonable?

MR. ALEXANDER: Even that's pushing it because we're talking subtypes. We're not even talking just autism, we're talking subtypes of a condition that's not going to be fully diagnosed probably till age three. So that's still going to be optimistic.

You can put 2015. It says five years anyway. So for our contribution, and there may be other contributions for this from NIEHS or others, it probably is going to be

more like 2015 instead of 2012.

MS. LAWLER: I think you should be able to use some of the international birth cohort, prospective birth cohorts that have, you know, samples collected, you know, either in pregnancy or, you know, the early postnatal period and, you know, have the kids who are of ages that the diagnosis is possible at this point. You could start --

CHAIRPERSON INSEL: That could be done now. It could be done next year. Story, could you do that?

MS. LANDIS: NINDS has a Norway cohort. There are blood samples from, I think, three months of gestation. They're identifying kids and I think the question there is what is the best use of those biological samples that have been collected and there's this conflict between using them now for what you think would be good assays, but then you won't have them later to use, but we certainly are very interested in this.

And NIMHS and NINDS have talked about maximizing the use of that from that cohort.

CHAIRPERSON INSEL: You know, I wonder, given that we've already got three institutes in this discussion, actually four, probably this should be an ACC effort, I would think, with a lot of coordination.

This is a chance to -- and I agree, Duane, that the National Children's Study will be an important part of it, but not in this first phase and we already have the two 100,000 children studies that we could begin to tap into and get some of this done.

So we've got some things that we would like to jumpstart in `09, I would think for this. So we'll have a chance to get it going quickly.

Anything else on this? So we've got agreement about basically the time frame, the dollars, and ACC will take the lead. Any questions about that?

(No response.)

CHAIRPERSON INSEL: Moving on --

MS. REDWOOD: Tom, this is Lynn. I just wanted to throw in again, I think we mentioned this during our last call, that I have some concern about utilizing other countries, and that I think the environmental exposures and the risk factors are going to be quite different, and I would really like to not see this focused specifically on Norway but also if we even have to, to create new specimens here in the U.S. for this investigation.

MS. LANDIS: So the notion of the Norway cohort is that that project has been underway for four years. It's not a huge cohort. It isn't going to answer all of the questions and it almost can be thought of as a pilot study that would then help focus what we would do in the National Children's study or other studies in this country.

I think Norway's not a bad

comparative. It's a developed country. The style of living is not that dissimilar. So it isn't as if we were looking at Iceland or sub-Saharan Africa. I think -- I mean, you do have a good point, but this is not meant to be the be all or the end all study, just a way to get a hook into the problem and have some idea of what one would want to follow up with.

CHAIRPERSON INSEL: I think the other concern here is just the matter of timing.

So, Duane, the National Children's Study actually started in terms of pulling together committees and the teams when?

MR. ALEXANDER: 2001.

CHAIRPERSON INSEL: So we're now seven years out and just starting to enroll the first kids. So if we started a new study today, we would not have really any data till 2019. So it makes a lot more sense to me to use some studies-- even if they're not perfect-- that are already completed, that you

could-- where we have the biosamples sitting and waiting to be analyzed. Otherwise we'll never get to where we want to be.

MS. REDWOOD: Could we utilize the studies in the U.S.? That was my point, Tom.

CHAIRPERSON INSEL: So the only study in the U.S. of this scope, of a 100,000 or greater, would be the National Children's Study. There really hasn't been done in this way before and it's just taken so long to get this off the ground, I just don't see anything else out there.

Duane knows more about this than anybody anywhere. So what's your sense?

MR. ALEXANDER: The only comparable population would be the Collaborative Perinatal Project that Neurology did back in the `50s and `60s. We still have the specimens from that, but the question is whether or not that's representative of what's happening today.

MS. LANDIS: Or relevant, which is

exactly the same thing, and I'm not even sure that the records on those kids -- just the practice of pediatrics, diagnostic criteria, recognition of symptoms, environmental factors. I think I'm not sure that's -- I'm not even sure that's as good as the Norway study which is actually a small study.

CHAIRPERSON INSEL: Okay. Onwards. A multisite study of the subsequent pregnancies of a thousand women with a child with ASD to look at the impact of environmental factors, five years, funding needed and $10 million in costs.

MS. LAWLER: So I think this objective maps very clearly on to sort of the multi institute-funded Craig Newshaffer early study. So there's already in place, you know, kind of a way to coordinate, you know, the programmatic administration of that study and so, you know, NIEHS is the lead on that.

So, you know, I'll be happy to, you know, continue that. Again, Child Health

and NS, NINDS and Mental Health, I mean, we're almost all equal contributors and that's a very nice collaborative project.

CHAIRPERSON INSEL: Cindy, should this be moved forward from a long-term to a shorter-term, if this is something that has a very high priority?

MS. LAWLER: Well, I mean, the problem is, you know, enrollment will be -- of pregnant moms will happen. It will start early next year. It's really going to be a 10-year study. So, you know, they will have some information, depending upon the frequency of exposures, you know, and the rate of enrollment, they will have some information within five years, but, you know, not enough. So don't think we can push it forward anymore.

CHAIRPERSON INSEL: And the other question that I had about it was with -- since enrollment is such a big issue, is this a place to involve Autism Speaks or ASA or some other -- one of the larger advocacy groups as

a partner to make sure that the numbers are high?

MR. SHIH: This is Andy. We are working with Craig on that issue and as well as exploring other opportunities where maybe we can supplement that particular project.

CHAIRPERSON INSEL: Okay. So I don't hear any questions about time frame, dollars, or leadership. So, Cindy, you're saying this is an ACC issue but one where the NIEHS is going to have a really important role, along with Autism Speaks.

MS. LAWLER: Right.

CHAIRPERSON INSEL: Okay. Moving on, genetic risk factors in at least 50 percent children with ASD by 2014. Again here, very broad range-- 30 million to 150 million-- and we'll need to refine that a bit as well as question about the number of years needed.

Comments?

MS. TANSKI: Well, I'm not saying

we have the money, but I am saying the Autism Consortium is doing some work in this area.

CHAIRPERSON INSEL: Is the number right? Should the number be 30 or 150? I think the IACC will need to know that. That's not really a workable range for them.

MR. BELL: I have a question. What does that involve? I mean, what -- you know, they're pretty simple words. Identify genetic risk factors in at least 50 percent of the children, but what does that mean? Does that mean that we actually have some sort of a test and can say that half the population have a specific genetic risk factor from the time of birth?

CHAIRPERSON INSEL: So the -- as I remember the discussion around this, the short-term objective had to do with identifying associations and the interest here was getting beyond that to look at actual genetic lesions; that is, understanding the functional variations in the genome. That

requires perhaps even something like whole genome sequencing or sequencing of at least 10 percent of the genome that's associated with making proteins and their regulatory elements.

The questions, as I recall from the discussion, the 30 to 150 range came about for two questions. One was the number of people needed and the second was how much of the genome you actually have to sequence. Would you have to sequence one percent which is what we do now when we just do exons, or 10 percent to do what we're calling the exome, which is all the regulatory regions around it, and I think they couldn't come to any real agreement in the group that met.

I think Dan Geschwind and several other people were at the table trying to sort this out, but I think that's where the range came from and then, as we talked about before, we just -- it's really hard to know what this is going to cost in 2014.

If we have a thousand dollar

genome which is what we're talking about, Jim, that's 2010, is that the plan, or `11?

MR. BATTEY: Within a few years.

CHAIRPERSON INSEL: All right. So certainly by 2014, you could have a thousand dollar genome which would mean that you could tout this for $30 million, and I think a lot of people at the table felt that was not too grandiose, that that was feasible.

