U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

STRATEGIC PLAN UPDATE

Working Group 3 – Question 3 – What Caused this to Happen and Can It Be Prevented?

Conference Call 1

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12:00p.m.

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PROCEEDINGS:

DR. SUSAN DANIELS: Thank you. Anyone else joining us?

(Silence.)

DR. DANIELS: We'll give us until 12:05 and then we can begin and if others call in we can have them join us. Are there any other working group members who joined who haven't said hello yet?

DR. ELAINE HSIAO: Yes, hello, this is (Elaine Chow). I just joined.

DR. DANIELS: Oh, hi Elaine.

DR. HSIAO: Hi.

DR. DANIELS: It's good to have you here.

DR. HSIAO: Thanks.

DR. DANIELS: Anyone else?

DR. CINDY LAWLER: Yes. Alycia Halladay has joined the call but she seems to be on mute.

DR. DANIELS: Okay. All right well anyone else join?

DR. LAWLER: So Dani Fallin has the same problem with not being recognized as a speaker.

DR. DANIELS: Okay. We'll make sure that folks have the correct code and everything to get on the speaking line. So we'll send that out to them.

Thanks. So we'll just go ahead and get started. I've kind of informally been taking roll so, so far we have David Amaral and Cindy Lawler who are the co-chairs of this working group for working group for question three of the IACC

strategic plan, “What caused this to happen and can it be prevented?”

And we have Alison Singer who's a member of the IACC and David and Cindy are also on the IACC or Cindy is an alternate on the IACC. Ray Bernier, Alycia Halladay, who I hear is trying to unmute her line, Elaine Hsiao, Elise Robinson).

And I know that Daniel Geschwind is not going to be able to make it on the call today and Irva Hertz-Picciotto will not be able to make it and Craig Newschaffer is going to join late.

Anyone else on the call? All right so let's go ahead and move forward and hopefully if other's join the call, they will speak up and we will be able to have them join our conversation.

So welcome everyone to this conference call of the IACC strategic plan update working group number three on question three which is about the risk factors for autism both environmental and genetic and welcome to our co-chairs David Amaral and Cindy Lawler who will be helping coordinate the drafting of the strategic planned chapter on this topic.

So on this call today our goal is to look through the past progress toward meeting strategic plan goals that were set for by the committee in the past. So the IACC strategic plan was first developed in 2009 and was updated each year subsequently and from 2009 through 2011 the IACC added new strategic objectives to the strategic plan.

So there's a current set of 78 objectives for the entire plan and over time, my office which is the Office of Autism Research Coordination at the National Institute of Mental Health which manages the IACC, we've been tracking progress toward meeting these objectives over time.

And we've been doing that by collecting data from all of the federal agencies and several private foundations that fund autism spectrum disorder research and analyzing it according to the different categories and the strategic plan to help understand which of those objectives are being met and which others may not have gotten as much attention and might be in need of more work.

So we've been collecting this information and the latest collection was for the year of 2013 and the information that's been provided on the internet, it's on the IACC website for those members of the public who might be listening in and then I sent it out to the working group, is information about our office's analysis of the 2013 dataset that we collected on research.

So I'd like to direct your attention to the first packet which is the data analysis packet that has a number of figures in and we want to just look through this. I was hoping that the working group might have had a chance to just browse through this.

And if you have any comments on the portfolio as we go along, you can feel free to make those comments because we will collect that information and try to work it into the eventual strategic plan update. So the…

DR. AMARAL: Susan I had a…

DR. DANIELS: Sure.

DR. AMARAL: Susan I had a question. Can I ask a general question?

DR. DANIELS: Yes.

DR. AMARAL: So since the last year that we have information on those 2013 and we're doing an update now that 2016 and going forward.

I wonder how, so I know for example in terms of the genetic studies that have been indicated or genetic goals that they were, they tended to be sort of underfunded in 2013 but since now SPARK and missing have been initiated, this, the whole feel is changed dramatically.

So how are we going to take into consideration those changes in the research portfolio that have taken place over the last couple years when the IACC wasn't in session.

DR. DANIELS: So I know that the members of this working group are aware some of those changes as we invited experts from the field to be a part of this group and so we hope that you'll just add those in verbally and that we can work that into a draft of the strategic plan update.

And we can mention these things but they won't be in this quantitative analysis so the office will continue to analyze other data that have come in so we are going to do a report on the 14 and 15 dataset and that will be the last dataset that will be analyzed against this old strategic plan and then the 16 dataset will start being analyzed against the new strategic plan.

So we are at the point of you know, we have the data already analyzed for 2013 and we'll be putting out that report as soon as we can and then we'll get to work on the 14, 15 report and get that out and so by the time you're doing the next update we'll be closer to being completely up to date.

