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Moderator: Heidi Mergenthaler
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9:00 am PST

Henry Greely: ...come in. Let's just do a roll call to make sure that we know exactly who's here and I think maybe the easiest way for me to do it is just go down the list of committee members. Dr. Blackburn; Dr. Cheshier; Hank Greely is here; Dr. Stock; Dr. Dorff.

Elliot Dorff: Yes.

Henry Greely: Dr. Gage?

Fred Gage: Here.

Henry Greely: Dr. McLean; Professor Rao; Dr. Martinez-Maza?

Otoniel Martinez-Maza: Yes, here.

Henry Greely: Dr. Lubin?

Bertram Lubin: Here.

Henry Greely: Dr. Lo?

Bernard Lo: Here.

Henry Greely: And Dr. Magnus?

David Magnus: Here.

Henry Greely: So we have seven present. We have a quorum. I think we probably should repeat for the record a couple of comments members made before the meeting started about new positions for the purposes of disclosure. Those of you who had those, you want to repeat them?

Bertram Lubin: This is Bert Lubin. I am now a member of the Independent Citizens Oversight Committee and the board of California Institute for Regenerative Medicine.

Fred Gage: This is Fred Gage. I am now the President of the International Society for Stem Cell Research.

Henry Greely: Anybody else relevant to changes? Okay. We have the meeting minutes - the next thing on our agenda - is the meeting minutes from our meeting last November. I want to congratulate the staff on doing a very nice job of making this all sound more articulate and coherent than my memory made it sound.

Are there corrections or additions or deletions to the minutes? I recommend the minutes this time - it was a very nice write-up - is there a motion to approve?

Man: I move.

Henry Greely: Second?

Man: I second it.

Henry Greely: All in favor say aye.

All: Aye.

Henry Greely: Opposed? Abstentions? Minutes are adopted. Now looking at the agenda we've got five items left. Item 3 - the first of them still left - Agenda Item 3 is really almost entirely language approval of decisions we took at our last meeting. I think that's right although there is one piece - the last pieces - the last of those pieces of language is one that we didn't discuss much.

Item 4 is on with respect I think largely to Dr. Lo's concerns about some of the consent issues. Item 5 is something that I'm not sure needs to be on here. David Magnus and I were talking about this and thought it should be on. A closer look makes me think maybe not so we may be able to work through that one, dispense with that one, I'm not sure.

Item 6 is a report from Dr. Lomax and Item 7 is a general research update. It is my hope, although I won't go so far as to say expectation, that this may be a short and productive meeting as opposed to a long and productive meeting so let's take a look at Agenda Item 3, the amendments to Sections 2, 5 and 10.

It's really useful for this I think if you've got in front of you the mark-up that the staff sent out with our meeting materials of the guidelines for human stem cell research. This is the one that has changes in is that blue or purple? Changes in a non-black color and says at the bottom last revised January 5, 2011.

Everybody got that or got access to that? I think it was sent out both physically and I believe it was an attachment to one of the e-mails; Heidi, is that right?

Heidi Mergenthaler: Correct, and it's also posted on the Website.

Henry Greely: Okay, good, so the first set of changes is at Pages 1 and 2 and that is a change to the definition of covered research which I think is mainly does two things: it makes the definition a little less circular - previously it had been covered research means research with covered stem cell line or that uses covered cells - and it also makes it clear that it's talking about research, well, so it says.

I'll just say what it says: covered research means research that derives a human pluripotent stem cell population that derives? Probably should be that involves, no? A human pluripotent stem cell population derived from an embryo or product of somatic cell nuclear transfer SCNT so this is saying that as I understand it correctly that iPSCs are not covered research.

Man: That's how I would interpret that.

Man: Yeah, me too.

Henry Greely: And I think that's what we wanted - most of us wanted at least - with the exception that the iPSCs come back in as human pluripotent cell research in a couple of respects notably with respect to their introduction into animals.

David Magnus: Or humans.

Henry Greely: Or humans, yes. Animals whether human or non-human.

Man: Right.

Henry Greely: So I do think that second verb in that sentence should be involves. Covered research means research that involves a human pluripotent stem cell population as opposed to derives a human pluripotent stem cell population derived from; am I right on that?

Bertram Lubin: That's right.

Man: Yeah, absolutely.

Henry Greely: Okay, so let's will somebody make a motion to amend this language to strike derives and put in involves?

Man: I make a motion.

Henry Greely: Okay. Any opposition? Okay. Friendly amendment adopted and I think well, I think I'll go through all of them and then we'll take a vote so I think that's fairly uncontroversial.

Geoffrey Lomax: Hank, can I - this is Geoff Lomax - sorry to be the and this is great actually. I think it's a terrific update. I guess the only question is do you is there for whatever reason it appears you're sort of just not addressing parthenote lines which are actually in use in California so is there any reason to include or not include those lines or are they not intended to be within the scope of this definition?

Henry Greely: I don't know. Any thoughts on parthenotes? I'm not sure they fall within our statutory mandate.

Geoffrey Lomax: Okay.

Henry Greely: But I'm not sure they don't. I'm not sure that given that these are guidelines, I'm not sure how important that is. Committee members' thoughts on parthenote lines? How widely are they being used?

Geoffrey Lomax: Well, if you could ask me in a week, I'm going to a meeting where there's this big discussion about them. I know there are a set of lines in use that have been derived and are being used in California but to be more - I can't be more - quantitative than that.

((Crosstalk))

Fred Gage: ...used, how do you mean they're being used? Are they part of protocols or published papers? Is there any evidence of their success?

Geoffrey Lomax: Yeah, I mean, they've been derived. That's been widely published or announced and then, you know, to what extent they're, you know, they're sort of utility beyond that, I haven't really been following the science other than to really know that they, you know, it is an area of active interest among some, you know, California research institutions.

Henry Greely: And these are human parthenote lines?

Geoffrey Lomax: Yes.

Fred Gage: So part of the issue in the IPS lines are that the evidence that there may be differences between IPS and ES at a fundamental level suggest that they're not the same thing and I'm wondering whether or not that same level of deep

sequencing, etcetera, has been done for the parthenotes compared to ES cells to see that they actually fall into the same category scientifically.

Bertram Lubin: Yeah. I don't think that's published yet but certainly the first part that you mentioned is definitely published and was presented at the last CIRM meeting the last week.

Fred Gage: Okay.

Henry Greely: Well...

David Magnus: To me, since this involves essentially creating a potentially pluripotent cell from a human egg, it does seem like to me that should be included so I think we should add products derived from an embryo, products derives from a somatic cell nuclear transfer or human parthenogenesis.

Henry Greely: Well, let's talk about that a little bit. It seems to me that the animal issues still apply so like iPSCs we'd be concerned about introduction into animals for the same reasons but to the same extent these parthenote cells are pluripotent cells, our guidelines as already proposed to be amended cover that.

David Magnus: That is a consent requirement, though.

Henry Greely: It's just a derivation in, well, huh.

David Magnus: If you're taking eggs from a woman and using them in this way, I mean, you don't have the...

((Crosstalk))

Henry Greely: Yeah, but that's a human subjects issue, isn't it?

David Magnus: Yeah, maybe, okay.

((Crosstalk))

Henry Greely: You're not destroying an embryo which is after all one of the main reasons for special status of review of these things. You're also not doing anything that can be described as cloning which is another substantial concern.

David Magnus: Yeah.

Henry Greely: I'm thinking out loud here because, you know, Geoff has seen it's probably obvious, we hadn't thought about - I hadn't thought about - the parthenote issue.

