U. S. DEPARTMENT OF HEALTH & HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

SUBCOMMITTEE FOR PLANNING
THE ANNUAL STRATEGIC PLAN UPDATING PROCESS

WEDNESDAY, OCTOBER 6, 2010

The Subcommittee convened at the Neuroscience Center at 6001 Executive Boulevard, Rockville, Maryland, at 9:00 a.m., Thomas Insel, IACC Chair, presiding.

PARTICIPANTS:

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DELLA HANN, Ph.D., *Executive Secretary*, Office of Autism Research Coordination, (OARC), National Institute of Mental Health (NIMH)

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COLEEN BOYLE, Ph.D., Centers for Disease Control and Prevention (CDC)

GERALDINE DAWSON, Ph.D., Autism Speaks

PARTICIPANTS (continued):

JENNIFER JOHNSON, Ed.D., Administration for Children and Families (ACF) (representing Sharon Lewis)

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

ARI NE'EMAN, Autistic Self Advocacy Network (ASAN)

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

ALISON TEPPER SINGER, M.B.A., Autism Science Foundation (ASF)

MARJORIE SOLOMON, Ph.D., M.B.A., University of California, Davis and M.I.N.D. Institute

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PROCEEDINGS

9:00 a.m.

Dr. Insel: Thank you. Good morning, everyone. This is the Subcommittee for Planning the Annual Strategic Plan Update, and this will be the second meeting we've had recently, getting ready for the October 22nd meeting of the full IACC.

We have several members of the Subcommittee in the room, and there are several on the phone. I'd like to just check to see who is on the phone, and then we'll go ahead and do introductions around the room.

Ari I know is on the phone. Has anyone else joined us by phone?

(No audible response.)

Dr. Insel: Okay, I assume that a couple of others, or at least a few others, we're expecting Ellen Blackwell, Lee Grossman, Marjorie Solomon and Stephen Shore should be joining by phone.

I wanted to introduce a new member

of the -- both Committee and Subcommittee, Dr. Coleen Boyle, who joins us from CDC. I think most of you know that Dr. Trevathan left to accept a job at St. Louis University. So he's no longer with the CDC. So Coleen will be taking over that chair. It's great to have you as part of the Committee.

A real quick round of introductions so that people on the phone know who is in the room. This is Tom Insel, and to my left is Susan Daniels, who is going to be speaking to us in a moment about all the things that are in these notebooks. But let's go ahead and do a quick round so you'll recognize voices, as well.

Dr. Dawson: Good morning. I am Geri Dawson, Chief Science Officer at Autism Speaks.

Ms. Singer: I am Alison Singer, the Founder and President of the Autism Science Foundation.

Dr. Koroshetz: I am Walter

Koroshetz. I'm the Deputy Director of the National Institute of Neurological Disorders and Stroke.

Dr. Johnson: I am Jennifer Johnson with the Administration on Developmental Disabilities, and I'm representing our Commissioner, Sharon Lewis.

Dr. Boyle: And I am Coleen Boyle with CDC.

Ms. Redwood: Hi, Lyn Redwood, Executive Director of SafeMinds.

Dr. Insel: Good. Susan, could you quickly just take us through this pile of really interesting papers that you've given us?

Dr. Daniels: So I'd also like to welcome members of the public who may be listening, and those who are in the room.

For the public, online, we have some materials available for you. We have the chapters of the Strategic Plan with line numbers that will be shown on the screen here

and also by webinar to help people follow along with what we're discussing.

We had some submissions of information within the last day of people's suggested edits to the Strategic Plan, and those are provided for the Committee members here for discussion.

And so you'll see the Strategic Plan line number documents are the first part of your -- the second section of your notebook, actually. We do have Subcommittee assignments, a procedures template and draft minutes that we'll go through in a minute, the line number documents, but then we'll be paying attention to the Strategic Plan edits that were proposed by Subcommittee members, and those are all in order of the Plan.

In the last tab of your binders, you'll have the draft portfolio analysis document that you've received for your reference. So hopefully that will be helpful information to you as you go through the

meeting.

Dr. Insel: We also need to look at the minutes from the previous meeting. That's the meeting that was held on September 21st. Are those in the document?

Dr. Daniels: Yes, they are Tab 3.

Dr. Insel: Tab 3.

Dr. Koroshetz: I move to approve the minutes.

Dr. Insel: There is one, essentially, typo, but just to make sure that before these become finalized, I believe it's the penultimate paragraph on page two, identifies Dr. Hann as Della instead of Dr. Hann, and since everybody else is identified with, usually a first name and last name, we should do that there, as well.

Any other changes or comments for the documents?

(No audible response.)

Dr. Insel: So we have a motion to accept. Unless I hear anything to the

contrary, I'll assume that we can go forward and the minutes are accepted.

Let's talk about the task of the day, and let me welcome Dr. Della Hann, who has just arrived.

Dr. Hann: Thank you.

Dr. Insel: We've got a lot in front of us here to try to get ready for ultimately what we will take to the full Committee in the way of a revision or an update of the Strategic Plan.

Before we get into the meat of this, I want to just step back and ask the Committee what it is you want to end up with? I'm a little confused because when we talked about this at the September 21st meeting, as you can see from the minutes, and also from a previous meeting, the gist of what I heard, but maybe I misunderstood, was that people did not want to do a major revision or a rewrite.

This was really meant to be an opportunity to take a look at the 2010 Plan,

and see how are we doing, essentially, use this as a progress report on those objectives that had been addressed and, more importantly, those that had not.

The only revisions or changes or updates would depend on having some major scientific breakthrough, and they're -- from what we received, in the way of the progress, the advances that we put out, I don't think we heard that there were any transformative breakthroughs, any really transformative findings from the first half of 2010.

Now I may be wrong about that. There may be something that you feel really is a game changer. But for the most part, I was therefore, surprised that we received as many new objectives. I think we have 34 new objectives that have been submitted, and I haven't seen the ones that have come from Ari. So it could be that there are many more that that, and also, there was quite a bit of rewriting of the plan.

So, you know, it's up to the Committee to decide how we want to -- Subcommittee, how we want to do this, but this is not where I thought we left off in the previous conversation. So I was a little surprised to see the number of changes that people made.

At the same time, it's clear that there are always ways to improve every document, and so you can understand the interest in either word-smithing, editing, revising or in some ways, adding to.

So let me, before we get started, just try to understand, at the end of the day here, what do you want? What is -- what do you want this to look like? Do you want it to be a new edition of the plan, or do you want it to be the 2010 plan with additions added at the end of kind of updates of things that -- you know, if there are, for instance, papers published in 2009 or 2010 that would change the references in the document, those could

certainly be added, but without having to do a major rewrite.

I'm just trying to get a sense of what the group feels would be best, and before I completely open this up, Ari, just a moment. I do want to say, which I think I said at the last meeting, that there is a risk, I think, in rewriting it every year because it becomes then, a document that doesn't provide the feel, with any sense of either priority setting or of stability, and if what we really wanted from this document was to set priorities for the field and we change the priorities every year, one can hardly hold a field, you know, as suspect, for not -- after a while, not paying attention to this.

So I think we do need to be mindful of what it means if we start making big changes on a yearly basis to this document. So let me stop there, and I'll open this up and just get a sense from the group.

There is an email that was sent in

by Ellen Blackwell. I don't know if that was circulated to the whole group.

Dr. Daniels: It was.

Dr. Insel: Okay, and I think -- right, okay, and that -- Ellen, who is not going to be here but may join us on the phone, time permitting, essentially said what I have just recalled that she didn't expect there would be any substantial changes at all. So comments or thoughts about this.

Mr. Ne’eman: This is Ari. You know, I certainly do agree that there is some value in holding findings constant year after year. I haven't seen -- and I haven't reviewed all of the other people's proposed edits, but I haven't seen any significant removals of proposed Strategic Plan objectives. But, you know, I do think we have to acknowledge a couple of things.

You know, the first is we have, I think, a broader representation now than we did in the past. So that's certainly going to

inform our work.

But second, you know, on a lot of things, particularly those related to adults and services and interventions, we're looking at a different reality, and it's not just a different reality relating to research, but since the last Strategic Plan, major healthcare legislation passed which included any number of different provisions which changed the service provision system, changed the access to the system by which people access healthcare, and all of those things have research implications or pose opportunities -- in a way that's going to improve the lives for autistic people and our families.

So, you know, I certainly do agree there is value in holding some things constant, but I think we can't pretend that we are not looking at a somewhat different set of circumstances toward formulation of this year's Strategic Plan, as compared to the

formulation of last year's Strategic Plan.

Ms. Blackwell: Hi, Ari, this is Ellen. I just wanted to agree with what you just said and also add that because we are having a Services meeting in November, I think we'll be better poised to look at those chapters of the plan in the context of health reform changes and what we hear from our speakers and other information.

Dr. Insel: Walter?

Dr. Solomon: This is Marjorie, and I really would like to echo what Ari said, only from the science perspective.

I mean, I think that a lot of things are changing in science, too, and if we don't acknowledge those and make the plan responsive to those, the plan is, in some respects, outdated.

So while I do understand that there's a need to make C- you know, we don't want to have a moving target all the time, I do think there is a need to, you know,

judiciously just update certain aspects.

Dr. Insel: Walter?

Dr. Koroshetz: So I think all the points made, I think, are probably compatible with one another. I would think that our first step is to try to understand how this should read, and I think there is two options on the table.

One is to go back and insert everything into the prose so that it reads as the original plans have in the past. I think the other option is to actually leave the plan as it was, fairly intact, or maybe completely intact, and then add pieces to the end of each chapter, saying, "This was our plan. This is what happened. These are the advances. These are the areas that we really haven't gotten anywhere in," and then -- and to Ari's point, adding in those areas -- in that section, you know, "These are the new things that came up."

Because if you -- and I would kind of like that because if you just redo the

whole thing as it is, it's really hard to know, you know, what's really been the impact of the plan.

It keeps changing and there's more things added. So to actually kind of hold the line and put the next piece in as, "All right, this was the plan and this is what happened, these are the new things," I think it distinguishes a little bit, you know, what's the past, what's the state now and what the future looks like.

But I think, Ari, we could do -- I mean, I agree with -- agree that adding things that are important, in, is fine. It would be nice to actually put it in in a section where it's indicative that, ghee, this is actually new now, and not something that's mixed up and no one will ever quite figure it out that it's something that -- that's happened recently.

Mr. Ne'eman: Well, and I think that's a -- and this is Ari, by the way. If the people in the room or on the call could

say their name before they talk for those of us who aren't in the room, I'd greatly appreciate it.

But this is Ari, and I actually think that the suggestion that was just made is a very good one. I'd take it a little bit further, though.

It does seem to me that in order to recognize both new developments and the more diverse representation of the Committee that it may be necessary to make some changes to the prose of this -- the prose of the Strategic Plan, and at the same time, I would agree that we do need to have some type of particular recognition of new developments.

So, you know, I don't see it as an either/or proposition. I think we can make some additional changes to the prose, but we can also really prioritize and put in place a new section, saying, "This is what happened in 2010, and these are why we're adding these new objectives or acknowledging these realities."

Dr. Insel: Lyn?

Ms. Redwood: Yes, and I agree with everything that's been said so far, but where I'm having a little bit of trouble is in the sections, the way it's laid out, what do we know?

I think some of those things need to be updated because we have learned new things, and it does create new gaps. So it may read a little awkward unless we insert those new what do we know into the what do we know sections.

So if we could do it at the end of what we've learned over the year, and then the other question I have is, you know, we had all these wonderful responses to the RFI, and we asked people to specifically comment on each question versus asking them, what were the new scientific breakthroughs.

So I would hate not to be able -- you know, to essentially, somewhat be ignoring all of the RFIs if we only respond to what

were the scientific breakthroughs. So those are where I'm in somewhat of a quandary with how best to update it.

Dr. Koroshetz: Well, I would agree with you, I mean, I would agree that -- Ari, this is Walter, again, that that -- what you said would be fine to do, and in the section, which is the update from 2011 to the plan, an add pieces, just as you said, in that section.

Going back into the prose, I think -- I guess what I'm afraid of is we'll get into the word-smithing business again, and we'll kind of miss our opportunity to really kind of assess the plan and assess what's new in the field and what we've -- you know, the new areas that Ari kind of brought up, and if we separate them out, I think, we could be much more, kind of clearly focused on new stuff. But that's --

Dr. Insel: Geri?

Dr. Dawson: So this is Geri Dawson. When I think about the Strategic

Plan, you know, we need to, first of all, think about the overall framework, which there was a tremendous amount of work done on identifying, you know, visions, identifying, you know, particular ways of framing questions, so the six questions, and even some of the overall strategic goals, and I don't really sense that there is any question that that Strategic Plan is changing.

What I sense is that people are wanting to, one, update the what do we know section, which, of course, we should, because there --

Dr. Koroshetz: What have we learned?

Dr. Dawson: Yes, there are new -- you know, we don't want an outdated what do we know section, and then if there are new objectives that reflect things that have happened, either because new members have come onto the group and they have a new perspective and they're bringing new information, or

because of things that have happened in the last year, to me, that's not completely revising the Strategic Plan. That's just adding some very specific new objectives.

And looking back on the last year, I guess I would see at least three areas in which I think we've made progress. One is I think that the stimulus funding is a big -- you know, has a big impact on what's happening in the field, whether we're talking about the, you know, Exxon sequencing project or some of the work that's being done on dissemination and early intervention in terms of getting this out into more rural and, you know, lower income communities.

There's a lot of work that's going on right now where when you think about having objectives and that those objectives would guide things like people coming in for a grant, which is now going to be a year from now, if we don't have -- if we're not sort of forward looking and have objectives that are

anticipating where we're going, I think it's going to be -- you know, it's going to be problematic.

So the three areas I see great progress in the last year or two, one is in the area of genetics and it's moving so quickly and this year, for example, there was a paper published that suggested that, you know, every child, as part of a diagnostic work-up, should have chromosome microarray. That's very new, and that has very big implications for thinking about diagnostic practices, and even research practices and things, in terms of say, pharmacogenetics approaches to treatment.

And then the second, I think, is in this area of moving intervention strategies out into the community and having more scalable approaches to providing services to a broader number of people, whether it's in the United States or internationally.

Then third, I think that the

recent NIEHS conference, where it really was focused on, you know, what are the new ways we can think about addressing the role of environmental factors?

There clearly were some strategies and gaps identified in that conference, that weren't incorporated into the Strategic Plan, some of the bioinformatics and infrastructure suggestions that came out of that.

So, again, I just see it as adding some objectives and then, updating the what do we know section, but not revamping the whole Strategic Plan.

Dr. Insel: Alison?

Ms. Singer: I actually really liked Walter's suggestion of creating a new section called what have we learned because I think it speaks to the issue that we identified at the outset, which is accountability.

You know, we really want to make sure that people are measuring their progress

against the plan, and if we sort of looked at a what have we learned as a part of the annual update, it would enable us to track year after year how well people are -- how well our research is moving forward against the objectives in the plan.

So, you know, for that reason, I really like that suggestion.

Dr. Insel: So if we just go back to what you were saying, Geri, against this recommendation, would that address the same thing, if you were put in an addendum to each of the seven questions about what did we learn, and incorporate in there, the NIEHS recommendations, or the issues around the dissemination of interventions, or even, you know -- there is a real shift in even the way we think about genetics, compared to when -- where we -- when we did this in 2009 -- or 2008. It's a different feeling.

Dr. Dawson: Right, the rare variant.

Dr. Insel: So rather than rewriting it, if we were to say what if -- if we made this what have we learned, and explained that shift, would that --

Dr. Dawson: Yes, well, I think --

Dr. Insel: -- address this?

Dr. Dawson: That's certainly one way to do it. I know that in -- for example, in the Autism Speaks Strategic Plan, where we update it every year, we have a section that's called what did we accomplish in 2000, looking back on that year, what did we accomplish, which is really different than what did we learn because if you're talking about accountability, then it's more like, you know, "Did we actually do anything this year, that mapped onto one of the objectives?"

What did we learn, you know, in terms -- like, for example, the NIEHS, you wouldn't say that we learned a lot from that, but we didn't really accomplish anything. All we did was kind of set the stage for new

information to be, you know, gathering through studies.

Ms. Singer: I think that one of the differences between this plan and a plan that's specific to an organization is that our level of accountability is different in that we put out this plan and we sort of encourage the private funders and the researchers to submit against the plan.

But there is not that much that we can do. In fact, I think the largest section for funding was other or work that was done that's not in the plan.

So, to me, that's one of the things that we have to really look at is, why was so much research -- you know, what have we missed, that there's still so much research that's outside the plan?

But I think that's really a difference between the way this plan and what we're able to do in terms of implementing this plan versus an Autism Speaks plan.

Dr. Dawson: Well, no, and I wasn't saying that they're the same. I'm just saying, it's good to have a section of what did we accomplish, right, because then, I think you have this metric of, you know, we have a plan. Have we actually achieved any of the objectives over the last year, which is a little different then forward looking of, you know, how does that impact now new objectives?

Dr. Insel: And the portfolio analysis is not sufficient for that in terms of at least finding out what's been funded? Is that -- or would -- is that --

Dr. Dawson: Well, I guess it's a difference between what has been funded and, you know, what were the outcomes of that funding, all right?