Jim, what's your read on this? You know this better than anybody?

MR. BATTEY: Well, I have a couple questions. Are you planning to lump all children with autism spectrum disorders in one bin and do a thousand or several thousand case control genome-wide association study? I mean, is that the plan? If so, I would ask the question, "Does it make sense to take as a single cohort all the children with the range of autism spectrum disorders and would that dilute out your likelihood of actually identifying associations?"

So I don't really understand what these people are planning to do.

CHAIRPERSON INSEL: So -- well, I'll just -- I'll convey what the discussion was because I was in the room at the workgroup and others may have been there and can explain it even better.

Their point was that the short-term objective would be used to get the associations. They felt fairly strongly, the group, and there were several people at the table who agreed to this, that in 2008, by the end of this year, we would be at a point where we could identify genetic lesions in 15 percent of children who came into the office meeting criteria for autism spectrum disorder. The 15 percent would be syndromic.

Most people in the group felt that that was just the beginning and that within two years, we'd be up to something like 20 to 30 percent, but they felt that this additional -- the 50 percent figure was going to be

captured by getting the genetic risk architecture; that is, understanding those kids who don't have a Mendelian or a large CNV or some mutation but have multiple risk genes that contribute and those are already being identified, and they felt that by 2014, you should be able to capture much of the group by having the risk architecture.

Fifty percent, I think, was where they ended up, knowing that you have 15, 1-5, 15 percent today with syndromic autism, as they called it, and the rest of it could go into this other mix.

MR. BATTEY: And syndromic means monogenic?

CHAIRPERSON INSEL: Means maybe not monogenic but mono -- a genetic lesion that's identified, whether it's a CNV or a single mutation.

MR. BATTEY: A single, a single genetic lesion.

CHAIRPERSON INSEL: A single

highly-penetrant mutation.

MS. MAMOUNAS: This is Laura Mamounas. To follow through that and actually to do functional studies to understand the nature of the risk, I would think would take longer.

CHAIRPERSON INSEL: Yes, Laura, I think that's coming up a little later in terms of -- maybe not, but I thought that there was another effort to look at the biology. If it's not there, then -- but I do think that the group was just looking for genetic risk.

MS. MAMOUNAS: Well, it depends on how you identify risk factors.

CHAIRPERSON INSEL: Yes.

MS. MAMOUNAS: You can certainly identify alleles, candidate alleles, but to actually understand how they would contribute to the biology is going to require all kinds of functional studies, development of animal models, so forth.

CHAIRPERSON INSEL: Right. So

this is short of that. This is really -- and I think the figure that they gave us at the time was this would do 15,000 cases for $3 million, basically assuming that it would be getting close to a thousand dollar genome by then.

So where I think the recommendation has gone in terms of refining these numbers, what we've been hearing more recently is that it's probably at the lower end of this estimate, the 30 million is probably a better figure than the 150, but not knowing exactly where we're going to end up, but we'll -- again, I think for this purpose, since this is a long-range six-year-out kind of estimate, it's certainly going to get revised in other iterations of the plan.

I don't know that we need to spend a lot of time on it, but I would recommend that we stay at the 30 million, not the 150, and NIMH will be -- just since we're doing the earlier genetics one, I think we're the place

to do this long-term one as well.

MR. SHIH: Tom, this is Andy from Autism Speaks. We agree with your general reasoning for the estimate and obviously we will be happy to help out where we can on this particular objective.

CHAIRPERSON INSEL: I think you already are, as far as I know, Andy. This is very -- this is again one of these very collaborative efforts with AGP and many others.

Okay. And actually, if Denise is on the phone still, I think SARRC is another potential player for this as well.

Moving on to the last one of the objectives from Question 3, support ancillary studies within one or more large-scale population-based epi studies for the nested case control data on environmental factors and as well as genetic data that could be pooled to analyze targets for potential gene-environment interactions.

So this is the one we've been sort of dancing around in many different places already today. The time frame here is five years, by 2015, again broad range, $5 million to $40 million.

To do this, the sense was that in the original discussion that much of this could actually be based on the Denmark and the Norway studies and wouldn't require an entirely new large-scale epi study, although additional pieces could come out of the National Children's study.

Ed?

MR. TREVATHAN: Yes, just for clarification, the SEED studies were here in the U.S., the sites here in the U.S., and then the advantage, of course, of the Denmark studies, I think, has already been discussed, is they already have very large banked infant blood spots that can be used, and I know there was discussion also of the Norway cohort here.

But it would be building upon

those platforms, but then additional funding on that. I think the low end of that range which I see the estimate used is at the top of the range, that low-end range seems quite a bit low to me. I think that it depends on, of course, how many environmental factors and how many susceptibility genes and how many sites we're really talking about, but I think we're probably much closer to 40 million than five million there.

CHAIRPERSON INSEL: Story, you -- this is where the Norway project comes in. So what's your sense?

MS. LANDIS: I think this is --

CHAIRPERSON INSEL: You have to use your mike.

MS. LANDIS: I think this is a really important thing to do. I think that what we've discussed is taking advantage of the samples that we have to do a number of biochemical and molecular studies looking for cytokine levels, looking for infectious

agents, looking for whatever, and the estimate for a screen on that early biochemical analysis is about a million dollars, I think, from -- just on a small sample.

MS. YEARGIN-ALLSOP: Tom, this is Marshalynn, and the previous discussion had CDC being at the 40 million range and, you know, I guess the Norway cohort being more at the five million. So that's how we came up with the range.

CHAIRPERSON INSEL: So it may be somewhere between. So, Story, --

MS. LANDIS: What we -- what I was referring to was the biochemical assays, not the genetics of all the patients and controls.

CHAIRPERSON INSEL: Yes, I don't think -- the genetics would not be a big deal because you're talking about just a few hundred people that would be genotyped, but what was the estimate that you had for the -- just the biochemical part of the Norway study?

MS. LANDIS: I don't think it was

as much as you are remembering, Tom, but since we haven't actually forced him to write a budget and had it scientifically reviewed, we may not have the best information about what that total would be.

CHAIRPERSON INSEL: So -- but if the five million came from -- and I don't remember this, but if the five million came from the Norway study, the idea that that's what it would cost to really exploit that as far as possible and 40 million was from SEED or from --

MR. TREVATHAN: I think that, Marshalynn, you were involved, too, but it was SEED and the Denmark both, wasn't it, or certainly the SEED study?

MS. YEARGIN-ALLSOP: Yes, I think that it would cost more to use the SEED study than to use Denmark, but the advantage, of course, is SEED is a U.S. study.

MR. TREVATHAN: Right.

CHAIRPERSON INSEL: So help us out

here. What's the right number? Marshalynn or Ed, what -- where should we end up? Where do we want to fill the IACC for a final number?

MS. YEARGIN-ALLSOP: I'm willing to say 20, somewhere in the middle.

CHAIRPERSON INSEL: But does that mean only half of the projects will get done? We don't want to be unclear here. I mean, if it really requires $40 million to get this done, we ought to be honest about it.

MR. TREVATHEN: Well, I guess that would be my concern. The history of these things is since we're looking at 2015, we're underestimating the cost. So I'm just wondering, if you look across SEED and the Denmark collaborative and Norway, is it 40 million, you know, really look and try to get all these things done, with some of them being more front-loaded, like maybe the Denmark and that sort of thing, but I understand the need for a U.S. sample if we're going to look at gene-environmental interactions.

So maybe it's 40 million for all three. I wonder if that's what was initially thought when the estimate was 40 million and--

CHAIRPERSON INSEL: Cindy, do you have a sense of this? I mean, do you know much about -- for these G by E studies, what do you usually think about?

