STATE OF CA

Moderator: Jackie Wilson
September 20, 2006
1:00 pm CT

Henry Greely: That sounds good. That sounds promising.

Coordinator: Excuse me. This is the operator.

At this time, I would like to remind all parties that today's call is being recorded. If anyone has any objections, you may disconnect.

Thank you.

Henry Greely: Thank you, operator. And thanks everyone who's here for this meeting of the California Department of Health Services, Human Stem Cell Research Advisory Committee.

Do we have anybody here who's present over the telephone connection? If so, would you identify yourself?

Gregory Stock: Yes. Greg Stock here, I'm on the phone.

Henry Greely: Welcome, Greg. How are you?

Sorry, we couldn't hold this meeting down in L.A. I promised to try and I did try -- Oto is actually here for which I thank him -- but it didn't work out this time. I'm not sure that it will ever work out. But it's nice.

Gregory Stock: But that's alright - because I'm in Princeton right now, so..

Henry Greely: Okay.

Gregory Stock: …I'd still be on the phone.

Henry Greely: All right.

Anybody else on the phone either from the committee or from the public?

Susan Fogel: This is Susan Fogel with the Pro-Choice Alliance for Responsible Research.

Henry Greely: Hello, Susan.

Anybody else?

Okay. I take that as a no.

We have number of members of the committee present. Why don't we go around the table and introduce their selves and then I'll ask the members of the public here to identify themselves so we got on record who else here.

I'm Hank Greely from Stanford Law School, chair of the committee.

Margaret McLean: Margaret McLean from Santa Clara University, member of the committee.

Bertram Lubin: Bert Lubin of Children's Hospital Oakland Research Institute, co-chair.

Otoniel Martinez-Maza: Otoniel Martinez-Maza from UCLA, member of committee.

Radhika Rao: Radhika Rao from Hastings College of the Law, member of the committee.

David Magnus: David Magnus from Stanford University, member of the committee.

Henry Greely: So I think we've identified all the committee members who are present currently. We have hopes that Dr. Elliot Dorff will be here in person, right?

Woman: Uh-huh.

Henry Greely: And are there any committee members we expected at this time in person or by telephone?

Elliot Dorff: Hi, this is Elliot Dorff.

((Crosstalk))

Elliot Dorff: How are you?

We took off and then went right back to LA actually because they couldn't retract the landing gear, so…

((Crosstalk))

Elliot Dorff: And then two hours later, they cancelled the flight so I figured it's better this way than…

((Crosstalk))

Henry Greely: We'd rather have you here…

Radhika Rao: Yes

Henry Greely: …but under the circumstances…

Radhika Rao: Right.

Henry Greely: …it sounds like a good decision was made.

Elliot Dorff: Right.

Henry Greely: Welcome. Sorry for your undoubtedly wonderful educational and enjoyable time.

Elliot Dorff: Right.

Henry Greely: Airport and in the air, but thanks very much for coming back and making the effort to call in.

Radhika Rao: Yeah.

Elliot Dorff: Sure.

Henry Greely: We've just started the introduction and figured out who all is here.

Gregory Stock: And, Hank, this is Greg Stock on the phone again. I haven't done this over the phone before. If we wish to make a comment at some point, how can we do that in a way without being too interruptive?

Henry Greely: I don't think there's a way you could do it without being too interruptive, so just go ahead and interrupt.

Margaret McLean: Yeah.

Henry Greely: We waive certain rules of politeness for the people who are unfortunately stuck on the telephone. That's, Susan I must footnote that as to say that applies to the committee members for public participants on the phone, we'll ask that you hold off until we get to a public discussion portion. But the committee members can feel free to interrupt or to try to interrupt anytime.

So, I think we've now got all of the committee members who we expect. I know I've heard from Bernie Lo that he's in Washington DC today and sent his regrets. The committee members are Irv Weissman and Samuel Cheshier.

Woman: …Weissman.

Henry Greely: Irv is actually literally my next-door neighbor. I will harass him about this. Peel some more tomatoes from his year. Just kidding.

So we've identified the committee members, we'll have the staff identify yourself and then we'll go to the public.

Shabbir Ahmad: I'm Shabbir Ahmad I'm with the California Department of Health Services (unintelligible).

Heidi Mergenthaler: Heidi Mergenthaler, Health Department.

Henry Greely: Anybody else in this category?

I'm sure (unintelligible) that should be recorded but Jackie Wilson is also here for…

Shabbir Ahmad: I just want to announce that Cindy Chambers got admission into medical school so she would not be with us full time so she's with UC Davis Medical School.

Henry Greely: Congratulation. Are you there right now?

((Crosstalk))

Henry Greely: Congratulations.

Now, you - medicine's gain is our loss. I'm not sure if it's your gain.

((Crosstalk))

Henry Greely: Bert looks ready to contradict me on that.

I'm not sure his heart is really in it. But his memory goes back far enough after first year of medical school.

Members of the public, could you please identify yourselves for taping purposes?

Don Reed: Don Reed, California (unintelligible)

((Crosstalk))

Henry Greely: Someone just walked in.

Yeah. I think we've now exhausted human contents with the room, at least in terms of the notification. And I hope we have exhausted the rest of your capacities yet.

I do want to start with two apologies and a hope. One apology to the committee members for getting you the draft of the recommendations so late. This is entirely my fault. David had his part done well before me. The start of the new semester, and a variety of other things pushed me off. But I think the draft recommendations which was sent around yesterday should not be too difficult - should not have been too difficult for you to read through it and assimilate. And that we'll be our main subject of discussion today.

The second apology leads into something that says our second agenda item to report on SB 1260. I wrote, I think, in the preface of the draft recommendation, that SB 1260 had become law. That was my mistake. It has been passed by the House, by the Assembly and the Senate. It has been enrolled which my being a lawyer who's lived in California for a long time, I misunderstood as meaning as it's signed.

It has not been signed. It may be signed. It may not be signed. I don't know what's going to happen with it. Presumably, the governor knows what's going to happen - well, there's a good chance the governor knows what he's going to do with it, but he has, I believe, until September 30 to make a decision about it.

I don't think that necessarily changes our discussion. There are aspects of the recommendations that were done on the presumption that 1260 will become law. Some of those we may want to vary a little bit if 1260 doesn't become law.

For today's purposes, we may want to note those when we come to them. But I think we're probably better off rather than saying all the different alternatives to assume for the purposes of our recommendations if 1260 becomes law, while noting how those recommendations might change if it's…

And then the announcement is I could be wrong and it's been known to happen. We are scheduled to run from 1 o'clock to 5 o'clock, but it is my hope and expectation that we might actually finish a little shorter than that. I know this would be a grave disappointment to everyone present, but (knock it off), try to be brave. If we finish by 3 o'clock - I'd be little surprised if we finish by 3 o'clock. But my hope is we'll finish before 5:00. I'll certainly without trying to cut off any committee or public discussion, I think that's probably feasible given what I think we have to do.