So, the achievement --

Mr. Ne’eman: I'm just -- I would add that I really think this idea of a section of what's new is a very good one, but, you know, there's also new policy developments,

which once again, you know, this is not a document that's focusing on that.

The research is impacted by policy, and so, you know, the increased focus on comparative effectiveness research, on closing health disparities, on increasing access to community-based long-term services and supports, all of these things should inform our research work.

But you know, I really do believe, and I encourage us to think creatively that there is a way to come to middle ground on here. I think that we should have the ability to make edits to the prose, where necessary. But clearly I think we can only benefit from the creation of a section where we can particularly call out new developments.

So I see no reason why this isn't an instance where we can have our cake and eat it, too, and really pursue both courses of action.

Dr. Insel: Walter?

Dr. Koroshetz: So, Ari, what are -- I mean, the other thing that we had talked about was not just what have we learned, but what are the gap areas, going forward?

So if an addendum included the what have we learned and then followed by what are the gap areas, the gap areas may be things that were identified earlier that really haven't had a lot of work in them, but they could also be new areas that have come up, you know, like comparative effectiveness research or something come out of policy.

So it would be, you know, not changing what we had before but, you know, evaluating it and saying, you know, in the gap areas, what's needed going forward? Would that hit your objective?

Mr. Ne’eman: Well, to a degree. To a degree it would, but at the same time, I don't want to limit the Committee's freedom of action before we've even started, you know, going through collectively. I mean, we've all

gone through this individually, but going through collectively, this document, you know.

We have the ability, obviously -- the difficulty, we're all very busy, but we have the ability, and I think we need to display the commitment to really -- to meet on this and to respect the people who have given public comment, and I thought there was a good recognition of that, somebody commented on earlier, and really incorporate whatever changes need to be made.

I think we can make mutual commitment to each other that we are not going to be sort of engaging in some sort of radical upheaval of the objectives that would have a chilling effect on the researcher community, but we can -- the new section and we can make certain marginal changes to the existing sections, as well, and I think that's my thought on that.

Dr. Boyle: This is Ellen. I'm just trying to understand what Walter is

describing so I can get a picture of what it would look like.

It sounds like there would be a section at the beginning of each chapter or at the beginning of the plan that says what's new, and then a section at the end of the plan or of each chapter saying what has been accomplished. Is that it?

Dr. Koroshetz: I mean, I think I was actually -- well, that would be fine. I was just thinking maybe, it would go at the end of each chapter, what -- that was the plan. This is what it looks like. What have we learned? What are the gap areas going forward, and if there is new areas that have come up like Ari said, I -- you know, I think identify them as the new areas in the gap, there's an advantage to that as opposed to hiding it in, you know, the previous plan, just in terms of how someone would appreciate, you know, the fact that here is something that really just came out, as opposed to in the

previous list -- laundry list of things.

So I think if you really were -- were concerned that there was something new that needed to be addressed, my argument would be that it would get more attention if it was, you know, kind of stated right out in that special section that this is brand new stuff. This is something that we didn't think about before, and we think it's important now, and that's why we're putting it in now.

Dr. Insel: You know, there is --

Dr. Koroshetz: It's a style thing.

Dr. Insel: Right, so this is Tom. One of the things we might want to think about if we're going to create a section of what have we learned is to try to incorporate all of the documents that we had to work with for this update.

So you could actually refer to, very specifically, ideas that came in from the RFI, ideas that --

Dr. Koroshetz: Yes, absolutely.

Dr. Insel: -- came in from public comment, without necessarily saying they have to be objectives, but these are things that we have learned as a Subcommittee, information that's come in.

In addition, talk about the portfolio analysis in terms of what the gaps would be, and then we have the summary of advances which captures the few things, not a lot, but it captures a section of what we think are the most important forms of research progress.

So all of that could go in, I think, in a fairly short document, short paragraph or two for each of the seven questions, and that would also allows us to put in the new references so that people would be up to date.

I keep thinking about, there's a section in here that deals with behavior -- ABA, and it's -- and the language is from 2008, there were seven, and clearly it's no

longer accurate, I mean there's now literature and a meta-analysis, two, actually, that you could say something much more positive than where we were then.

So those kinds of things, I think, need to be reflected at some point. I just -- I guess my personal reluctance here is, I don't want to go about another line-by-line rewrite because we just did that, and to do it again, at this point, I feel is -- like it's not in anybody's interest. Whereas, we do want to capture some of these important changes.

Mr. Ne'eman: And I think we can reflect that by simply asking the question of the IACC, where do people feel there is a need for change, and some of that change may result from new information. Some of it may result from new facts on the ground. Some of it may result from new representation on the IACC, and I think all of that is legitimate.

You know, my concern is I just

want us to keep our options open procedurally because I think that's a reflection of the trust that we have with each other to approach this in a responsible fashion, and I know I certainly appreciate those members of the research community who are on here and who have lent a perspective about how important continuity is, and I imagine others on the Committee from areas outside of research feel the same.

Dr. Koroshetz: We're all nodding our heads. We agree.

Ms. Redwood: Tom, the only thing is, we've already taken off on this subject --

Dr. Insel: This is Lyn. You have to speak up a little bit.

Ms. Redwood: Okay, this is Lyn, is that we've taken off in this other direction for the last two weeks. So in terms of taking all the comments that have been incorporated into the plan, now in all these different sections, and I hear us now creating something

different that would be a document at the end, whereas what we've done to date, or at least what I did, and I'm sure other members of the Committee were sort of line-by-line edits, and incorporating that new information into the plan. So we've wasted two weeks.

Dr. Insel: No, I don't know that we wasted it because a lot of what --

Dr. Koroshetz: The instruction was to fill out that template.

Dr. Insel: Yes, so what OARC asked us to do was not -- sorry?

Mr. Ne’eman: I guess maybe we're not entirely on the same page then because my impression was that the documents that we've just put together are, in fact, going to be utilized and that as s supplement to them, we're going to talk about this new section, but certainly not that all of our comments are going to have to go through this new section. Which one of those is currently under discussion?

Dr. Koroshetz: The latter.

Dr. Insel: So OARC sent a template out to be filled out, but then some people did that and many people did not.

Dr. Dawson: I guess I was -- I just want to say, from my point of view, I didn't realize I wasn't following the instructions. So I wasn't trying to be, you know -- I thought that -- what I did is, I thought -- was what I thought was expected of us. So I just didn't understand.

But I do think it would be possible, right, to go back and the changes that were incorporated into the text, to, you know, pull those out, that's the beauty of track changes, and put them into a section that says, you know, what have we learned.

I think, you know, there is -- it's inelegant for the NIH to have a section that says what do we know that's very outdated. If you imagine someone reading it for the very first time, it's just something

about that that kind of bothers me.

But on the other hand, if there is a section that says, this is what we knew in 2008., now this is the way we look at it, in 2010, and I think that's all right.

Dr. Hann: So this is Della. Just on that particular piece. I hear what you're saying, and one of the options we could also think about, if you want to go this way, is to actually insert more dating essentially, into the document, and so --

Dr. Dawson: You would have to --

Dr. Hann: So you'd say --

Dr. Dawson: I mean, there are inaccurate --

Dr. Hann: Right.

Dr. Dawson: -- statements in it now, that says what do we know, and that's a little embarrassing, you know, because this is the NIH telling the world this is what we know.

Dr. Hann: Right.

Dr. Insel: So just to be clear, it really isn't the NIH. So it's all of us.

Dr. Dawson: Oh, the IACC.

Dr. Insel: So, I mean, this is your document --

Dr. Dawson: Okay.

Dr. Hann: Okay, I see.

Dr. Insel: -- as much as anybody else's. So, that's not say we want it to be wrong, but I think we just all need to understand that we're taking ownership for this thing.

Dr. Dawson: Yes.

Dr. Insel: But I hear your point.

Dr. Dawson: Well, that's even more embarrassing then.

Dr. Hann: Yes.

Ms. Redwood: I agree with Geri in that going through it there are areas that are obviously outdated and need work, and we're somewhat wishy-washy.

Dr. Dawson: And that's good,

right? That's a good thing that things are changing that fast, I think, but we need to do it in the most efficient and least onerous way.

Dr. Insel: So given that, how would it work to simply have what do we know in parenthesis, 2009, or --

Dr. Hann: That's what I was talking about.

Dr. Dawson: Yes.

Dr. Insel: And then to add a section at the end, post healthcare reform/post lot of other things, about -- that would say, update 2010 what have we learned -- or -- yes, 2011, actually.

Would that be less -- I mean, in terms of efficiency, rather than doing a line-by-line edit, would that work better? Although, Lyn, I feel your pain for having done all of this. I'm not sure it's in vain because a lot of that can simply be put into a new section.

Ms. Redwood: I'm just afraid it's not -- it's going to read awkward not being really current.

Dr. Insel: Coleen.

Mr. Ne’eman: I have some concerns even around that just on the grounds that, you know, once again, this is a Committee with new representation. You know, I know that the other Committee members are very engaged on this, as well, and while there is certainly a desire, I think, to ensure we don't throw out the -- years of very good work, all of our names are going to be on this document.

And so I think it's important that if there are discussions about values or language that need to happen, certainly within reason, that we afford the opportunity to have those discussions.

Ms. Blackwell: This is Ellen. I just wanted to say, I'm going to have to sign off here in a minute here, but I would certainly support the bookend approach, that's

how I'm thinking of it, that we talked about earlier. That's kind of where I am as far as 2011 goes.

Dr. Insel: Ellen, if we're going to lose you, can -- I'd like to actually get the Committee -- the Subcommittee to vote on this so I get some clarity about what people really want.

Ms. Blackwell: Okay.

Dr. Insel: It's seem like there are two -- if I'm hearing this right, there are two options. One is to go through a line-by-line rewrite, which some of you have already done on specific chapters.

The other is to take some of that information but to basically incorporate all of the changes in a new section that will be dated as an update.

Mr. Ne’eman: I actually -- there is a third suggestion on the table, which is namely to do both --

Dr. Insel: Okay.

Mr. Ne’eman: -- to reflect the developments in a -- the bookend section, but also to be open to, as necessary, making edits to the prose of the Strategic Plan.

Dr. Insel: Right, so those are the three options. Can I get a show of hands, who wants to do the first option, which is really kind of what we've started, or some of you have started, is the -- is essentially, within the document, doing the revision the way we did last year.

If you're on the phone, you'll need to say aye or here or something.

The second option is the -- incorporating, essentially, all of the changes in a new section that will be called update or what have we learned or something like that.

Dr. Boyle: Can I make an addendum -- amendment to that, a little bit, and I guess, in -- for the current plan, the 2008/2009, whatever it is, I really like there to be some kind of hyperlink or somehow

reflected that that's sort of the static document for 2009, and if you really want to see the current state of the art, you know, somehow, make it obvious to people when they, you know, on a website or they actually read the plan, that -- that was the look then, and that, you know, there is an update, so it's obvious to them.

Dr. Insel: Okay, but that could -- so the -- the 2011 update --

Dr. Boyle: Right.

Dr. Insel: -- will be what will come up as -- that will be the plan people will see. So each of them are dated, just like now you have the 2009, somewhere. We don't have it here, but it has a --

Dr. Daniels: We put out a separate plan every year.

Dr. Insel: Yes.

Dr. Daniels: So there will be a whole new document with a new cover and everything.

Dr. Insel: So let me see a show of hands or voices for people who want to restrict this to an addendum section, in each chapter.

Dr. Koroshetz: This is the bookend, right?

Dr. Daniels: The bookend.

Dr. Insel: We have one, two --

Ms. Blackwell: This is Ellen. I --

Dr. Dawson: Well, I'd be willing to go either way.

Dr. Insel: All right, so we've got --

Dr. Daniels: And that's without any edits in the text?

Dr. Insel: Without edits in the text. So we've got five in the room.

Dr. Daniels: Five, and then Ellen.

Dr. Solomon: And this is Marjorie on the phone. I'll go with bookends.

Ms. Blackwell: Yes, this is Ellen,

me too.

Dr. Hann: Six, seven --

Dr. Insel: Seven, okay, and then the other option, which is to do both, to do both the line edits and the bookends, or the --

Ari, I assume you were there because that was your proposal.

Mr. Ne’eman: Correct.

Dr. Insel: Okay, so there are --

Ms. Redwood: And also --

Dr. Insel: And so, we have two people who want to do that. I think we're -- it sounds like we're going to go ahead and do the -- do this as an addendum.

Dr. Dawson: So Tom?

Dr. Insel: Yes.

Dr. Dawson: So I'm assuming that the reason for this approach is to make it more efficient, right, and to -- right, so, I'm just wanting to put out that probably there will be the same -- you know,

machination over every one of those bookends, line-by-line.

Dr. Insel: Yes.

Dr. Dawson: So whether or not it will be more efficient in the long run, it actually might end up being less efficient. So just kind of -- you know, we should think about that, if that's the issue that's on the table, is efficiency.

Dr. Koroshetz: I think it's focus more than efficiency.

Dr. Dawson: Okay, then that's --

Ms. Singer: I also think it's accountability, in addition to --

Dr. Dawson: Yes, then that's fine. I just think it's not going to be necessarily more efficient, but yes.

Dr. Koroshetz: The truth of the matter is, you go through it and something really looks better in the prose, and who is going to object, you know.

Dr. Insel: The other thing is that

it gives us the first opportunity we've had to reflect the public comment, and the --

Dr. Dawson: Yes.

Dr. Insel: -- RFI, which we don't --

Dr. Dawson: Yes, that rationale makes total sense.

Dr. Insel: -- which we haven't had in this document, and it's missing. I mean, people do all this work to tell us things they really feel are important for us to hear, and that's never reflected in anything that we put out there. So we can now do that for every part of this plan.

Okay, is there anything else about the big picture before we start to actually look at individual chapters? Any other issues?

Dr. Dawson: I have two quick questions.

Dr. Insel: Yes.

Dr. Dawson: One is, wanted to

clarify, and I mentioned this before, the difference between what we've learned, right, or a new perspective. So, for example, let's say a new technology came onboard, like, say, induced pluripotent stem cells, right.

In a way, that's an achievement, but in terms of our objectives, we didn't say our goal is to develop induced pluripotent stem cells, right. Our goal was to treat autism or something like that.

So the question of what's new, what did we learn that might influence objectives is very different than what did we actually accomplish? Did we actually discover, say, a new gene? Did we discover a new environmental risk factor that we know affects autism that could lead to a prevention strategy? Did we develop e new treatment?

Or even if you think about the objectives that are written, you know, one could say, "You know, in progress, it's being funded," right, versus, still hasn't been

funded at all, versus, it's been funded and accomplished, right.

So I just wonder about that more, you know, accomplishment aspect of it.

Dr. Insel: So, I'll answer, unless somebody else wants to jump in.

What we did last year was to use the update, to reflect new opportunities, as well. So, if my memory is right, we never mentioned microbiomics in 2009, but we did in the 2010 version.

So, and yet, there is no search on that in autism. It's simply to lay out, for the research community, that, here is a new opportunity. It's something that's really have a huge impact in diabetes, and maybe it could be relevant to the way we think about autism.

So, I think if something like that has emerged, it's a little hard for me to think about -- I guess, I could come up with a couple of examples over the last four or five

months, but there haven't been a lot of large scale technical breakthroughs in 2010, for whatever reason, compared to 2009 or 2008.

But then again, like that, I think that we feel, that the community needs to know about, I hope that we'll at least flag them and say, "Here is a great new gap area for us," that we're hoping by next year, will actually be an area that people will pursue.

Dr. Dawson: And then, in terms of the objectives then, is it noted whether they have been funded versus, you know, they actually -- the objective is now accomplished or --

Dr. Insel: Right, so, that was a question I was going to put to the group, and going through this, and I hope we do this for each chapter.

Is if there is something that was listed, that we've now finished, let's check it off. I didn't see a lot of those, going through, but I would love to know whether

there is any -- or if there is something that you see, that you think now, two years later, or even one year later, was a real mistake, and you want to take this to the full Committee, to say, "Let's remove this from the plan," that would be good to know, as well.

And again, I don't -- I saw mostly, additions. I don't think we saw a lot of subtractions.

Ms. Redwood: What about in the area of research opportunities, because there are, as Geri pointed out, in research opportunities, bioinformatics and toxicogenomics.

If we don't list those under new research opportunities, then those will go in this bookend, and I just don't know that they're going to get as much attention as they would, if they weren't actually highlighted as research opportunities.

Dr. Insel: So, maybe I was thinking about this differently.

I thought we were going to do an addendum to each chapter. So, each chapter would have, you know, `what have we learned', including `what new opportunities would exist'.

So, if something like what you just mentioned comes up, probably in -- I'm not sure if that's Chapter 2, but you could -- that's where it would go.

I think it's important to -- and maybe the most important piece to have in here are the new opportunities. I think one could --

Ms. Redwood: But would it not, I guess -- the way I read it, it would be a little awkward to not have it in the research opportunities now, unless we're going to label these as research opportunities for 2008 and 2009, and then have a new section of research opportunities for 2010.

Dr. Insel: Yes, it would be --

Dr. Koroshetz: Yes, new research,

everything would have new --

Ms. Redwood: So, what would --

Dr. Koroshetz: You would give it more attention. That's the old stuff. Don't do the old stuff. Do the new stuff.

Ms. Redwood: But there is still good old stuff, so, but --

Dr. Hann: But pay attention to the new.

Ms. Redwood: Right.