MS. LAWLER: I think the higher side of the estimate makes the most sense, I mean, because you really start running into power issues and a lot of it depends, too, on whether you're sort of building on an existing infrastructure or having to, you know, just identify kids and the diagnosis has already been made and as part of a larger study, like with the Norway, the infrastructure for that identification is in place. So, you know, more toward the 20 to 40 million.

MS. YEARGIN-ALLSOP: And Tom, I can provide a little more breakdown of that. You know, we were thinking SEED. It was six grantees, and it was about a million dollars

per site, you know, per year, and that's how we came up with the 40 million over five years.

CHAIRPERSON INSEL: So what would be lost in using the higher number, and if we could get it done for -- if we could solve this for $5 million, great, but why not put in the actual amount that we think it's going to cost based on what we know now? Okay?

MR. TREVATHAN: Agreed.

CHAIRPERSON INSEL: All right. So if the number -- let's go with the higher number on this, and then what do we -- in terms of the leadership on this, it sounds like CDC would be the place to go, but I can tell you that both NINDS and NIMH are trying to get a project going.

We would like actually to do this as one of the spin-offs from the Strategic Plan. It's one of the first things we want to be able to push out the door in `09 or some time in the next year.

MS. LAWLER: NIEHS would be interested in participating in this one as well.

CHAIRPERSON INSEL: Okay. But --

MR. TREVATHAN: We'd be happy to take the lead but certainly don't want to own all of it. I mean, we'd be happy to collaborate with NIMH and NINDS, all of you, yes.

CHAIRPERSON INSEL: Okay. You got it. We're moving on. Thanks.

Question 4 - Costs, Organizations, and Milestones

CHAIRPERSON INSEL: Question Number 4, which treatments/interventions will help? Short-term, we got -- launched-- four research projects. We just cut to the chase here. The cost estimates in all of these were based on what the group felt it cost to do an RCT, randomized clinical trial, and they tried to work that out and then just scaled it up according to what was required.

So it was generally around $2.5 or $2 million per study, as I recall, and so if you had four projects, it generated a number like seven million.

If there are thoughts as you look at this that can be refined better, be good to know, but I don't think we need to spend a huge amount of time on changing it from seven million to 6.5 or six.

But in terms of years needed and costs, any comments? And then leadership, who's going to take on accountability for this? This is the biomarker that goes with the clinical trials.

MS. WAGNER: We're doing that.

CHAIRPERSON INSEL: Okay. So we being?

MS. WAGNER: NIMH.

CHAIRPERSON INSEL: Okay. Done. Oh, by the way, is there anybody else who needs to be in that mix? I assume Autism Speaks has got a lot of interventions, trials

going on and we ought to make sure that we are using some of the same potential biomarkers, moderators as we call them, so that we can work together on this.

Peter is shaking his head, so Andy, you're signed on.

MR. SHIH: Yes, we're obviously working in this area, and we, as you know, we started funding related research. So I do see an opportunity for us to work together in this area.

CHAIRPERSON INSEL: Terrific.

MS. TANSKI: The Autism Consortium, also.

CHAIRPERSON INSEL: Are you doing intervention trials?

MS. TANSKI: Yes.

CHAIRPERSON INSEL: Good. All right. Three randomized controlled trials that address co-occurring medical conditions associated with ASD by 2010. I assume that ATN would be helpful for this. Again, figures

around 7.5 for three years. Besides ATN-- and the Intramural Program is doing some of this as well-- anyone else who's in this mix?

MS. MUMPER: ARI would like to be involved in that. It's an area of great interest for us.

CHAIRPERSON INSEL: Peter, is this a place where ATN ought to take the lead?

MR. BELL: Well, I think we can take the leadership role. I think, you know, there are a number of organizations that would be interested in this. So I guess I have a fundamental issue with us kind of taking the leadership role here and I think that, you know, perhaps you have gotten the sense that we all want to contribute and make this a collaborative process.

Whether or not, you know, who takes the leadership role or whatever, I mean, I think we're here to talk about the Strategic Plan for the IACC and so --

CHAIRPERSON INSEL: I just -- I'm

still mindful of the language about a public/private partnership. If it comes out that all of the initiatives are NIH or CDC, I'm not sure that's the right --

MR. BELL: I appreciate that, but we will take on an active role in this.

CHAIRPERSON INSEL: I can tell you that, if it makes you feel any better, that our Intramural Program is already deep into the Sleep Study, that I'm sure they would want to have included in this effort and it's quite a big investment for us. It also is fascinating to see. So that's -- so it would not -- we're talking about at least NIMH and there may be other parts of NIH as well.

MS. MUMPER: Tom, I'm feeling like it's a good time for us to jump in and say that ARI will actually take a leadership role on this particular initiative. I think that's an area that we have not only interest in but expertise. So I'm jumping up to the plate and offering to help.

CHAIRPERSON INSEL: All right. So you'll have to fight Peter for it, though.

MR. BELL: Yes.

CHAIRPERSON INSEL: Okay. So this will be ARI, is that okay? Peter, that's fine with you?

MR. BELL: Yes.

CHAIRPERSON INSEL: Conduct five randomized controlled trials of early interventions for infants and toddlers by 2011. So $15 million because it's five trials and they will be more expensive than your typical trials and the five years of funding that were thought to be needed.

Any questions about the time frame or the dollars? This is one where again NIH has got already a fairly large investment. I think this will help to expand it. As I look at what we were given in terms of what is in the portfolio, it's NICHD, NIMH, I believe. I think even maybe NINDS has something here.

Is this an IACC project?

MS. WAGNER: Yes, I think so.

CHAIRPERSON INSEL: Okay. Any problems with that? I'm sorry. ACC. Excuse me. They're all IACC projects, but the ACC will be the -- Ann, you're going to have a lot on your shoulders here.

Launch three randomized controlled trials of interventions for school-aged and/or adolescents by 2012, again five years of funding, $14 million.

First of all, time frame and dollars. Questions, comments? Looks like that's acceptable. What about leadership?

MS. WAGNER: NIMH has interest in this area.

CHAIRPERSON INSEL: Okay. So NIMH has got -- is there anybody else who wants to jump in on this?

MR. GERHARDT: This is Peter Gerhardt. We would be interested in supporting it.

CHAIRPERSON INSEL: I'm sorry, I

couldn't hear who that was.

MR. GERHARDT: Peter Gerhardt.

CHAIRPERSON INSEL: Okay. Thank you, Peter.

All right, moving along. Standardize and validate three model systems. So, Laura, this gets back to your question before. Cellular or animal systems that replicate features of ASD will allow identification of molecular targets.

MS. MAMOUNAS: Right. So I think this will take longer and I think the budget will be more.

CHAIRPERSON INSEL: So give us what -- this is great because this is actually something we can change.

MS. MAMOUNAS: I would say five years to really develop the testing.

CHAIRPERSON INSEL: Other thoughts about this?

MS. LANDIS: So one of the things that's interesting is as we learn more about

etiology, the models -- so you might be able to develop three quite credible models within three years for that price, but as the other studies go forward and you learn more about potential etiologies, you would probably not be satisfied with the three you'd done with what you know now. So it's kind of a moving target.

MS. MAMOUNAS: And it also might be a place to look at sort of common pathways across, you know, disorders that have an autism phenotype, Fragile X Syndrome, tubular sclerosis, and in order to understand a little bit more about the biology.

CHAIRPERSON INSEL: So the IACC at the last meeting heard from Mark Baer about the way this was used to develop new medications for Fragile X and I think was far more expensive than this. It took certainly more than three years in that disorder and if I look at just what our institute alone has invested, it's many times this number. So

that would be some indication at least for that disorder what it would cost.

Jim?