Geoffrey Lomax: You do cover it. What's useful is the way you for your review of research involving oocytes, you don't actually say covered research. You say human stem cell research so I think you actually do cover it.

David Magnus: And think I think will cover it. Yeah, I think we're set then.

Geoffrey Lomax: I think you're set because I was worried. I was worried you might just be excluding it but it appears you're not because for reasons you've sort of just touched on so like I say, I was just thinking out loud and I didn't mean to sidetrack the discussion.

David Magnus: As long as the oocyte procurement issue's covered, I think we're set.

Henry Greely: So parthenotes-derived cells would be covered under the oocyte provisions of this as well as under the transplantation into non-human animals provision?

David Magnus: Right, right.

Henry Greely: Other thoughts on this question? Okay.

Otoniel Martinez-Maza: I think that's right.

Henry Greely: Okay, good, and Geoff, thanks for bringing it up because it's good to at least now we have a record of what the committee thinks it means with these guidelines with respect to this. It's something I don't think we'd really given specific attention to.

And I hadn't really realized that people were moving forward substantially with the parthenotes. I'm sort of curious about the justification for it given the reasons for the interest given both HESCs and iPSCs.

Elliot Dorff: This is Elliot. My only question is shouldn't this be, I mean, if this is part of the ongoing research, shouldn't - and then we know about it - shouldn't those be deliberately and explicitly part of the guidelines rather than just the committee notes?

Henry Greely: Well, the question I think Elliot is whether we think parthenotes should be covered like embryonic stem cells in all aspects of the guidelines or whether more like iPSCs, they should be covered only when specifically - only in ways that are of specific interest or that are specifically covered like the transplantation into non-human animals and the use of oocytes.

Elliot Dorff: Right. I understand that. My only question is given that we discussed it and I think have come to a consensus, shouldn't that consensus be written into our guidelines rather than just simply part of the background material?

Henry Greely: Right. I think that makes sense but where would we write it in?

Elliot Dorff: I don't know.

David Magnus: I hate to interrupt but I'm leaving in like 30 or 60 seconds so if there's any vote that you need me for, you've got about 30 seconds.

Henry Greely: Right. I don't think there's anything we can vote on yet. Sorry, what?

Bernard Lo: I was wondering when David's lunch would be over, whether we can try and get him after his lunch.

Henry Greely: And we are expecting Radhika on you said at 10:00?

Heidi Mergenthaler: At 10:00.

Henry Greely: When is your lunch over, David?

David Magnus: Sorry?

Henry Greely: When is your lunch over?

David Magnus: It should be over hopefully, in about an hour to an hour and a half.

Henry Greely: Greg, are you on now? I have an e-mail saying Greg is online now.

Gregory Stock: Yes, I'm on. Can you hear me?

Henry Greely: Okay, good. I didn't realize you were on. In that case...

Gregory Stock: I just didn't want to interrupt you earlier.

Henry Greely: We're back to a quorum, right?

Gregory Stock: Yeah.

Heidi Mergenthaler: Yeah.

Henry Greely: Okay, David, have a good lunch.

David Magnus: Okay, thanks. Bye.

Henry Greely: All right, so let's get back to Elliot's question. I think I agree with you in principle, Elliott. I'm not sure where we would put it since it shouldn't I think go into this initial section on the definition of covered research because it's not covered for all purposes, although it could be.

I'm not sure that I care strongly about that. Covering it for all purposes would mean that the derivation of stem cell lines from parthenotes would have to go through SCRO approval. That doesn't strike me as terribly burdensome.

On the other hand, other parthenotes I think have some controversial aspects. They're not as ethically, morally or publicly as controversial as either embryo derivations or SCNT. We could cover parthenotes for everything.

If we only cover parthenotes in relation to our oocyte guidelines and our non-human animal guidelines, then I'm not sure there's a good place to specifically say that. What's the committee's sense here? Should we cover parthenotes generally; parthenote-derived stem cell lines?

Bertram Lubin: It's seems - why not - I'd ask that question.

Elliot Dorff: Well, and I think Hank raised some issues as to why not, mainly that the concerns are not the same kinds of concerns as you have for destruction of embryos. This is, you know, this is an egg. It's not a full - it could never become - a full-fledged human being or at least that's my understanding of it.

Otoniel Martinez-Maza: Well, you know, there are some serious issues regarding procurement of eggs that are addressed by this and maybe they should be applied to this research as well.

Henry Greely: Although I think that the procure - well, you know, I think that's right - I think the procurement of oocytes provisions would cover parthenotes but it would cover it more clearly if we included parthenotes in the definition of covered research and the downside I suppose is instead of just requiring SCRO approval of the oocyte procurement aspects and the non-human animal transplantation aspects.

It would require people to put in a protocol every time they were planning to derive stem cell lines from parthenotes.

Otoniel Martinez-Maza: Wouldn't it also make it not allowed to pay women for donation of oocytes for that purpose?

Henry Greely: For research purposes, that's true. Do we know whether the current parthenote research is using paid donors? I mean our census here is there isn't a lot of paid - if any - paid egg donation - paid research egg donation - going on in California but you're right. That is another thing. This would too.

Fred Gage: My only concern is it's a slippery slope argument that you're deriving ES cells from a single cell...

Henry Greely: Right.

Fred Gage: ...will this eventually sort of...

Henry Greely: Why is this different from IPSC??

Fred Gage: Yeah, exactly, and if we do it, I would consider have the committee considered not calling it a parthenate which has a variety of meanings to different people and call it what it is, you know, deriving directly from oocytes or something like that, more the definition of what it is that you're really protecting against.

Henry Greely: We'll look. I think we've got protections in the current guidelines with respect to the things that would be of most concern, the transplantation into non-human animals and issues around the oocyte donation.

I think I agree in principal with Elliot's point about it would be nice to state clearly somewhere that these are covered. I think I'm convinced that they probably shouldn't be covered to the same extent as embryonic and SCNT-derived cell lines.

So my suggestion at this point would be that we'd leave this language as it is and we think about if there's some way we want to, yeah, my problem Elliot is I don't see an obvious way to say in the context of these guidelines to say what we want to say about parthenotes so I want to punt it.

Elliot Dorff: I understand. Let me suggest...

Henry Greely: And not punt it - I don't mean punt it - by ignore it but think about before our next meeting if there is a language fix we can use.

Elliot Dorff: That's fine. The only question that I would ask is at the beginning here in the definitions, all we're talking about is what is covered.

Henry Greely: Right.

Elliot Dorff: We're not talking about how it's covered...

Henry Greely: Right.

Elliot Dorff: ...right, so that's why it seems to me that it should be covered because otherwise we have no jurisdiction to deal with it altogether as far as...

Henry Greely: Well, no, that's not quite right because we do later - covered here is a term of our - the guidelines apply to things that aren't covered cells in some context...

Elliot Dorff: Oh alright.

Henry Greely: ...so they apply and that's another aspect of the changes that are proposed in this version, they apply to IPSCs even though IPSCs aren't covered lines but there are a few provisions that talk about pluripotent lines...

Elliot Dorff: Okay.

Henry Greely: ...and those would cover parthenotes. Those are the animal provisions and then there are some provisions that deal with getting oocytes for research.

Elliot Dorff: Sure enough. Good.

Henry Greely: I think those would be covered so let's go on to I think the next changes...

Geoffrey Lomax: Hank, could I just - sorry to interrupt - but again, Geoff Lomax. I have just for one point of clarification because it came up in the conversation that I think it actually introduced an inaccuracy into the record and that just as a reminder, the issue with regarding oocytes and payment were covered in the actual - the enabling - legislation for this committee, that's SB 1260.