Dr. Hann: So, I mean, what I'm hearing for formatting is, this would -- there would potentially be like, a line drawn at the end of each chapter, if you want to think of it that way.

And then it would say, 2010 or 2011, whatever year we're calling this, 2010 updates, and then we would have sections on `what's new'. We would have a section then on `what's learned', as well as `gaps', and then, at the end, you would have potential new opportunities, based on all of that, and if

the Committee believes that there is any new objectives.

Ms. Redwood: Okay.

Dr. Hann: So, does that make sense?

Ms. Redwood: Yes, it's just some -- I'd like a different format, than before, but it --

Dr. Hann: It is the --

Ms. Redwood: I'm just having a difficult time, incorporating that into the plan we have now.

Dr. Insel: Yes, it is truly an addendum, right. This is not -- it's not a revision, in that sense.

Anything else, on the major part, but I guess the other thing I should just -- I have to say this, is, we're always going to struggling a little bit, that the summary of advances that we have, and the portfolio analysis are kind of off. The summary of advances, we're now a little bit more up to

date, because we've to the mid-year --

Ms. Redwood: The mid-year.

Dr. Insel: -- 2010, but the portfolio analysis, we're looking at 2009, and this plan will have a 2011 date on it, right, just like the current one has --

Dr. Hann: Yes, because I don't think we'll have it done in December.

Dr. Insel: Well, I think that even if we do have it done in December, it goes in January, to the Secretary.

So, if it's a 2011 plan, unfortunately, we're stuck with 2009 portfolio analysis. I don't know what else we can do about that. That's -- it just takes us a year.

Dr. Daniels: Well, unless we change the date of the plan, and have the plan come later in the year.

Dr. Insel: Yes, I think -- we have made a commitment to stay on target, which is January 23rd.

Dr. Daniels: But if you have the plan come out in May, you would have enough time to get at least the previous year's analysis.

Dr. Insel: I think we're going to -- I think we're stuck with what we've got.

Mr. Ne’eman: Well, speaking of that portfolio analysis, I wanted to add one additional thing.

It occurred to me that, you know, that would also have to figure in how we structure this addendum.

So, if we were looking in an area of research and we're finding that we're not seeing new developments in it, even if we previously acknowledge the area of research or there hasn't been new research in it, that may spell that there is a need for a more specific objective or focus, because it would appear that findings are not materializing in that area.

So, I just wanted to put that on

our agenda, as well.

Dr. Insel: Yes, so, I'm glad you mentioned that, Ari.

So, before we get started, could I ask for a read from the group about this portfolio analysis, because this is really an important document, before we dig into the rest of this, and how you saw it, and what, you know, kind of -- when you look at -- what's great about this, I should tell you is, I don't think there is anything comparable in the rest of biomedical research.

There are very few opportunities to look at the entire landscape of funding, public and private.

But when you look at what is being funded, both publically and privately, does that give you any reassurance or heartburn, or does it tell you anything that we need to do differently, as Ari suggested?

Ms. Redwood: What gave me heartburn over it, when I looked at it, was

the amount of money that's going for genetics, and what percent of our overall budget.

There were two questions, two objectives, that had something like, I want to say $55 million, out of the whole -- what was it, a total of $300 million?

Dr. Insel: Well, $396 is the -- I'm sorry, $316 is the total budget.

Ms. Redwood: I guess it would have been question -- it's on question two, is that it?

(Simultaneous speaking).

Ms. Redwood: I'm sorry, it's question three, what caused this to happen and can it be prevented? When you look at 3LB identified genetic risk factors, that was $44 million, 14 percent of total funding, and then up on 3SA, which was another $11 million, of this $12 million.

So, that sort of jumped out of me, in terms of some of these areas that have absolutely no funding at all, and then we see

this huge amount focused on genetics.

Mr. Ne’eman: Well, it strikes me, and I didn't precisely hear the comment that was just made, but correct me, but I think you were just raising concern around under-funded areas, and it strikes me, the two most under-funded areas here are Chapter 5, `where can I turn for services', and Chapter 6, which didn't even make one percent, in regards to the bills.

So, you know, it does seem to me that those may be areas where an added focus, in terms of edits, may be appropriate because we're just not seeing the research dollars.

Dr. Johnson: The other thing that I -- this is Jennifer. The other thing that I was struck by, and this is something that Alison brought up, is the number of `other', and it made me wonder what is being funded that we're missing? Are these important areas that we're missing, that should be looked at, or are they not important?

So, that raised questions for me, and the other thing is, I wanted to know specifically, what the research was, that was be funded under each objective, and so, having that information would be helpful, in the future.

Ms. Singer: Yes, we had that last year.

Dr. Hann: We will have it.

Dr. Johnson: Okay.

Dr. Hann: It's taking a while to format it. This is Della. So, it's -- the double-checking that goes on with these tables is a little much.

Dr. Johnson: Yes.

Dr. Insel: Do you have a general sense of what `other' would be? An example?

Dr. Hann: So, I think we have to remember too, that the way that this is coded is by the funders.

The funders are taking the information and telling us, based on their

opinion, whether they believe the research that they're doing matches a specific objective, matches a particular section of the plan, or does not.

So, that's the first thing to keep in mind. Sometimes, what is sitting in `other' can be -- and I'm trying to remember, there was an example. Actually, there was an example that I'm thinking of, that was in your portfolio -- it was in the Autism Speaks portfolio.

It was very, sort of infrastructure, and it wasn't prepared -- but it wasn't specific to the things that are in Chapter 7, and so, it was sort of -- there wasn't any place to put that kind of thing.

So, that's one tiny example. Some time, last year, when the Committee did look at the specific announces the Committee, made recommendations to move things, and so, that will be your prerogative, to do so, again. That's why this is all draft. This is not

final. So --

Ms. Redwood: In Section 2, or question two, 42 percent of what was funded was unrelated to any objective.

Dr. Hann: Correct.

Ms. Redwood: Or went into `other', but then when you go down to question three, that dropped down to only 10 percent that was unrelated.

Dr. Hann: Right.

Ms. Redwood: So, yes, what's going on?

Ms. Singer: But you know, I think what we're struggling with here --

Dr. Insel: Before we move on, is there --

Dr. Daniels: Well, the objectives, my understanding was that, you know, this plan started before I got here, but -- this is Susan Daniels.

The objectives of the plan were really to address gap areas that existed. So,

you didn't write objectives for things that were well underway already, and so, my interpretation is, those areas may have been placed, that were already well funded before the plan came into existence.

Dr. Insel: Okay.

Dr. Dawson: So, I just wanted to make a couple of comments.

First of all, I think this is, you know, incredibly important to do. I think there is a few limitations, and having now done this for Autism Speaks now, for a few years, one is that most research really touches on multiple areas.

So, let's take genetics, for example, right. So, we might be funding a project that's looking at the relationship between a specific genetic mutation and sensitivity to an environmental risk factor, in an animal model.

And so, I could code that genetics. I could code it environmental risk

factor, or I could code it underlined biology, right, and even treatment and prevention, you know.

So, this -- we've really, really struggled with this, and so, one of the thought is to actually have multiple designations, so that -- because most research does fall into multiple, and the reason for that is that, you know, I think that if you have a -- you know, genetics is often our first tag on things.

But if you look closer, you'll notice that actually, it has implications for other areas, particularly, at least for our work in environmental risk factors, and yet, it gets kind of put into the genetic, you know, area and it kind of over-represents what's going on in the area of genetics.

So, anyway, and then the other issue is that we -- you know, you have to also think about the costs of the actual studies, right. So, you know, that's something that's

not accounted for, is that the technologies to do certain kinds of work are more expensive than the technologies to do another work.

So, that's something I struggle with, as well.

Dr. Insel: But I think what we're trying to make sense of here, is that in some of these objectives, the not-specific for any sub-objective is almost -- is half or -- it's a very large chunk of many of these.

So, is that because, just as Geri is saying, the projects are not specific, but they apply to, let's say three or four of the sub-objectives, or it's because they're not related to any of the sub-objectives?

Dr. Daniels: There are some. There are training programs that may cover multiple topics and they weren't able to be categorized, because they're --

Dr. Hann: Can I give an example? I think you're -- we might have some confusion. This is Della.

So, I'm looking now, within a given question, and at the end of -- I'm looking in the appendix --

Dr. Insel: So, look at number two.

Dr. Hann: Yes, right, so, if you look at question two in the appendix, and it lists the objectives and the dollars and the projects, and at the very bottom line --

Dr. Insel: Right.

Dr. Hann: -- there's a not specific to any objective.

What that means is, that the funder believed that the work -- the research project that they have before them was relevant to, how can I understand what is happening, okay, but it didn't neatly fit into one of the specific objectives.

Dr. Daniels: Okay.

Dr. Hann: So, it could have been addressing one of the research objectives, you know, other -- yes, the -- what do we call those? I'm sorry.

Dr. Daniels: The questions.

Dr. Hann: The basic question, and particularly, in this area, I could see that happening, where you could have a lot of basic neuro-work that's going on, that was not -- didn't neatly fit in any of the specific objectives, but it's still relevant and it's still very important to advancing that area of science.

Dr. Insel: But if 49 percent of the projects don't fit, in some ways, does that mean that we need to rethink how we're doing this?

Dr. Insel: Yes, we could do that.

Ms. Redwood: I don't think we'll know, until we actually have a list of what's --

Dr. Daniels: No, you wouldn't really expect, out of nine objectives, that that -- those nine descriptive sentences would describe all of research that's going on in basic biology for autism, though, right?

(Simultaneous speaking.)

Dr. Johnson: And that might be actually, an area to look at, in terms of the objectives that need to be added, right?

Dr. Daniels: That's right.

Dr. Johnson: So, if there's important work going on, that hasn't been reflected in the objectives, that's interesting.

Dr. Insel: Or could be that the reason it becomes not specific to any is because it's related to all of the current ones.

Dr. Johnson: Right.

Dr. Insel: So, we can't distinguish that with what we have here.

Dr. Johnson: Right, and that would be -- in doing this, again, an addendum to this process is to maybe not say, not specific to any objective, but related to these objectives, so, we'd have an understanding of maybe some research projects, suggesting

multiple objectives, instead of just one.

Dr. Insel: Yes, it would be interesting, if 49 percent of the work is going on in areas that are completely related to any of the objectives we have here that would be intriguing.

Dr. Solomon: This is Marjorie, and as I look at that, I say that perhaps, our Strategic Plan isn't really responsive to what scientists are doing in the field, and to what study sections are approving and that, I think, is a little bit of a problem with the plan.

Dr. Insel: Well, we'd like to think it would go the other way, right. So, we'd like to think that we're ahead of the curve and that people just haven't caught up with us yet.

Participant: They're not responsive.

Dr. Insel: Alison, yes?

Ms. Singer: Well, I was going to

say that one thing that I thought could be added to this section, to make it more robust was to really look specifically at the plan spend versus the actual spend, and really pull that out.

I mean, the data are here, and you can pull it out and -- and I made columns, but I think to see that graphically, would be very informative, to see what the Committee budgeted for a specific objective, versus the actual scientific community spend.

Dr. Insel: That would be a good --

Ms. Singer: Yes.

Dr. Insel: -- idea to share with the IACC, you know, to let them know when the --

Ms. Singer: And the data are here, it's just pulling it out.

Dr. Insel: Right, good idea, good idea.

Mr. Ne'eman: I have something to add to that, just in the sense that it strikes

me that it would be useful if we're associating what's going on, in the research arena, which is both the private and the public sector, if we had more desegregation on the basis of some -- and I understanding of some of that, we distinguish between what's happening, in regards to Government funders, and in regards to private funders.

But we could do that, and I believe we have the data, since the funders forwarded it, we could dig down deeper and see with each individual funder, what the break down was. We might have a clear idea of where the disconnect is coming from.

If it's coming from within NIH, then you know, conceivably, that's more of a problem, than if there is just a select few private funders, just -- that just flat out disagree with our approach to priorities, and I guess, there's probably relatively little that we could do.

Ms. Redwood: One of the things --

this is Lyn, that I wanted to mention too, is that when we do see these gaps in the plan, on things that we really think are critical issues that we need to get answers to, I think it would be wonderful if we create some type of mechanism to get those answers, because right now, the scientists are driving the research and they're putting in the proposals and then they're retro-fitted back into the plan, to see how they fit, and I understand you can't, in any way, control what the private funders are funding, but I think for the NIH funding, that if there's a way to better disseminate this to the study sections, or to create RFAs, to be looked to -- to go out, to get specific answers, I think that's really important to do.

And to date, to my knowledge, we have not been doing that, with autism research. Maybe I'm wrong, I'm a consumer on this Committee, but I see a lot of important critical things that we should be following

up, that are falling through the cracks, and this is something that came out at the NIEHS workshop, too.

Dr. Insel: My understanding is that that's one of the real deliverables from this process, is that we see where the gaps are, and then to go back to what we were talking about before, around accountability, part of our task is to then figure out how we're going to address those gaps, and then, to come back and find out whether we've done it or not.

Now, the original idea with the plan was, we were going to focus up there, and everybody would follow it, and if that's not happening, so, if we still have large areas that no one is funding, or no one is applying for, then we have to ask, did we make a mistake here? Is there no traction in this area, so nobody could actually feasibly do this work, or is that people just aren't getting the message of how important this is?

But that is part of our role, in this accountability frame, that we have to circle back to see what impact this has had.

Ms. Singer: But I think Lyn's point is a good one, in that I get this question all the time, people say, "How can they apply specifically, for some of the objectives in the plan," and there really is no specific mechanism.

It's through the regular NIH processes. There's nothing that specifically calls out, any of these specific line item objectives, and it may be -- that may be an opportunity for us, to try to look at how we can go out into the community and encourage people to really follow the plan.

I think it really represents one of the biggest challenges that this Committee has, is that with regard the private funders, there is not -- we have neither a carrot nor a stick, but we can try to be persuasive and that this plan was the work of a lot of time

and effort and energy of the community, overall.

But with regard to the NIH funding, I think that is a different story.

Dr. Insel: So, I think I am with you, a little bit.

Mr. Ne'eman: I would just --

Dr. Insel: Let me just finish, Ari, just to comment on something, because in the Recovery Act, RFA we did, which was a very large one --

Ms. Singer: Right.

Dr. Insel: -- it specifically said, "This is to address the objectives of the Strategic Plan."

Ms. Singer: That is true.

Dr. Insel: What would be really interesting is to see how much that happened, you know, to see again, out of the 68 objectives, how many of them ended up in the -- and I can't remember how many --

Ms. Redwood: I sort of did that.

Ms. Singer: But maybe there is something that we can learn from that, because that money is going away.

Dr. Insel: Right.

Ms. Singer: And you know, a lot of the research that we've been able to fund with that money is -- I'm going to now fall of the cliff, and I think that's also something that as a Committee, we need to talk about, and that the funding is going to go down, in subsequent post-stimulus years, and how are we going to focus on this?

Dr. Insel: So, we've said -- yes, go ahead.

Dr. Dawson: Well, so, to address this issue, which I also think is very important, the way that we're doing it at Autism Speaks, just to throw it out, is a strategy, is that instead of just having investigators come with what they come, what we're saying is that there is well defined, what we call targeted research emphasis areas.

This is actually, the strategy that the Juvenile Diabetes Association works. So, each year, they have, if you go to the website, a set of targeted research emphasis areas, and so, we've defined those, if you go into our grants program, you can see them on there, and then when you come in with a proposal, you have to explain up front, how that proposal maps onto a targeted research emphasis area.

And so, that's one way, besides RFAs, you know, there are special and targeted, that you can influence, kind of the broader things like R01's, or in our case, basic or clinical or pilot research awards.

Ms. Redwood: And let's look at Department of Defense, too. They also have very specific categories and you have to --

Dr. Dawson: And those are also then -- when we have a review panel, those are circulated, and people are reminded that, you know, think about this, because sometimes, a

quick proposal comes in and we'll say, "You know what? There is already a ton of funding going on in that area."

So, it's not one of our targeted research areas this year, because we're trying to really build this other area.

Mr. Ne'eman: Well, this is Ari. I want to sort of echo comments and build on the comment that, I believe it was Alison, the person didn't identify themselves earlier, which is, we should be out there really encouraging, to the extent that we can, private funders to follow the Strategic Plan.

But in order to do that, I think we must have a clear idea of what the break down is by funders.

So, I would really hope, some of the stuff and formulations, and I recognize this is a draft, so, maybe this is one of the things we can change for the final, that we can take a look at the 10 or dozen or so, top funders and then get a break down of their

funding for each of these seven questions, of the Strategic Plan. That way -- and you know, also for stuff that was not fitting within the Strategic Plan objectives, and then we can have a very clear idea of who is going off-message and you know, we don't really have any type of arena.

Dr. Hann: Ari, this is Della. That will be part of the detailed analysis that we'll be providing.

So, the detailed --

Mr. Ne'eman: Can we present it in the same way, with the graphs and everything, that we're representing it, across all funders?

Dr. Hann: It doesn't lend itself well to the graph modality, and I think we do present the information on how much each funder is contributing, and so, that is there, and available for people to see.

I think it's really in the details, that it comes through, in terms of

what the different areas that the funds -- because some of the funders are very specific, in terms of the kinds of research that they're interested in.

As we've just talked about, there are targeted areas that they each sort of focus in on. So, I'm respectful of that, of the fact that we have diversity amongst our funders, and I think the detailed analysis will provide that information.