MR. BATTEY: On the cellular models, did you imagine IPS cells from patients differentiated in neurons? Is that the sort of thing you were thinking about?

CHAIRPERSON INSEL: You know, so we do have -- we have one grant already, it's not yet funded but it will be funded after next week or the week after that involves IPS cells and he's going to be focusing on children with autism who have, I think, a 16 P11.1 mutation to understand how the neurons that grow out from those stem cells are different from other neurons from kids who have autism without that mutation and normally developing children who don't have either autism or the mutation.

So that's one approach, but, you know, one could argue that you need 25 people doing that, not just one lab.

So, Laura, back to your comment. It was five years and $5 million. Again, these are sort of really broad estimates.

MS. MAMOUNAS: I mean ballpark.

CHAIRPERSON INSEL: Okay.

MS. MAMOUNAS: One and a half-two million a year, five-year period.

CHAIRPERSON INSEL: Well, that would be more like 7.5. So what's the best sense of the group about what this should look like?

MS. MAMOUNAS: I mean, it depends on how deeply we get into it, but it really blossoms into, you know, a larger effort as time goes on. As you said, it's a moving target and as we start to identify risk factors from the genetic studies as well as environmental factors --

CHAIRPERSON INSEL: Yes.

MS. MAMOUNAS: -- and as we start to understand the neurobiology of some of the monogenetic disorders and we want to start to

understand the common pathways, this could become -- you know, may become a bigger effort.

CHAIRPERSON INSEL: So I -- just again an editorial comment. If we were talking about cancer, heart disease, diabetes, this would be the major part of this plan, right, because in those illnesses, you say we'll develop the treatments after we have the targets, and for whatever reason, this ended up kind of getting sandwiched in between lots of other treatment interventions where we often don't know what the target is.

So one could argue that this is not only short-term but really the most urgent thing to do is to come up with a set of targets based on understanding the pathophysiology at a molecular level so you'd know actually what the next generation of medications might look like.

MS. MAMOUNAS: Exactly. This is like early target identification and then it

would be early translational research, you know, to develop clinical strategies. Then I think it would be a lot more than even six million, but I'm just trying to be prudent here.

CHAIRPERSON INSEL: But the -- so what I'm hearing from you, from the NINDS side, is something like five years and somewhere between five and seven and a half or something like that.

MS. LANDIS: And a lot of interest from the institute in this area.

CHAIRPERSON INSEL: Okay. So is this one that you want to take the lead on? We'll help you.

MS. LANDIS: With NIMH, yes.

CHAIRPERSON INSEL: Okay. Absolutely. This is one we're very committed to, and probably spending more than $7.5 million already, maybe in that range anyway, but it's one that we're going to be heavily invested in until we get the targets.

MS. TANSKI: It's also where the Autism Consortium's focus is.

CHAIRPERSON INSEL: Are you -- do you have an IPS program or a stem cell program for autism?

MS. TANSKI: Not yet.

CHAIRPERSON INSEL: Good.

MS. TANSKI: It's coming.

CHAIRPERSON INSEL: Okay. Well, let's hope that -- because I think this is something that has to happen in many different places very quickly.

Okay. We're moving along here to test the safety and efficacy of five widely-used interventions that have not been rigorously studied for use in ASD by 2012, five-year initiative, $15 million.

So first, a comment on time frame and cost, or no comment on time frame and cost.

Jim?

MR. BATTEY: If you're imagining a

randomized clinical trial, I think the time frame and cost is reasonable.

CHAIRPERSON INSEL: Okay. Any other comments? And what about leadership here?

MR. BATTEY: Tom, what do you already have cooking in this area? I've got to believe you've got something.

CHAIRPERSON INSEL: We have studies of diet and we have range of studies with anti-inflammatory compounds and recently -- there's a bunch of things going on. It's -- another player here could be NCCAM, which is not part of the IACC but could be brought in to help us all think about this better and to think about how it can be done.

This is also a place where there's a lot of interest outside the NIMH and some of the groups that are around the table, I think, have even probably a bigger investment than we do.

MR. SHIH: Tom, this is Andy, and

we're funding some of these grants already, looking at some of these alternative approaches. So we'll be happy to participate in this as well.

MS. LANDIS: So it seems to me that this points out a really critical role that the Coordinating Committee can play, which is to make sure that you don't have unknowingly four different organizations doing the same trial.

Maybe you want to have four different or maybe you want to have one collaborative trial with four times the power, but what we've discovered with a recent publication with Lithium helps -- appears to be of benefit in ALS is that there are three different groups running off, each do their own small underpowered study and that does not benefit anybody, especially the patients who either have ALS or who get ALS.

CHAIRPERSON INSEL: And then when you try to do a meta analysis, you discover

you can't really combine the data because they've all used different time points and different measures.

MS. LANDIS: Yes, and patients with different levels of disease.

CHAIRPERSON INSEL: We've been there. That's where I think the IACC really can agree, can be very, very helpful.

MS. LANDIS: And I'm not sure that every one of those studies that may already be underway would necessarily make it to clinicaltrials.gov which in principle could serve as a resource for making sure that there's not redundancy.

CHAIRPERSON INSEL: Especially in this area, that may be the case.

Other players in this arena of widely-used interventions, like the ones that sometimes are complementary and alternative, whatever that means?

MS. MUMPER: Which prompts me to say that we would like to be involved, but I

don't think we can commit to a leadership role on that, but we certainly have lots of interest in that area.

CHAIRPERSON INSEL: Who would be -- who's the reasonable lead for this kind of thing? Who's the -- who's got the greatest expertise in how to do this or the greatest investment? We could volunteer NCCAM.

MS. WAGNER: We could volunteer NCCAM. We could try to pull in NCCAM for their expertise.

CHAIRPERSON INSEL: I'm sorry?

MS. WAGNER: We could try to pull in NCCAM for their expertise.

CHAIRPERSON INSEL: Yes, okay, we'll do that and we'll bring them into the ACC network and at least for this. I know that when we've embarked on some of these in the past, they've been extremely helpful in teaching us what to do and what not to do. So having them at the table is useful.

MR. BELL: I think that's an

excellent suggestion. I think it's also something that all of us -- I don't think there's anyone here in the group that's going to take the lead and we're all kind of cautiously dipping our toe into the waters and trying to figure out what's the best way to do this, but it's absolutely something that's critical to this community and there's a lot of things that are being used, a lot of things that are working. We don't know why necessarily, some people probably do, but, you know, I think this is something that's worth looking at and really requires a broad group to do.

CHAIRPERSON INSEL: Just one other comment here.

I think this is an opportunity as well where the IACC can be helpful. One of the issues that comes up, particularly in this area, is the lack of trust about people's data and so whether it's coming from the pharmaceutical industry or from an advocacy

organization, people see it and say, well, of course, but it's not credible.

One hope would be that if by bringing everybody together at the outset and having some agreement about how the studies would be done, that whatever results come out actually would have a much greater impact and would actually be able to effect practice better.

So maybe even a better reason to make sure that NCCAM and lots of other people are at the table at the very beginning.

Moving along, --

MS. MUMPER: Tom, I've got one other person. The AAP has a CAM division that we are officially collaborating with at ARI. So they would be perfect and I will try to hook that person in, Kathy Kemper, when I talk to her next week.

CHAIRPERSON INSEL: Great. See, we wouldn't have known, so that's very helpful.

Two multisite RCTs of comprehensive early intervention that address core symptoms, family functioning and community involvement by 2013, five-year trial, again thought to be a $15 million investment.

MS. LANDIS: So I think we've discussed the possibility that the Department of Education could take a role in this. I don't know if there's a representative on the phone or formally committed to the Coordinating Committee, but given the way this is structured and its broad base, it seems to me that this would be a good candidate for them to take on.