DR. AMARAL: Yes. And when just, again, just very general, when is this update draft on, I'm sure we got this material, but when is this update draft supposed to be finalized?

DR. DANIELS: So our goal is to get the substantial amount of work done before December and then at the January meeting of the IACC, we

can discuss the update by then, we should have a draft or a strong draft of the strategic plan, do any final approvals and then be able to publish it in 2017.

DR. AMARAL: Okay.

DR. DANIELS: It usually takes several weeks after the committee completes things for the office just to get everything lined up to get everything published but we expect that the working group will have finished its work by the end of the calendar year.

DR. AMARAL: Okay. And your 2014, 2015 summaries will be done by when?

DR. DANIELS: That's not going to be out before this strategic plan update is done so you will be…

DR. AMARAL: Okay. Okay.

DR. DANIELS: So right now when we report on past progress, we will be looking at the 2013 analysis and you'll be talking about that in the strategic plan update and then the 14 and 15, that will be a standalone document and probably won't even be used as much for the next update because hopefully we'll be on to the 16 by then.

DR. AMARAL: Okay thank you for that classification.

DR. DANIELS: So we'll, our office will provide a full report though so the public and congress and everyone will have that information and it can be taken into consideration.

DR. AMARAL: Okay.

DR. DANIELS: So, but thanks for, thanks for asking. I know that for many people this is a new process doing a strategic plan update for some like Alison. It's one of many that she's been

involved in so anything else that our questions before we just take a look through the data?

So we provide a packet here. The first figure is one that just shows what the proportion of federal versus private autism research funding is and this proportion has been relatively the same over several years since 2008 as we've been tracking it. It's changed a little bit but, you know, approximately three quarters of the portfolio that we are tracking is funded federally.

Of course it is important to keep in mind there are some private foundations that aren't a part of our portfolio analysis, certain family foundations that also are contributing so this is just based on the foundations that we have participating at this time.

In the second figure, we tried to provide a sense of the different funders of the proportion of the whole research portfolio that they're funding and so as you can see, NIH is the largest funder.

And we also have a number of private organizations and other agencies that are doing various, they're funding various proportions of the research and to the right, you can see a table that actually gives you finer details about the amount of funding.

On the third page, we provided the percentage of 2013 funding that was devoted to each of the questions and the strategic plans and keep in mind that each agency and organization is doing their funding independently so they're not necessarily aiming for a particular percentage.

They're just funding what is in their mission to fund and this is the result when you combine all the information. So you'll see that question

three in to 2013 was about 18% of the portfolio by funding and about 11% by project count.

The next figure shows funding alignment with the IACC strategic plan objectives. So this is something that the committee was interested in understanding how much of the funded research portfolio in general is relevant to the IACC strategic plan objectives.

So when the IACC created these objectives, they were trying to target areas that they thought were new, emerging, underfunded in need of additional assistance and focus and so those objectives don't really represent the entire breath of the portfolio because areas that were well established weren't targeted with specific objectives.

But in terms of the objectives, how much of the funded portfolio that's out there addresses those objectives and we found that 75% of the portfolio that's funded is related to our objectives and about 25% is not related to our objectives and so that represents areas that are already well established that may not have been covered by specific strategic plan objectives.

And the committee named that area core other. Meaning that much of that research is foundational important. In the next page, we looked at each question individually to see how well the portfolio that's funded aligns with the strategic plan objective.

And you can see that for question three that most of the funding goes to projects that do in some way relate to our objectives and it's only a small proportion that is funding other things that outside the objectives.

And when we get to the fourth page which is quite text heavy, you can get a sense of where we are with the different objectives. So this

question has a number of objectives and you'll see that in green are the objectives that have achieved the recommended budget which was as Alison has quoted several times, is a ceiling, not a floor.

The committee came up with these recommended budget figures to help funders understand what it might cost to do some of these objectives but in some cases, objectives are able to be achieved with less money.

And it wasn't limiting funders from being able to fund more but this was the floors or what they thought was a minimum that should be used to try to stimulate these areas of research.

And so you can see that by the color coding-so green is represents the objectives that have achieved their recommend budget as well as achieved the general content of this objective and then the yellow are the ones that are partially completed. If there were some that had no work at all, they would have been in red but there aren't for this particular question.

Does the committee, or does the working group have any comments on specific objectives or on the question three profile overall?

Speaker: Yes I have a question. So on this page, there's some that are indicated as yellow but don't have a funding amount associated with that. Is that because the funding hasn't been a time that this is done that and administered yet or for example on the second 3SB…

DR. DANIELS: Sure. So in some cases, if there's no funding indicated that might mean that there are projects that were not counted in the autism research portfolio that achieved the objective or achieved part of the objective.

So there for example could be, there in some cases grants that are for general science areas or general neuroscience areas that help achieve some autism objectives but they were never really specifically being about autism but they did help achieve the autism objective if that makes sense to you.