Dr. Dawson: I should say, Ari -- Ari, this is -- this is Geri Dawson. I wanted to say that if you're interested in Autism Speaks, just go to our website and every year, we provide an extremely detailed portfolio analysis and so, you can look at that, and this year it will be more detailed than ever, because we have a new system. So, that will help.

Mr. Ne’eman: Well, I appreciate that, Geri. The concern that I have, however, is right now, we have information as to how

much money each funder is contributing, and I know that OARC has the data and it's largely the same formulations.

So, I'm not entirely sure as to what these logistical challenges are, largely the same formulation as the data representing the break down of the aggregate. So, you know, I think it would be very useful, to see where the major funders are placing their priorities, in comparison to the Strategic Plan, and across all public and private funders, how funding is being allocated, and that would strike me as really, the only way that we can drill down and find out how we can rectify the imbalances that are leading to a bias of autism research agenda.

Dr. Insel: Well, as Della said, I think you will get all of the details, and the time-line for delivery is like?

Dr. Hann: We're hoping to have it by the 22nd.

Dr. Insel: Okay, by the IACC

meeting. So, you'll get a pretty good view of who is funding what.

We're going to -- we have a lot to do, still, and I really wanted to hear these kind of general comments about the portfolio analysis, because it does need to inform what we do, and I think these issues about identifying continuing gaps has got to inform how we do the updates. So, I don't see any way around having to talk about this.

Are you ready to go into now, just doing a chapter-by-chapter look at kind of suggestions that have come in, so we can get the Committee's read on changes you want to make?

We could take break, if everybody wants to stretch for a minute, or -- okay, let's take a three minute or four minute break. There are restrooms just down the hall, and those of you who are on the phone, we'll be back -- I have 10:11 a.m. We'll be back at 10:15 a.m.

(Whereupon, the Subcommittee members took a brief break starting at 10:13 a.m. and reconvening at 10:16 a.m.)

Dr. Insel: Coleen, you had the Chapter 1, that you had looked at, so, we're going to start with you, and I guess this will be a little complicated, because what we'll be doing, instead of actually doing the text rewrite is, we'll just want to quickly go through what you thought were the major issues.

Dr. Boyle: Okay.

Dr. Insel: And we did fill out the section, the template, about what progress has been made. So, hopefully, the group can focus on that, as what might be the basis for the addendum, and you've included some new references, as well.

Dr. Boyle: They're all done.

Dr. Insel: So, you've got some --

Mr. Ne’eman: Are we talking about something straight from Chapter 1, or are we

going to be discussing the introductions?

Dr. Insel: We are going to start with Chapter 1. We'll circle back and do the introduction at the end. But the main thing we want to grab is the new objectives and those issues around the new substance.

Ms. Redwood: Tom, I was also wondering if the preface -- if we could put something at the bottom, because it summarizes why we're doing this, the Act, funding, how much was spent in the last year or two.

Dr. Insel: You mean, for the --

Ms. Redwood: On the preface, the very first page of the --

Dr. Insel: At the very first page, sure. I think we'll capture those introductory sections at the end. I want to make sure we get through the substance, where the objectives are, and the `what have we learned' sections.

So, Coleen, do you want to just quickly take us through, and I think you and,

I believe Lyn, have both contributed to -- I'm sorry, Geri, have both contributed to Chapter 1.

Dr. Boyle: Right, so, help me with the tabs here.

Dr. Insel: It's Tab 13.

Dr. Boyle: Tab 13?

Dr. Insel: And Tab 14, on Geri's --

Dr. Dawson: I have my own notes.

Dr. Johnson: Actually --

Dr. Insel: Geri's notes.

Dr. Johnson: It was Walter, myself and Coleen.

Dr. Insel: Oh, okay.

Dr. Boyle: Yes, yes.

Dr. Insel: Okay, and it looks -- you're right, so, Jennifer and Coleen, looks like you've already collaborated on this?

Dr. Boyle: Yes, we have.

Dr. Insel: Okay, so, can you just quickly take us through what you think would

be the most important changes, and what you'd want to see incorporated into something that may be half of a page, or -- we have a relatively tight addendum, on `what have we learned'.

Dr. Hann: Or what is new.

Dr. Boyle: What is new?

Dr. Hann: What is new, yes.

Dr. Boyle: Well, I mean, I think what is new, has really come up from the -- both the work from the ADDM Network, and the King study, in terms of the screening and pediatric practices.

Dr. Insel: So, basically, it's what you've already written there. So, you've given us the basis for the `what have we learned' section.

Ms. Singer: And you're in Tab 13.

Dr. Insel: Tab 13, so, it's the last part of Tab 13.

Dr. Hann: Page five, page five in Tab 13.

Dr. Insel: Yes, there is a section that says, "What progress is being made in fulfilling the objectives?"

Dr. Boyle: And right at the end, there is -- which is the paragraph we were asked for.

I think we have to work on it a little bit, based on the frame that we talked about.

Dr. Insel: Right.

Dr. Boyle: Particularly, the context of sort of the ACA, and the changing environment and the healthcare reform. I think that was -- those are opportunities that we might be able to position here.

So, do we want to talk at all, about proposed new objectives?

Dr. Johnson: Sure, I think just in terms of what I thought, in terms of what we learned from your research, I think I was particularly struck by the research that was done, to look at the early signs of autism.

It was a good study, but we had, you know, some sample issues, because it was a small sample that was done, but I think it does change or offer some new information, as to how we think about how autism emerges, and the notion of there being different ways in which it emerges.

So, I think that was an important study, that, I don't think, ultimately changes the objectives, but is important information to include in the update.

Actually, I think what happened was that the template that I filled out is not included in the notebook, and I had that, and I think what ended up getting included in here --

Dr. Hann: I don't know if we ever received it.

Dr. Johnson: It was the first email that went out to the group, was my template, and so --

Dr. Hann: Okay, I think yes, we

assumed that --

Dr. Johnson: Right, yes, I think what happened is that what was in my template was incorporated into what Coleen worked on.

Dr. Insel: Okay.

Dr. Johnson: So, I did have -- but I did incorporate that into the -- what ended up getting edited into the chapter.

So, I do think that's important, to include -- pardon me?

Dr. Daniels: So, if we're taking notes on what things we would want to conclude where -- where is the --

Dr. Hann: It's not here.

Dr. Johnson: It's not there.

Dr. Hann: It's in an earlier email that she left out.

Dr. Johnson: Yes.

Dr. Daniels: Okay, so, we'll have to do it after.

Dr. Hann: Right.

Dr. Insel: So, can I just -- back

to -- I want to make sure I understand what you're thinking about, when you say earlier diagnosis, are you talking about bio-markers or behavioral --

Dr. Johnson: What the researchers did is, they really looked at, I think, behavioral features and how that's observed.

Dr. Insel: So, which is this -- are you thinking Amy Weatherby or --

Dr. Johnson: It was -- I don't actually know.

Dr. Boyle: Sally Ozonoff?

Dr. Johnson: Yes.

Dr. Insel: Sally Ozonoff, yes.

(Simultaneous speaking.)

Dr. Johnson: Right

Ms. Singer: And is that in the 2010 mid-year or the 2011?

Dr. Johnson: This was in the 2010 mid-year.

Ms. Singer: Okay.

Dr. Insel: So, I have a question

about this, and I think some of you are going to be closer to this than I am.

But in -- you recently had presentations by people like Ami Klim and people who were doing a lot of the very early work on social engagement, cognitive features, eye- tracking, all of that, which shows that there are -- there already is a separation at two months, and a large number of children who are on this pathway.

But it just felt to me that that was for the 2012 Strategic Plan, or 2013. I just can't imagine that that's something that's ready for prime time. I mean, that work is underway, but didn't seem to me --

Dr. Solomon: Actually, Sally Ozonoff's paper in the article that we nominated, it doesn't suggest what you're saying.

Dr. Dawson: Yes, I'm surprised you're saying two months.

Dr. Insel: Yes, so, this was

presented at the Simons meeting.

Dr. Dawson: Oh, okay.

Dr. Insel: About two or three weeks ago, and it just blew people away, because it's the first time any of us had seen -- they were doing this every -- I think every month, or every other month, throughout the first year, and the lines clearly started diverging, just kept diverging.

Dr. Dawson: Right, but that is different than predicting, you know -- either in a population or a high risk population, that being a predictor, specific of autism later, right, so --

Dr. Koroshetz: Well, no --

Dr. Insel: No, this is a -- basically, would be like a bio-marker. It's what we have now, for Type I Diabetes, with the auto-antibodies, you know, the same idea, that you're well, well before the period of first behavioral observational kinds of clinical features.

Now, would you do this in the general population? Well, you know, in Type I Diabetes, they're actually starting to melt a large population screening effort, to look for auto-antibodies.

So, if you had something that was clear enough, you could -- all I'm saying is, I don't think we're there. I think this is two years in the future, or so. That's what I was asking is, if that's where we're going, because clearly, that's where the science is.

In this case, the science is ahead of our plan, instead of behind it. But that's where I think a lot of the excitement is, on the research front, is not so much on what Sally is doing, which is kind of behavioral pheno-typing, but developing very careful, either cognitive or bio-marker kinds of tests that could be done in a large population, as a screening test.

But I just don't think that that's ready for prime time.

(Simultaneous speaking.)

Dr. Insel: No, this is eye-tracking, cognitive --

Dr. Koroshetz: Eye tracking?

Dr. Insel: -- it's social engagement measures, that look pretty exciting.

Dr. Dawson: Yes, but again, I think we're getting -- it's going to take a while to get this sensitivity and specificity of those kind of measures, to really map onto, you know, as a screening.

But I agree, that that's the future, but --

Dr. Johnson: And that's why I don't think the objectives would change in any way, as a result of the research, but I do think it's important research, because it does challenge current thinking, in terms of the different ways in which autism might appear early on in a child's life.

And so, I did note that in

something that should be included in this year's updates, and then also -- and I think you noted this, as well, Coleen, the research that looked at extremely pre-term babies as at risk for autism, and that is an indicator that should be taken into consideration when thinking about tracking children and later, testing them for autism.

Then also, there was a research study in the screening, at pediatric practices, and how that study --

Dr. Dawson: Yes, that study, right.

Dr. Johnson: Right, I thought that was also important, and I think we mentioned this earlier, the research on the genetic, the chromosomal micro-array, and I wasn't sure how that could be incorporated, but it seemed important.

Dr. Dawson: So, I had, based on that, because, you know, there has been a fairly substantial paper this year, that

recommended that as part of the diagnostic, that all children have chromosomal micro-array.

I thought that there were two objectives that kind of came from that. One is to conduct at least one study, to determine the yield and clinical utility, for example, predicting comorbid conditions, et cetera, of chromosomal micro-array genetic testing, for detecting genetic diagnosis of ASD, in context of a clinic based sample, consecutive referrals. That's never really been done, right, and that's critical.

I mean, right now, it's almost theoretical, right, we don't know. It's a nice recommendation, but if you actually use this, as a part of a diagnostic assessment, what is the yield and also, what does it tell us about course, and comorbidities, you know, prognosis, response to treatment, all of that, right.

And then the second, I think

that's in parallel, is to conduct at least one study to examine the attitudes, needs and parent -- of parents of children with autism, and persons on the autism spectrum, regarding the need and clinical utility of genetic testing and genetic counseling.

I think that, you know, that's a very important study to do, too, because I think there are a lot of ethical and sociological issues that go along with those kinds of recommendations. So, those were the two that came out of that.

Dr. Koroshetz: And the other thing, so, we -- I wasn't quite sure, but it sounds like the 2009 advances were not in the original plan.

So, there were -- so, I think that we should go back into those, too, if we're going to add -- so, I have little hand-outs for people. These are the 2009 advances, and I tried to break them down into questions.

In terms of question one, there

are a couple of other things that were in the 2009. So, there was the -- let's see, the -- the Trevelyan study. There was a study on racial -- there were two studies that looked at racial disparities.

One of them was a large study, showed that diagnosis was delayed in females and black children. There was another study shown on the black children, they were less likely to be diagnosed.

And so, I thought that those two were important, because that was in the plan, from the racial aspects and so, I think we can incorporate something that's been learned from that.

Mr. Ne'eman: And we should recognize that there are a number of situations here where we mentioned socio-economic status and racial and ethnic diversity, but leave out gender, and certainly, you know, you just cited a study and there are a number of others, and we're

received public comment that experiences and the access of the diagnosis of women on the spectrum and girls, represent a fairly crucial area.

So, that may be another area where we would like to make an addition.

Dr. Koroshetz: Exactly, so, it's stated that -- you know, maybe a culture is such that a shy girl is thought to be fine. A shy --

Mr. Ne'eman: A shy --

Dr. Koroshetz: -- little boy is thought to be, you know, in trouble. So, that's a good point.

Dr. Johnson: This is Jennifer. I thought with the changes that we made last year, we tried to -- and maybe -- and I think this was one of the questions that I raised, when were looking at this chapter is, maybe there needs to be more specificity in who we identify, in terms of disparity, because I know the issue of identification of girls came

up last year, gender disparity.

Again, maybe it just needs to be more specifically stated, so people understand that that's included, in terms of looking at disparities.

Dr. Boyle: And we, in our rewrite, tried to do a little bit of a tweak of that. I know we're going to -- we've decided not to go back and rewrite the objective, but just to --

Mr. Ne'eman: Well, we have a few areas here. I mean, in the short term objectives B and C, and I think there are a few others here, we don't mention gender and in C, we don't mention age.

You know, I personally think it makes sense for us that, just generally include age and gender, whenever we're talking about disparities.

So, if we can make that broad decision, across this chapter, even across the scope of the Strategic Plan, I think it would

be a powerful statement, of our intentions for inclusion.

Dr. Boyle: We could say that in the background, based on the accumulation of information from 2009 and 2010, and applying that, disparities.

Dr. Johnson: Right, yes.

Dr. Koroshetz: And the other one was that, you know, the study of the general maternal age, in California, that study, I think is --

Dr. Insel: Would that be a big enough effect size that you'd want to tell parents that that's the reason why they should be concerned?

Dr. Koroshetz: Well, I had that question, and in someone's pros, they mentioned high risk kids, and they mentioned--

Dr. Insel: So, that would be Chapter 2? I mean, I think the next chapter will deal with, what are the risk factors of--

Dr. Koroshetz: Oh, okay.

Dr. Insel: -- I think we've been talking about a real risk factor and maternal age. But this is really population based information.

That's why in the original formulation it was mostly about screening and developing screening tools to do large population based studies, think about PKU, or something like that.

Is there something we could put in place that will pick up -- that will increase detection in the whole population? That's why they have to --

Dr. Boyle: I think the disparity is, it's still important, obviously, with respect to the early identification and screening.

Dr. Insel: Right.

DR. Boyle: I think that is --

Dr. Insel: That's a population issue not a risk issue.

Dr. Boyle: Yes, right.

Dr. Insel: So, that's why they separated it from the parental age, which is, I think, a risk issue, not a population issue.

Mr. Ne’eman: I'd like to call attention to gaps, and the one, I think Jennifer already raised, which was, you know, we have not seen any serious funding or any real findings, in regards to ethical considerations, in respect to genetic testing and other diagnosis and screening processes.

So, I think it might make sense for us, particularly since we are seeing some fairly significant advances, in regards to genetic research, to include the new short term objectives, specifically around those lines.

And I'll hold off on the other gap, until we get a chance to discuss that one.

Dr. Insel: Yes, I think that's a great point, Ari. This is Tom. It may be that part of what the Committee was thinking

was that we could leverage all the work that's already been done by NHGRI in what's called their ELSI initiative, ethical, legal, social implications of genomics and genomic research.

The advantage of having Alan Guttmacher on the ACC is, that was a lot of what he was in charge of, when he was Deputy Director at NHGRI, and he may be able to help us to think about how to focus this specifically on autism. It was not in the plan before, and yet, as genetics -- you know, if we're starting to talk about genetics as a screening tool, this becomes -- we know enough from what NHGRI has done, to know that's probably an essential piece of whatever we put out there, and it needs to be thought of, in the context of autism.

Dr. Dawson: So, that's why I did add that objective, right, in parallel with the idea of trying to look at the clinical utility and prognostic abilities of that kind of genetic testing, to be used in a clinical

context. Yes?

Ms. Redwood: No, go ahead, I'd just like to --

Dr. Dawson: This is a little bit of a change of topic, so --

Dr. Dawson: I was wondering, circle back to what you said earlier, Tom, about finding something similar to PKU, to do screening, and I do think there are some opportunities that are there, that we could -- we've got to first, replicate, like the study that came out by Yap, that looked at these urinary metabolites that were very different, and that we need to replicate that, because that does provide an opportunity for early screening for risk, and the same thing with oxidative stress and low glutathione levels.

If we can identify those children at birth, who already are under oxidative stress, have low levels of glutathione, we know they're not going to be able to effectively deal with environmental toxins and

the parents can be counseled, to please, you know -- clean out your home, don't -- make sure there is not lead or different chemical contaminants in the home, and I think we could start replicating those studies and doing that now.

Dr. Insel: So, I think what you're -- if I think about this more generally, it sounds like objective here is shifting a little bit, from where we were two years ago, which was really, kind of epidemiology, based on clinical features, to now, thinking about whether genomics or some metabolomic measure, trying to come up with bio-markers that could be used for screening, at a population level.