And based on that legislation, that is the driving piece of public policy that imposes the payment restriction so any and that incorporates any use of oocytes for research so I just wanted to make - add that clarification - because I felt what was said previously I found a bit confusing. Does that make sense?

Henry Greely: I'm not sure, you know, my recollection of the language of the bill is not entirely clear. Is it your understanding that the statute limits the use of oocytes or is it - you talking about oocytes specifically - not embryos?

Geoffrey Lomax: Oocytes specifically.

Henry Greely: Okay.

Geoffrey Lomax: And that was, yeah, so it was, so any, the sort of the, the framework regarding payment is effectively set by the legislation.

Henry Greely: Right and the legislation bans the use of any oocytes for which there was payment beyond whatever small reimbursements it permits?

Geoffrey Lomax: Correct.

Henry Greely: But that isn't the setup with respect to embryos.

Geoffrey Lomax: Correct.

Henry Greely: Got it. Okay. Thank you. Take a look at Page 5 and Page 5 of the guidelines, Section 5(b), we're adding creation or use of embryos, covered research involving creation or use of human embryos may not commence.

We had some significant discussion last time about whether it should be creation procurement or use of embryos and ended-up coming down on the side of just putting creation in and I think this amendment only reflects the decision we made at the last meeting. Questions, comments?

The next proposed language changes are at six and seven and these are the two spots or at least these are two spots where I think David noticed somebody - or maybe Bernie - somebody had noticed that we were still using the covered stem cell line term when we wanted it to be broader and include all human pluripotent.

So (d) on Page 6 is human clinical trials and (f) on Page 7 is transplantations in non-human animals. These are both areas where the committee believes that iPSCs should still be covered and we're doing that by changing the

coverage for these from covered stem cell lines to human pluripotent stem cell lines which would cover iPSCs as well as presumably cell lines - pluripotent cell lines - derived from human ova. Questions on that?

Okay, then turn to Page 16. These are informed consent requirements in both Section 10(b) and 10(b)(1). Based on our discussion from last time, we're adding SCNT so the consent applies when you're getting donation of gametes, embryos, somatic cells, or human tissues for purposes of SCNT as well as for purposes of derivation of new covered stem cell lines.

The SCNT is a new addition in part because the covered lines, well, I guess it's just to clarify it because SCNT lines are covered lines but just to make it more specific, I do think that there may be a need for language change in (b)(1). If you look at just (b), it says for purposes of SCNT comma or derivation and (b)(1) says for the purposes of SCNT to be used to derive stem cell lines.

And I don't think we want one to be solely about SCNT so I think there needs to be an or added someplace in there but this also I think with that possible amendment reflects our conclusions from last time. Comments, questions?

Fred Gage: A friendly amendment that we include the or.

Henry Greely: Yeah, thanks. For the purposes of SCNT comma or to be used to derive stem cell lines, I think that's where the or would go. Objections to the friendly amendment? Hearing none, it's adopted.

And then the other change reflected on this draft that we received on Page 18 and this is provisional language that the staff came up with after reading through the transcripts of our last meeting and Bernie, I think this is aimed at

some of the concerns you have but since you were not able to be present for the entire meeting, this is language we didn't discuss at the meeting.

It's language that you didn't discuss at the meeting. It says new Section (c) saying though not a requirement, these guidelines encourage researchers to incorporate informed consent in their research design for any human tissue procurement that might potentially be used for any human stem cell research.

So as to avoid retrospective consent, paying particular attention to sensitive areas such as the creation of human gametes. So there are I think two different levels of issue around this. One is do we like the idea of this putting this encouragement into the guidelines which I recall we discussed last time.

And then second is this language the right language for it and I think the first is probably the more important. Anybody want to speak to that? Bernie, do you have any thoughts on this?

Bernard Lo: Yeah, so let me take a step back and try and think through what the issues are that we would want people to pay specific attention to in addition to creation of human gametes.

Henry Greely: Okay, so these are issues that we would want to make sure the consent specifically raised for people; is that it?

Bernard Lo: Yeah, so what I think the, you know, I think it would be helpful to try and say to researchers look, if you're going to collect tissue from which you're going to create a stem cell line, here are specific things you might want to try and put into the consent so creation of gametes is clearly, you know, the most sensitive.

I guess another thing I would raise as a suggestion is this notion of allogeneic transplantation for therapeutic purposes so in other transplantation contexts, we recognized that there were some potential donors who have concerns or objections about using cellular material derived from their tissues to be transplanted into another person even though it would potentially be lifesaving.

And so I guess other issues like that that we would want to have included a consent so that later on you would avoid the situation of a donor saying oh, when I consented, I had no idea that this was part of the potential future use of these cells and had they told me that, I would not have, you know, I would not necessarily have consented.

I think it's particularly - it may be particularly - important in the iPSC derivation context assuming for example that they're able to be used clinically, scientifically for transplantation and that there should be no - there's relatively lesser problem - with finding alternative donors as opposed to human embryonic stem cells.

So I guess one thing would be to sort of think are there other issues and again I don't mind just saying as a for example not a requirement. So that would be one set of issues I'd like to hear other people's suggestions on.

Bertram Lubin: One of the comments I want to make that's related but somewhat tangential to the discussion you were having - Bernie and Hank are having - is CIRM is going to be in my opinion moving more and more to clinical trials.

They're recognizing that the public wants to see cures or treatments of patients and I think there's going to be an emphasis and Geoff you could

correct me if I'm wrong in this, an emphasis on more studies that would involve infusion of cells into humans.

And so I think that whatever we do in considering these guidelines should keep that in mind and I think we have. I'm just saying we're going to see more of this now and I just wanted everyone to know. Hello?

Henry Greely: Yeah.

Bertram Lubin: Okay, sorry.

Henry Greely: Well, Bert, I think that's certainly right and useful. Bernie, going back to your point, do you have language that you would particularly like or is this idea of encouraging do you think enough or...

Bernard Lo: Well, I guess...

Henry Greely: Where would you have us go?

Bernard Lo: So one question would be to, are there other - paying particular attention to sensitive areas - do we want to include other...

Henry Greely: Specific examples.

Bernard Lo: ...and, you know, while sensitive may be, you know, it's one of these elastic terms and perhaps just to give more examples would be useful and whether sensitive's the right adjective or not, it's not clear.

Another one just to throw things out, is this whole notion of patenting discoveries and commercialization. I mean, there are some studies suggesting

that some percentage of donors object to the patenting and commercialization although that may forestall as we know the development of therapies.

Again the idea would be to put it up-front so that people who do consent know it's going to happen and therefore there are no barriers to the therapy development and commercialization process downstream.

Henry Greely: Other thoughts, so I think Bernie's making a strong argument for at the very least encouraging researchers to think through possibly - I'm going to use the word sensitive Bernie - because I'm not sure what else captures it for me.

Sensitive uses of materials up-front in the consent, I find that personally I find that fairly appealing. I wonder about what language would most accurately capture it and I wonder if maybe this is something that we don't try to draft language at this meeting but agree that it's worth trying to consider such an addition and before our next meeting, have some proposed language.

It sounds as if the current language doesn't capture all of what you're concerned about, Bernie; is that fair?

Bernard Lo: That's right. I think I agree with the creation of human gametes being a particularly sensitive issue but I think there are others that may also merit explicit attention. The other thing is I think retrospective consent again is a term that people may interpret differently. I'm wondering if we can...

Henry Greely: Yeah, I'm troubled by that term in this context too.

Bernard Lo: Yeah, avoid that and introducing a new term that people may interpret differently by giving specific for example including but not limited to.