So in those kinds of cases then they don't get assigned a number because we're only when we're counting the dollars, we're only counting things that projects that are autism related projects.

DR. AMARAL: Susan, this is David. So 3SA is one of the examples of an objective that I was talking about before where it's yellow now but it should be green based on for example the sparks study 50 thousand subjects. So I wonder if anybody else on the call notices any other yellow areas that have been supported over the last few years and would have moved into the green.

DR. DANIELS: And this is great. We do want to note those things because as we did in the last strategic plan update, we did have information that came in from the committee that we were able to use to give a little more context about what's going on with those objectives so we'll definitely note spark for that one.

DR. LAWLER: Susan, this is Cindy. What's not noted here because they weren't funded until the last two years, we've added I believe about 13 more grants that are looking at various ways on environmental risk factors and those include in model (unintelligible) some different kinds of exposures being investigated.

And also many of the human studies that we supported were leveraging existing investments so that sprinkling would be across a number of different objectives.

It's hard to say whether that would turn the yellow, all the yellow screens were leading I think in the right direction with that and the other comment I'll make is it's a little bit hard to assess this. I think question three really suffered from at least in the environmental risk arena.

The field was so nascent at the time that we started. We just, you know, everything was on the table. Everything was needed and we kept added more objectives and never got rid of any and any one study often times you know, could be characterized in more than one of these but of course they only get counted once.

So it's you know, kind of hard to get a gestalt as to whether you know, I definitely think there's progress but it's hard to look at this and you know, necessarily convince anyone else that there's not still you know, a lot of areas that you know, need much more attention.

DR. EICHLER: This is Evan Eichler. Can you hear me?

DR. DANIELS: Sure. Yes we can, welcome.

DR. EICHLER: Well thanks. I've been on mute for about 15 minutes. I just want to add one comment I think it was David's comment about the Spark. I think we have to be careful about a lot of these projects that are basically just starting out like Spark in terms of what does it actually realize what it delivers.

We shouldn't assume that it's actually done at this point, right? And I guess I'm a little bit concerned, even about the missing comment that was made up in the beginning, getting access to these data or even getting all the data complete.

These are projections. They're not done yet, right? So I think people have to be careful about

this specifically as it relates to strategic planning.

DR. DANIELS: Right.

DR. AMARAL: Evan, this is David. So you're points well taken. I think if I understand but Susan please correct me, I think this is really thinking more in terms of funds allocated or projects allocated towards a goal, not necessarily that they're completed because a lot of these projects have not completed.

But you know the goal has been addressed by some funding agency or some projects. So I guess…

DR. DANIELS: That's correct. What I was going to jump in and say is that with the way they, the strategic plan is designed, it really was to try to ensure that work is at least begun in several areas but it isn't necessarily tracking the absolute completion of every area.

DR. EICHLER: Right. But I guess I would say that one has to be careful because sometimes these other initiatives don't achieve the goals, right, and so if there's, if there's an initiative, that's great but if it's essentially you know, gets bogged down and it doesn't deliver, you'll have a hole in your strategic plan going forward because you assumed that by another area. But…

DR. AMARAL: Right.

DR. LAWLER: So this is Cindy again. You know, I agree. I think that's definitely a risk when we are relying on just one or two large studies to address a gap and I would be much more comfortable in cases where we have a number of different you know, efforts that are underway simultaneously that then that's going to be a less risky proposition but you know, I agree with your point (Evan).

DR. DANIELs: Yes and so with this particular exercise looking at what's been funded, that's one way of us looking at the portfolio but we're also you know, on the next call going to talk more in terms of qualitative achievements of some of these areas.

And so hopefully with the whole strategic plan update looking at both quantitative data and qualitative data will be able to get a well-rounded picture or what's happening.

DR. EICHLER: Okay.

DR. DANIELS: Any other comments in here? So and I know that with the last working group they commented that as they read through the objectives, they felt that reading through them really reinforced to them how much the field has changed.

And how if doing some priority setting exercises now, they've probably would have really different priority areas because the field has made so much progress and I'm imagining that that's probably the case in this area as well so hopefully you'll all have a chance to comment on that at the next, on the next call. So the last…

DR. LAWLER: Susan, this is Cindy again. Could you just remind us, we want in the long run to end up with a small number of objectives that are broader and will replay, so this is almost a reset as opposed to tweaking around the edges of what we see here.

DR. DANIELS: Right. You will have the opportunity to create brand new objectives. The committee discussed this, and this is good to discuss on this working group call as not all the members of the working group might have had a chance to listen in to the IACC meetings.

But the IACC agreed that they would like to see a smaller number of objectives in the next strategic plan and so we set the approximate number at three per question area and that these could be very broad objectives and that under each objective there could be examples of kind of projects that could be responsive but the objective itself wouldn't be very specific.