CHAIRPERSON INSEL: Other thoughts or suggestions? It's easy to volunteer someone that's not here.

MS. LANDIS: That's why you should always be here.

MS. BLACKWELL: Hi, Tom. This is Ellen Blackwell. I just wanted to let you

know that I am here.

CHAIRPERSON INSEL: But you're not Department of Education.

MS. BLACKWELL: No, but I would say, you know, and I'm not volunteering, but we, you know, do, of course -- I don't know if you guys realize this, but EMS also has involvement in funding educational services in full.

CHAIRPERSON INSEL: But does Department of Ed or CMS actually fund RCTs?

MS. BLACKWELL: We have never funded anything like this, no, and I can't speak for Gail, but we do have projects that look at, you know, family functioning and community involvement, not necessarily for people with ASD.

MS. WAGNER: So we have efforts on interventions, early interventions at NIH, and we could certainly think about ways to address family functioning and community involvement as outcomes in these trials.

MS. BLACKWELL: Is the right way to address this through a multisite randomized controlled trial?

CHAIRPERSON INSEL: Yes, in this case, I think the group felt -- it's a good question, Ellen. The group felt that the -- they wanted to look at how interventions were having effects beyond just the reduction in symptoms. They wanted to look at what does it do for families and what does it do for community involvement, and I think this is -- there was a lot of enthusiasm for doing this and it also -- we talked before you got on the phone about the gaps in the portfolio and it was striking that, in addition to having very little data about adults and interventions and long-term outcomes, we have very little data about family functioning and so this was thought to be a place where rather than just describing it, we could actually look at what the interventions would do to impact family functioning.

Wolf?

MR. DUNAWAY: And the other thing, if I remember correctly, is that the main focus was to try to understand the quality of life and gauge quality of life for the -- not only just the autistic person but the family as a unit because, of course, autistic people belong to the family and also belong to the community, and trying to develop a good idea of what the quality of life and how different things impact the quality of life. That's important.

MS. BLACKWELL: I guess my only other question could be does this go beyond, you know, early intervention? Does it go to, you know, across the life span?

CHAIRPERSON INSEL: Yes. So this one, when the group looked at it, they wanted to, I think, focus initially on early intervention with the idea that you could see how great the impact would be. It may be that in the longer-term goals we'll be able to see

something more extensive, but I -- as I remember the conversation, this had to do with other things that I know are going on in NIH where we're looking at the -- what we're calling comprehensive interventions that are far more than just focused on symptom reduction.

MR. GROSSMAN: Yes, so on -- this is Lee from the Autism Society of America. This is a program actually that the Easter Seals and ASA are starting to work on where we are looking at early intervention and how that impacts and building comprehensive services around individuals to prove the concept that early intervention does in fact work and we've already pretty much put the business plan together and are going to be marching out on this pretty soon.

CHAIRPERSON INSEL: So this is one where it -- Ann, if the ACC is going to take leadership, it's going to be ASA and Easter Seals are going to be the major partner. I

had forgotten and I think you actually talked about this at the workgroup, that was part of what got this on the list. Thank you.

Anything else on the short-term list? Okay.

We're moving on to the long-term objectives. Complete RCTs in humans on three medications targeting core symptoms by 2014. This was a five-year effort, $7.5 million. Questions about time course, time frame, questions about costs?

MR. BATTEY: I think the cost is low.

CHAIRPERSON INSEL: Low?

MR. BATTEY: Yes.

MS. LANDIS: I mean, unless there -- unless those trials are going to be conducted in the context of A centers with a hub-and-spoke mechanism, I also think the cost is low.

CHAIRPERSON INSEL: So give us a better number. What would you say?

MS. LANDIS: I would probably have three times that, unless you're working with infrastructure that already exists. I don't know if any of NICHD's networks would represent a possible structure for these trials. I can't remember the last time NICHD did a trial that came in at $2.5 million if they're going to be Phase III.

Now if they're Phase II, that's going to be a different time frame. So I think not specifying Phase II/Phase -- Phase IIB versus Phase III represents some complexity vis … vis price --

CHAIRPERSON INSEL: Yes, but I -- again, I don't know that it was specified at the meeting, but I don't think anybody feels there's something ready for Phase III at this point. I think they said earlier phase.

MS. LANDIS: So Phase IIB?

CHAIRPERSON INSEL: Yes, just really looking at early efficacy.

Jim?

MS. LANDIS: So 12 million?

MR. BATTEY: So are you talking a few hundred patients?

CHAIRPERSON INSEL: The group didn't go there.

MR. BATTEY: That's the driver of what the trial's going to cost.

MR. BELL: You're probably not going to find a hundred patients, that would be my guess, per trial per medication.

CHAIRPERSON INSEL: So that times three.

MR. BELL: I think you're probably looking at $3 to $4 million per trial.

MR. BATTEY: That sounds like a reasonable number to me, if you're talking about a hundred patients. If it were 3 or 400 patients, I'd say it was low, but if it's going to be a hundred patients, that sounds reasonable.

CHAIRPERSON INSEL: Okay. So $12 million is the number we'll send to the IACC

and five years of funding is kind of where we're at.

Again, leadership on this?

MR. BELL: We'll take an active role in this. We have our Clinical Trials Network which we, you know, have a number of medications that are currently under investigation.

MS. MUMPER: Can I just make a strong suggestion that when you're enrolling those 100 people, we need to deal with the heterogeneity aspect of things and not have effects wash out if we pick a hundred kids that are different in so many ways that the mechanism -- that the medication that we're testing on them wouldn't have a biologically plausible reason to work.

CHAIRPERSON INSEL: Yes, this goes back to that very early concept we talked about of sort of building in a biomarker into the interventions trials and being able to segregate or stratify the population. That's

always a reason for doing more rather than fewer and it has to do with how you construct the trials with more moderators at the outset to be able to come up with an individual medication.

MS. LANDIS: And it's probably having some sort of compendium of trials that are underway with enough detail about patient selection, protocol, outcome measures and some, if possible, agreement on some of those things so that you don't end up with 10 different groups doing 10 different trials, the results of which can't be compared at all.

CHAIRPERSON INSEL: So on that topic, if you asked who's doing large-scale clinical trials for autism, NIMH is involved as well as NICHD through the ACEs, and ATN or CTN. Is there anything going on through Autism Speaks with what we're talking, you know, 50 or a hundred subjects?

MR. BELL: We have two trials within our Clinical Trials Network, one that's

currently active, that is a trial with a quick dissolve form of fluoxetine. The sponsor of that is Neuropharm which is a U.K.-based pharmaceutical company, and we're, you know, well along the way of recruiting the population.

We also have another trial that's actually on hold right now with an FDA hold around Memantine and that actually started two years ago but for a variety of reasons, the FDA, you know, obviously put it on hold and so we're not actively recruiting, but it's a trial that was originally funded by Autism Speaks.

CHAIRPERSON INSEL: And you said, Tish, that Autism Consortium is also supporting some trials?

MS. TANSKI: We're supporting work that's going into some pilot work on Rett Syndrome and we're participating in Fragile X.

CHAIRPERSON INSEL: But in terms of sort of -- so for ASD more generically, and

in terms of double-blind RCTs, who are the other major -- is there another major player here? There's nothing going in pharma.

MR. BELL: No, actually, there are a few trials that are happening there as well. Rispiridol, Bristol-Meyers is doing a trial there. I suspect that Jansen probably will continue to do some Phase IV on Rispiridol and so forth. So.