There is a lot in that, and I was just at a meeting yesterday, with FDA, around how they -- they're about to put out language on what they will require to qualify those kinds of bio-markers. That will be out, I think, very quickly, very soon.

But as a goal for the Strategic

Plan, when -- I mean, we're talking about trying to get ahead of the curve. I mean, isn't that one way where we could establish, I mean, you know, put a stake in the ground, someplace a little bit ahead of where I think most of the field is right now?

Dr. Hann: It's there, or part of that language is there.

Dr. Insel: Where is that?

Dr. Hann: So, I'm looking at the long term objectives in Chapter 1. So, pick what version of Chapter 1 you would like, because this one didn't get tampered with.

It's long term objective A, and it's to identify behavioral and biological markers that separately or in combination, accurately identify before age two.

Dr. Insel: Okay, let me --

Dr. Koroshetz: So, where are we? So, I would resonate exactly with what -- with what is said, that the issue with the -- the issue we are at now is, that we have a lot of

studies, and they have a lot of reports, and in the field, like this, like any of the field, the next question is how do you validate them?

So, the replication is really, the critical point, because otherwise, you end up with a whole bunch of stuff and it just is useless.

So, some way of going, when somebody publishes like this, you know, to replicate it and then validate it, because that's what the FDA will probably be thinking, you know, what are the steps, to qualify for bio-marker, and the problem with -- there is lots of bio-markers, the problem is, they're useless, because no one validated them.

So, I think that -- I was thinking the same thing, that this issue of replication and validation really is what you are investing in the bio-marker identification for.

So, I would -- I'm really with the

idea of, that is a gap, and now that we have these reports, how do you actually go to the next step, replication and validation?

Dr. Insel: So, it would be okay to say that? I mean, maybe that would be the language.

Ms. Redwood: And I think that's something that we should identify now, as critical to get an answer to, as part of an RFA or some, you know, special study section, to accomplish that objective.

Dr. Insel: It would be important, too, to standardize the measure in some way, so that it becomes more than just another one-off study, because that's, I think, what we've struggled with so often, particularly on something like the metabolomic measures, where you -- you know, the reason why FDA has really had heartburn around this is that it's so difficult to compare across studies, because the measures are so different.

So, we do need to make -- and

that's a little bit in the Chapter 7, the standardization of measures, which will be really important.

So, it sounds like this is building on a -- the objective that's there, to simply say that well, progress has been made. There is a need to replicate and leverage what has already been done. That's different, though, than the C-

Dr. Dawson: So, I think we also -- but also, I think that it does relate, in some ways, because -- so, for example, if you think about the micro-array testing, and you're coming up with risk markers, some of which you can't really interpret, unless you have a pretty large data base of how often do these -- are these specific to autism, right?

And so, for example, the work that David Ledbetter is doing right now, that's funded through the stimulus funding, right, where he is actually developing a very large data base, with lots of different conditions

of how often you see these different, you know, C and B's, and rare variants and so forth, and without that kind of a comprehensive data base, it's very hard to interpret or give information to parents about the meaning of it.

So, it really does have to do with validation, standardization, but you know, again, it requires collecting that data in the clinical context and then, looking at that in reference to it, a standardized data base.

Ms. Singer: I just wanted to add that one thing we did last year, is we pulled out all of the infrastructure issues, including replication, and moved them into Chapter 7.

So, I think we should just -- as we're talking about some of these issues, we should just see if they are in Chapter 7, because I know we have an objective specifically about the necessity of rapid replication, and that there should be funding

for that.

Now, I don't understand how much -- it's seven -- well, we pulled it out, and I think that one came out of -- I just want to see if -- where the funding is, because this is all in different places.

So, seven efforts actually won, where there was no funding. So, that is something that I think we should flag, because it comes in every chapter, this need for these rapid replication, and that was one that -- were there was nothing.

Mr. Ne'eman: So, I think to put out there, quite frankly, and we're talking about an objective around bio-markers, you know, the question that arises, do we talk about the inclusion of ethical conservation, as -- objectives, you know, dependent clause, within the objective around bio-markers, are we to talk about that as a set objective?

I think there is something to be said, to really looking at that as a separate

objective, because it would seem there is something of a conflict of interest, if you're going to people who are against bio-markers, and presumably, are more likely to be thinking about how this is going to be used, and one does not do research, unless one, you know, thinks it's going to have some net positive to society, and then you ask them, "Well, you know, how could your research have some potentially negative ethical implications?"

We hope every researcher gives that fair consideration, but it does occur to me that you know, in the interest of child stability, and clearly, we're going to need to look out then on this discussion, it makes sense that a separate objective around ethical considerations that will give this critical area an independent look.

Dr. Insel: That's very much the way Geri had framed this. So, she has two separate objectives. One on using micro-array technology as a screening technique in clinics

with ASD kids, or developmental disabilities, and a second was to look at the attitudes, needs and concerns --

Dr. Dawson: We could add ethical issues.

Mr. Ne’eman: I'm sorry, what was the second? I didn't catch that.

Dr. Insel: Geri, do you want to --

Dr. Dawson: Well, so, the -- Ari, the second objective was to conduct at least one study to examine the attitudes, needs and concerns of parents of children with autism and persons on the ASD spectrum, regarding the need and clinical utility of genetic testing and genetic counseling, as part of the diagnostic assessment.

So, we could certainly add ethics, ethical issues, but that's what I was trying to capture, when I said attitudes, needs and concerns.

Mr. Ne’eman: Well, I think that's great. I mean, I think if we can use -- and

Tom mentioned this, a specific term of art, ethical, legal and social implications, in addition to attitudes, needs and concerns, that would be very positive.

Dr. Insel: Yes, that is the term we use at NIH.

Dr. Dawson: Yes.

Mr. Ne'eman: And I really appreciate you including that, Geri.

I guess the only thing I would add to modify that somewhat is, I would broaden that, to include, certainly, genetic testing is the big one, but there are others, all bio-markers and I would -- let's see, yes, I think that was the major thing I was going to call attention to, to ensure that we're including all bio-markers, in respect to that.

Dr. Insel: The first objective you have, the new one, Geri, does that --

Dr. Dawson: Well, okay, so, this one, basically, I think there is a lot of interest in doing international work on

screening, because -- and diagnosis, because of -- it allows everything from new opportunities for research, to comparative epidemiology, etcetera, and the issue is that when you go into these countries, they don't have well baby check-ups or developmental pediatricians. So, all of the mechanisms and models we have, you know, for screening and diagnosis, when you move into developing countries, are not appropriate.

So, the idea here would be to fund at least one study, to test a model for screening and diagnostic methods that could actually be integrated into existing practices for screening in, you know, under-served or under-represented communities internationally, and particularly, internationally.

So, for example, in other disease areas, you know, they have to basically -- or they tend to use community workers to do screening and diagnosis, rather than -- but we had never really tested or validated any

kind of model like that, and it's a huge barrier to doing that kind of research.

Dr. Insel: So, was the main interest there the international?

Dr. Dawson: It is, although I think it would not a bad idea to consider it in under-served rural populations, because they actually, in the United States, face the same issues, that there just aren't the levels of expertise in the community to use the kind of models that are out there, that are being suggested by the American Academy of Pediatrics.

I mean, they are great suggestions, it's just impossible to actually screen kids out there, in that way, because there is just not the technical expertise available.

Dr. Insel: That goes back a little bit to Coleen and Jennifer's point, as well. They talked about how the AAP recommendations are less successful at making referrals to

early intervention or --

Dr. Dawson: Right.

Dr. Insel: This is from the King paper.

Dr. Boyle: Right, exactly, and so --

Dr. Insel: Can those two things be put together --

Dr. Boyle: Combined, I think so.

Dr. Dawson: Sure.

Dr. Boyle: Because we had -- we added the --

Dr. Dawson: That's a great idea.

Dr. Boyle: -- in collaboration, we added a new objective there. I think we can put those together.

Dr. Johnson: Well, and I guess for me, I don't -- I was -- I guess I didn't see, necessarily, a need to add an objective because there are currently -- or we added them last year, and specifically, short term objective C, around looking at health

disparities and accessing early screening and diagnostic services.

So, to me, I felt like that was being addressed under the objective, but maybe it's just written to broadly, to get at some of these, you know --

Dr. Dawson: You could add to that objective, by saying, "Including testing models of," because I think that's the issue, rather than just assessing disparities, it's really, well, what models could you use, that could address the disparity?

Dr. Insel: Yes, so, this gets to -- when we first developed this, and we had a lot of discussion about what was this first objective all about, and where we ended up, we were really talking about screening instruments and that what -- at least at that time, well, I don't know if it's still true, the field lacked the instruments needed to do population based screening, even at a behavioral level, at a clinical level, for

ASD. Is that still true?

Dr. Dawson: Oh, yes.

Dr. Insel: A rapid, efficient way to do it.

Dr. Dawson: Right, but it's -- yes, it is -- it's a little different, what we're saying here, but it's very closely related, in the sense that I think we're really talking more about, you know, work force and skill level and you know, these issues that other diseases have really routed with.

Dr. Insel: So, it feels to me, just from reading your comments and hearing this, that what would be really great here, would be a paragraph that sort of said, "This is what we've done," from the -- and the American Academy of Pediatrics, and from research that we've seen already, "but there remains the following," that you know, is a new opportunity that we need to focus on, and then you've got, I think it's three

objectives, if I'm reading this right.

So, you've got the ethical, legal and social one, and then you've got one around genetics/bio-markers, and then you've got this other piece, which is, how to take the screening efforts that we now know how to do, and disseminate them globally, under the minorities, under sort of communities, all of that. Is that -- are those the three?

Dr. Boyle: And there's also a sort of understanding that barriers, in terms of -- both from a parent and a provider perspective, actually getting action on that, and getting things to move along. So, I mean, I think those are the issues.

Dr. Johnson: And I think also, cultural.

Dr. Boyle: Yes.

Dr. Johnson: Is an important consideration, and you commit barriers.

Dr. Insel: Walter?

Dr. Koroshetz: I don't know, I'm

not sure if it's correct, but are we at the stage where we can say that we're getting behind the Academy of Pediatric guidelines and now, we're -- now, the object should be to get them into practice and --

Dr. Dawson: Well, that's one issue, but I think that actually, the guidelines are not feasible in a lot of -- in some of the developing countries, for cultural and/or infrastructure.

Dr. Koroshetz: Well, let's keep it to the U.S. So, the way I read that article in the U.S., the parent forms -- surveillance forms, they got, but after that, everything broke down.

Dr. Dawson: Right, right.

Dr. Koroshetz: So, it seems to me that one -- if you wanted to, you could just focus on the U.S., saying, "Okay, you know, we got this tool," we're behind what the pediatricians are wanting, but it's not -- it needs a culture change in practices, to get

the kids cared for, after they get the surveillance.

But that would be different. That would be saying, you know, almost dropping out of this one, saying we did that, we have this now, let's make it work.

Dr. Dawson: Well, there's a little more work to be done.

Dr. Koroshetz: Okay, all right.

Dr. Dawson: On the recommendations --

Dr. Insel: So, that's what I was asking, if we could capture that in some language, I think for all of us, it would be helpful to get clear on -- for this first piece, about, when should I be concerned, the whole screening, population based element.

What's the next step here? What do we really need, and what's missing in the current instruments? Ari, go ahead.

Mr. Ne’eman: Perhaps -- I'm sorry, I thought it was muted. Let me put something

out there on that.

It would seem to me that instead of looking at not exactly new research, but the -- only about a year old, we may want to think about doing a version of the study that was done in the United Kingdom, by the National Health Service, to identify the prevalence of ASD in the adult population, and you know, there were certain challenges with that study, but I think it yielded some interesting information, and it would be very valuable if you could include an objective to really do the same, in the United States.

That would give us very useful information, and if we're talking about where the gaps are in population level health surveillance, in regards to ADS, I think adults are a critical component.

So, I don't know if this goes within question one. It would seem, there is a connection, or in question six, but I'm going to put it out there, particularly given

that there has been research being done around this in the United Kingdom and it would make sense to get similar data for the United States.

Dr. Insel: I think the heads are nodding here, about this, Ari, thinking that it's more of a question six opportunity, than a question one.

Ms. Singer: Or really, a question seven, which is surveillance.

Dr. Insel: Yes, but it's a great point to make because that is clearly a gap that could be followed here, and we've already got this very interesting project to lead us from the UK.

Anything else on question one?

Dr. Johnson: Just going back to our conversation about this whole issue of the screening process and looking more closely at that.

Is it a matter of revising then, what with the new objective C, last year,

short term objective, and just specifying a little bit more on what is meant there, because that is the one that C-

Dr. Insel: Health disparities?

Dr. Johnson: Right, getting at this notion of disparities and screening, so do we want to keep that in or just again, offer -- or have more specificity in that objective, to get at some of these issues that we're talking about?

Mr. Ne'eman: We need to capture gender there. So, the question arises, do we just say, in the addendum, "Well, this objective now includes gender," and you know my concern there is, it runs the risk of just somebody is just reading the Strategic Plan and doesn't truly explore the addendum, because they only are going to interpret the new objectives in the addendum as some priority, so that could miss that IACC is interested in looking at gender based disparities and diagnosis and service

provision.

Dr. Johnson: This is Jennifer. There is the short term objective B, that looks C- it addresses more, the looking at specific populations, and objective C is really addressing the issue of accessing screening and diagnosis services.

Mr. Ne’eman: Well, my apologies. I thought you were referring to B. So, I'll hold off, but after you finish with C, I'd like to raise the issue of making sure that gender is appropriately included in B.

Dr. Johnson: All right.

Dr. Dawson: I think we could do it either way. I don't think it really matters, as long as it's in there and it's called out, personally.

Dr. Insel: It wouldn't hurt, though, you know, if we feel like this is an area that isn't getting addressed, although there are a couple of papers now, on the health disparities issue, maybe not so much on

the mechanisms, but certainly, on the delay in diagnosis of --

Dr. Dawson: But they were -- they're more on detecting the disparities, rather than testing the solutions.

Dr. Johnson: Exactly.

Dr. Insel: Right, and so, it wouldn't hurt to put in an objective that tries to capture that, and flags it as a continuing problem.

Dr. Johnson: That's the big issue.

Dr. Dawson: Yes, okay.

Dr. Insel: Is there anything else on Chapter 1, before we move on? Della?

Dr. Hann: Procedures, sorry, to be -- that note again, but how -- now that we've had the discussion, in terms of what elements might be included in the addendum, how are we going to proceed in producing the addendum?

In years past, it's been basically, the responsibility -- last year, it was the responsibility of the people on the

Committee, to -- just as you've been doing, to do that.

But since we've got several people working on this particular one, it might be useful to identify sort of a key person, to draft it and then circulate it, kind of thing. So, I just offer that as a potential.

Mr. Ne'eman: Are you willing to take our comments?

(Off the record comments.)

Dr. Insel: Yes, so, Coleen, could you be the --

Dr. Boyle: Yes, that's fine.

Dr. Insel: -- and then maybe you could just go to the sub-Subcommittee, in this little group.

Dr. Boyle: That's fine.

Dr. Insel: And then, and Walter, you're part of this one.

Dr. Koroshetz: Yes.

Dr. Boyle: Well, you all are.

Dr. Hann: Do you want to clarify

which people need to get this Chapter 1 for review?

Dr. Boyle: And Sarah, if you could send a form out --

Participant: Yes, I'd be happy to do that.

Dr. Hann: And this time, we would like you to follow the format. It wasn't clear before. You had every right to say that, but this time, we will have a format that we will ask you to follow.

The people that I heard, that have been identified to work on this particular one are Coleen Boyle, Jennifer Johnson, Geri Dawson and Walter Koroshetz.

Dr. Insel: And what we'll do -- I mean, you've got -- I think you've got all the elements here, it's just putting them into a document, and we'll give you a sort of template of a half-page or whatever it is, that will kind of capture both, the language -- anything that's `what have we learned', as

well as the objectives. Walter?

Dr. Koroshetz: So, just one question one, I don't know if, I don't know about the -- but the gap areas, are we going to talk about?

So, if you look at the portfolio analysis, on one of the -- we have two studies for early diagnosis, treatment, intervention. There's no studies in any -- disparities, there's one study.

So, I thought that those were the things that we should underline as areas in the plan that just doesn't seem to me --

Dr. Boyle: So, where did you find that?

Dr. Dawson: In the portfolio analysis.

Dr. Boyle: The portfolio, okay.

Dr. Koroshetz: Yes, it's going to be --

Dr. Insel: It's in the appendix, right?

Dr. Dawson: Yes, they don't have it.

(Off the record comments.)

Dr. Insel: So, this is the page -- the first page of Appendix A.

Ms. Singer: I think you have it.

Dr. Insel: And these are the disparities, which is kind of what we talked about. There's only one study, early diagnosis and early intervention, outcomes, nothing, for those two.

This is where it gets a little tricky, because we have 38 projects that are not specific to any particular -- I mean, we just don't know, you know, how -- whether that's actually the case, but --

Dr. Boyle: So, do we want to capture that somehow, in the format --

Dr. Insel: Well, we'll be able to look, when we get the --

Ms. Singer: I think you have to look at them.

Dr. Dawson: Yes, look --

Ms. Singer: And see what's in that bucket.