Our agenda today is relatively short. We start with the report on SB 1260, which I'll ask Dr. Ahmad to give and so the rest of us may kick in with a little bits on it. And then talk about the draft of the recommendations for guideline talking first about what I think is probably the more substantive set, the ones dealing with guidelines on issues - I'm sorry the less substantive set - the one dealing with guideline and issues other than clinical trials. And then the meatier set I think the recommendations for guidelines on clinical trials.

We then will go into committee discussion of areas that we think that could use new guidelines or could use some more development or discussion with respect to the ethics of Stem Cell Research in California. We will have public

comments and we'll talk about the next meeting, if there is any, that mindful of some comments that we made in our last meeting.

Though I don't frankly know - I did not checked out the legality of the timing of public comment. It does seem to me that it makes more sense to open up public comment after each agenda item, if I can - if the public comment is short. So rather than try to hold public comment at the very end, I think there is some significant merit in letting people, letting the public comment immediately after or as part of discussion on the agenda item rather than at the very end, unless there are some strong objections for the committee that (unintelligible) the course I expect to pursue.

Seeing and hearing no objection, if there any other introductory information that from the Health Services or any committee member, I think we need to hear before we go to Agenda Item 2.

Dr. Ahmad, tell us about SB1260?

Shabbir Ahmad: I don't have much to add to what you already informed the committee about 1260. It's all the provisions which was in the SB 322 are there except the advisory committee for human stem-human embryonic stem cell research has been not there in 1260 anymore.

The sunset date which is January 1, 2007, that has been removed from the 1260 - 322 and in 1260, all those provisions are extended.

There is an addition of the use of SCRO, the stem cell research oversight committee. And there is a whole addition of the process of procurement of oocytes in the 1260.

The bill passed overwhelmingly in Assembly and Senate and it is on the governor's desk as we speak. So I don't have for much more to add to it at this moment.

Henry Greely: I'm sure it would be inappropriate to ask you for your best guess about what would happen, so I won't.

My guess is it may get signed and it may not.

Shabbir Ahmad: That's what I would say, yes.

((Crosstalk))

Henry Greely: Yeah.

Bertram Lubin: Yeah, that's usually a safe bet.

Henry Greely: It's not your fault.

Radhika Rao: The newspaper articles about the bill have been saying that the governor is being lobbied extensively to not sign it, as an organization.

Henry Greely: Well there were certainly objections to it, and some of the people in this room or on the phone who had been involved in discussions about amendments to it, and some substantial amendments were made from the time of its first task at the introduced and agreed to by Senator Ortiz and the other senator whose name (unintelligible).

Shabbir Ahmad: Senator Runner
((Crosstalk))

Henry Greely: Okay. Thank you.

Which I think as you all recall at our last meeting, the committee agreed to - agreed on some concerns and objections to the bill. Most of those were taken care of which was also the amendments. I know that some of the research institutions had other concerns and some of the professional organizations had other concerns. Some of which I think may have been mitigated to some extent, but I don't think they were - based on the discussions I recall, I don't think that they were completely eliminated. So it doesn't surprise that there is still some controversy over the bill.

Radhika?

Radhika Rao: I found the newspaper article is a Los Angeles Times' piece written by Lee Romney on September 13, "New Battle Lines Are Drawn Over Egg Donation." And in it she says, "The American Society for Reproductive Medicine recommends paying $5,000 for eggs regardless of whether the eggs are used by scientists or fertility clinics. The group is pressing Schwarzenegger to veto the Ortiz-Runner bill."

So it's the American Society for Reproductive Medicine apparently that is lobbying against it.

I think she also said that the Center for Genetics and Society in Oakland and the Pro-Choice Alliance for Responsible Research in Los Angeles are two of the most vocal supporters of the bill. So…

Henry Greely: So I learned long ago that predicting political outcomes was not a safe business. Slot machines are probably a better chance.

We'll see what happens on or before September 30 in terms of this bill.

Even if I don't have any deep information, I'm not sure I could share it if I did, but I don't have it. I don't know what's going to happen. And I accept that I think there is some pressure from both sides on the governor's - in the governor's office.

If the bill passes, the regulatory authority for these guideline does not disappear as it would under the sunset for 322 as of January 1. Whether the bill passes or not, the legislative mandates for this committee disappear because the bill does not contain it, and SB 322, which did contain that mandate, does disappear except to the extent as continued by new legislation. There's not likely to be any other new legislation other than 1260 between now and January 1. I think that's fairly safe.

So the committee will either - the legislative mandates for the committee will either continue - will not continue in either case. It is likely the case that no legislative mandate is necessary for there to be such an advisory committee, but whether the Department of Health Services decides to continue to have such a committee or have the funding that allows them to have such a committee, if they are not required by the legislature to do it, is a question to which I do not know the answer.

Shabbir Ahmad: So some discussion haven't happened yet at the department level. But the program (feels) that such committee would be needed because of the dynamics of research in stem cell - embryonic stem cell and the department may not have such expertise as we have around this table.

So there would be a need for advisory committee. And as Hank said, the - there are programs were - which have advisory committees and they are not legislatively mandated. So as I said, such decisions have not made yet at department level. So probably by next meeting, we will have some answer, yeah.

Henry Greely: So, any other comments on 1260?

Gregory Stock: Yes. This is Greg Stock.

Henry Greely: Go, Greg.

Gregory Stock: I was wondering if 1260 which prohibits payment for oocytes for all sites that will be used for research purposes. If that is the case, then I think there was a discussion at the previous meeting about the guidelines and whether the guidelines should allow payment or not. And I'm - if you could remind me, but if the bill passes and it were illegal to do any research involving those, is it a necessity to have the guidelines also agree - concur in that?

In that one of the reasons that was stated was that, you know, it was important for them to be matched with the previous NAS guidelines and such. Is that - any comments on that?

Henry Greely: 1260 bans any payment in excess of the amount of the reimbursement of direct expenses incurred as a result of the procedure and be made to any subject to encourage or to produce human oocytes for the purposes of medical research.

That's the language of 1260. If the bill is signed by Governor that will become state law. I imagine it is. But it is inconceivable that the department would issue guidelines that directly contradicted a statute.

Gregory Stock: Uh-huh.

Henry Greely: Because I suppose conceivable though, I think a little silly for the committee to recommend the issuance of guidelines that would directly contradict a state statute. We can say that, but I'm not sure what the point would be.