CHAIRPERSON INSEL: So this goes to Story's question, and it is something that I think the IACC needs to deal with. We won't deal with it today, but it ought to be on their agenda, is to think about if it's mostly Autism Speaks or the CTN and NIMH or NIH, how do we coordinate this so that we're using the same measures and same time points and not ending up with parallel efforts that don't really synergize?

MS. LANDIS: Or if you're not, that it was a conscious choice to do something different and not just random chance --

CHAIRPERSON INSEL: Right.

MS. LANDIS: -- and I think NIH, NINDS has found it quite hard in some of the diseases that we're interested in, in actually ferreting out what drug companies are doing now. The principle of that should be easier as there's more and more pressure to use clinicaltrials.gov, but I think it's critical that there be, for the kids' sakes, that there be a single site where all that information is collected and results, both positive and negative, are put.

CHAIRPERSON INSEL: Yes, I guess I'm suggesting something a little different. This is -- this, we can table this till the IACC can deal with it, but I think what we want to have is some conversation way ahead of time so that when the grants come in, before there's a decision to fund, that people sit down and say, you know, you do this, we'll do that, we'll put it together.

Well, so this comes up here

because if we are trying to do this long-term objective and let's say it is going to be 12 -- is that what we said? Some greater amount of money. We'd want to make sure that we build into that some kind of prospective way that coordinates and that if there are many different partners involved, that as grants come in, there's an opportunity to figure out how to get the best use out of clinical trials that are done, that they're not isolated.

Moving along, --

MS. BLACKWELL: Tom, this is Ellen. I have a quick question. This goal just mentions trials in humans and I just heard someone reference children. Are the trials going to be on people with ASD of all ages?

CHAIRPERSON INSEL: This says humans and I'm not --

MS. BLACKWELL: I know. That's why I asked. I'm sorry.

MS. WAGNER: I think the word was

changed to humans at some point just for that reason, to make sure we included the life span.

MS. HANN: Well, it was also to get us out of the animal models in terms of testing for targets and so forth, too. So I remember someone very clearly saying make sure this is really working with human beings in this.

MS. BLACKWELL: What if we said people with ASD of all ages or just, you know, that way we'd be talking about people definitely and not animals?

CHAIRPERSON INSEL: Thank you. We'll put that.

MS. BLACKWELL: Thanks.

CHAIRPERSON INSEL: When we get to the meeting, that's a good point.

Finally, develop interventions for siblings of people with ASD with the goal of reducing risk recurrence by at least 30 percent by 2014, five years, $6 million.

Any comments on the time frame or the dollars? Hearing none, this sounds like a Baby Sibs effort which means I'm assuming NICHD or NIH ACC. What's the best group?

MS. KAU: ACC would be good. We are currently funding one study through one of our A centers.

CHAIRPERSON INSEL: Good. And I know that this is another place where Autism Speaks is probably going to be interested in participating.

MR. SHIH: Correct. Thank you.

CHAIRPERSON INSEL: Yes, we're moving along to the fifth question.

Question 5 - Costs, Organizations, and Milestones

CHAIRPERSON INSEL: Which is where I can turn for services and this one begins with the state of the state's assessment. This is existing state programs, getting a survey out there. We want to do this in 2009, so it needs a year of funding, a cost of

$300,000.

Any questions about feasibility of getting this done in a year for that amount of money? I know this is already underway, I believe, and I think the people involved are at the table.

All I need to know here is who's really taking charge or is there even a need to do that, if it's already along the way.

MS. BLACKWELL: Tom, this is Ellen. We have a project at CMS. We are only permitted by OMB to look at nine states at a time. So we have a project that sort of fits into this basket but it isn't the entire United States. It's nine states.

CHAIRPERSON INSEL: So if you're going to do nine, can someone else do the other 41?

MS. BLACKWELL: There you go.

CHAIRPERSON INSEL: I didn't hear -- hadn't heard that before. So if -- we want to get this done and we want to get it done

within a year. So what's the best way? Who's the one -- who's going to get this over the goal line for us?

MR. GROSSMAN: Well, I think that this could be a priority effort for the Services Subcommittee to organize the federal agencies to identify what services they're providing.

We've already initiated a study of legislation on a state by state basis and we published a booklet on that recently with Easter Seals as well and UCD, University Centers for Disabilities. So that was actually a start of finding out where the legislation stands and I can provide you with the website so that you'd have that information.

We intend to expand that even further so that we can get an assessment of what's going on in the states, but a lot of this could be driven by the Services Subcommittee, I believe.

CHAIRPERSON INSEL: Who does -- Lee, who does the state of the states for developmental disabilities? Who publishes that or puts that together?

MS. BLACKWELL: That's coming out of -- it's David Braddock's study, Tom.

CHAIRPERSON INSEL: Right, right. Where does he live?

MS. BLACKWELL: David -- hold on. I was trying to find my copy of it.

MR. GROSSMAN: Well, and Morrissey would have --

MS. BLACKWELL: I want to say David's at the University of Colorado.

MR. GROSSMAN: And Morrissey at ACF would have access to getting that information through the Developmental Disabilities Council. They oversee that and every state has a DD Council.

CHAIRPERSON INSEL: So what's -- I think everybody who was involved thought this was an important thing to get done quickly.

Is it realistic to say one year or is this going to take longer? If it's nine states, Ellen, is it nine states in a year or is it --

MS. BLACKWELL: Yes, I don't think -- I mean, our project isn't constructed to get this done in year one and that's nine states. So I think it's a reasonable expectation. I think the cost is reasonable. I think the problem is, you know, how -- who's going to -- how do we go about doing this, who's going to be responsible for it.

MR. GROSSMAN: I mean, there's been suggestions about having OMB or other -- or the Government Accounting Office oversee this. There actually was some legislation introduced last year that hasn't moved forward yet that was part of that legislation, also, to do the state of the state assessment.

CHAIRPERSON INSEL: So I'm amazed by this. Is this a place where it actually would be better to have it done outside the

government to get -- to just get this done, if it's going to -- because once you involve OMB, you're talking not months but decades. They're not going to respond quickly.

MR. GROSSMAN: I -- you're talking to somebody that would absolutely agree with that and it's just a matter of getting the funding.

I think that an organization, like ASA or Easter Seals, could do this, if we have pretty much the authority. We've been trying to work this through the IACC and I know the Services Subcommittee was going to be discussing this, too, as part of the roadmap, but I think it can be done and should be done and it's part of an ongoing effort that we have.

A lot of the details will be coming from and through federally-funded programs that the state agencies are running.

MR. BELL: What does this actually entail? What is CMS doing with the nine

states? Are they just doing an inventory of what exists today?

MS. BLACKWELL: Hold on for a second, Peter. Let me actually look at the task order. We envision this as sort of a mini -- have you seen the state of the state document for people with developmental disabilities?

MR. BELL: Yes.

MS. BLACKWELL: Okay. We envisioned a document like that with different, of course, measures. So that's kind of what we had in mind and as far as the nine state report, hold on for a second, we want a summary of ASD-related services and funding in nine states, including overall longitudinal trend analysis, identification of gaps in state systems and Medicaid spending, information regarding youth and adults is especially sought, data collection procedures shall include acquisition and analysis of financial and program documents from each

state, development of a survey instrument regarding program and budget structures related to services and supports provided to people with ASD in each state, implementation of the survey in each state in cooperation with state officials to obtain, verify and interpret information.

So, you know, the answer to your question, Tom, is -- I mean, when you said is it important, yes, I think it's really important because the way the service system is set up, there are great variances from state to state and until we get a snapshot of what's happening in the United States, my feeling has always been how do you measure progress if you don't have a baseline?

So this would be kind of a baseline assessment of where we are in the United States right now.