So that would give a little bit more room for including various projects. Right now what these strategic plan objectives in some cases they're super specific.

And it made it really difficult with trying to code the research portfolio because incase, in some cases there were projects that probably met the spirit of what the IACC was looking for but didn't really fit the specific criteria in the objective and so hopefully by making these priorities broader, it will make it easier to be able to track how we're doing in those areas.

So you will have that opportunity on the final call of the working group or the third call anyways. I guess if you need an extra call we can always schedule another call but on the third call we'll be talking after you've discussed this and then discuss more recent progress.

You'll have a chance to try to look through all of it and decide what possibly three areas you would like to really target for the next strategic plan as areas that we need to expand, grow, simulate. So any other comments on this?

The last page in the packet is an analysis that our office did that we kind of overlaid on top of the strategic plan objective analysis. So with the per analysis according to objectives, it showed how much of the portfolio was devoted to all of those objectives.

But it did not include anything that might have not been related to objectives and something that our office found is that it might be a little bit easier in some ways to get a sense of the portfolio overall if we simplify and have some really obvious scientific subcategories that we could assign each of the projects to and to give you an idea of how the portfolio divided.

And so our team went through, and this was true for the entire strategic plan, there are subcategories for every question area. There are only four that we created for this particular question because they seem to be, they seem to capture the areas that are of interest to the public and are pretty obvious ones for the scientific community as well.

So you'll see that there is divided according to genetic risk factors, environmental risk factors, epigenetics, and gene environment studies and you can see the proportions there. Any questions about that?

DR. DANI FALLIN: This is Dani Fallin. I think I can finally be heard. Can you guys hear me? Oh great. I would just comment on that that no surprise but you can see if I'm riding these pie charts right that the environment in epigenetic ones you know, appear to be you know, lesser proportion for the same number of projects in terms of funding.

So if you think about you know, the funding attached to any particular project, it's clear that their ratio is less funding per project and the genetic based ones are more funding for project and it would, I don't think that they are eccentrically that much cheaper if done well and so paying attention to that ratio of project to cost.

(Crosstalk)

DR. ALYCIA HALLADAY: Just going on but I also wanted to say that I've been in contact with some of the NIH staff about what was categorized under gene environment and I'm not, this isn't first, the staff did a great job.

But I have to worry about what investigators put into their abstract that triggers gene environment and how much those abstracts really do reflect whether or not the study is truly looking at a gene environment interaction.

DR. DANIELS: We're happy to share the specific data with you if you want to revisit it and look at it but in general if the study was looking above genetic risk factors and interactions with the environment, it got categorized to gene environment.

DR. HALLADAY: Yes sometimes the abstract say things like you know, it's a genetic study or it could be an environmental study and they then say something like well, then genetic risk variables will be investigated and that's like, in 3B and it never really ever gets done.

So I guess we just have to be wary of that but in my opinion over the, you know, the project I have experience with.

DR. LAWLER: So Alicia, is your point from that that there's, that categories look, is over represented?

DR. HALLADAY: Yes actually, I maybe thought…

DR. LAWLER: It may be less of a proportion of studies in that category?

DR. HALLADAY: things like Craig said the EARLY study and the SEED study, those definitely belong in there but you know, and I haven't had access to the whole data. I've talked to staff and they're doing exactly what they should do and maybe it's a

little bit of you know, inside information that you know, just because someone lists something in their abstract, it's not the first priority.

It's in the abstract to attract the you know, to attract those who want to see that type of research get done when in fact it's not a priority at all.

DR. DANIELS: We could say that for the entire portfolio of research across all of autism, I mean, we're going by the abstract for everything because unfortunately we don't have access or time to read these full applications for every project out of the 13 hundred projects. So we are dependent on those abstracts being somewhat accurate.

Speaker 2: Is there a way to easily determine whether the projects are data generating our secondary data analysis? That might be an easy way to figure out a little more insight into the distribution of spending for type of project.

DR. DANIELS: Just based on the information that's in the abstract, so if somebody wanted to look at that.

DR. LAWLER: Well I agree, the categories probably over represented because there's, or the studies haven't been very successful because we know that there's very few examples of published examples of gene environment interaction in this area but I don't want to get derailed on the call today with you know, refiguring out how to go back and you know, that recode these.

If maybe we can just agree that they, that the proportion is probably smaller than it appears to be in this analysis.

DR. DANIELS: Potentially so if you know, someone from the group wants to look through those abstracts, you're welcome to. We have the data and

it would be easy for you to look for example at 2012. That's already in the IACC web tool online.

And so you could look at that category and see the kinds of studies that are in there so it would be very similar because when we do coding, we try to stay really consistent with how it's been done in the past unless there's a specific call to do something differently.