Gregory Stock: Right.

Henry Greely: There is I think still - and this is one of the provisions that got changed slightly through the legislative drafting process. There may still be some questions exactly what the amount of reimbursement of direct expenses incurred as a result of the procedure encompasses, specifically whether it encompasses reimbursement for lost wages or other income.

The earlier draft specifically bans that. That phrase is gone. But CIRM regulations I believe encompass lost wages as part of direct expenses. So there may still be a little bit of interpretive room for guidelines for this committee to make a recommendation to the department about guidelines that would interpret and apply the language even if 1260 is signed.

Gregory Stock: Does this mean that oocytes that were actually procured for donate - for reproductive purposes and paid for as a result, could not be donated for research purposes? It seems to.

Henry Greely: That would - boy, without having given it a lot of thought, I think that's probably right at least in California.

David, do you…

David Magnus: No I'm just trying to think of how that works So - if a couple is paying for eggs for reproductive purposes and (transfer) to and freeze them and then they have some leftovers.

Gregory Stock: Precisely.

David Magnus: Yes.

That's a truth - that's a tricky population for two reasons. One is the payment issue that you just mentioned and I don't know whether that's going to contradict that.

Then the second problem that we've already identified is that you sometimes don't have consent of the gamete donors which is actually required. The people who actually own the eggs; they might be willing to donate are not the gamete donors. And I know the CIRM regulations require that the actual gamete donors...

Henry Greely: Well though - if it's an oocyte and not an embryo, it will be (the same).

David Magnus: Well no because you would fertilize the egg.

Henry Greely: Right, but if it's just - if it's purely the oocyte…

David Magnus: That is being used. You couldn't - right now, you wouldn't clinically freeze the oocyte. You create an embryo and freeze that.

((Crosstalk))

Radhika Rao: Right.

Henry Greely: Right. I understand. Well maybe I didn't understand your point fully.

So if you're using - what 12-125-355 deals with production of human oocytes for the purposes of medical research, not paying anybody to encourage that.

David Magnus: Okay, so then this wouldn't apply to that.

Henry Greely: Right. It doesn't apply to embryos or to…

Radhika Rao: Embryos that are donated for research.

Henry Greely: If you oppose to oocyte, result of manipulation of an oocyte whether we want to call it an embryo or not, I remember substantial discussions in our last meeting about what embryo meant and didn't mean. We all heard those. Let's just pretend that embryo - let me use a broad term for embryo right now just to prevent semantic distraction.

So it wouldn't apply for that section; it wouldn't apply to…

David Magnus: So I think then that gives us the answer. It could happen to somebody donating eggs for another couple. That couple then have those eggs fertilized. Transfers a couple of them, freezes the other embryos. And then if they're wind up having any excess, it's that couple that would then be donating it and would not be paid. So that's not a problem.

The bigger problem is the consent of the gamete donors.

Gregory Stock: Right.

Okay, thank you.

Henry Greely: Right. Although, you know…

((Crosstalk))

Radhika Rao: Basically these require the consent of the gamete donors then I think. Does it?

Woman: Yeah.

Radhika Rao: Because they're not donating the eggs for the purpose of research. So all of the informed consent regulations of 1260 apply only if you know that the egg is going…

((Crosstalk))

Henry Greely: The NAS regulations, the NAS guidelines required.

Radhika Rao: Yes, and the CIRM regulations as well.

Henry Greely: Yes.

Radhika Rao: The CIRM regulations deal with the issues that Greg just hypothesized. And the CIRM regulations say that not only must the original oocyte donor sort of go back and consent or has consented to using the eggs for research but also if they were paid, the eggs can be used - the embryos can be used only if they're essentially - the clinicians determine that the oocytes are unusable - that the

oocytes failed to fertilize or otherwise are biologically unusable for reproductive purposes.

I think I've read that in the CIRM regulations. It says, "If the procurement" -- this is Page 19 of the handout we were given. "If the procurement of oocytes involved use of materials donated for reproductive use by another woman and with valuable consideration in excess of reimbursement for permissible expenses for the oocyte donor."

So the woman was paid for providing eggs to a couple for fertility purposes. Then the oocytes may not be used for CIRM-funded research except when all the following applies: A, the oocytes failed to fertilize or otherwise are biologically unusable for reproductive purchase; B, the clinician determining that the oocytes are unusable for reproductive purposes, does not know whether the donor has consented the donation to research at the time making such a determination; C, the clinician has no conflict of interest.

David Magnus: I think that we're jumping ahead in the agenda because obviously SB 1260 only prohibits a very narrow range of things, and the purposes of our guidelines that we're developing is to fill in the rest and make us consistent with the CIRM…

Radhika Rao: CIRM.

David Magnus: …regulations.

So it sounds like SB1260 certainly leaves open the possibility that we could put regulations that are very similar in place.

Radhika Rao: Or different to CIRM.

Henry Greely: Dropping the caveats and although Radhika and I are both attorneys our legal conclusions expressed here should not be relied upon.

Radhika Rao: Right.

Henry Greely: In terms of what a court would actually make of the language from 1260.

Radhika Rao: Yes.

Henry Greely: But I think it sounds positive, may make a difference.

Basically what we're saying is it may make a difference whether it is a donation directly of an oocyte embryo or other entity produced ultimately from an oocyte in terms of the application of 1260. That may or may not make a difference for purposes of whatever guidelines we propose and the department proposes.

Gregory Stock: Okay.

Henry Greely: The other side of it which makes things a little more complicated, and I don't want to get into this in detail right now, but that could - that portion of the firm proposed regulation 100095 has - in a section that has three different options. I see a hand from Geoff Lomax from CIRM who may be able to enlighten us some on that.

Geoff Lomax: I refrain from interrupting other than the fact that…

Radhika Rao: Yeah.

Geoff Lomax: …I'm concerned with the record reflects accurately what the final decision was in CIRM regulation.

Radhika Rao: Okay.

Geoff Lomax: So in this scenario whether there's been payment for an oocyte to a third parties, that oocyte can then no longer be used in CIRM-funded research, so the final decision that was made…

Radhika Rao: Oh, not at all.

Geoff Lomax: Because that would constitute a violation of the provision prohibiting compensation for the research material.

So in a sense, if there has been a payment made for an oocyte and it remains as an oocyte failed to provide otherwise, that material was still not available at the CIRM-funded research.

Radhika Rao: Okay.

Henry Greely: So then it becomes an embryo?

Geoff Lomax: Embryo is a different matter.

Henry Greely: So a scenario where a couple is interested in having babies, they need egg donation. They pay a young woman to be the egg donor for the purpose of providing them with babies.

Geoff Lomax: Yes.