Elliot Dorff: Right. This is Elliot. If you're worried about the word sensitive, I mean, I think what you have in mind is applications of their donations to uses to which they would object so you could just simply say that specifically instead of using the word sensitive because that's what you have in mind, I take it, right?

Bernard Lo: I like that language and I hope it got recorded on the tape recording and will get captured in the minutes.

Henry Greely: And it's applications to which we think what, substantial?

Elliot Dorff: Donors would - to which the donors would - object, something like that. Why they would object is their business.

Henry Greely: Right, but it wouldn't necessarily be all donors.

Elliot Dorff: That's correct.

Henry Greely: And it wouldn't be and if there's one donor out there who would object, we don't want to capture that so it's...

Elliot Dorff: Very good.

Henry Greely: ...that some and I'm not proposing the word non-trivial but some significant percentage of donors might object to.

Elliot Dorff: Exactly right.

Bernard Lo: The way we framed it for our researchers at UCSF and I think it's been successful, is the notion that if you develop a line and it becomes for whatever reason a line that many other scientists want to use and might even have

therapeutic application, it would be incredibly inefficient and unfortunate if downstream uses were blocked because the donor later said wait a minute, I sort of infer these are derived from cells I donated.

I had no idea you were going to do this and I would have objected so it's more of the sort of the retrospective withdrawal or refusal that I think would really be unfortunate in terms of barriers, delays to research that could have been avoided had the consent been a little more comprehensive at the onset.

Henry Greely: Okay, what I think I'm going to propose subject to of course committee members' thoughts, is we accept the idea that we should have a provision along these lines and we agree to come up with thought-through language by our next meeting. Is that fair? It always makes me a little nervous to try to craft language in the middle of a meeting, particularly a teleconference meeting.

Elliot Dorff: Absolutely.

Bernard Lo: I agree.

Elliot Dorff: Right, and that sounds right to me as well. I do have one other thought though in doing this. We say at the beginning of this though this is not a requirement. I think we should say why we think it's not a requirement.

Is it because there are so many uses for which the materials might be used that we can't possibly imagine what they would be at the time or because these are materials after all, they are not the human being him or herself or both of those reasons or other reasons?

I mean, I think, you know, this is after all a legislative - this is an advisory committee - to a law, I mean, to applying a law so if we are saying that it's not going to be legally required, I think we need to say why.

Henry Greely: Okay, so Bernie, having heard all this and since you're the person who has expressed these concerns most seriously, no good deed goes unpunished and I hope that you will give some thought to specific language that we might debate and approve at our next meeting.

Bernard Lo: I'll do that and try and work with you Hank and others on the committee. I would just like to follow-up on Elliot's - I think it was Elliot, I'm sorry - I have trouble...

Elliot Dorff: Yes, yeah, this is I, yes.

Bernard Lo: ...comments about so what's the ration - and it doesn't necessarily need to go into the actual text but maybe it would help me certainly to understand - the rationale for why not requiring it and to me it seems to be a matter of flexibility and assuming that standards and best practices will evolve and that there are things that we can't necessarily anticipate.

But I'd like to have a sense from the rest of the committee as to the rationale for that at the beginning of the section.

Henry Greely: I can't speak for the whole committee. I think the questions of uncertainty, change are certainly part of it. We're not wanting to try to come up with a specific list of here are all the issues that people might be concerned about with the implications that yeah, these will always be issues people should be concerned about so you should always ask about them on the one hand and the

negative implication that if it's not on the list, you don't have to worry about it on the other.

Elliot Dorff: This is Elliot so maybe the language ought to read something like because the uses of donated materials cannot be, well, cannot be foreseen, informed consent is not required but where the use of a particular donation is expected, then informed consent is encouraged or is appropriate or something like that.

Henry Greely: Yeah, so remember the context here. This is in Section 10 of the guidelines which are the informed consent requirements and it basically Section (b) of that goes through a fairly long list of nine specific things that should be included in the consent form. Actually, it's even more than nine.

Elliot Dorff: Mmh-hmm, right.

Henry Greely: That's funny.

Elliot Dorff: Right, even in I on Page 17 that the results of the reagents may be patentable or have commercial potential, what Bernie was talking about before.

Henry Greely: Right and it's both...

Elliot Dorff: It's already on the list.

Henry Greely: ...right, we've got nine under (b)(1) and then we've also got a (b)(2),(3),(4) and (5) so (c) is kind of the proposed (c) would be kind of the clean-up in addition, you know, the Columbo, one more question, in the memory of Peter Falk, the late Peter Falk.

But I think those are good suggestions for us to think about as we try to draft this language but remember it's in a context where we've already listed a whole bunch of specific stuff that needs to be included and I think this is something that says and apart from all the things we've already listed that should be included, think hard. We encourage you to think hard about this.

Bernard Lo: Heidi, if you or your staff can forward me the comments that Elliot and others made in this last go-around I think would really help with the drafting process.

Heidi Mergenthaler: Sure. No problem.

Henry Greely: Okay. I think we may be ready for a motion on these proposed changes from the staff as amended in two cases - not proposed changes from the staff - but the language the staff has proposed to incorporate changes we said at our last meeting we wanted done.

And I'm going to - I think it would be good to - get a motion to approve the changes with the two friendly amendments to Sections 2, 5 and 10 that we have discussed excluding at this point the proposed new 10(c) but with the intent to bring back language for that at our next meeting.

Elliot Dorff: So moved.

Henry Greely: Is there a second?

Man: Second.

Henry Greely: Is there any further discussion? Should we be asking, is there any member of the public on this line apart from invited guests but also member of the public

Dr. Lomax? Does any member of the public including but not necessarily limited to Dr. Lomax want to comment on this before we vote?

Man: No.

Henry Greely: Okay. All in favor say aye.

All: Aye.

Henry Greely: Aye. All opposed? Any abstentions? And now feeling a little anal about wanting to do this but I just want to make sure that we still have seven at the time of these ayes so I'll go by names and give me an aye? Greely, aye. Lo? Bernie, you still on?

Bernard Lo: Sorry, this is Bernie. I just popped out for a...

Henry Greely: So you voted yes, right?

Bernard Lo: Voted yes.

Henry Greely: Greg?

Gregory Stock: Yes.

Henry Greely: Elliot?

Elliot Dorff: Yes.

Henry Greely: Fred?

Fred Gage: Yes.

Henry Greely: Oto?

Otoniel Martinez-Maza: Yes.

Henry Greely: Bert?

Bertram Lubin: Yes.

Henry Greely: Okay, so we got seven yeses.

Radhika Rao: Hank?

Henry Greely: Yes?

Radhika Rao: This is Radhika. I just joined your call.

Henry Greely: Hi, Radhika.

Radhika Rao: Hi.

Henry Greely: You want to vote yes?

Radhika Rao: Uh, sure.

Henry Greely: No, I think we should probably list you as just having joined the call after the discussion.

Radhika Rao: Yeah.

Henry Greely: Thanks for coming on.

Gregory Stock: Hank, will there be any more votes?

Henry Greely: I don't know. I don't think so but I don't know.

Gregory Stock: I may have to leave and I just wanted to check ahead of time. Rather than interrupting people, I'll just escape now that you have an extra person coming on.

Henry Greely: Okay. Thanks for being on.

Gregory Stock: You bet.

Henry Greely: So we're playing rotating quora, quorums, quora, but we have a quorum still. I'm not sure that we need any more votes. Let's look back at the agenda. We've finished Agenda Items 1, 2 and 3.

Radhika Rao: Okay.