So I mean, offline I'm happy to talk with anyone who's interested in more detail at the dataset. We have all the information available but you know, I appreciate the comment and it is true that that area has not had as many publications as yet.

So moving on to the next packet we have here, we provided the data, the multiyear funding table that shows kind of how the progress has been over the last few years since 2008 through 2013.

And the last column is similar to the fourth page of the previous packet where the yellow and green show the overall. That's where the objective is whether it's completed according to the recommended budget and the types of projects that were supposed to have been funded and yellow is only a portion of that work has been done or has been funded so far.

In the annual categories, if you look through 2008, 2009, and through 2013, the colors represent an analyzed version of that recommended budget and so for example, on the second objective on 3SB, you'll see that 2009 through 2011 are red.

And that's because it didn't reach the annualized, but actually red is not a good example so I just, I should be talking about yellow because red means that nothing was going on.

But for example in 2008 for 3.3 which became 3SB, that was being looked at against an

annualized version of the recommended budget. So that's how we kind of estimated progress as we went along.

So that just gives you a sense of where some of things have gone and there are some objectives where there wasn't any working, work going on in certain years but they ended up being partially achieved or completed.

Are there, and then there's just a little figure on the fourth page that kind of represents all of that too. Any questions about that? Okay.

DR. AMARAL: Okay Susan, question. I'm just looking at a specific, one of the objectives which is the conduct a multisite study of the subsequent pregnancies that one, and the green color across until the last, until 2013 and then in our, in our summary, it, which one that now becomes 3LA…

DR. DANIELS: Umhumm.

DR. AMARAL: yellow, and it only has the last year funding's.

So I guess I was miss interpreting, so if I were to look at the entire portfolio, I would say so over the majority of the years, it's actually achieved it's appropriated funding and it's only the last year that's actually dipped below what was the IACC has suggested so that yellow is a little misleading I guess in the slide summary that you showed us initially.

DR. DANIELS: Right. So it's just, so it's compared against the annualized budget but by the time 2013 had rolled around, this had already been completed overall so yes, I guess that could be a little bit confusing for someone who's looking at it.

But again, those numbers in the in the columns are, in all the annual columns are against the

annualized budget and it just gives a sense of whether that annualized budget wasn't reached but in that case was already done by then.

DR. AMARAL: Yes so I guess I would, what I'm saying is I would use this analyzed budget summary to make, to make overall summary of whether these goals have been accomplished or not and not use that chart that has only the 2013 funding because that gives you, that, a snapshot that might be misleading.

DR. DANIELS: Right and so that's why we have this table so when we, when we put out this report we use this table and it's something that gives you a sense of where it's gone over the entire time.

We just you know, in order to see, to have a specific information there in front of people, we put it together in this, in single year table but certainly the context of what's been happening before that is really important.

DR. AMARAL: Yes. Okay thank you.

DR. DANIELS: Sure. Anything else on this?

(No response.)

DR. DANIELS: So do you have any comments overall about I guess that we've been kind of talking about this the whole time, each of the objectives or areas where you think there might be any particular gaps when you looked at the actual portfolio of projects, did you again, now the portfolio you're looking at is for 2013, that's the one that I gave you in that attachment.

And if you clicked on the link in this multiyear table, it had the projects for previous years but I know it's a little bit difficult to look across all the years but if there's anything

that really stood out to you that was missing as far as those objectives go.

DR. LAWLER: So this is Cindy. The second objectives that has to do with exposure assessment, it always seems problematic because the issues are not specific to autism.

It's you know, very difficult to you know, collect reliable exposure information but it's really important and so there have been a number of efforts particularly of ongoing spear headed by this institute environmental health science is to get a handle on the exposed zone which is sort of the you know, analogues to the genome.

And but we funded, and one way to do that is you know, one of the approaches in the (unintelligible) approach, there's always been a handful of studies have addressed that to my knowledge in the context of autism.

So I think kind of agnostic exposomic approach apply to autism is a real gap and it does address the very clumsy objectives that's in here now that is related to exposure related assessment issues.

DR. DANIELS: Great. So we can definitely note that and you might take it into consideration when thinking about future objectives and how that area will be represented. Anything else?

DR. AMARAL: I guess I have a comment and maybe I'm missing it in the objectives but I think, you know despite all the recent successes that have been in terms of identifying genetic risk factors, there's still a big problem in terms of really penetrance and variable expressivity.

So a lot of patients, when you actually bring them back into the clinic that has a similar type mutation don't manifest the same, many of them don't even manifest autism and I, I think this is a bigger question.

It actually probably bridges many institutes at NIH but it's this question of how genetic risk basically contributes to really so many different diseases so for example, intellectual disability, epilepsy, and autism in different individuals as a different seems to manifest very differently.