Henry Greely: They make ten fertilized embryos.

Geoff Lomax: Yeah.

Henry Greely: They implant two. They get twins. They're thrilled. There are eight frozen embryos left. Three years later, they decide we would like to help humanity by allowing our frozen embryos to be used for embryonic stem cell research. How would this – what's your understanding of how the proposed CIRM regulations…

Geoff Lomax: Again, the scenario you've just described, those embryos could be (donated) for research provided the original donor of the oocytes consented…

Radhika Rao: Oh, okay.

Henry Greely: Okay. That's consistent with my understanding.

And then the three options, how do the three options play out in ten - in 1000095?

Radhika Rao: Yeah.

Geoff Lomax: The three options are a relic of the California Administrative Procedure Act process. What we put before in the ICOC in August was where each of the three provisions and the provision that was ultimately approved by the ICOC (unintelligible) purpose of regulation contained the provision which I just characterized where if there's been any type of payment for the oocyte, the oocytes failed to fertilize or otherwise could not be directed towards research because the payment itself the material violates the payment provision…

Henry Greely: And could you help us out if your memory goes to…

((Crosstalk))

Radhika Rao: You know, which option?

Henry Greely: Is that Option 1, 2 or 3?

Geoff Lomax: The third option I believe.

Henry Greely: Thank you.

That's very useful.

Anything else on SB 1260, which I think is where we still are? It occurs to me looking at this agenda and looking at the materials provided by the staff, I've forgotten one important thing that we need to do. We have minutes- the draft unapproved meeting minutes which were in your packets and were also distributed by email to all of you. We should approve, disapprove or amend the minutes.

Is there a motion to approve the minutes?

Elliot Dorff: I move.

Henry Greely: Seconds?

Margaret McLean: Second.

Henry Greely: Are there any discussion, the motion, any amendments to the minutes, changes…? I want to complement the minute taker for actually making us sound more rational and coherent than perhaps we were.

All in favor of the approval of the minutes say aye.

Man: Aye.

Man: Aye.

((Crosstalk))

Henry Greely: Opposed? Abstention?

It is unanimously approved.

Okay. Anything else now before we get to the draft recommendations, the document that starts off with preface in your packet?

No? Okay. Well then let me - oh, I'm sorry. Although given the information item, I'm not sure there's much stand for this. Having said that, I would take public comment after each section of the agenda.

So anyone from the public care to comment on our information discussion of SB 1260 beyond the useful contribution we've already had from Geoff Lomax from CIRM?

I don't see anyone on the room jumping up and down.

Anybody on the telephone jumping up and down? Okay. We move on then.

So what we've got with and we set out in our June meeting was we would come back at this meeting with language for recommendation, and the goal of this meeting would be to approve our recommendations to the department, as to what guidelines the department should create.

We're not regulatory or guidelines drafting agency ourselves, but we're here to make recommendations to them. We split it into two working groups. One to look at clinical trial issues, and one to look at all other issues.

As fate would have it, time chance and other barriers, the working groups didn't get called on very much to do some work, although we did get some usual suggestions from some of them.

I have to take responsibility for the non-clinical stuff, and David Magnus I think deserves the credit for - note the difference in phrasing. Deserves the credit for the recommendations with respect to clinical trials.

With respect to the - in the documents you see before you, it's something that I drafted, David - the section on clinical trials is taken from what David sent me. I tinkered with it in some ways that may well have messed it up.

So anything bad is my fault. Anything good in it is David's responsibility.

I started out on this document trying to give some background as it turned out some inaccurate background with respect to SB 1260 about what the current state of play is in terms of the law in California. SB 322, the Section 125, 118.5 which creates our a committee, the role of Prop. 71 and the CIRM, and the current status of the CIRM proposed regulations.

Now, actually Geoff, can I interrupt myself here and ask you those regulations are still at this point proposed regulations. Is that correct?

Geoff Lomax: The regulations have been submitted to the Office of the Administrative Law. So in a sense they're - they reflect the aspirations of the ICOCs in terms of what we would like to see as regulations.

I would anticipate that any modifications with the regulation by the Office of Administrative Law would be purely technical in nature give that they're not evaluating them for their substance or content.

Henry Greely: So you've put things out for notice and comments. You've received the comments and modified your original draft as you thought was appropriate, if to the extent necessary in light of the comments…

Geoff Lomax: Yes.

Henry Greely: …with the three revisions that you put out. And you're done with it. It sounds to me like we can't say they're actually law yet or regulations yet until the Office of the Administrative Law blesses them, publishes them, does whatever it does with them.

Geoff Lomax: That's certainly our position.

Henry Greely: But they're in the hands of the lawyers who are not supposed to make substantive changes.

Geoff Lomax: Right.

Henry Greely: Okay. So with the - this document reviews the regulations and talks about some of the similarities and differences in the statutes and in the CIRM funding.

And we've talked about this before, but it is a little quirky that the CIRM funding, because CIRM can fund any kind of human stem cell research, the CIRM regulations apply to all human stem cell research whether it's embryonic or not.

Our legislative mandates - department legislative mandates to produce guidelines and our mandates to advise them is limited to human embryonic stem cell research. Presumably, we can offer (unintelligible) advise on non-embryonic even stem cell research and perhaps the department has authority to publish such guidelines -- that's the question I don't know the answer to and don't want to speculate on now.

In addition though, SB 253 from 2002 did require IRB approval for all of stem cell - all human stem cell research whether it's embryonic or not. And it is my understanding that neither 322, passed in 2003, nor 1260, if it's signed, amends that provision or removes that provision of 253.

So we're in a sort of an odd circumstance I think where there are multiple overlapping jurisdictions. The legislature in 1260 -- and this certainly (stands) as the intent of the legislature whether or not the governor signs 1260 -- expresses its intent as we try to have as consistent a scheme as possible, regulating both CIRM funded at non-CIRM funded research.

The CIRM regulations themselves broadly implement the National Academy of Sciences report, as with some variations for the special context of Prop. 71's provisions.

So I started with the CIRM regulations as I tried to pull them together. Unfortunately, the document I gave you is in a somewhat different order from the order that we're covering these. So I'm not sure I'm looking at exactly the same paper you are.

David Magnus: Page four of this one that begins with the preface.

Henry Greely: Yeah, but I printed out mine. So on the line stuff. Right.

So the version you have with the numbers from the line is in reversed order from our agenda. So skip from the second page – I'm done explaining the preface -- through the heading at the bottom of the third page, the third page and whatever's on the fourth page.

As I went through the CIRM guidelines, the CIRM proposed regulation and looked at what we had discussed and looked at the minutes of our last meeting for issues that we had discussed there, not dealing with clinical trials, there was very, very little that, where I thought we could not just adopt and recommend the CIRM guidelines.