Henry Greely: Agenda Item 4, let me skip over Agenda Item 4 for a second and then plan to come back to it because I do want to nail down Agenda Item 5. I think this may not need to be on here. This is the question David Magnus had raised it to me and I'd raised it to Heidi who as a result put it on the agenda, the CIRM regulations as I understand have changed in the not too distant past in a way that now allows the use of embryos that were created for reproductive purposes in CIRM- funded, well, in research if, well, allows the use of cells from cell lines created from embryos that were created for reproductive purposes to be used even though some of the donors of gametes for those

reproductively-purposed embryos were paid. Is that right, Geoff, Bernie? Am I...

Geoffrey Lomax: Yeah, well, either the cell lines or the embryos themselves may be used.

Henry Greely: Okay, okay.

Geoffrey Lomax: The point is there - as long as they were produced for reproductive purposes...

Henry Greely: Right.

Geoffrey Lomax: ...there's no intent to impose any kind of restriction on payments.

Henry Greely: And David said well maybe we need to change our guidelines to correspond to this and I said well it sounds like something we should put on the agenda but as I look back over our guidelines, I think we're already okay on that because our guidelines only limit payment for when the gametes were donated for money for research.

Radhika Rao: Research.

Geoffrey Lomax: Yes. You were very eloquent and insightful in that scoping statement you made, yes.

Henry Greely: So I think we're all right.

Radhika Rao: Uh-hmm.

Henry Greely: Which means that Agenda Item 5 I think was my mistake and can be stricken.

Radhika Rao: Yeah.

Henry Greely: Unless somebody else sees something I'm missing.

Elliot Dorff: Well, again, this is Elliot. The question is whether you want to be specific about the fact that it is in other words what you just said is in the guidelines as stated and I think it can certainly be read that way.

The only question is that if CIRM in particular is allowing the use of gametes where payment was used because they were originally for reproductive purposes, whether we should be explicit about allowing that as well or whether that has to be something that's inferred.

Henry Greely: Right. Trying to find - anybody have handy - the specific section number?

Radhika Rao: Yeah, it's...

Henry Greely: 6(a)(2)(B), right?

Radhika Rao: Yeah. (2)(B).

Henry Greely: Or not to be.

Radhika Rao: I say to be. Donors of human gametes or embryos did not receive valuable consideration for participation in research.

Henry Greely: That seems pretty clear, Elliot.

Elliot Dorff: Sure enough.

Henry Greely: We could say, no, I'd be inclined to let it ride.

Radhika Rao: Me too.

Henry Greely: Again, I appreciate and agree with in general your interest in being express but adding language is always a little bit scary.

Elliot Dorff: Okay, fair enough.

Henry Greely: So let's circle back then to Agenda Item 4 and Heidi, would you give us some background on this one because I'm still being a little thrown by the citation to Section 5(f) which is the animal section.

Heidi Mergenthaler: Well, I think at the last meeting, Dr. Lo was expressing the same concern that he had with what we had inserted into 10(c), the language that we had inserted in there. I think that he had the same concern in 5(f) about the downstream usage and we never got around to discussing it again before he left the phone call so we included it in this.

Bernard Lo: That is the connection. Thank you so much for clarifying. So, you know, this is again another example of procedures or activities that are generally regarded as the standard part of research but to which some people - potential donors - might object and I'm particularly thinking, you know, at UCSF my office is located so that when the animal rights people demonstrate, they sort of hook themselves onto the front of a building and they sort of dangle outside my window with the police underneath.

And so, you know, animal objections to research though some people do object to that and I guess again the issue is that do we want to make - to do - what we can by making this explicitly the expectation that the cells derived in

this manner will be injected into animals as part and parcel of the research enterprise.

Henry Greely: Okay.

Bernard Lo: So that people don't later say well gosh, you never told me and I never would have agreed.

Henry Greely: Right. I see that and so but it strikes me that this is really part of what we just discussed in the language that you could propose for a new 10(c) could also encompass animal uses.

Bernard Lo: That's right. I think Heidi made that connection very nicely for us.

Henry Greely: Okay, so in effect we don't really need to do anything under this agenda item except to make sure that it's included in whatever language we propose in the spot of the previously-proposed 10(c), right?

Bernard Lo: Right.

Geoffrey Lomax: Although just as a - again, Geoff here - to point out that in Section (b)(1)(E) you actually incorporate animal transplantation into your general consent requirement.

Henry Greely: In 10, right?

Geoffrey Lomax: Yes.

Henry Greely: Which is at Page 17.

Geoffrey Lomax: Big letter E.

Henry Greely: Right, derived cells or cell products may be transplanted into humans or animals, but there may be more to be done. I mean, I think Bernie think about this one as you think about language we might want to work with the staff and others of us to think about language for our next meeting.

Bernard Lo: Absolutely. This is complicated and as Hank said, we're not trying to do this on the fly.

Henry Greely: Okay. I think we're done with Agenda Items 1 through 5 at this point. Anybody disagree? Is there something in there that I missed? Well then, let's turn to Agenda Item 6 and I will with great pleasure turn the floor over to Dr. Lomax to tell us about what's going on with CIRM these days.

Geoffrey Lomax: Good, thank you and thanks, everyone. This is always very helpful to hear the committee and have a sort of a second opinion on a lot of the stuff we're doing. I thought would you like to start with the clinical trials piece because it's actually kind of interesting.

We just had a resolution passed and I know that's something that you all have been encouraging us to look at and hopefully I think Bernie could help me with this one so that would be a good place to start?

Henry Greely: Sure.

Geoffrey Lomax: Okay, so the standards working group that's responsible for the CIRM regulations is also mandated under Prop 71 to address clinical trials as you all have noted and I know and, you know, the guidelines actually are a little bit

have sort of touched on sort of the role of the oversight committees with regard to clinical trials.

We had a meeting of the standards working group and looked at first within that meeting, you know, what we did at the staff level was try to identify for the working group the whole series of public policy and regulations which would govern a clinical trial.

In this case we have the sort of Geron example to look at because that's the trial our board has approved funding for so we were in the context of that trial we were able to sort of describe the sort of public policy universe in relation to a trial registered with FDA for under an IND.

And so those regulations really encompass a number of aspects including the sort of the safety of the product that it would be introduced to a human in terms of a whole series of testing requirements for purity and safety and the details that come into the product on the product development side so we touched on that.

In addition, the common rule, the IRB, the consents and those set of activities and then I think what, again for the purpose of pulling it together in one place, this was a resolution.

We were trying to sort of illustrate to the working group all the various things that come into play because you can't just go to one piece of regulation. You have to pull from sort of FDA and a whole variety of regulatory agencies.

But then I think out of that discussion, I think the working group and perhaps Bernie, you know, if you could, you know, chime in here, I think they were encouraging us to really sort of amplify on issues around sort of transparency

and information reporting which, you know, I thought was, you know, extremely healthy and very interesting.

It's a bit different than sort of what you all have sort of where you've gone in terms of encouraging, you know, review up-front. This was more in regard to sort of publication, results reporting and adverse events and Bernie, would you like to comment at this stage?

Bernard Lo: Yeah, no, I just want to put in the big picture context so this follows-on from what Bert Lubin had mentioned earlier on and that CIRM is really looking at trying to facilitate stem cell-based clinical trials.

And that obviously as the science progresses, they wanted the standards working group to think about the ethical and policy issues and so the standards working group with Geoff's staffing has really been trying to think about these issues and I think we're just sort of saying this is where we think we're headed.