I think that could obviously involve epigenetics environmental but also invokes this kind of idea that they were other kind of genetic background effects that kind of dictating what pathology in particularly a class of mutation takes.

And this seems to be more the rule than the exception so I think it's worth probably thinking about this in a little bit broader way.

DR. LAWLER: This is Cindy, I completely agree with that. I think, and looking at things that way I believe opens up new or encourages kind of new research on environmental risks as well. We're not focused just completely on an autism genotype.

But we're looking more in a quantitative multidimensional way with the expectation that these risks are not you know, not only going to lead to an autism genotype. There are you know, other related conditions as well.

So people are, I think you know, this is a good number of investigators that are you know, following that track but it's not necessarily reflected in the strategic plan and I do think it merits consideration.

DR. DANIELS: That sounds like an area that we'll want to maybe write up a little paragraph about in the strategic plan update and maybe get some input from someone at NIMH that might be looking at that for various psychiatric and mental conditions. They may have some information that

they can add. Anything else that you would like to add?

DR. LAWLER: This is Cindy again. I have just a general comment and that is I think the best you know, examples of studies are ones that are taking I mean, question three seems to be very focused on identifying the risks of epigenetic or environmental where the underlined biology, you put that into question two.

But really the most successful studies are the ones that are kind of going back and forth in how to, it's a general question, how do we encourage that sort of multidisciplinary work so that there's more of a back and forth between the, you know, the biologist trying to understand what the genetic risk means and the same for the environment.

Because right now it just seems very you know, divided almost artificially between two and three.

DR. DANIELS: Right. Any other comments about all of this? In terms of the recommended budgets, I don't know that if anyone has any comments about what ended up being invested in various areas and whether those recommendations were realistic at the time.

Whether we need to take anything into consideration when we go forward into the new strategic plan. Have we learned…

DR. ELAINE HSIAO: Yes, this is Elaine HSIAO. I just have a comment, looking over the multiyear funding, I'm noticing that across the board the projects that or the topics that seem to be underfunded across the, what is this, the five year period are the ones that are dedicated solely to environmental risk factors.

I guess in the pie charts it seemed obvious as well that gene environment interaction and just

gene, genetic factors were dominating whereas purely environmental factors were a smaller piece of the pie.

And so I think that moving forward it would be great to still you know, focus at least integrate environmental risk factors. Another thing that I notice here is that it seems that the emphasis on environmental risk factors is on the particular factor itself.

For example, determine this factor, at least five different factors or the other aim initiates studies on at least 10 environmental factors and I think what would be useful at least in my opinion moving forward is actually to integrate the various environmental risk factors and also genetic factors into converging pathways.

I think that several of environmental risk factors may follow converging pathways based on immune activation or epigenetic profiles that they listed and the greater focus on pathways rather than the individual factors themselves may be useful.

DR. EICHLER: I would just extend, I would extend that to the genes as well.

DR. HSAIO: Right. Right.

DR. EICHLER: …the genes, the really significant findings are coming up in terms of (unintelligible) the networks and the pathways whether that be protein interaction or gene expression and I think maybe this idea of a pathways emphasis going to be the way that we ultimately start treating these patients.

And I think that would be a, kind of a future direction that's important for this strategic plan going forward.

DR. HSIAO: I would also in both the projects and budgeting…it could be nice to see some explicit consideration of data sharing and try to estimate what proportion of the activities and what proportion to funding it's resulted in the generation of publically available data.

DR. DANIELS: So certainly we could say something about data sharing there in terms of like, the office being able to track that, I don't think we would have the capability to be able to track that information but you certainly could emphasize the importance of it and lay out some suggestions or recommendations for that.

DR. EICHLER: I agree. I think that's really important because a lot of big projects have been initiated and data access can happen at various levels and so not everyone gets equal access to the data or you have to pay for access and I think this really does have the ability to really leverage you know, something, some of these resources that have been built.

DR. LAWLER: So I'm assuming you're talking about resources that aren't funded by NIH because at least with NIH we have…

DR. EICHLER: No, no, I'm talking about, I'm talking about, I'm talking about NIH resources that have significant amounts of money have gone into and in fact getting the access is encumbered.

DR. LAWLER: Through NDAR?

DR. EICHLER: Not just NDAR data release with publications. I'm not going to go into specifics but very large…

((Crosstalk))

DR. LAWLER: That's a, that's an important issue.

DR. EICHLER: It's critical because what it does is it creates essentially balkanization of investigators and that shouldn't be specially when it's NIH funded. In fact, some of the private funding have actually been more open with data sharing than some of the actual public.

DR. DANIELS: Is there any angle to this that involves kind of international data sharing and collaboration that needs to be?

DR. EICHLER: I think I mean, like NHGRI for example has you know, they initiated these CCDGs which are these sites of complicated genetic disease and they're being very hardnosed about it which I think is good that a lot of people bring forward collections of you know, patients that need to be sequenced, need to be analyzed at the whole genome level.