And for the most part, what this - what the document I've given you does takes the CIRM regulation - the CIRM proposed regulation -- in the version that I had which I've not yet chosen which of the three options there are -- and so that's a qualification that needs to be added to it -- and said well what would we need to change if anything or what would we want to change if anything in terms of the guidelines the department should recommend, and came up with very little.

So for the first section of the regulations, they talk about the scope, the CIRM funded projects, well obviously the departmental guidelines apply more broadly than CIRM funded projects. So it would be the full statutory language of human embryonic stem cell research.

In section 100020, the definition section, definitions will be revised if needed. The only one that's really jumped out at me was that Subsection C in which CIRM - in which CIRM has defined covered cell line more broadly than just human embryonic cell lines.

Let me put a flag there and suggest we may want to come back in discussion to whether we as a committee want to recommend to the department that these guidelines should go beyond the statutory requirement of embryonic stem cells and encompass at least the other covered cell lines that the CIRM regulation encompasses.

David?

David Magnus: Don't we also need to get rid of Definition D "funded research".

Henry Greely: Yeah.

And there'll be a number - there are a number of things that would be clear both to us and to the department where, you know, when it says "CIRM", we don't want to say CIRM So - but the substance - but I think C is the more important substantive one.

Section 100030, activities not eligible for CIRM funding. These are all activities, I believe, that are not considered appropriate by the National

Academy of Sciences recommendations or that are dealt with in California statutes for things like reproductive cloning.

And so I would propose that the guidelines be amended only from the CIRM regulation only to not say they are not eligible for CIRM funding but say they shall not be done.

These include human reproductive cloning, the culture in vitro of any intact human embryo or any parts of SCNT, parthenogenesis or androgenesis after the appearance of the primitive streak or after 12 days, not counting frozen time, the introduction of stem cells from the coverage stem cell line into non-human primate embryos.

A little footnote, the NAS says blastocysts rather than embryos, but I'm not sure that there's any reason we would want them to be introduced to the embryos that were passed either before certainly or after the blastocysts stage.

B, as the introduction of any stem cells whether human or non-human into human embryos which is directly from the NAS guidelines.

(E), bringing any animal into which stem cells from a covered stem cell line have been introduced. Again, that would have to be changed by the department because of the coverage stem cell lines or else they would have to use the coverage stem cell language in the definition and apply it for whatever these guidelines are to apply to. And the transfer to the uterus of the genetically modified human embryo, which I believe is also set from the Prop. 71 or the NAS guidelines or both.

Anyone remember? Somewhere.

Geoff Lomax: As a result of public comment, (unintelligible).

Henry Greely: Also this was in - on the section of the regulation.

Geoff Lomas: Conditional provision (Unintelligible).

Henry Greely: Does any remember whether there's anything in the NAS guidelines dealing with this particular issue? I guess there probably isn't.

Radhika Rao: I think not.

Geoff Lomax: There is none.

Henry Greely: So flag that as another thing we may want to come back to -- the arguments for consistency between the two regulatory schemes we'd say we should recommend it.

But it isn't something that's either banned by law, or the NAS, or covered by the NAS guidelines.

David Magnus: Though at present time it's universally – it's deemed as unethical in almost all the special guidelines, you know, the Human Gene Therapy Society and all those sorts.

So…

Henry Greely: So it may well be something that…

((Crosstalk))

David Magnus: …germ line gene transfers.

And I think there's other NAS reports, not this one, but there are other NAS reports that do recommend that that's something that at present times should (not be allowed).

Man: Yes.

Henry Greely: But hold that for - I'm going to read through all of them and then come back and pick up these flag things.

Radhika Rao: How was genetically modified embryo defined?

Henry Greely: That's the problem.

Radhika Rao: Uh-huh.

Henry Greely: But that's why we should come back and discuss this.

One thousand forty Institutional Assurance of Compliance, I saw no reason to change that. It seems to me the guide - the department may also want to require Institutional Assurance of Compliance.

Section 100050- compliance, now this is a bunch of ways in which CIRM says it's going to…

Man: Enforce.

Henry Greely: …enforce largely through cutting off funding. Obviously that's not a possibility for the department guidelines.

Radhika Rao: Yeah.

Henry Greely: I frankly don't know how the - what the department would view as either within its statutory authority or appropriate activity for it enforcing guidelines. Obviously there should be some enforcement - well I shouldn't say obviously. So one may well want some enforcement stability, but my view is we'll probably leave that up to the department unless people around the table have a strong view about what enforcement mechanisms the department should use.

Radhika Rao: Presumably, they should be consistent with other methods that the department uses to enforce similar prohibitions. So, for example the prohibition against human cloning…

Henry Greely: Right, although…

Radhika Rao: …how is that enforced.

Henry Greely: But that has some statutory enforcement provisions that arguably limit or at least expressly the authorized and may limit what the department can do…

Radhika Rao: Can do. Uh-huh.

Henry Greely: …which I think it doesn't necessarily exist here. So I don't know legally exactly what the department can do in terms of enforcement.

There's also this little odd quirk and that the statute talks about guidelines and not regulations. And it's never been entirely clear to me what they meant by guidelines. One might try to make an argument that guidelines are aspirational hopes with no enforcement mechanisms.

My own preference would be that there'd be some sort of enforcement mechanism, but let's tag this as the third thing to come back to.

Radhika Rao: Uh-huh.

Gregory Stock: Yup, just to interrupt. I - you know, you were saying it was saying obvious -- this is Greg Stock. It feels to me that guidelines in a way that enforcement mechanism don't necessarily belong in guidelines in that there are various other mechanisms that one can enforce the guidelines by- that are external to the guidelines themselves. In other words there are legislative possibilities in terms if one does not follow the guidelines then whatever. But it doesn't seem to me that an enforcement mechanism is appropriate for guidelines at this point.

Henry Greely: Greg, let's - we will come back to this. What I'd like to do is get through all of - a brief overview and all of the sections come back to flagged areas.

Gregory Stock: Okay.

Henry Greely: This issue about compliance and enforcement is certainly a flagged area.

Well, and I don't even know how to say these, 1060 and it sounds like 1-0-6-0. So 100,060. I don't know why our regulations have these kinds of sort of and numbering system. It's worse than having five digit numbers on one block along the street, which is also a California specialty.

Sixty, I'll just call it Section 60. Our SCRO committee membership and function, in our recommendations from our June meeting, we noted a couple of places where CIRM was proposing a different membership criteria than the

NAS and we said we'll have to recommend that that'd be followed. Well several of those June provisions it seemed really the easiest thing to say was, we'll just adopt the CIRM view, the CIRM position.