We are not proposing new regulations at this point but really view it as a sort of raising the awareness of both the potential recipients of CIRM grants that involve clinical trials and also CIRM staff and the CIRM reviewers who will be looking at these grants to keep in mind the ethical issues as well as the scientific issues.

And so there is going to be some guidance issue but it will be guidance as opposed to regulation.

Geoffrey Lomax: And I think, you know, what we're specifically incorporating along those lines and where this is at the moment is in our - they're incorporated in - the

application and I anticipate they'll be ultimately incorporated into our grants administration policy.

The application applies to the specific funding program whereas a grants administration policy is sort of a broader document that applies to, you know, all funded research but it would be first of all there's a requirement - basically a publication requirement - that the results of the trial are disseminated in a timely manner for the benefit of the field.

And again, that was something the working group was very adamant about. There's already a requirement - again this goes to the application but it will move to a broader CIRM-wide policy that - the trial is registered clinicaltrials.gov and the IRB is an IRB that is registered with OHRP so this is sort of a transparency requirement.

And then that CIRM itself is providing active oversight which is sort of a third part here and that there would be a very timely reporting of any kind of significant adverse event, again so that we would be informed of anything that would come up on a kind of risk safety side in a very timely way.

So that again, that information would be available in the event that there was any need to sort of communicate that or sort of reflect on any other trials that may be going on where that, you know, that event, you know, would have any bearing.

So I think those three specific aspects, the working group, you know, as we, well we ended-up redrafting again a resolution - I think you have the draft and not the final, I apologize for not sending the final - if you look at the final version of the resolution, it really I think calls out those areas more sharply than they were initially and again, that was really through the input of the

working group. And that resolution was approved by our board last Thursday.
Are there any questions there?

Henry Greely: How many clinical trials have you guys funded at this point?

Geoffrey Lomax: At the moment it's just the Geron trials, the primary trial. I mean, there are a number of other studies which are on a clinical trajectory but have not resulted in the filing of an IND at this stage, of May.

Henry Greely: Five, 10, 20?

Geoffrey Lomax: I'd say on the order of there's roughly five in the pipeline that have or that in and I'll - roughly with a capital R - but really to answer that I should probably check with the scientific team but I think kind of of that magnitude.

Henry Greely: Okay. Not a hundred.

Geoffrey Lomax: Not a hundred at this time.

Bertram Lubin: Can I interrupt just for a minute? A very beautiful annual report was handed out at the meeting last week which I'm sure is online and available which I think every member of this committee - it's the annual report from CIRM - and then the other is that the President Alan Trounson's report is going to be put on the Website for CIRM and that gives you a timely up-to-date on the new announcements and on some significant publications that have come out and I think our committee would benefit from reading that as well.

I'm sure CIRM could send it to the state if you want and they state could but if you look on the CIRM Website, it's on the Website.

Henry Greely: Okay. Thanks. Heidi, why don't you e-mail all the members that are on this call as well as those not with that link and Dr. Lubin's recommendation and let me take a look at it.

Heidi Mergenthaler: Sure.

Henry Greely: All right. Well, it's interesting to see how you guys have gone with the clinical trial approach. Anybody else have questions or thoughts about CIRM's clinical trial activity?

Bertram Lubin: Well I can just comment, and Geoff correct me if I'm wrong, because I'm a new member to the board but basically applications that have in them an IND or at least a plan to get an IND are the ones that are being requested now.

So clearly the intention is to do something that can eventually lead to a clinical trial and fortunately CIRM has resources to really support a clinical trial which I think is going to be important for this state and also adds importance to our committee at the state level that we're discussing right now.

So I think we're going to see a bit of a change in paradigm and Geoff, if you wouldn't mind, could you say who the new chair of the board of directors is for CIRM?

Geoffrey Lomax: It's Jon Thomas who's replacing Bob Klein and he's got I think there's an announcement on the Web in terms of folks want bio, background, etcetera.

Henry Greely: One sentence bio?

Geoffrey Lomax: His background is in - his most recent background - is in bond financing and areas around public financing and then sort of in a previous life, he's a sort of biologist and well, that's three sentences; how about that?

Bertram Lubin: And he's a lawyer.

Geoffrey Lomax: And a lawyer.

Henry Greely: A lawyer, a biologist and a financier.

Geoffrey Lomax: Yeah.

Bertram Lubin: Mostly lawyer and financier.

Henry Greely: Okay, good. And then the usual combination of skills and backgrounds?

Geoffrey Lomax: Yes.

Henry Greely: Geoff, other things about CIRM you want to tell us about and, you know, are there things the working group has on its agenda to take up?

Geoffrey Lomax: Yeah, well, I think the other side of this and again this is an area where we will I think continue to hopefully communicate and collaborate as sort of policy committees is we and I was hoping to get you a copy of this report.

We just got our final, you know, we just had the draft circulated to the working group on Friday and I just couldn't spin it around over the weekend but we are looking in quite a lot of detail about issues related to the IPS cell repositories.

Henry Greely: Mmh-hmm.

Geoffrey Lomax: And so we're sort of doing this is sort of two stages. The first stage is we're going to collaborate with the National Institute of Neurological Disease and Stroke, NINDS of the NIH who have an agreement with Coriell which is a big IPS bank in New Jersey and this really does tack directly back to the conversation you were just having around kind of consent and uses.

And so, you know, I think it's very relevant and so what we are going to - what we're doing there - is we are going to be collaborating with the idea of getting IPS lines that relate to certain neurological disease, you know, kind of work with our grantees to have them deposit it in the Coriell bank so that they're widely available.

And I think it, you know, so that was sort of part of the discussion we had recently with the standards working group but I think again it sort of comes back to, you know, maybe something to think about in terms of both our regulations and your guidelines is, you know, we don't actually in the sort of consent piece call out the sort of, you know, distribution of lines and deposits to repositories.

So one of the things that for example will appear in the report, you know, from this meeting is just to, you know, our basic inclusion is that our established rules for consent which are consistent with your rules as well for IPS derivation is that the other they're basically effective and sufficient for the purposes of banking given, you know, the list of things it goes through.

But perhaps it may be useful particularly for lines, you know, that are clearly eligible for deposit into this bank that, you know, indicate that, you know, it

may be, you know, the lines may be deposited to an outside bank for, you know, broad distribution, again just a level of detail.

I think when you explain that to somebody, it's kind of very tangible actually. You can talk about it's a, you know, the researcher may give them over to somebody else who will, you know, widely distribute them. That's important information for a donor.

And I think that's sort of a trend that we're going to see increasing so first off I think Step 1 for CIRM is through this collaboration, which is in the process of moving forward, we're going to learn more about I think the real mechanics of banking and sort of the process.

And then from that there's been discussion about the development of a CIRM bank and I don't think it would be on the order of like we're actually going to be physically building a bank, but maybe developing something in California through the existing infrastructure to develop a set of disease-specific induced pluripotent lines.

And I think if you, you know, sort of on the scientific side there was a workshop report that came out earlier this year that really describes the thinking there that there may be within California unique populations either on the disease side or just because of California's diversity overall, there may be opportunities for California to develop lines that are unique - have unique value - as a scientific resource.

And this initiative would be geared towards really basic research to develop a set of sort of standardized lines and again articulated in the scientific report and so there in that case it would be something where the lines would be being derived presumably with some sort of CIRM support.

So again sort of looking at, you know, the up-front issues of consent but one of the particularly interesting aspects of this proposal is that there is a sense that in developing these lines there may be a need for sort of ongoing sort of aggregation of health data so it would be more like in a study mode where the individual donating wouldn't sort of come and go but they would continue to have human subject status because you'd envision incorporating health information prospectively over some time course.