And it has be totally explicit that you know, not only the fact that the patients are consented for full data release which are always has been an issue in the past but that the data will be put up in a timely fashion and will be released even before the papers are actually published which I think is a step in the right direction.

And so this is, this is something to where you know, NHGRI, you know genome sequencing is their lifeblood so they have to be sure of this but as they move into patient collections, the data isn't necessarily publically available but it's data used so you know, it's data certification through NDAR or through DBgap for those datasets.

Speaker: They recently instituted a series of similar policy that for family center at the (unintelligible) Institute but the reality is it kind of differs a lot across different disciplines, for example the epidemiology studies that are being conducted with the large Scandinavian registries have completely different

limitation towards data sharing and aggregation that they're working out in their own way.

For example, using cloud based computing to do limited analysis for everything remains private within the country and then go back down.

But in understanding how data sharing limitations differ across the various project types would help interpret the extent to which the, has funding is being equally distributed to the community at a large, not just to the individual investigated groups.

DR. EICHLER: I mean, I think we understand that the same problem with others like Iceland and others that they have certain rules that the data can't be you know, shared in certain ways.

But I think to me honest what has happened for some of these projects is that there's a coordinating committee and also kind of a review committee that looks at the cohorts that are going to be sequenced and that's all things being equally and that's one that has restrictions and one that doesn't in terms of release that when moved ahead in terms of the queue.

Because the most researchers that can access the dataset, the better off it will be, right? So I mean, the Swedish registry isn't the only one out there. There are others and you know, we've been working with as part of this effort for example with different groups in Australia and China and their cohorts didn't meet spec.

And so what is come back is that they've gone back in and made sure that they now have things that would actually pass (unintelligible) that can be released in NDAR no restrictions and that's great.

That means that those datasets are ready to move forward. So I think the way to control this

is at the level of the task, right? It's so basically what projects and what cohorts enter you know, these sequencing queues? They should be open and successful to the maximum number of investigators.

Speaker: I agree completely.

DR. DANIELS: So it's great that Alison Singer is on this call. She's chairing question seven which deals with data sharing and bio banking, et cetera so…

MS. ALISON SINGER: Writing it all down.

DR. DANIELS: Yes so and we're taking notes too so we'll be able to try to integrate some of this into that discussion as well. Any other comments about the portfolio before we move on to duplication? So the fourth item on my agenda was to ask the working group if you noticed any areas of this question or specific projects that you feel any concerns about related to duplication of effort.

Or if you have any suggestions of how duplication of efforts can be avoided in this area of looking at risk factors, so this is question that we're asking because the new law, the autism chairs act requires that the IACC and its strategic plan provides some recommendations about avoiding duplication of effort.

And so we wanted to follow through on that and let everyone one of these working groups have a chance to take a few comments about this. So does anyone have any thoughts about duplication? Any concerns?

DR. EICHLER: I mean, I can comment because I've seen it. I think the most important thing is to have the manifest of the datasets that are actually being sequenced by whom available to all and I noticed, so we know that in the actual

sequencing of autism genomes, there's been redundancies between missing and other efforts.

And that's in part because the data manifest in terms of what samples were being sequenced (unintelligible) and other questions were not made publically available. So I think that what we really need to have is an open dialogue between NIMH the foundations that are sequencing for examples, that's one area, and just making sure that those manifests are in place long before sequencing starts.

And all it requires is kind of a higher level coordination and people can find additional samples to sequence or you know, or not to sequence. If they…

Speaker: That sounds like a great…objective

(Crosstalk.)

DR. EICHLER: Well it's a pain, I can tell you it's a pain because someone has to sit there and actually do this kind of coordination but it in the end saves millions of dollars to do it, right? And so…

DR. HALLADAY: Well you know, yes say it's the cost of a person or a part, a part of a person's salary to do all that, I mean, to make sure that happens, that seems to need a minimal amount of money to make sure it happens.

DR. EICHLER: Agreed. And just, and the only thing you need which is the biggest problem was basically having all the foundations agree that they would share what their sequencing and that has not always been transparent.

And that's, I don't know how you leverage, I mean, just having one person unless they don't have a stick it doesn't make any difference, right? They won't release, they won't release. But

I think in the end, everybody wins if people are open about what they're sequencing for example.

But that just, that's been a little bit slow in this area.

DR. AMARAL: Okay, Evan, this is David. I just want to understand what you're saying. So initially was thinking that you were saying that there was redundancy and different efforts sequencing the same subjects and wasn't clear about that.

But then at the end of your comment, it sounded like there was something else but I'm not sure if I understand exactly where you, what you're indicating is the redundancy. Could you try one more time so we understand it, I understand it?