That variation with CIRM I think was a patient advocate addition and maybe an addition of an outside member. Some slight variations on the membership from NAS that seemed completely reasonable, and the interest of having uniformity and not having inconsistent rules for what a SCRO should contain seemed to me overwhelming there.

So I thought we should just adopt 60.

Seventy-SCRO committee review and notification. Similarly I thought here, we should adopt, we should recommend that the department adopting its guidelines. The substance of this again deleting reference of things like CIRM funded research so that it clearly applies to our scope.

The same is true in my view of Section 80, acceptable research materials.

Section 90, Additional requirements for CIRM funded derivation. Again, unchanged except for deleting CIRM specific references.

Section 95, additional requirements for CIRM funded research involving oocytes. That's the section that has already been a subject of some discussion involving oocyte donation.

I'm glad to know now that the CIRM has settled on Option 3 and would recommend that we adopt - that we accept option three.

And similar throughout the rest of it, Section 100 informed consent requirements.

One-ten, fairness in diversity and research.

One twenty, record keeping.

All of those seem to me things we could recommend, again with the technical deletion of references to CIRM funded research.

So I've now spoken for longer than I intended to. The bottom line of which is it seems to me that our best bet is to recommend to the department for things other than clinical trials which an area that CIRM has not spoken very much at all on, for the good reason that I don't think they intend to fund any clinical trials anytime real soon. It's not a matter of great urgency for them I believe.

The - what CIRM has done seems to me broadly consistent with both state law and the NAS guidelines and that to drive the importance of consistency between the two regulatory systems, which we already recognized even before the legislature reiterated it at 1260 seems to me they argue very strongly towards adopting - recommending that the department adopt in its guideline, the position that CIRM has taken.

So I have on my list of things to come back to.

The definition of covered cell line; the issue of compliance. There was one other…

David Magnus: (Genetically modified).

Henry Greely: The issue of genetic modification in Section 30. And one other I should have mentioned, by adopting the CIRM proposed regulations on oocyte donation, we would be defining direct expenses to include lost wages.

Radhika Rao: Oh, we would be defining.

Henry Greely: We will, the CIRM has defined it using the language direct expense that direct expenses including compensations for lost wages.

Radhika Rao: Where is that?

Henry Greely: In the - it's in…

Geoff Lomax: Look in the definition of (permissible)…

Radhika Rao: Okay, (permissible)...

Henry Greely: The sound of shuffling paper.

Radhika Rao: Necessary - okay, Page 4.

Henry Greely: Yes, Page 4.

So this is 120,028 each. Permissible expenses means necessary unreasonable cost directly incurred as a result of donation or participation research activities.

Permissible expenses may include but are not limited to cost associated with travel, housing, childcare, medical care, health insurance, and actual lost wages.

If we compare that with SB 1260, SB 1260 says no payment in excess of the amount of reimbursement of direct expenses incurred as a result of the procedure shall be made to any subject to incur or to produce human oocytes for the purposes of the medical research.

So, I think this language, the CIRM language seems to me at least is consistent with 1260. So one could argue with and we also have the question of whether we as the committee want to recommend permitting, not requiring but permitting the reimbursement of actual lost wages as part of the - part of the direct expenses for which oocytes donors could be compensated.

So I've got those items to revisit.

Anybody have anything else?

Gregory Stock: Greg Stock again. If we're actually going to make a modification such as making a recommendation or not adopt CIRM and its entirety then why limit it to simply the lost wages?

Henry Greely: Well, because that we would run into both the conflicts with the National Academy guidelines and possibly though - certainly not certainly, a conflict with 1260 if it's signed by the governor as well. It would certainly be a conflict with 1260 if it's signed by the governor.

Gregory Stock: But if there is - doesn't -- 1260 -- signed by the government - by the governor trump any guidelines essentially.

Henry Greely: That's true, but in that case we'd be recommending the department issue illegal guidelines which strikes me as aesthetically unpleasing.

Gregory Stock: You know…

Henry Greely: It's not impossible.

Gregory Stock: I wouldn't say that they are illegal guidelines. It's saying that - I mean, I think that's an excessive statement and that what you're really saying is that you could meet the guidelines and still run afoul of the legislation.

David Magnus: That seems to me a good argument against making our guidelines. If you have a guideline and say here is what you should do, oh but by the way, if you do what we tell you, you should do to do this research, it's going to be violation of the law then that's a bad guideline.

Gregory Stock: Is the - okay.

Henry Greely: You know, Greg, I'm trying to organize a narrative structure here, a theme and a flow, and I wanted to come back to this. This is Item 4 - well 2 on our list of four substantive things.

Gregory Stock: I wasn't going outside of that, but you were saying that those were the only issues to revisit in Item 4.

Henry Greely: So, do you have any other issues you think we should revisit where we may want to differ from the CIRM guidelines?

Gregory Stock: So I was - still back on the issue of payment or aspects of payment and I understand the arguments that we really, you know, want to confirm - conform but - so I was wondering why we were not entirely conforming and --

because I am not comfortable entirely with that decision. But I'll forego with it. It's all right.

Henry Greely: No, but my recommendation is that we do entirely conform to the CIRM regulations on payment of oocyte donors.

Gregory Stock: So it's 1260 that was different.

Henry Greely: No, I actually think that the CIRM regulation is consistent with 1260, although I could understand some people who might read 1260 otherwise.

Gregory Stock: Okay, I would…

Henry Greely: It all depends on what you mean by direct expenses under 1260.

Gregory Stock: Okay. Thanks. I'll…

Henry Greely: I think that's (a subject) significant argument back and forth and the people who wanted a tight reading of that, I think probably still think there should be a tight reading of that. So - and they might convince the judge the best way it should be read.

David Magnus: Is there anybody here in this committee - any committee members who think that the language of SB 1260 is incompatible with the language involving direct permissible expenses of CIRM?

Henry Greely: Well…

Radhika Rao: I think it's a matter of interpretation as I said.

Henry Greely: Yes, right.

((Crosstalk))

Radhika Rao: As I said, there are two for possible interpretations. One is direct permissible expenses does not include lost wages but only the other kinds of expenses. The other is that it also includes lost wages.

Henry Greely: So for what it's worth, Mr. Philosopher, our two - the two lawyers on the committee are in agreement in that we can't say for sure.

Radhika Rao: Right, we can't say for sure. But I think…

((Crosstalk))

Gregory Stock: But I think that your point about my comment is appropriate and that we should just let it go at this point.

Henry Greely: You don't want hear the lawyers argue either…

David Magnus: So I suggest since nobody's committed to the view that they're incompatible...

Radhika Rao: Right.