MS. HANN: But, Ellen, I think in your description of that, this is Della, I think that's why I could imagine why you're

limited to the nine states, is because of the survey and that's --

MS. BLACKWELL: That's correct.

MS. HANN: So that's the limit for OMB, for the government essentially, to go out to do surveys.

MS. BLACKWELL: That is correct.

MS. HANN: And in order for us to do beyond nine states for the non-federal people here, in order for us to do that, we have to go through OMB clearance. OMB clearance requires at least a year's time to get that cleared.

MS. BLACKWELL: Yes.

MS. HANN: So if the government is going to do this, and I think this -- I'm not trying to say whether this is good, bad, or anything. I'm just saying if the government is expected to do this, it will take longer than a year just because of the structures that we have to deal with in order to make it happen.

MS. BLACKWELL: That has certainly been our experience.

CHAIRPERSON INSEL: So we have a great opportunity here because we're not all government.

MR. GROSSMAN: I think what can be accomplished here, in November at the NATAP meeting, for example, there will be a minimum of 38, we're hoping as many as 45 state autism teams there, and I can easily convene a meeting there of those state teams to have them get organized to get us the data that we need, and I think in conjunction with some of the other national associations, such as the Developmental Disabilities Divisions and the special ed administrators who also will be there, they will have representatives from there that we can convene a meeting that will at least get us to the point where we can figure out how to best do this.

I guess the thing that we've been struggling with is if ASA or Easter Seals or

whomever comes out and presents this data, it's how will it be accepted? I mean, we're advocacy groups versus if the government comes and presents and gets this -- if the group here feels that the private organizations can address this and it will be received well, then we'll move forward and that's what we've been struggling with.

MS. LANDIS: Well, an alternative -- so there should be some validation if it comes through the IACC and is blessed. The alternative is to pool funds and maybe time to get a disinterested third party who would have -- who would not be perceived as having a dog in the fight.

I also think that this would be incredibly useful because there's a lot of folklore about which states and where's the best place to go, where are the best services, and that may or may not be true, and also if there are significant differences, it gives families a tool to actually press for better

services in places where services aren't included.

Of course, we don't know what the best services will be, but --

CHAIRPERSON INSEL: So in the interest of time, let me make a suggestion. Why don't we remand this to the Services Subcommittee?

I love the idea, actually, of having this be an IACC product ultimately. I think that would be great with Autism Society of America taking the lead on getting it done, coordinating with people, collecting the data.

The Services Subcommittee could help to figure out what the questionnaires would look like and what kind of data would be collected.

I do think that a one-year time frame is probably pushing it but maybe we could say two years and try to get something -- okay? All right.

Let's move along. Two studies

that assess how variations in access to services affect family functioning in diverse populations.

This is the issue that came up before about getting the family data along with individual data. Three years of funding, $900,000. It was thought maybe this could be done through supplements or some other mechanism.

Any questions about the time frame or the cost?

MR. DUNAWAY: I'm sorry, but I have a problem with this, the two studies part of it. I know you say we can't change anything, but hopefully we can make the recommendation.

I kind of think it's -- with just the two studies, when we're talking about how people access services -- again, I mean, this is a thing where I wonder why it is that when we talk about people being able to access the services, we don't seem to be as aggressive as

when we're doing research.

It's just like the older people, the adults, not -- seeming to be underrepresented. I mean, when we're looking at how well people access the services and if we're penetrating certain communities, I think that's the most important thing because that's the people, you know, being able to get in and be helped.

If we're not looking at making sure that the pathway between, you know, a person out on the street and a person trying to get access to services, if we're not making sure that that's easy to do, then I don't understand, you know, all the rest of it seems for naught if we're not able to make sure a person can get services and it's just the two -- whether it just be two of these -- you know, two of these -- what do they call it? Studies.

It's just -- I mean, it's like taking two teaspoons of seawater and saying,

well, we can analyze the entire ocean based on what we get here. I mean, it just doesn't make sense.

CHAIRPERSON INSEL: It doesn't and so the explanation is that there's another whole effort that Lee is part of around the services agenda. It's less involved with the research and more involved with trying to understand where the biggest challenges are and what the Strategic Plan ought to be around access to services, dissemination of services and all of that.

That's a whole parallel effort to this one which is very much focused on research. This comes up over and over again in the discussions and that's why we created this parallel effort and they -- as Lee mentioned, they'll be meeting next week. They have a whole program going on which will help the IACC to figure out what needs to be happening most of all to provide access and what are the services that people need to have

access to.

So understanding that this is really just about studying the variations in access and trying to basically dissect out where the problems are and what the impact is on family functioning, is this a reasonable approach to take, make this a short-term objective, three studies, 900,000, knowing that there's this whole other effort that will be taking a much better view of the whole landscape?

MR. DUNAWAY: Okay. That makes sense.

CHAIRPERSON INSEL: Who would do this? Who's the -- what's the right home for this?

MS. WAGNER: NIMH Services Research Group.

CHAIRPERSON INSEL: Okay. So NIMH has got a Services Portfolio.

Long-term objectives. Four methods to improve dissemination of effective

interventions in diverse community settings by 2013. So this is issues around things like telemedicine, other dissemination strategies for evidence-based treatments. Five years and $6.3 million. I'm not sure how this one became so precise but that's what we've got.

Comments about the time frame or the cost? It was thought to be sort of $1.25 million per year for five years.

In terms of leadership, is this a HRSA/CDC/Department of Ed? What's the sense of -- Ann, is this some place where the Services Portfolio would fill in? What is your --

MS. WAGNER: Well, the Services Portfolio could look -- can investigate effectiveness of different dissemination methods, but they're not doing the dissemination. So it's a little unclear which this means, but they have some similar things that they can build on, so they can participate for sure.

CHAIRPERSON INSEL: So who's the right program for meeting this, the right agency?

MR. GROSSMAN: I would refer this to the Services Subcommittee again since we have a broad representation therefrom CDC and NIH and HRSA and SAMHSA, Department of Education, et cetera.

To me, if we're looking at four methods, to me five years is kind of long and it could probably be done in a shorter amount of time, particularly if we're looking at more of psychosocial, behavioral, educational interventions. Then we could easily put together four groups.

I don't know if Doreen's still on the phone, but I know that she's been working on some of these as well at her centers. Is she still there? I guess not.

CHAIRPERSON INSEL: The plan here would be to actually test the methods to figure out what works for dissemination.

But I like the idea of actually having this go to the Services Subcommittee. That's much of their mission. That's where the expertise is. So why don't we do that? We'll stick with this as it is now and if it needs to be modified, we can deal with it in the 1.1 version because it's a long-term objective.

Efficacy and cost-effectiveness of three evidence-based services for people with ASD of all ages in community settings.

So this is a more ambitious effort, five years, $7.5 to $10 million, and here we need again a sense of -- so this will be actually doing the trials, sort of -- this would be effectiveness trials, I guess. Much bigger effort and this sounds -- this is the NIMH Effectiveness Portfolio, so I think that's probably the place this would live, right?

I'll go through very quickly because we only have 10 minutes left.

Develop and have available to the research community means by which to merge or link databases, two years of funding, $1.2 million. This is basically NDAR.

Any questions?

(No response.)

CHAIRPERSON INSEL: Moving on, launch at least two studies to assess and characterize variation in adults living with ASD by 2011. Three years of funding, $1.5 million was the cost estimate.

This gets back to what we're doing with adults and the need to have some studies in that arena. We have a single study currently. It's clearly a gap in the portfolio.

ASA has got something going. This is an Easter Seals-type effort.

MR. GROSSMAN: Right. Yes, and I'm wondering how this really varies from that previous initiative of doing the state by state because in the state by state, it would

obviously be looking at -- I mean, a critical aspect of that would be assessing the adult service delivery.