DR. EICHLER: The redundancy is really just what you first mentioned, same samples being sequenced twice by a different competing efforts, right? That's the redundancy.

DR. AMARAL: Okay.

DR. EICHLER: The problem is release of what we call the sample manifest, who's sequencing what? And that you know, centers have been I don't for unintelligible) trend or they necessarily had their manifest all in place. I don't know what the issue has been but that has required a lot of effort to convince people to release their manifest to each other almost if that was a sequence in itself.

So I know NIMH can obviously make all its investigators that are getting funded make it really clear what you know, what samples are being sequenced but if the same samples are being done by missing or being done by you know, by the Simons foundation or something to that effect, that's not always clear.

Nor are those places obligated to share those, that information. So that's a separate issue so that's what I'm saying it's not just having you know, one FTE focused on you know, coordinating or even half an FTE to do that. But it would be nice if there was just one clearing house where we knew all the samples that are being sequenced by whom.

And I predict that would save money and lots of it but does that make sense (David)?

DR. AMARAL: Yes, no, it does make sense. So what you're asking for is more of a formalization because if understand correctly, I know that Spark is declining subjects that are being sequenced by missing you know, at least that's what they tell people who are involved in the studies.

But you're saying that may not necessarily take place and even if it does that it would be better to formalize that and publicize the, as you say the manifest of what they're doing? So I think that's a good point and I just wasn't aware of how problematic that is but if you think it's a big issue, I think that it's something we should address more formally in the next go around of this.

DR. EICHLER: And I think this is also totally intertwined with data access because if you have to pay Google for example to access missing, a huge amount of money, right, that will exclude most investigators from actually analyzing that.

So some colleagues have said you know what? We're sequencing the same sample but to be honest, we're going to make it publically accessible so that data can be accessed and downloaded and as opposed to having to actually maneuver through you know, the fee structure of actually you know, analyzing or manipulating data on the cloud.

So these, these are complicated topics to be honest. It sounds simple, share manifest, but it's also important to know you know, how accessible is that data going to be and to whom and how much is it going to cost.

And this is where I think the institute or NIMH in particular should be playing a big role because like I said before, it benefits a lot of people if all this data can be put on one platform and made freely accessible at least to qualified researchers.

DR. AMARAL: So I do think it would, it's under the purview of the committee to recommend that some funding be allocated for coordinating meeting genetic data that is coming in through various sources that are relevant to autism research.

So if it isn't being done know, you know, I think it's something that when we get to the third call where we'll be talking about new goals or maybe this is actually better for Alison’s, you know, in question seven.

But somebody should say that some funding should be allocated to bring all the critical parties together and solve this problem so that you know, so that you and other investigators who are dealing with these kinds of data don't feel that access isn't open and rapid.

And you know, it shouldn't be as costly I mean, I think that this is really an important point and I don't think I was aware of the depth of this issue so we should certainly keep it on the, on the front burner.

DR. EICHLER: Yes. The good news is that the data coordinating centers from the CCDG at NHGRI are beginning to do this for you know, a little bit for autism but for many of the other diseases that are going forward for genome sequencing.

So it's starting to happen but it just needs to be I guess coordinated I guess is the point, coordinating the coordinating committees I guess.

DR. AMARAL: Yes. Good point, (Evan).

MS. SINGER: This is Alison and I also wasn't really aware of this. So I do think this is exactly the kind of thing that we include in chapter seven. So I think what would be great is Evan is if you could just maybe shoot me an e-mail with a couple of sentences about this and I can bring it up on our chapter seven call.

DR. EICHLER: Okay I will do that. I will probably send it to you in a couple days. I'm sorry I have to run guys but this has been an interesting discussion. I'll talk to you guys later.

DR. DANIELS: Thank you, Evan. Being sensitive of people's time, we have gotten through the agenda that I had planned for us in terms of emerging research that doesn't appear to be strongly represented in the portfolio area. You've already talked about that and we'll have time on the next call to discuss that.

So for the next call, we will be convening to talk about the public comments that came in through a request for public comment that our office put out on the street and you'll have access to kind of a short summary of what was in those comments and then of course, to the full text of the comment that we'll be putting online.

And then we'll talk about research updates and what has been happening in research recently and if you would like to just note anything that you are going to want to bring up on that call, any particular findings that you think have been real breakthroughs or that have revolutionized the field or particular needs in the field will be discussing that next time.

So are there any other questions before we wrap up?

(No response.)

DR. DANIELS: Well thank you so much for all being here and for this great discussion. We took good notes and certainly we'll also try to coordinate with question seven's working group and glad that Alison was on this call. Thanks so much and we'll be sending out information about the next call.

DR. AMARAL: Okay thank you, (Susan).

DR. LAWLER: Bye.

DR. AMARAL: Bye everyone. Thanks.

(Whereupon, the conference call was adjourned.)