Dr. Insel: And then the other request would be to go through, just -- in this case, I don't think there are very many public comments or RFI comments.

But those are also organized in this way, so, if there's anything there, it would be great to identify something that we heard about, that you think needs to be recognized in this.

Okay, can we go into Chapter 2, so, we -- starting now?

Ms. Redwood: I was just going to say, there was some things missing, in the RFI. I know that the SafeMinds have -- and I haven't seen a new one sent out yet.

Dr. Hann: That's correct. We've gone back to the drawing board. Thank you for drawing that to our attention, that that one was missing, and we have identified some other

glitches, and so, that's why it's been delayed.

But it was not systematic, by any means. It was random.

Ms. Redwood: So, when will we -- because I think it's important to have captured all the RFI comments, when we look at these. So, when do you think that will be ready?

Dr. Daniels: I believe within the next few days, that should be available. We can just -- would we send the -- just the missing information separate or --

Dr. Insel: And the, yes, the RFI is in a format that is pretty easy to ascertain. Most of what's in there, you can get quickly.

Ms. Redwood: Okay, there were just some things missing, that was --

Dr. Insel: Okay, Chapter 2, we've got --

Mr. Ne'eman: Before we move on,

Coleen, can you loop me into the discussion on language around Chapter 1, as well?

Dr. Daniels: Sure, yes.

Dr. Insel: Yes, actually, I assumed, everybody will ultimately -- everybody is going to see this.

Dr. Hann: So, right, so, while we're on process, we will send you the short template, to help structure it. You all will work on it, and be sure to copy Susan and myself, when you circulate it around.

I think the question will be, Tom, in terms of a meeting on the 22nd, if any -- if the Subcommittee feels is has things to take forward on the 22nd, or the 22nd will simply be a description of the process and the decisions that you've made, to date.

So, that's going to be something to think about. So, if, for example, for this one, if you all felt that you basically had a good draft, that you wanted to take forward for the 22nd, that we could do that,

potentially, and then let the entire Committee see it, at that moment in time, or -- you know.

Dr. Insel: We could shoot for it. Does the group want to have a chance to look at it, as a Subcommittee, before it goes to the full Committee?

Mr. Ne'eman: That's probably a good idea.

Dr. Insel: What is the -- heads are nodding here.

Dr. Hann: The timing might be a little off.

Dr. Insel: So, this could be -- it could be, but it could be that, Coleen, you know, let's say, you get something in pretty good shape, a week before the 22nd, if it goes out, and even if there were comments, you could take the comments, as well to the full IACC.

Dr. Hann: Right, yes, I think we would -- realistically, we would be aiming for

next Friday, which is the 16th, I think, next Friday, to have a draft that could be circulated to the Subcommittee, and then we can see from there, if it's something that can go forward to the full Committee, on the following Friday.

I'm also just thinking of the meeting preparation materials and so forth, to give us an opportunity to make sure we can catch up with you.

Dr. Insel: Well, we're one-seventh of the way through. Actually, less than that, because we have the prep function, and we have an hour left.

What I'm going to suggest is that we go into Chapter 2, and we just continue to plug through here, until we get our rhythm and figure out how to get this done. We do have to end at noon.

So, let's move on. We've got four different people who have contributed to Chapter 2. Does anybody want to start off and

just talk about the suggestions that they felt would be good for, how can I understand what is happening?

Ms. Singer: I'll start.

Dr. Insel: Alison?

Ms. Singer: I focused specifically on the portfolio analysis here, which I think the most concern was the fact that the vast majority of studies and dollars were not specific to any objective. So, I think it really speaks to the need to get that specific funding data.

I also -- when we had the scientific workshops last year, when we updated the plan, I co-Chaired the Chapter 2 with Dave Amaral, and all of the members of our Committee that put together our presentation were almost unanimous in the need to focus on biobanking and to leverage the new technology, with regard to skin fibro-blast and pluripotent stem cells.

I know we're looking at 2009 spend

and 2010 objectives, but if we look at what's happened against those objectives, it's really a little bit disappointing.

The bio-bank objective specifically was moved into Chapter 7 and I think that's really an area where we want to draw additional attention. I don't think enough has really gone on there, and that, I think, speaks to the issue of having to go out into the community and make sure that people are aware of this.

This is a big scale project. It's definitely an infrastructural investment. I don't know who would take something like that on. But it was clearly called out by all of the members of that group, that that was an area that we really needed to make an investment, and that really hasn't happened.

So, that would be my main point, and I'll wait until everyone else has had a chance to speak.

Dr. Insel: Okay, but just to

clarify, since that's in Chapter 7, as an infrastructure project, does it also need to be in Chapter 2, because we moved it last time, or is it just because we wanted to feature it, in its own place, that was actually the main reason for creating this infrastructure project.

So, are you suggesting we move it back or what would you like to do with it?

Ms. Singer: We can talk about it again in Chapter 7.

Dr. Insel: Okay, okay, but I hear you.

Ms. Singer: But I just wanted to raise that as something that when we did talk about Chapter 2, it unusual that there's unanimity in the Subcommittee and there almost universal -- I mean, that was really -- everyone agreed, that was key, and it really hasn't gotten a lot of time or attention.

Dr. Insel: Good point, maybe worth bringing to the IACC as a continuing problem.

So, others? Walter, Lyn, who else? We've got --

Dr. Dawson: Marjorie.

Dr. Insel: Marjorie, you're on this one, as well?

Dr. Solomon: Yes, thank you.

Dr. Insel: So, comments on Chapter 2, particularly if there are new objectives you think need to be put in here.

Ms. Redwood: Tom, when I went through this, I added in more -- some of the new research, on the very first page, that's just come out this past year, that I felt was important, so, possibly, that could be incorporated into what we'll be doing for the update.

Dr. Insel: And Walter did that, as well. So, you gave us a bunch of new references, to --

Ms. Redwood: Right, and then the other section that I thought was important to add here, was the section on metabolomics, as

being a new area of research that has unique opportunity, to look at genotype, as well as -- genotype, phenotype and genographic type, environmental interactions.

Dr. Insel: I think that was in there before. The short term objective A was metabolic or immune system interactions, and then we had a new objective that -- where was that, metabolic and mitochondrial dysfunction and there was one place where we actually talked about using metabolic markers.

Ms. Redwood: It just wasn't reflected in the `what do we need' section. So, I was trying to explain it a little bit more, so, when people saw this, they could see what the unique opportunity was. Do that make sense?

Dr. Koroshetz: The metabolics field is really progressing substantially, in certain areas. So, I mean, it's reasonable to think about. It's got a lot of control problems, but certainly, cardiac care is,

they've hit a couple of home-runs.

Dr. Insel: Just as a point of reference, we tried to float a large metabolomic project through the Foundation of NIH for bio-markers for, I think this was depression.

Dr. Koroshetz: Yes.

Dr. Insel: And nobody would invest in it. It went to something like seven different companies, which is what NIH does, and it's an interesting way of seeing what people think is ready for investment.

So, there is a lot of concern still, about the concern and the technique, but it's -- you know, what's wonderful about it is, it's one of these omics. It's a discovery tool, and so, you'd be hard put to argue against it, at this point, since it's not hypothesis driven. It's just putting something out there, to try to see what may show up as being different in any C- with any phenotype.

Dr. Koroshetz: The thing I've seen that -- there was metabolics conference at NIH, was, do you have like, a test that you can do, in certain populations, and then you check the metabolites during the test, or before and after, and the patient serves as their own control.

The best data was when we studied glucose tolerance testing, and they found metabolomic profiles that were more predictive in diabetes than the glucose or the insulin. But, you know, it's real focused.

Dr. Insel: Right, so, there are seven metabolomic markers that are being developed as a new bio-marker assay, as an early predictor of Type II Diabetes.

So, there are areas where this has worked. CNS just has not been as -- so far, as productive. That doesn't mean that it won't be. I just -- I think that these discovery tools like this, that's the state of the art, you know.

An area like this, we could be out there fishing, for what might show up, whether it's immune-markers or metabolic markers.

So, I just thought it was in there before. So, if it isn't, and I can't find it quickly here, just -- but I'm pretty sure there was some language that mentioned bio-markers, including metabolic bio-markers.

So, it's -- but I see your point there. So, you were wanting to put in -- what it says is multi-disciplinary assessments of brain imaging metabolic and immune markers, micro-biomics, and you thought we needed to add metabolomics, and I thought that metabolic markers was metabolomics. So, I'm not sure it's worth -- if people -- other people think that that would be --

Ms. Redwood: I just was thinking it should be identified as a new emerging area that shows promise, in developing bio-markers.

Dr. Insel: Okay.

Ms. Redwood: And so, that's why I

put it in there, in terms of whatever we need.

The other thing that I added, in terms of new objectives was to just flush out a little bit, this whole idea of regression, because I think there is an opportunity there to really intensively study children during regression, to understand what is going on biologically, during that time of regression, and this came out of the workshop that we had on environmental factors, too, as one of the opportunities.

So, do I try to identify the trouble during that opportunity that I think is important to research further, is that a fever, but fever associated, not only with regression from the work of Shoffner and mitochondrial disorders and autistic regression following fever, but also, improvement during fever, because there are children -- you know, it's documented now in the literature, who have fever, and a lot of their behavioral abnormalities disappear, and

I know that happened with my son, during times of fever.

And so, that sort of tells me that there is some promise there, that these pathways and networks are still functioning, if they can recover during fever, then, you know, they regress back into autism afterwards.

So, I think that's an opportunity, that we should --

Dr. Dawson: Is there an objective that has to do with understanding the role of the immune system, and could that be incorporated into that, as a -- sort of a sub-strategy?

Dr. Insel: It's a system --

Ms. Redwood: There are several that have immune system and immune system interactions --

Dr. Dawson: And so, you could certainly add the fever to that, right, and at, particularly, the role of fever as either

being associated with regression and the -- well, I guess it couldn't be and/or, but or, just or --

Ms. Redwood: Yes.

Dr. Dawson: -- or improvement.

Ms. Redwood: So, I guess we could accomplish that by specifically identifying. I just think that that's a unique opportunity, but may not -- if somebody were to read this and just looked at immune system, they might not be aware of the research.

So, that's why those were -- that was one of the things I highlighted, as well, trying to see --

Dr. Insel: Okay, is there other comments on Chapter 2, other --

Dr. Solomon: Yes, this is Marjorie, just in that --

Dr. Insel: Marjorie, you're dropping in and out.

Dr. Hann: Marjorie?

Dr. Insel: We lost you.

Dr. Hann: You're not there for us.

(Comment by operator.)

Dr. Insel: Okay.

Dr. Hann: Thank you.

Dr. Insel: While we're waiting, Ann Wagner, do we have -- is there a metabolomic project now, that we're supporting?

Dr. Koroshetz: The gap areas for Chapter 2, I thought were the -- in the neuro-development of females with ASD. Risk factors have shown its regression and increased awareness in brain donation. But if you look at the portfolio, those are the ones that --

Dr. Insel: And this is what we're limited to saying, not regression.

Dr. Koroshetz: Right.

Dr. Insel: Okay, so, that's a good reason to feature this in the new section.

Let's wait a moment for Marjorie to come again and finish.

Dr. Solomon: Here I am.

Dr. Insel: Okay.

Dr. Solomon: I'm back again.

Dr. Insel: All right.

Dr. Solomon: That was the iPhone 4, you know, dropping calls. But the comments that I was making is that I found that absent from this chapter, was really a more serious and foundational look at structural and functional neuro-imaging, and how they might help to explain biological differences.

You know, Cindy's paper, that was being accepted as one of the advances in one of the examples of this kind of work, but I don't think that we give a lot of serious treatment, to looking at either structural or functional imaging, and what's going on, you know, both early in development, in adolescent development and then, in adult development.

So, I found myself a little bit at a loss for how to add that into the chapter and personally, I think that could be a reason why there is such a mismatch between the

portfolio analysis and what we're funding.

Dr. Dawson: I was just going to say that.

Ms. Redwood: Yes, I agree, Marjorie, I think that's probably where a lot of that `other' category falls.

Dr. Insel: Yes.

Ms. Redwood: Is structural imaging.

Dr. Insel: Does the imaging go into risk factors or does it go into Chapter 3?

Ms. Redwood: It's probably in the `other'.

Dr. Hann: It's probably sitting in the `other'. I mean, I don't know --

Dr. Insel: The `other' in Chapter 2?

Dr. Hann: Correct, I'll bet that's where it is.

Ms. Redwood: Yes, I think that there is quite a bit --

Dr. Insel: So, the longitude and imaging, there are a number of people who are doing now, longitudinal imaging of kids at risk?

Dr. Hann: Yes.

Dr. Insel: That's not --

Dr. Hann: Don't know, but we'd have to look, for sure.

Dr. Koroshetz: In the Courchesne studies, I have that in this chapter, as an update.

Dr. Insel: Right.

Dr. Koroshetz: Of what we've learned, but we've could, certainly, you know, amplify that, you know, this is the type promise in the area.

Dr. Solomon: Yes, I would be --

Ms. Singer: It's interesting, though, because we did talk about this and we said that that's a technique, and therefore, it's not necessarily an objective, nor our objective is not to utilize a technique.

So, we didn't put it in as an objective, but it probably does account for a lot of that `other' in there, and I know that in a lot of the titling of these studies, it does say function, the fMRI study, and so, maybe that's -- to get that in.

We should just look at it, you know, again, it speaks to, we have to have that more detail to it.

Dr. Koroshetz: Right.

Dr. Insel: Because the -- remember, the featured questions at the beginning of the chapter, one of them was, "What is happening early in development," which is what those studies are really all about, and are there known biological differences? Could that help explain ASD symptoms?

So, again, I guess that is Chapter 2, if we don't have it in here, it needs to be captured. So, maybe --

Dr. Solomon: Yes, I mean, not only

if it's the early studies, but I think there now are a ton of, you know, cognitive neuro-sensory research, looking at the whole adolescent period and, you know, even some work starting in the adult period, that will help us to understand the development through life span, and I think that that's sort of an important part of what's going on.

I also think, Tom, your whole objective, looking at the endo-phenotypes of different disorders, is relevant here. You know, I think that we should have a point of contact, you know, with understanding the range, specifics and potentially, piece of endo-phenotypes are operating in ASD's, you know, as that will help fertilize our search for genes and, you know, our transmitter development, and you know, facilitate the search for drugs, and so forth.

Dr. Insel: Yes, I'm not sure what to do with that here, though, Marjorie. It's not -- again, it's probably a little early.

But what the AR-DOC project, which is a project about changing the way we do diagnosis, what it will probably rely on will be all of the research that's going to be in Chapters 2 and 3, that gets away from the term autism, and looks much more at dimensions of social cognition or dimensions of attention, a whole range of things.

I'm not sure that I would know how to put it in here, and it feels a little bit early. Again, that might be easier to do in 2012.

Dr. Solomon: But just to prepare, so that we make a point of contact with that, eventually, you know, just -- I think we do need to beef up the sections on just neuro-development.

Dr. Insel: Okay. So, does someone want to volunteer to help us pull those objectives together and any language that needs to go with them, along with the business about what's coming from the RFI and the

portfolio analysis, and the public comments?

Dr. Solomon: I'd be willing to help with that.

Dr. Hann: Marjorie, you'd be willing to take the lead, in terms of drafting that?

Dr. Solomon: Yes, I will.

Dr. Hann: Okay.

Dr. Insel: We'll send you the template of what it needs to look like.

Dr. Solomon: Okay, great.

Dr. Hann: All right, and the piece, the metabolomics piece, Lyn has already written a fair amount of that.

Dr. Solomon: Yes, I know, I saw that. Thank you, Linda.

Dr. Hann: Right.

Dr. Solomon: And I'll incorporate that, as well as Walter's changes.

Dr. Hann: Okay, great. The sub-group consists of Lyn Redwood, Walter Koroshetz and Marjorie Solomon.

Dr. Insel: So --

Dr. Hann: I'm so sorry, Alison.

Dr. Solomon: I'll run it by you all, and I think what was the time table, next Friday, where we want to have met as a Subcommittee, to get -- so, that we can have it for Friday.

Dr. Insel: So, before we go on, I can't remember if this chapter, since it's about risk, whether it captures the epi-genetics issues. There's a piece out in Science, two weeks ago, that shows that there are these stable epi-genetic marks that look like they're highly connective of BMI and vulnerability to diabetes, from Andy Feinberg, a person who came and spoke to the -- and it just begs the question about whether there might be something similar, that could be picked up in an 18 month old or in a 24 month old.

Dr. Koroshetz: There was a paper by -- I think that was -- with the look at

ASD, identified some abnormal methylation.

Dr. Insel: Okay. So, it's in Chapter 3, I guess, not Chapter 2.

Dr. Dawson: Are we moving onto Chapter 3 now?

Dr. Insel: No, no, no, I'm asking this -- whether this is a -- could it be a risk measure? Could it be a bio-marker? We're talking about metabolomics. I mean, this would be the other thing to consider about, or epi-genetic bio-markers.

We haven't thought about that way, because we did the --

Dr. Dawson: I sort of put it into the environmental, is where I put it.

Dr. Insel: Yes, the cool thing here, though, is that it would be --

Dr. Dawson: Be like a bio-marker --

Dr. Insel: It's like a scar, and you know, you'd know who was exposed by their epi-genetic --

Dr. Dawson: Right.