So, you know, one of the areas that again we didn't, I don't think we've finished the conversation but we recognize is a very important conversation is beyond what's already required for someone to withdraw, someone can always withdraw their participation in research under the laws that govern us.

There are some outstanding questions with regards to materials that are either in a bank or materials that have been substantively transformed and the status of those materials in relation to any sort of repository with regard to sort of future distribution, redistribution, what have you.

And again that is something that we've tried to articulate a range of issues in this report and we've kind of, you know, put forward some preliminary positions about what should and should not be withdrawn and why.

But again another I think very, you know, hot topic in the sense that, I mean, this isn't necessarily a new issue but it's a nuanced issue when one's considering sort of pluripotent cells.

And so maybe I'll stop there and again I know, you know, Bernie was extremely helpful both in facilitating the conversation and helping edit the report so I don't know if you have anything to add, Bernie.

Bernard Lo: Well Geoff, thanks very much for your summary and also for all your outstanding work on this. I just want to sort of point out that we at CIRM thought a lot about how best this sort of issue - the role of guidance as (unintelligible) relation - and we really wanted not to sort of step in with regulation at a point where they may not be needed and might (unintelligible) thought in these two new areas, stem cell banking and clinical trials.

It was really important to set broad guidance then to let the field move forward and find best ways of organizing this research and so I think the CDPH approach of guidelines as opposed to regulations was something that we found very attractive.

Henry Greely: Okay. Other questions for Geoff about CIRM?

Bertram Lubin: Geoff, you want to comment on IOM, the IOM, consideration of an IOM report?

Geoffrey Lomax: You know, actually I don't because all I know about - all I know is - IOM report and I have no detail on where that's going to tell you the truth.

Bertram Lubin: So I think CIRM is going to request an IOM report. I mean, that was with the discussion at the last board meeting. It hasn't been finalized and I don't think there was - I think they're exploring what that would involve - and I suspect that that's going to happen.

Henry Greely: Report on anything in particular?

Bertram Lubin: Overall the functions of CIRM, what it's done, how it's related to, how it was funded, etcetera, etcetera.

Henry Greely: Well, that actually may be connected at some level with the question that I had that I invite anybody with knowledge to speak to and Geoff may have some special constraints but well actually Geoff, you can answer part of it anyway. When actually does CIRM's clock run out and are their thoughts about what happens then?

Geoffrey Lomax: Well, I think again I forget the details. I mean, you know, the clock runs out I suppose when the money runs out as a practical matter and then there's, you know, there's - I forget the exact timeline - but there's the Institute is authorized to sort of issue bonds up until some point in the future which is sort of longer than the, you know, sort of people often used to sort of say 10 years since the initiative.

But it's some time horizon that's broader than that and I forget but I think that was, you know, I think that's kind of the kind of the interest in, you know, our new chairman in some ways that he brings expertise in sort of bond financing I know and, you know, Dr. Lubin I think was probably- the board knows more about this than I do.

You know, I think that was part of the discussions with the candidates in terms of looking at, you know, sort of getting their thinking in terms of ways in which, you know, there may be opportunities to, you know, prolong that time horizon.

And I think there was a discussion of sort of various sort of mechanisms, the details which I've, you know, I think it was fairly conceptual in terms at the time because that was the nature of the conversation so all, you know, in short it's something beyond, you know, I forget what the projections are for. I think they're almost like another seven years.

There is actually, I mean, if you go look at the financial projections that get put forth at board meetings, they do run for I don't know another six or seven years but then within that there's been these discussions with the new chairs about their thinking with regard to mechanisms of additional funding and then of course Mr. Klein's talked about another, you know, another initiative.

So that's where the discussion is at this time and Bert, I don't know if you can add any more resolution to that.

Bertram Lubin: I can't, but I think you're right on the timeframe, about another seven years and the issue is whether more bonds, philanthropy, private donors, all those kinds of activities are activities that are envisioned to be part of the future sustaining what CIRM initiated.

Elliot Dorff: Hank, this is Elliot Dorff. I'm wondering whether our committee needs to either at least consider the guidelines that CIRM is creating for, you know, for applications and for banking and then to either include them just as, you know, just include them completely or write some variation of them in our own guidelines.

Because at the moment as I understand our guidelines, it's completely for research and not for application or for banking; is that right?

Henry Greely: I think that's right although to the extent the application is in a clinical research context, our guidelines cover that.

Elliot Dorff: Okay.

Henry Greely: And I'm not sure, well, I think your suggestion's a good one. We should take a look and think about it. We'd have to go back and look at the statutes that created us and also see what DPS - DPH - wants in terms of whether we're limited to discussing research or whether our purview goes beyond research or not.

Once you get into non-research applications, there's a whole host of other bodies and issues that come into play starting with the FDA. But yes, I think we should think about whether these latest CIRM activities are things we should parallel.

Elliot Dorff: Okay.

Henry Greely: And that's something we should think about and maybe bring for discussion at our next meeting.

Geoffrey Lomax: And like I say, as soon as we're - I suspect this week - I mean, we've tried to format this report in a manner really for conversations like this really down to sort of three or four key topic areas, four or five sort of key things to think about and I hope that, you know, is helpful.

So we will in short order we'll get the more detailed description of this and like I say, it is current. As we like to say, this is clearly thinking in progress and we are, you know, in a sort of intermediary phase here.

Henry Greely: Okay, well if you can send those to Heidi when they're available and she can distribute them to the committee, I think that'd be very useful. Other questions about CIRM since we've got an ICOC member, a working group member, and the regulatory and ethics staff leader all on the phone. We may not have this opportunity again.

Bertram Lubin: This is great, this is great, actually.

Henry Greely: Okay. Well then I think we're down to our last agenda item which just says general stem cell research update and I don't know what all was intended when that was put on there. Heidi, did you have somebody in mind to give a specific update or...

Heidi Mergenthaler: No. I think you had asked that it be included but a lot of the topics you were thinking about were actually covered by Dr. Lomax in the CIRM discussion about clinical trial.

Henry Greely: Right. I guess I am interested though from the committee members. If there's anything that you see out there that you think that apart from what we've already discussed that you think the committee needs to be paying attention to, either new science or new ethical concerns that demand our attention or merit our attention.

Fred Gage: Well, I don't want to open a Pandora's box. I'm still on those interested in Greg's comments, this is Rusty, but I think that directed reprogramming, this is taking somatic cells and directly programming them into other types of somatic cells by introducing factors is something we should at least say falls outside of our purview or weren't included.

But what will be happening is that those cells will be transplanted, will be worked on in the same way that IPS cells but they're slightly different in the sense that they're not being reprogrammed back - the fibroblast - not being reprogrammed to an ES cell and then to a neuron but rather presumably and we don't really understand the mechanisms directly programmed into a neuron or some other cell type.

Henry Greely: Right, so they're not going back to the pluripotent stage...

Fred Gage: Right.

Henry Greely: ...which is - raises some of the - which mitigates some of the concerns that we have about pluripotent and embryonic cells.

Bernard Lo: Rusty, could I just ask a point of information? Are there safety concerns about errors in this directed programming in other somatic cell types that need to be addressed?

Fred Gage: Yeah, because in some cases, I mean, this is a little bit of a Pandora's box I guess but we don't know. In some cases there are still viruses that are being used in this directed programming so there are mutations that are being made.

Now presumably all this will be in the years forward abrogated by chemical reprogramming but that still may result in DNA mutations so to answer your question specifically, to the extent that there are modifications to the genome in the process of directed programming then one has to accept that there might be - there could be - some risks.