Gregory Stock: …that we recommend the same guideline.

Henry Greely: Well…

Elliot Dorff: It sounds good to me.

Henry Greely: Good, although that's actually the second of the four that we're now approaching.

So if I can once again try to get us - so you guys are worse than first-year law students. It's pretty bad.

((Crosstalk))

Henry Greely: So hearing no other subjects that we need to bring out, I think that we start with this issue of - in the definitions what's a covered cell line. And what we want to - whether and what we want to tell - I've got four: the covered cell line, the reimbursement, the enforcement mechanisms, and the genetically modified embryo.

Radhika Rao: I have one more - one question.

Henry Greely: Yes.

Radhika Rao: One thing that I don't think we covered which the CIRM regulations do is the whole issue of medical care cost being reimbursed. Now it seems to me it looks like that's part of Option 3 of 100095 which was adopted by CIRM.

Yes? So the CIRM has in fact required that that there'll be procedures to ensure that an individual who donates egg for CIRM funded research has access to medical care at no cost to the donor.

Geoff Lomax: Correct. And that's an informational note consistent with 1260(unintelligible).

Radhika Rao: Right.

Henry Greely: And it's also consistent with the decision we reached at our June meeting that we wanted to do that.

Radhika Rao: We wanted to (include) that.

Henry Greely: So by saying that we're adopting - by recommending to the department that its guidelines follow the CIRM guidelines, that would encompass that requirement.

Radhika Rao: Okay. Yes, I want to make sure of that.

Henry Greely: So right. A lot of what we said - we have five or six particular points reflected in the minutes from the June meeting where we thought we wanted to make sure that rather than take the National Academy position…

Radhika Rao: Right.

Henry Greely: …we took the CIRM position.

Radhika Rao: Yes.

Henry Greely: By switching from taking the National Academy as our template and say department, here's what we recommend with these changes in the National Academy to saying CIRM is our template, here's what we recommend that these changes from CIRM. We've automatically encompassed those CIRM variations from the National Academy guidelines. And those are largely things that we thought in June were good - I think entirely, things we thought in June were good idea.

But at least one of them raises I think interesting questions and that's this issue of what should be covered.

SB 322 said the department should make these guidelines on human embryonic stem cell research, and said that it should appoint a committee to advise it on those guidelines.

CIRM, of course, has the power to fund all sorts of research on stem cells that are not just human embryonic stem cells.

As a legal matter barring the authorization from 322 or 1260 for the department to make these guideline, I frankly don't know whether the Department has the authority and other respects to give out guidelines, although this may to some extent go back to Greg's question about what is a guideline. If it's just a recommendation for good practices, maybe the department has full plenary power to do that. I don't know the answer to that.

But I'll let the Department's lawyers worry about that for now. I think the interesting question for us is do we think that the guidelines we're recommending should encompass things beyond human embryonic stem cell research, and specifically, things that we could recommend that to the Department, the Department would then figure out whether it (thought it could) do it or not.

Specifically, the things that the CIRM regulations defined in 100,020 C as covered cell lines. Covered cell line means a culture-derived human pluripotent stem cell population that is capable of one, sustained propagation in culture, and two, self-renewal to produce daughter cells with equivalent in developmental potential. This definition includes both embryonic and non-embryonic human stem cell (lines) regardless of the tissue of origin,

"pluripotent" means capable of differentiation into mesoderm, ectoderm and endoderm.

So, the question I've put to the committee is do we want to recommend to the Department that if it thinks it has the legal ability to do so, it extended guidelines to cover all of the covered cell lines covered by the CIRM regulations, or merely human embryonic stem cell lines.

My tentative vote on that. You know, I'm not - you know, there are things I'm convinced about before I hear discussion and there are things that I'm genuinely up in the air on it.

This one is very tentative. I'm up in the air and could be talked out of it. It seems to me that a lot of the things we worry about with respect to embryonic stem cell lines would apply to other (pluripotent) human stem cell lines.

That's included some of the ways in which they're derived in which arguably they may not be human embryonic stem cell lines. They might still require human gametic medic, human gametes, human (concepti), human reproductive material.

So, for example one might argue that the product, parthenogenic construct is not human embryonic stem cells. But you'd still worry about I think where the eggs came from that were used for the parthenogenesis.

So I am slightly in favor of adopting - of recommending the department if it thinks it can use the broader CIRM definition. But I can easily be talked out of it or confirmed in it.

Elliot Dorff: What harm would it do to apply into that as well?

Henry Greely: I'm sorry?

Elliot Dorff: What harm would it do? I mean what's the downside of applying it to that as well?

Henry Greely: As you know, it may be that some of these of the cell lines that are covered by the CIRM regulation don't raise the same concerns. But I can't think of any offhand that it does raise at least some of the same concerns.

Presumably, the department - the CIRM's regulation, if somebody magically were able to take fully differentiated adult cells and dedifferentiate them back to pluripotency but not to totipotency, then you don't have the reproductive materials issue. But you've still got some of the (chimeric) issues, you've still got concerns about a radically new treatment, the uncertainty about control and so on. It makes to say the oocytes donor aspect of it irrelevant. But it doesn't I think make the idea of special guidelines being useful irrelevant.

So I don't – that was Elliot who asked that question?

Elliot Dorff: Yeah, it was.

Henry Greely: So, this - so I think the only potential downside I see other than arguably going beyond what we were ordered to do is that maybe by doing this, we might inadvertently apply it to recommend this department create guidelines that might in some cases not maybe - very meaningfully apply, but those are cases that I think are quite remote scientifically and medically and that could probably be dealt with subsequently if it comes up.

Elliot Dorff: Uh-huh.

Henry Greely: So, basically, I agree with you Elliot.

Elliot Dorff: Okay.

Henry Greely: Never ask a lawyer for a short answer.

Elliot Dorff: It's all right. Don't ask a philosopher or a rabbi for one either.

Henry Greely: Any other comments? David?

David Magnus: So, at one point, and I believe it was one – a version of the CIRM guidelines that didn't make it into the final one. It was all – I believe it was there, not in the National Academy guidelines.

There was some discussion not under covered (cell) line, but there was some requirements elsewhere about dealing with neurogenic stem cells that were going to be placed in human brains.

I believe that those - that part is not in the final regulations event, correct?

Geoff Lomax: If I may.

That part is in the final regulations under the specifics to see kind of an exceptional circumstance that was (thought) appropriately nested within the (Chimeric) research provision.

So, it indicates that the oversight committee should review any research involving, neuroprogenitors.

Henry Greely: Even if they're not a covered cell line.

Geoff Lomax: Exactly. So it was trying to capture any implantation of a human material to an animal brain and that was what I would characterize as an exceptional (circumstance) or provision.