CHAIRPERSON INSEL: I think this is trying to assess not just the service delivery but the quality of life for people, for adults, and trying to characterize that.

MS. BLACKWELL: I agree, Tom. I think they're two different things.

CHAIRPERSON INSEL: Okay. So who would be the lead on this one? What's the right group for this?

MR. GROSSMAN: It's one of ASA's major initiatives, is adult services, looking over the next four and five years.

CHAIRPERSON INSEL: So you want to take this on as the lead and we'll work with you?

MR. GROSSMAN: Yes.

CHAIRPERSON INSEL: Okay. The next one actually is a little more intense. It's around clinical trials, to look at cost-

effectiveness and efficacy of intervention services and supports.

Again, this is going to adolescents, adults and seniors living with ASD, 2012, five years, $5 million, and I'm going to presume that, given the fact that this is again in what we would call the Services Research Portfolio, that it's really going to be NIMH and don't think anybody else at the table does this, as far as I know. Maybe Autism Speaks, but I doubt that others, you know. Okay. So, Ann, we'll sign you up.

MR. SHIH: Tom, we'd be interested in supporting that with you as well.

CHAIRPERSON INSEL: Okay. Andy, thank you.

Two long-term objectives and then we'll finish this up. One is develop at least two community-based interventions with individual specificity that improves outcomes as measured by educational, occupational, social achievements. 2015 is the delivery

date, five years of funding, $8 million, same sorts of issues.

Who's in the community-based intervention developments business, and are these about the right costs?

MS. WAGNER: We have some of that in our portfolio and NIMH does this, and I think we thought this was a good estimate.

CHAIRPERSON INSEL: Yes, okay. It's so tempting to nominate NICHD to do this. Would that be cruel? They're not shaking their heads, so I think -- but it sounds like an NIMH project.

MR. GROSSMAN: I could easily nominate the Services Subcommittee for this as well since a lot of this is psychosocial, educational, behaviorally-based, and would be a great project for that committee to head up.

MS. BLACKWELL: I don't know. As the co-chair of the Services Subcommittee, I really see this as more of a research -- this is very specific.

CHAIRPERSON INSEL: You know, I think we can get input which would be great.

MS. BLACKWELL: That sounds reasonable. That sounds absolutely reasonable.

CHAIRPERSON INSEL: So, Ellen, while we have you, the last item on the -- don't go away. Develop and have available to the research community means by which to merge or link administrative databases for tracking.

This was one-year funding needed for $500,000. Tell us, is that reasonable?

MS. BLACKWELL: I don't know. I absolutely don't know.

CHAIRPERSON INSEL: So the question -- I think where this was coming -- again, the group was looking for a way to be able to bring Medicaid database, Medicare databases into a research format or something like that.

MS. BLACKWELL: Well, the problem we constantly run into when we're trying to

find people with ASD and Medicaid and Medicare is that we use ICD-9 codes and, you know, the person is not always tagged with an ICD-9 code when they see a physician.

So we have -- the data we have shows about six and a half percent of our Medicaid beneficiaries, they have ASD, but I don't find it reliable. So we really have to, you know, get kind of deep in the weeds.

Now, our states have other ways of identifying people that we don't have access to. So that's kind of the big problem here.

MR. TREVATHEN: Yes, I think Ellen's just identified the reason why surveillance for ASD is so time-intensive and expensive. So when we discussed this, we talked about having Medicaid, you know, CMS work with CDC and I think specifically our Workgroup on Disabilities but I think even more importantly the National Center for Health Statistics to perhaps just look at -- take another look at what's out there and what

are the shortcomings and can we -- what can we do, and I would think this is another -- I hate to keep bringing up education, but I think this is another area in which it might be nice to bring them to the table.

For $500,000 per year, I would think what we could do would be just to sort of give a state of the state of this situation and say what is it that needs to be done going forward. I don't really think that it's reasonable to think we could link administrative databases to really know what's going on in the communities with autism.

I don't know if, Marshalynn or Ellen, if you all agree with that.

MS. BLACKWELL: I think it's totally reasonable to think that we could all sit down at the table and talk about what we could do. You know, I don't know if we're really talking about a grant here, but the first step is definitely to get together and talk.

We have some people here at CMS who are very interested in this sort of project.

MR. TREVATHEN: Yes, I agree HRSA would be good to bring to the table.

CHAIRPERSON INSEL: This was put up as a long-term objective and maybe, as Della was saying, what this requires is really a needs assessment, I think, to get a lot of people involved.

It could be transformative. If it's done in the right way, you could use this for monitoring prevalence and even incidence if you did it right, but it's, I think, going to need a lot of people thinking carefully about it.

I don't know what to do with the budget or the time frame of this.

MS. BLACKWELL: I mean, this project may get into, you know, actually going out and interviewing state folks, you know, getting their permission to get information

from their databases. This could be bigger than $500,000 in a year.

CHAIRPERSON INSEL: So maybe this is -- you know, we -- I don't know if you were on the phone before, Ellen, when we talked about this, but it's what we called the "verb" problem here.

It may be rather than -- what we want to recommend to the committee is not developing this but beginning a process to get this done. This wasn't meant to be done by -- until 2018 anyway, but oddly enough, it only proposes one year of funding. So I guess that would be in 2017.

I think this is one of those actually potentially very important initiatives that needs to be looked at a little more carefully by the --

MR. TREVATHEN: Yes, I would say this is a needs assessment, I agree with you completely, and maybe we -- it's the verbature that we need to change at the level of the

IACC, but it would seem to me we do need CDC and CMS and HRSA and a few of us to get together and look at this and say, well, what are the needs and plot it out longer-term.

This fits together, too, with the really big picture of tracking and populations in the future with electronic medical records and merging datasets and how to do that. So $500,000 obviously won't do that, but it will, I think, bring people to the table and perhaps do a needs assessment. So we can have autism at the table when these issues are discussed with a lot of other disorders.

CHAIRPERSON INSEL: So what about moving this forward, so not doing it in 2017 but maybe 2009?

MR. TREVATHEN: Right, right. Exactly.

CHAIRPERSON INSEL: Okay.

MR. TREVATHEN: Change the date.

CHAIRPERSON INSEL: All right. And, Ed, do you want to take charge of this

and be the convener because this is not -- we're not talking about a big research project at this point. I think someone needs to figure out what different pieces are and what's the hub going to be and who are all the spokes because this is --

MR. TREVATHEN: Sure. I think we can convene the group and, Ellen, I assume you're on board and we'll get our friends at HRSA, Peter Van Dyke and company.

MS. BLACKWELL: That would be great.

CHAIRPERSON INSEL: I don't know that $500,000 is -- I don't know if that would be -- so we may want to rethink --

MR. TREVATHEN: We'll need to relook at that.

CHAIRPERSON INSEL: Yes, unless you want to meet in Maui or something and have a monthlong meeting to do this, that seems to me to be good.

MR. TREVATHEN: We can meet in

Atlanta, cut the costs.

CHAIRPERSON INSEL: Cut the costs by about 98 percent.

Are there any -- anything else in here that we need to talk about? We're right at 3 o'clock, and I know people have to run to other commitments.

(No response.)

Summary

CHAIRPERSON INSEL: Well, thanks for staying the course. I think this was very helpful for the IACC. We got a number of things refined and a number of additional items that we're able to put in here in terms of leadership.

I think we're ready now to go back to them with a much more filled-out plan.

I appreciate everybody's best thoughts about this and their hard work and the meeting is now adjourned.

Thanks to those of you on the phone for joining us.

(Applause.)

(Whereupon, the meeting adjourned at 3:02 p.m.)