Dr. Insel: -- mark, and what we didn't realize until two weeks was the stability of some of these marks.

Dr. Dawson: Right.

Dr. Insel: And what Andy is arguing is that these might really be the way of now, not just identifying who has been exposed, but predicting who is going to go on to develop a particular disorder.

Actually, in the discussion of this Science paper, he talks about this, that this could be a very important way of developing, kind of the pre-diagnostics, or something like that.

Ms. Redwood: Tom, could that be --

Dr. Insel: It's pretty neat. He's really sort of leading this field, to help us think about the use of this as a clinical tool.

Anyway, it may be just -- if you're going to put in metabolomics, that may

be one other thing to think about. Should we -- we'll make sure you get that.

Chapter 3, should we take a look here and -- who -- let's see who we have on this one.

Dr. Hann: There is a number of people.

Dr. Insel: Lee Grossman, Walter Koroshetz, Lyn Redwood, Tom Insel. So, who wants to start off? Lyn or Walter?

Dr. Dawson: I added a bunch, even though I wasn't on the Committee, coming out of NIEHS workshop.

Dr. Hann: Geri's is number 17.

Dr. Insel: Yes, okay.

Dr. Hann: And Lyn's is in 19.

Dr. Dawson: You know, first of all, I want to apologize for looking at this over, it's a little piece-mail. You know, I was in a rush, because we had a week, and I was trying to get everything in there, figuring we would have it -- a chance for

discussion, because I think some of these could be combined, and so, it doesn't end up being, you know, such a long laundry list. So, I apologize for that ahead of time.

But so, the first concept there, in terms of the objective, is to, you know, support at least three epidemiological surveys in different populations, to really identify -- well, special populations in which either unique genetic and/or environmental risk factors could have contributed to heightened or lessened risk for autism.

So, that was one of the major strategies that came out of the workshop that, I think there was an obvious one, but one we haven't actually utilized, or called out as a strategy, and if you look, there is really some different examples of that, that are flushed out in the next objectives I list.

So, for example, clinical populations that may have unusual or high levels of exposures. So, this would now

include prematurity, maternal infection, vitamins, nutritional deficiencies, other toxins, exposures.

Dr. Insel: Then there is the prematurity paper that's out this year.

Dr. Dawson: Right, right. So, another special population, which is an `eye', is immigrant population.

So, there was a lot of interest in phenomena, like the Somali population, you know, have we really, you know, investigated that?

I know that Linda Birnbaum was very, very interested in that, and you know, do we really understand that?

But if it's not that population, are there other populations where we see either an increased or reduced prevalence of autism that could give us clues into potential environmental risk factors?

So, I think the first set are really under this issue of utilization of

special populations, to try to look at environmental risk factors.

Dr. Insel: So, were these the product of the NIEHS workshop?

Dr. Dawson: Yes, so, these are all --

Dr. Insel: So, maybe that could even be framed that way.

Dr. Dawson: Yes, absolutely, and there's a draft --

Dr. Insel: So, they're based on 2010 workshop.

Dr. Dawson: Right.

Dr. Insel: Sponsored by NIEHS. These are the priorities that were noted, as opportunities.

Dr. Dawson: Yes, definitely. Another area that came out, that I don't think is quite represented in the plan yet, is some pretty phenomenal bio-infomatics tools.

Dr. Insel: Now, that sounds like it would go into infrastructure.

Dr. Dawson: Perhaps, yes.

Dr. Insel: Okay.

Dr. Dawson: So, yes, that's fine. But I think it needs to be in there. So, just some -- you know, we actually talked about whether the science of autism, in terms of genetics, is ripe enough to use some of their databases, where you can map the genes on the specific pathways, and then the databases will tell you what environmental exposures are mostly likely to impact that pathway, and then, shines a light on particular environment, and that's very cool, and we haven't really done anything like that.

Ms. Redwood: And I think it's ripe to start doing that.

Dr. Dawson: Yes, so, then, the other, I think, issue has to do with really, moving the field, in terms of the development of vertebrate and invertebrate model systems, for looking at the role of environmental risk factors and the interaction with genetics,

susceptibility, things -- a very strong focus on that, and just some of the really innovative, even using zebra fish or other kinds of in vitro methodologies that could be used in autism, certainly, you know, even stem cells, and you know, induced pluripotent stem cells, as a way of starting to look at sensitivity to environmental exposures, and other null techniques that were talked about there, such as, you know, cell phones and passive modeling, dermal patches.

There really is, I think, in the area of environmental exposures, a lot of new technologies that could be brought to bear in autism, that we haven't considered.

So, there might be, I don't know, an objective that talks about bringing some of those new technologies, as well as one that focuses on the need to develop vertebrate and invertebrate model systems.

So, anyway, those were the general kinds of ideas that came out of that workshop.

Dr. Insel: So, how would the group feel about doing this? If we were in this new section, how -- just essentially, have a summary of priorities, rather than -- because what we've been tending to do is taking a -- three project by 2013, I'm not sure with this long list, you are recommending that.

But if you were to at least say the need for increased emphasis in all of these areas, because this, again, as you look at the portfolio analysis --

Dr. Dawson: Yes.

Dr. Insel: -- this is not an area that's gotten --

Dr. Dawson: No, I mean, it's --

Ms. Redwood: But if we summarize it, how will it be measurable? If we don't have a specific date and time, you know, I think it's going to really hurt us, when we go to measure --

Dr. Dawson: Yes, we could take it the next step further. I mean, I don't think

it would be -- I've tried to say, you know, support a study that will, you know -- for example, examine, you know, vertebrate and invertebrate model systems, you know.

Dr. Insel: So, maybe you could say, support studies in each of the following, and then might be able to --

Dr. Dawson: Yes.

Dr. Insel: Something like that.

Ms. Redwood: Right.

Dr. Dawson: Yes, that would work.

Dr. Insel: And I think, you know, this accountability issue, again, you need a date.

Dr. Dawson: Yes, I think we could do that, and I could also just work with Cindy Lawler, and she's now had a nice draft that comes out of that workshop, that really identifies the priorities and really -- try to map those onto the priorities that came out of the workshop.

Dr. Insel: Okay.

Mr. Ne’eman: So, I would --

Ms. Redwood: Walter, did you have -- yours was the next section.

Dr. Koroshetz: I think you described my points. The only thing I would say, the focus seems to -- should be on pregnancy and early development, in terms of where this environmental questions may --

Dr. Dawson: Yes, I agree, and I think that was clearly evident in the conference, or workshop.

Ms. Redwood: Tom, when I went through this, I'm trying to look at the comments --

Dr. Insel: Let's see, there is 19? Nineteen.

Ms. Redwood: I, again, had just added in more research about methylation profiling, which we could possibly incorporate.

Dr. Insel: Yes, that's actually -- I think that's one of the fields, that's that

just changed tremendously in the last nine months.

That's really what I was trying to say at the beginning, the purpose of this update is to capture something like that, that wasn't on the radar two years ago, or a year ago, and now, we have the tools -- we have CHARM, that's a tool that anybody can use, it's quick, it's genome-wide and it allows you to --

Ms. Redwood: And we're assuming methylation realities in children with autism, already. So, I think it's --

Dr. Dawson: I guess, for me, that calls a question as to whether a specific opportunity is to try to really drill down on the issue of advanced, you know, parental age, because it has really, seem to be one of the more replicated factors and its relationship to, you know, methlyation patterns in offspring.

Ms. Redwood: See, I think of

environmental toxins, but then, that fits into it, as well.

Dr. Dawson: Yes, exactly.

Ms. Redwood: But the older you are, the more body --

Dr. Dawson: Right, or exposure -- yes, that's another, it kind of brings together this --

Dr. Insel: So, yes, there's another paper, which I'll have to -- and we should probably tee-up, both for IACC and for this group, about the relationship of gene sequence to methylation, so, that it really does matter, you know, what your sequence is about what you get -- how much methlyation you see in a genome and different areas.

So, we've treated these two things as being independent, and they're really not, which is a very surprising, but maybe we should have understood that sequence is all about vulnerability, vulnerabilities to exposures, exposures, methylation.

Dr. Dawson: Right.

Dr. Insel: So, maybe this would have been very predictable but it's helping us to understand that we've got to look at both.

There's a wonderful autism paper from -- I won't be able to -- Gregory is the first author, from Peggy Vance's group in Michigan, showing that one of the places we're going to --

Dr. Dawson: Oh, yes, that's the C-

Dr. Insel: -- yes, oxytocin receptor, they also have hyper-methylation of the same gene.

Dr. Dawson: Right.

Dr. Insel: And people with a perfectly normal sequence, meaning that you can -- there is lots of ways to remove oxytocin receptors from expression.

Dr. Dawson: That might be a great workshop in the Spring, right, it's just to bring in people, you know, on the cutting edge of doing work in that area, because there is -

- and people are approaching it in a lot of different ways.

Dr. Insel: But I think for us, I mean, it seems to me that what this really does is, it shifts this whole issue around environmental exposures onto -- it's giving us a tool now, that we didn't have before.

Dr. Dawson: Right.

Dr. Insel: So, it's giving us the traction that was missing in 2009.

Dr. Dawson: I agree.

Dr. Insel: So, in line with having had this workshop and having the tools, it's a chance to march forward, and especially, if the exposures in the second trimester, it would be hard to do that in any kind or prospective way.

Ms. Redwood: Tom, the other thing I --

Mr. Ne’eman: I'm kind of curious if this fits in here. Some studies, which have identified certain factors, which have

been responsible for the increase in diagnosis that are social.

For example, there is a California study, which is -- it's on correlation on the basis of education status and also -- and location and also, one that looked at -- one that found -- and I think was in last year's, that advances -- one that found about 25 percent of the increase in incidents and diagnosis could be attributed to, people at one point would have had the intellectual disability label.

And I wonder if this could be incorporated under risk factors, just to recognize that when we're talking about epidemiology, we want to also understand, you know, what some of the social determinants are going to be, otherwise, we may spent a considerable amount of time looking for something in the hard science realm, where socio-economic factors may have more of a role to play.

So, I think just to think about in an objective in that direction.

Dr. Insel: This would be a great conversation to have, Ari, and it's a very interesting body of work from Peter Bearman, at Columbia. This is -- he has a Pioneer Award from NIH, to pursue this work and it's -- it could be read either way.

There's a 16 percent part of the increased that can be explained away by the diagnostic change, and on the one hand, that seems very substantial. On the other hand, you know, when you add all of the social factors that he's been able to put together, they came to about 41 percent, or something like that. It's still less than half of the increase, can be explained away.

So, people have looked at this in both ways, on the one had saying, "Well, you know, some of this is just the social determinants," or ascertainment. On the other hand, when you add it all together, you still

have a very real increase that can't be explained away.

So, it's kind of hard to know what to do with that information, as a result.

Dr. Dawson: Well, I think --

Mr. Ne'eman: And I think the appropriate answer is to research both possible avenues.

So, I mean, nobody is saying that we should eliminate Chapter 3 and just look at socio-economic factors. I'm just proposing that we also make available, within Chapter 3, an objective focusing on that kind of research, so that there is funding and may explore some thing that we might currently be missing.

Dr. Insel: It would be interesting to see how Peter Bearman was -- ended up in our portfolio analysis.

Mr. Ne'eman: Yes.

Dr. Insel: He must be the `other'.

Dr. Dawson: Absolutely. You know,

I think, actually, the most phenomenal paper that's coming out, of that body of work, recently, is the 2010 -- I don't even know -- I can't remember if it was listed or not.

But basically, it's a study of looking at the, over time, the concordance between fraternal twins, as compared to dizygotic twins, and showing that over time, we're seeing an increase rate of concordance among --

Dr. Insel: Fraternals.

Dr. Dawson: -- the -- well, no, it's decreased for fraternal and increased for monozygotic twins, and the reason -- and his prediction is, is that what's happened over time is that parent age has increased, you're seeing higher rates of rare de novo, CNDs, which could be environmentally induced or you know, other mechanisms, and both.

And so, what's happening over time is, because these are rare events, if you have identical twins, the concordance is increasing

and in fraternal twins, you see it decreasing, and look at the data, it's phenomenal. His predictions were born out.

So, what's very amazing about that work is he's bringing together social change, having children later, with environmental exposures, with genetics, right, in these fields where we used to say either/or, you can see something converging, three lines of evidence in one phenomena.

Dr. Insel: Yes, and I guess the piece of it that we haven't really thought about much before, is how the CNVs could be created by environmental exposures, over time.

Dr. Dawson: Absolutely.

Dr. Insel: Whether they're just due to toxins, we don't know.

Dr. Dawson: Right, right.

Dr. Insel: But you know, this is a very cool area. We obviously need to have a scientific seminar here, at some point, because there's a lot of really interesting

stuff going on.

But in terms of Chapter 3 --

Ms. Redwood: I would still finish --

Dr. Insel: Let's let Lyn finish, okay.

Ms. Redwood: Okay, one of the things in here that we mentioned before, very briefly, was the Institute of Medicine, the 2008 report, and just saying it summarized what was needed in the field, but we really didn't incorporate of that into this document, which would require somebody to go back and read the 2008 report, to know what were the highlights of that.

And one of the things I thought was most important, because I went back and read through the report again, was this concept of children with autism, being a vulnerable phenotype, and this is based on the work of Jill James and then all the recent work that's just come out, this year,

documenting oxidated stress in children with autism who are highly oxidized.

And so, I've put something in there, adding language around this vulnerable phenotype.

Dr. Insel: So, I see that, but my only issue with that, Lyn, is that no one has ever shown any specificity for this. So, we've got almost the same findings for schizophrenia, for lots of developmental disorders.

So, while it's an interesting piece of bio-chemistry, there has never been anything that links it specifically to autism, as opposed to all these other developmental disorders, which is kind of like --

Ms. Redwood: And maybe, all the developmental disorders are in some way linked.

Dr. Insel: Yes, I mean, Walter knows more about this, than any of us, but this is just the problem we're struggling

with, with all kinds of CNS problems, where you've got changes in oxidative stress pathways, and it's hard to know -- there's no specificity for any of them.

Dr. Koroshetz: I spent years trying. I thought I had something. Let me just -- it was just an artifact. So, you've got to be really careful about these measures.

But it could be true, it's been like a wholly-rail, people trying to get this oxidated stress measure and nail them down, no one has been able to do it, in any disease, as far as I know.

But it still means it's incredibly --

Dr. Insel: But everybody has done -- every disease has a report about this.

Dr. Koroshetz: Yes.

Dr. Insel: So, it kind of goes both ways. It's --

Dr. Koroshetz: We've acted on it. We found studies that, you know, antioxidants

in Huntington's disease and Parkinson's disease, because of these studies, but the truth of the matter is, they've never been really validated.

And so, I think I agree with your point, I just think that before we go there, we should push for validation, because they are treacherous assays, really hard to review.

Dr. Insel: This gets to the replication issue, that we brought up before, the importance of -- and standardization, this is an area where we've really got to standardize your bio-chemical assays, and it's been a real headache, not so much for autism, but for some other areas that we fund.

Ms. Singer: Is it possible that in the portfolio analysis, Della, that replication studies were coded in their subject area, as opposed to being pulled out as replication studies, and that may be the reason why there is a zero in that column?

Dr. Hann: It's a possibility, but

I'm also -- just knowing how NIH approaches its portfolio, I think that the probability of finding replication studies is very low, across NIH, not just for this area, but across --

Dr. Koroshetz: We actually started -- because we're doing clinical trials, based on studies that are not replicated, and they didn't work.

So, we're like, "Okay, we're not going to do anymore," because now we'll find replication studies, just for that purpose. That's how bad it is.

Dr. Dawson: Well, moving to -- for example, if you take the earlier study, we did it a one site. Now, it's being done at multiple -- it's a multi-site. So, that's our replication, right. So --

Dr. Hann: But they probably wouldn't frame it --

Dr. Dawson: Yes, so, I'm just saying, there is an example that may or not

have been framed that way.

Dr. Hann: Right, right.

Dr. Dawson: -- that is currently happening.

Dr. Hann: Right, right.

Dr. Insel: So, as I look at the recommendations you have here, Lyn, and some of what Geri has put in, I think they can come together and probably, we could do it in a way that's a little tighter, not so many bullets. But do you want to take it -- since you have --

Dr. Dawson: Sure, I can work with Lyn on it.

Dr. Insel: And then Walter, you're on this one, as well, and I am, as well. So, if we could circulate this around, you will, again, we'll get you the template, you'll take responsibility and we'll get this done between us.

Ms. Redwood: Tom, and the last thing that I wanted to bring up is, there is -

- in the plan, we had that we would continue to work with NVAC, and coordinate with NVAC, and there was a report that just came out, well, in 2009, which were their research recommendations, and there were three recommendations in there specifically, that related to autism.

So, I incorporated that, in there, as well, since that was part of their report, and we said that we would continue to work with them.

Dr. Insel: So, that sounds more like a comment for the IACC, rather than for the Strategic Plan. I mean, it sounds like the original plan was that we -- that IACC, that's the discussion we had, would be working with NVAC. Does that need to be in the Strategic Plan?

Ms. Redwood: It was in there already.

Dr. Insel: Right, there was -- okay, so, what's the -- what is the revision?

Can you go -- where is this?

Ms. Redwood: It's in the --

Dr. Hann: It sounds like what is -- it sounds like progress, is what you're talking about.

Ms. Redwood: Yes.