Henry Greely: I think this would be a good topic for our next meeting - just consideration of how if at all this fits within our regulations or within our guidelines or within our purview as a committee.

And it does seem to me that it - my initial take - is that maybe it doesn't at all because it doesn't involve destruction of embryos and it doesn't involve putting pluripotent cells into non-human animals which are the two things that have - and it doesn't involve SCNT - which are the ethical and publicly-

controversial issues that have I think driven the special regulatory context here.

But that probably deserves some more attention so maybe for the next meeting to have somebody and Rusty you might the right person to do it, tell us a little bit about what's going on scientifically in this field and then have us decide whether or not we think this is something that needs to be discussed in the guidelines.

Fred Gage: Yeah. That would be great. I'd like that.

Henry Greely: How confident are people that this can be reliably done in human cells?

Fred Gage: Very.

Henry Greely: Yeah, okay.

Fred Gage: Now whether or not the cells that are generated - the phenotypes that are generated - will be viable for transplantation and successful human therapy. That of course is unknown but that's true also for ES cells and IPS cells so...

Henry Greely: Right, right.

Fred Gage: ...but the ability to differentiate the cells into to directly program somatic cells into a completely different lineage has been replicated by a variety of labs, published in a variety of different cells using a variety of different methods and they're happening every day, publishing, publications are coming out. It has a growth theory...

Henry Greely: That's really fascinating knowing. Does it go from you know, I'm a fibroblast in this cell division and in the next cell division, bam, I'm a neuron?

Fred Gage: Pretty close. It's pretty remarkable.

Henry Greely: And is it one neuron and one fibroblast or do both the daughter cells change nature?

Fred Gage: Yeah, that's not known and what actually is happening mechanistically is not known. Sometimes you can do it with one growth factor and, I mean, one factor instead of the conical four that are years reprogramming or fewer cells and whether or not it's lineage, restricted, or even cell type restricted within a lineage by virtue of not going all the way back is not known.

But that phenomena can occur and it's not just hypothetical, that you can actually see a neuron with action potential within, making synapses that was previously a fibroblast is now recorded.

Henry Greely: Wow. This sounds to me like a very good potential agenda item for next time. Other thoughts? And it's an example of the sort of thing I was looking for with this last agenda item. Is there anything else going on out there in the science or in the politics, the ethics, the legislation that the committee really should be thinking about.

Maybe it strikes me from our earlier conversation, I'd be interested in our next meeting hearing a little bit more about what's going on with I'll avoid the word parthenote with ova/oocyte-derived cells. Anything else going on that we should think about?

Bertram Lubin: I think it would be nice if we could have the next meeting in person if we're going to hear this presentation, it'd be nice to be there rather than over the phone.

Henry Greely: Yes. If possible. I think we've got - Elliot, are you on the East Coast right now?

Elliot Dorff: No, I'm in Los Angeles.

Henry Greely: Okay. I'd seen an e-mail that led me to think maybe you were someplace else. David was on the East Coast. One of the nice things about the telephone conferences is they make scheduling a little bit easier but yes, it's good to see each other face to face, person to person from time to time.

Gregory Stock: Yeah, I'm calling - this is Greg - I'm in Princeton right now. It would be nice to have it in face to face if possible. I think it's a lot better.

Henry Greely: Yeah, okay. Any other ideas people have, any other things we should be thinking about paying attention to? Is there anything going on at NIH that we should think about?

Radhika Rao: The only thing I was thinking about - this is Radhika - is that they were thinking about changing or revising guidelines for human subjects research but of course if that happens, you know, then we would of course have to comply with those to the extent that the research is governed by it but I wondered if there had been any developments that anyone knows about?

Henry Greely: You know, I've heard rumors that that's in the works but I haven't seen anything specific. Bernie, do you know anything more about that?

Bernard Lo: Well, there are rumors and also the President's Commission was charged with making a report on that so my guess is that we're likely to have to wait until that commission has issued a report and that's usually a 12 to 18-month timeline.

Radhika Raor: Okay.

Henry Greely: Yeah, although I think they're working to move the report which is connected to the STD research in Central America in the '40s. I think they're trying to get that out unusually quickly. Yeah, I had heard that Zeke Emanuel was working very hard to get some changes to the common rule before he left government service.

Radhika Rao: Yeah, yeah.

Bernard Lo: Yeah. One has heard those rumors. Never underestimate Zeke's energy level.

Henry Greely: Yeah, but I think underestimating any of the Emanuels is probably a dangerous thing.

Radhika Rao: Okay.

Henry Greely: Well, anything else people think we should be concerned about, paying attention to, thinking about? I hope that by the next time we meet there'll be a final resolution to this litigation about the federal regulations. That should be winding down soon I think but is still pending. All right. Any other subjects, comments, questions?

Shabbir Ahmad: Professor Greely, this is Shabbir Ahmad from California Department of Public Health with Heidi and others. I just want to announce a change in the

leadership at California Department of Public Health. I don't know if Heidi gave the update in the start of the meeting or not.

Dr. Mark Horton was the previous director. He completed his tenure and we have a new director of the department. Dr. Ron Chapman. He was the Chief Medical Officer for Partnership Health Plan California and before that he was the Health Officer for Solano County and he joined in May, end of May as the Director of California Department of Public Health.

And with him both the chief deputies were also changed. The new Chief Deputy Director for Programs and Policy, it's Kathleen Billingsley. She was Assistant Executive Officer for Health Policy and Planning at CalPERS but before that, she was actually part of California Department of Public Health as the Deputy Director for the Center for Healthcare Quality, here in the Department.

And the Chief Deputy Director for Administration is the new Chief Deputy Director is Daniel C. Kim and he came from Sacramento County so I just wanted to let the committee members know the administrative changes here in the California Department of Public Health.

The administration is very supportive of the continuation of the committee-advisory committee- and also appreciate your voluntary time for the Department and it can't be done without your participation and your input and your expertise. I just want to announce that and I just want to share with the committee members. Thank you.

Henry Greely: Well, thank you for that update. I take it none of these changes is reflecting any changes - involves any changes - in the California employees with whom we regularly deal I hope, you and Heidi and Patricia and so on.

Shabbir Ahmad: No, there won't be any, at least as far as I know, hopefully.

Henry Greely: Okay.

Elliot Dorff: Do we officially have to be reappointed by the new governor or how does that work?

Shabbir Ahmad: It's the Director of the Department is designated to appoint so I think I will check with Heidi and Pat if we have to send the new member letters to all the committee members and also we are like - there are some - vacant seats for the committee and I would like to have some suggestions from you to bring the scientist vacancy to our committee, yes.

Henry Greely: Who has stepped off?

Shabbir Ahmad: I think it was - Heidi, who was it - Dr....

Henry Greely: Was it Dr. Cheshier or Dr. Weissman?

Shabbir Ahmad: I don't know.

Shabbir Ahmad: Dr. Weissman from Stanford, yes, yes.

Henry Greely: Okay. All right, so committee members and actually Heidi again because we only have about half the committee actually on the call, if you can send out a message to committee members seeking recommendations for nominees, I think that'd be useful.

Shabbir Ahmad: Thank you very much. We will do that, yeah.

Henry Greely: Okay. Is there any other business or is it possible that we might adjourn our meeting early? Not to put any pressure on anyone.

Man: I'll move to adjourn the meeting.

Henry Greely: Is there a second?

Man: I'll second.

Woman: I'll second.

Henry Greely: All those in favor, hang up. Thanks a lot, guys. Good meeting.

Man: Man.

Woman: Bye.

Henry Greely: Bye.

END