Dr. Hann: Progress has been made.

Ms. Redwood: They've actually --

Dr. Hann: So, that that's part of the objective --

Dr. Insel: So, in the addendum, you want to say what their --

Ms. Redwood: What their recommendations were, that were specific to autism, in the 2009 report.

Dr. Insel: Okay, so, we can work that in? Okay, Chapter 4. We've got --

Mr. Ne’eman: Where are we, on Chapter 4?

Dr. Insel: We're on Chapter 4, and that includes Geri Dawson, Stephen Shore, Lee Grossman, Ari Ne'eman, Lyn Redwood.

Mr. Ne’eman: We actually have an issue I wanted to raise, in regards to Chapter 3, if we can just spend a little bit more time on it.

Dr. Insel: I don't think we're going to have a lot more time. We still have four chapters to do, and 20 minutes to do them.

So, unless it's very quick, do you want to just let Geri know what it is, or you can let Geri know off-line, as well.

Mr. Ne’eman: Well, it's very brief. I just wanted to ascertain A) whether or not we're going to be doing something -- we're going to be putting in an objective around socio-economic factors, and then B) you know, just in the spirit, since we do have a specific objective around it in Chapter 1, which is comparative.

But I encourage us to also mention ethical, legal and social implications, additionally, in each of the objectives, where

we mention genetic risk factors, so, that we're approaching it from both directions.

Dr. Insel: So, Ari, I guess I just contest that, in the spirit of trying to keep this -- I think if you deal with the ELSI, ethical, legal, social implications up front, in that first -- the first chapter, where we'll essentially be charging people to look at this, and as you said, keep those independent from the people doing the work, then I'm not sure that we need to do this for every chapter. It becomes, in some ways, redundant, unless you really wanted the people doing the genetics to also be doing the studies of ethical, legal and social implications, and I thought your recommendation was to keep those independent.

Mr. Ne’eman: No, and I do believe that they should be independent. The issue is, is that, you know, what one would hope is, as a result of independent into ethical, legal and social implications, there is going to be

additional consideration of those factors, in the context of the broader scope of genetic research.

I mean, I look at it somewhat similar to environmental impact statements, you know, really, we do not go to, you know, those people and say, "Well, in the standard, we come up with the numbers and the metrics by which you're going to be assessing your impacts on the environment."

But on the other hand, once we do have that information, from an independent body with expertise and credibility, you know, we do expect those who are going to be having an impact and proposing these formalities to society, in that respect, to be engaging in dialog and to be undertaking some consideration of that, before they undertake their project.

So, you know, I see it very similarly, in regards to genetic research. Maybe what we need to do here is to make clear

that in the independent objective, we're talking about the framework and the metrics and then, in some of these dependent clauses, we're talking about ensuring that that independently arrived at framework is being included in the actual scope of research that's being done.

Dr. Dawson: Yes, I think that --

Dr. Insel: I think we hear you. I'm concerned about spending a lot more time on this issue, because unless you want to have another meeting in the next two weeks or next week, there's a lot to get done. We still have three chapters -- four chapters to do --

Dr. Dawson: But Ari, I will definitely be happy to talk to you off-line about this, and see if we can come to some solution around this. So, yes.

Dr. Insel: Let's move onto Chapter 4, which treatments and interventions will help, and let me see if I can -- it looks like we've got Geri, then Ari, I think you're on

this one, and Stephen Shore, who is not with us today. So --

Mr. Ne'eman: My suspicion is that we've got four chapters to go through in 20 minutes, that we're going to need another call, no matter what.

Dr. Insel: Let's see how far we can get. So, help us out with Chapter 4. Geri, you want to take us through?

Dr. Dawson: All right, so, in terms of the update to `what do we know', I'm happy to take all of those edits and put them into a bookend, so to speak.

In terms of short term objectives, there were two that we recommended. One has to do with beginning to use and test the fidelity and outcomes of evidence based medical treatment protocols, in community physician settings, and then the second one, sorry, was to -- it really --

Ms. Singer: Where are these? I'm sorry, I can't find the page that you're on.

Dr. Insel: It's page eight, under 20.

Dr. Dawson: Tab 20, page 8G.

Ms. Singer: Thank you.

Dr. Dawson: And I'm sorry to hurry, because of time, and then the second one really is a parallel to what we talked about earlier, about this issue of, we have these recommendations for interventions, but when you get out into particularly, you know, developing countries or rural communities, they're not scalable and not -- and so, is this to develop and evaluate and disseminate appropriately scaled early intervention programs, for under-served, low resource or low -- and low literacy populations, not only in the U.S., which I think we had, but to expand it to international.

Dr. Insel: I thought originally, Geri, that these kinds of dissemination objectives were in a separate area.

Dr. Dawson: Well, it's not just

dissemination, because you're actually going to have to develop different intervention techniques, because the validated intervention techniques that we have now, it couldn't even begin to use them in most --

Dr. Insel: Yes, I'm sorry, I was thinking about the earlier one, the one about evidence based medical treatment in community physician settings.

Dr. Dawson: Oh, I'm sorry.

Dr. Insel: So, that --

Dr. Dawson: Or that should be under dissemination?

Dr. Insel: Well, I don't know.

Dr. Dawson: No, no, that's fine, yes, that's fine.

Dr. Insel: If it isn't there, it needs to be some place. We can worry about --

Dr. Dawson: Okay.

Dr. Insel: -- where we'll move it, but C-

Ms. Singer: Can we get -- can you

give an example of what a study would be that would fall under that objective?

I mean, you're talking about sort of the way Connie Kasari is doing --

Dr. Dawson: Are you talking about the second objective now?

Ms. Singer: I'm looking at G, but are you thinking of doing pharmacological --

Dr. Dawson: So, a medical treatment protocol would be, for example, the screening for seizures, right, in children with autism, when they are provided a diagnostic evaluation.

Currently, there are no guidelines, of whether -- when you really do an EEG and if -- when you develop a guideline, which is a very intensive process, you actually have to pilot them and then you have to validate them, against --

Dr. Insel: But would community physicians do that?

Ms. Singer: Yes.

Dr. Dawson: Well, eventually --

Dr. Insel: Or is that something you would want --

Dr. Dawson: Well, so, eventually, I think this is -- yes, actually, they would be learning to screen and make the referral, in many cases, because in fact, if you think about the prevalence of autism, we're not going to be able to serve all the kids in specialty clinics.

So, the longer term goal is to develop methods that could be used to be able to screen and --

Ms. Redwood: And some of the children have underlying seizure disorders that aren't being picked up and then when they're treated, there's a lot behavioral improvements.

Dr. Dawson: So, I think it really -- it could be rewarded to be at two levels. I do think, ultimately, you have to address this at the community level, because you know,

let's say that you are a primary care doctor and you're taking care of a child with autism, right, and there are no specialty clinics within 200 miles, how do you know when you should be referring to have this child have an EEG, because the child may have seizures?

I mean, there are no guidelines for that. There are no guidelines in the specialty center, either. But so, it really does need to be --

Dr. Hann: But doesn't that have to happen first, though?

Dr. Dawson: Yes, so, maybe this is premature and we should -- but the thing is, that's already being funded by HRSA right now. So, either it's not in here, but you know, maybe we want to put it in here, because then we can say, we did it, but no, I'm serious, it's a pretty important objective that is being funded.

And so, then the next question is to try to move that information out into our

communities.

Dr. Insel: Could you do both? So, could you --

Dr. Dawson: Yes.

Dr. Insel: -- simply expand this to say, create -- and this is -- this gets to this issue of the standardization of --

Dr. Dawson: Yes.

Dr. Insel: -- assessments, that we talked about before. Now, in this case, it's in a clinical setting, not a research setting, but the need to have those SOPs there.

Dr. Dawson: Right, and then another would be for sleep, you know, and what they -- okay, if you try a behavioral intervention for sleep, what's the next step and you know --

Dr. Insel: Walter, are the -- are docs, community docs doing more sleep assessment now, the --

Dr. Koroshetz: Well, it's mostly

referrals.

Dr. Insel: But what about -- because we have ambulatory recording. Is this something that is just found in specialty care, or is it --

Dr. Koroshetz: Generally, it's specialty care. It's in there.

Dr. Dawson: So, right now, there is randomized clinical trial being conducted through the Intervention Network for Physical Health, where they're looking at the efficacy of a nurse based intervention -- education intervention program for improving sleep, that could be implemented in a community setting.

Dr. Insel: But that --

Dr. Dawson: So, yes, I do think we're going to be moving in that direction, because there is -- this is such a highly prevalent disorder, there is now way, if you had to refer -- can you imagine this parent, this kid is having sleep problems and then you refer and get on a waiting list for six

months, to a specialty clinic? It's just not going to work.

(Off the record comments.)

Dr. Dawson: So, anyway, I can tune that up.

Dr. Insel: Other thoughts? But Lyn, you had a =--

Ms. Redwood: Yes, one of the things that I reflected in here, because I think it's such a big opportunity, and Geri alluded to this in her presentation, was the presence of all of these medical comorbidities, that should be addressed now and they're being often times, overlooked by the medical community, because the children don't have language, and I just think that's an opportunity to improve their overall health and functioning that we're missing, and I really think that that should be incorporated into the introduction too, as one of those cross-cutting themes.

Dr. Dawson: Yes, I did include

that, in my update, you know, the part that I'm now going to put in the bookend.

Ms. Redwood: Okay, great. So, that was one of the things that I thought was very important.

The other thing was developing techniques because of the heterogeneity that we see within the disorder, one of the things I think we do as a mistake, is that we try to acquire one treatment across the entire spectrum.

And so, if we can separate out these different sub-types, clinical sub-types, and then apply treatment to those, I think it's going to be more effective and but you also need multiple treatments at once.

So, we need to develop some type of assessment tool,that can look at multiple modalities over regimes.

So, let's say combine the sleep regime with something that's improving either nutritional status or dietary status, because

if we just do one, we may not capture the whole benefit from treating the whole person, medically. So, that was the other comment that I had.

Dr. Insel: Yes, I thought we did this last time. If we didn't, we really -- remember, we had these conversations --

Ms. Redwood: There is nothing in there about --

Dr. Insel: -- about the importance of looking at sub-groups, that was the essence of --

Ms. Redwood: But my point is to then, take the sub-groups and aim your clinical trials at those sub-populations.

Dr. Insel: And we didn't do that?

Ms. Redwood: I didn't see it in here.

Dr. Insel: Because that was -- I thought we talked about personalized care and developing interventions, based on identifying sub-groups for the different kinds of ASD and

--

Ms. Redwood: If you can find it, or Geri, if you can find it --

Dr. Dawson: Yes, I don't know --

Dr. Insel: We talked about this last year.

Dr. Dawson: But I think that was --

Dr. Insel: If we didn't do it, we need to do it. That was part of the -- one of the main things we wanted to do with the revision in 2010.

Dr. Dawson: Well, there is convening workshops but that's the --

Dr. Insel: No, that's actually --

Dr. Dawson: Okay, so, the first one is --

Dr. Insel: We did this last year. It was very --

Dr. Dawson: The first one is three randomized clinical trials to address co-occurring medical conditions. So, that's

there, thank goodness.

Then there is also a -- where is the one on sub -- okay --

Ms. Redwood: Are you looking at the ones on --

Dr. Dawson: No, you're right, it is a convening workshop.

Ms. Redwood: It's a workshop.

Dr. Dawson: It's a workshop. Linda is right.

Dr. Insel: Okay, have we done that?

Ms. Redwood: No.

Ms. Singer: We haven't convened the workshop yet.

Ms. Redwood: Now, there is something -- Geri, you said at one of the meetings, there was something in January? Is it January or February, that was --

Dr. Dawson: Well, but when we talked about what workshops to do -- but that's all on -- that's different, it's a --

Dr. Insel: Translation based.

Dr. Dawson: Yes, it's different. It's on outcome measures and it's not specific to, I think, the issue that this is really addressing.

Dr. Insel: Sounds like that's something that needs to be done in 2011, all right. Okay?

Dr. Dawson: All right, I guess that's it. All right, so, moving on.

Dr. Insel: No, no, I actually thought we had built that in, when we talked about --

Mr. Ne'eman: Can people try and be a little bit more clear? It's very hard to hear.

Dr. Dawson: Sorry, Ari, we're mumbling, I'm sorry. I think it's our hurrying.

So, the only other long term objective that we had suggested was to try to build in some language around the comparative

effectiveness research opportunity.

So, this is a very broad, but long term objective would be to conduct at least, you know, several multi-site comparative effectiveness studies that start to look at the relative efficacy of different pharmacological, nutritional and behavioral interventions.

So, I think the reason why that's it, it maps onto, if there are CER opportunities, then it can map onto them.

Dr. Insel: You may want to use the word `effectiveness' instead of efficacy.

Dr. Dawson: Yes, actually, it is effectiveness, and I said efficacy, by mistake.

Dr. Insel: Okay, so, anything else on Chapter 4,that we want to see, in the way of new objectives? I think this personalization, we need to really hammer. I thought we put it in last year. I thought we had, but all right.

Ms. Redwood: So, we can add those in the objectives?

Dr. Insel: Well, unless you want to base it on what comes out of a workshop, that may -- I mean, if we're going to do a workshop, it's just like we do with the environmental stuff?

Ms. Redwood: So, should Lyn and I do that one too?

Dr. Dawson: Okay, so, we've got two, all right.

Dr. Insel: Anything else, on four?

Mr. Ne'eman: Yes, this is Ari. I have three new objectives and a note that I just would like to see if we can include.

You know, the first is, particularly in light of the health reform law, and you know, there is currently, within HHS, negotiating rule making committee, which is looking at the definition of under-served population, but I think it's very likely that disability and particularly developmental

disability, because there is some albeit, not as extensive as necessary, but there is some research really supporting disparities and access to health care and in health care outcomes there, is likely to be included in that.

I really do think we need to see some kind of objective that looks in -- that looks at disparities in access to health care, and health care outcomes, including checking conditions, that often arise as a result of the lack of access to health care.

I think the best way to do something like this would be through a participatory action research study, or something of that nature, but I wanted to put it on the table, for the consideration of the Committee, in light of the fact that this is now, you know, a major Federal policy objective, within the Affordable Care Act.

Dr. Insel: Okay, other comments or other thoughts about --

Dr. Dawson: So, is the F the personalized medicine one, if you read it carefully?

Dr. Hann: I don't read it that way.

Dr. Dawson: It's --

Mr. Ne'eman: I'm sorry, could you repeat that?

Dr. Hann: No, I don't believe it is.

Dr. Dawson: Okay, it's not. It's not enough, even with the biological --

DR. Insel: No, that's not what Lyn was talking about. Sorry, Ari, we're just still stuck on personalized medicine. But it sounds like we're going to have to really put better language in the update.

So, your comments, Geri and Lyn are going to work on developing this piece for Chapter 4. We've got five, six and seven to do. We're out of time. We're going to have to do this with a conference call.

In some ways, five, six and seven fit together, at least five and six, so, you know, it might make sense to put all those on the table at the same time, and in the meantime, we can work up the template that we -- and I think we can get this set for one chapter, we can follow it for the others.

Are there any final issues before we break, to reschedule it, for a phone conference?

Mr. Ne'eman: The only additional thing I would raise is that it strikes me that the conversation on four is only half complete.

So, I'd encourage us to include that in the follow conference call, you know, and in a lot of ways, four fits with five, six and seven, many of the same specs. So --

Dr. Insel: Well, I think what we'll end up doing -- this group is going to look at whatever comes forward, from the little work group leads. I don't mean the

people are little, but the groups are little, and we'll have a chance to reroute through this Subcommittee.

So, I have a feeling that all of the things that we talked about today, we're all going to revisit and have a chance to tweak a little further, but we have done a lot here, by at least providing a process and providing the structure that's really different than the way we came in.

We are almost at noon. Della, last words?

Dr. Hann: Yes, so, OARC will send out the template for the now -- for the addendum, essentially. That should hopefully be out by tomorrow, will be my goal, is to get it out to you by tomorrow, late tomorrow.

For those folks who are working -- you progressors, for Chapters 1, 2, 3 and initial work on 4, I think if there is any -- if we're thinking of taking it forward to the full Committee on the 22nd, that means those

first drafts need to be circulated next week, no later than Friday, of next week, and then we'll try to clean it up and get it ready to take forward to the full Committee on the 22nd.

We will also work to find another time for our second conference call, to finish up in terms of five, six, seven, any comments on introduction, etcetera, and stay tuned, we'll have to look at a calendar to try to figure out what we can do on that particular score.

Susan, are there any other logistical pieces I need to mention?

Ms. Redwood: Just the updated RFI.

Dr. Dawson: Yes, so, the additional piece, so, the updated RFI and the detail for the portfolio analysis, our goal will be by end of this week, to get that out to you. That's our goal.

Dr. Insel: That's your objective.

Dr. Dawson: No, that is my goal.

I don't have objectives.

Dr. Insel: But you will be held accountable.

Dr. Dawson: I'm always accountable.

Dr. Insel: Thanks, everybody, and for those who joined on the phone, we appreciate your listening in, if you were public participant, and for those who are members of the Subcommittee, thanks for joining us by phone, as well.

We still have a lot to do, but I think we've made some progress today, and thanks, for those of you who came from far away, to join us here for this meeting. We are adjourned.

(Whereupon at 12:02 p.m. the Subcommittee adjourned.)