And if I made this scenario, you described about the cellular programming…

David Magnus: Right.

Geoff Lomax: …is really the only functional significance of this definition. Because if you look at the regulations and if you will adopt them in all the consent additional protection and other requirements apply to human (gametes) and embryo.

So, anything involving egg sperm or embryo apply under every provision…

Henry Greely: Whether it's a covered cell line or not?

Geoff Lomax: It will…

Henry Greely: Because for us, it might not be a covered cell line.

Man: Correct (unintelligible).

Geoff Lomax: The only - if you were to sort of (sift through these) regulations, think how does this definition change anything into a scenario you describe where it was the reprogramming of a theoretical somatic cell back to the theoretical pluripotent state.

So, that what's made - that's the functional relevance of this definition in terms of the regulation, in terms of what gets regulated. Because otherwise, any use of sperm, gamete, any gamete or embryo is covered explicitly in all the (consent) and additional provision (unintelligible)

David Magnus: So I recommend that we add neuroprogenitor cells that if I will – if we're going to start from the beginning (unintelligible) and we're making an exception, I recommend that we make neuroprogenitor cells that are placed – that are going to be placed at least in the brains of animals.

What about in humans? And - you don't care about - you guys didn't really address clinical trials at all. So, you didn't address about what happens if you put neuroprogenitor cells into human brain.

Geoff Lomax: Any – if any implantation of a covered stem cell line.

David Magnus: But neuroprogenitor cells are not covered…

Henry Greely: May not be covered stem cells.

David Magnus: Are not covered stem cell lines.

Geoff Lomax: Correct.

David Magnus: So, if you put those into a human brain, those are not - there's nothing in the - during the course of the clinical trial, that's not covered by the CIRM regulations.

Geoff Lomax: Correct. But the reason they're not covered is because that would have been duplicative (unintelligible).

So one of the things that we're attempting to do here is not…

David Magnus: There's no regulations that require ESCRO approval for that kind of research.

Geoff Lomax: That's right. (Unintelligible).

But it would require IRB approval (unintelligible).

David Magnus: Right.

But that's all. Whereas, I think (Bernie)'s made a pretty good argument and I agree with them that some of the special issues that that kind of research (raises), would benefit greatly from ESCRO approval.

Henry Greely: So, I would note, David, that because we're adopting 100070 which is is a (70), which says what the SCROs should do, is that would also be adoption of the neuroprogenitor cell limitation with respect to…

David Magnus: (Chimeric) research.

Henry Greely: …non-human animals.

David Magnus: Right.

Geoff Lomax: But you're right it would not put it into the human animals unless we either did that in our subsequent clinical trial recommendation.

David Magnus: Right.

Henry Greely: Which I think it is – we will require ESCRO approval of any sort of clinical trial, oh but it wouldn't be a covered cell line…

David Magnus: Right. That's why I'm recommending, if we put it in as a covered cell line, we get all the advantages of doing the same thing that they do, but we also get the advantage that any clinical trial in which it's placed in humans would require ESCRO approval, which I think would be a good idea.

Henry Greely: Now, the alternative to that would be to expressly add neuroprogenitor cells to a - to the clinical trial provision…

David Magnus: Correct.

Henry Greely: …which has the advantage that then we're not picking them in covered cell line definition, which might trigger something some place else from the regulation that is not appropriate for neurogenic stem cell line, so I can't - on the top of my head, using my neuroprogenitor derived neurons, figure out something that would fall into the category right now.

David Magnus: I just thought that was an easy way to get it all, is just to put that in…

Henry Greely: I think the easier way might be to stick that into the substantive provision coming back to yours.

David Magnus: That's fine.

Henry Greely: If I can try to pull it back to the core issue here, we want to make our recommendation to the department, broader than just embryonic stem cells or not?

Anybody else want to talk to that?

David Magnus: Can I ask Shabbir, given what the legislation said, is it appropriate for us to make a recommendation that exceeds our statutory authority?

Man: Hang out.

Henry Greely: Statutory requirement.

((Crosstalk))

Radhika Rao: Statutory mandate.

Henry Greely: Mandate.

Shabbir Ahmad: Yeah, of course these – whatever the recommendations going to be, going from this committee that would be seen by the department lawyers and they may line out some – those which are outside 322 or 1260.

So, I can't say at this moment to what will be their interpretation.

Henry Greely: Will people view us badly as having been bad actors if we recommend broader guidelines from the statute (unintelligible).

Shabbir Ahmad: It's totally up to the committee how they want to feel. At this moment, I don't think the department should say a committee to do this or don't do this, and so it's up to the committee how they want to go forward with this, so…

David Magnus: Then I would recommend that we go forward with the broader definition. And truly SB1260 seems as if it's - it's theoretically broadening it in certain ways (unintelligible) stem cells, generally in terms of at least the IRB provision.

So, I would recommend that we come up with the best guidelines that we think should govern the research and then the department can decide if they have to limit it (because of legal reasons).

Henry Greely: Anybody else want to speak to that?

Woman: I agree, I agree.

Henry Greely: Okay. I want to hold off taking any votes on these issues until the end of our discussion of this part and until the public discussion of this part because what the public has to say might inform or influence or both, but I think we're done with the first of those four items where we might vary.

Our tentative conclusion is we don't want to vary it. Want to use the same broad definition as CIRM with respect to covered cell lines, even though it goes beyond (322), what (322) told us to do.

The second issue is - comes from - also, in the definition section (100,020) the definition of permissible expenses and (H) Page 4 of the CIRM regulations as we have them lines 3 through 6.

We've already talked about this a couple of times as to whether or not we want to vary from the permissible expenses as laid out by CIRM.

And I think we've talked about the implication in either direction either by saying it should be narrower and shouldn't allow wages, (lost) wages, or it

should be broader and we should encourage broader compensation even though that would violate both - well, even though that would be inconsistent with the (NAS) guidelines and would be inconsistent with the as yet unsigned and possibly never to be signed 1260.

((Crosstalk))

Henry Greely: Comments on that?

David Magnus: I recommend we do the same thing that, say the same thing as CIRM, seems like, but it looks like it's probably consistent. It's a good clarification of it and there's no reason not to be (unintelligible).

Henry Greely: Greg, this is an issue you care about, comment?

Gregory Stock: I'm sorry. I just stepped out. I came back into the room, so I didn't…

Henry Greely: You owe us all $100.

Elliot Dorff: This is Elliot. I mean I…

((Crosstalk))

Elliot Dorff: …is consistent with the act. I think the fact that - but it's an argument from silence, that is, I think the fact that (1260) does not mention wages probably is not just by accident, but because they didn't really want to include wages.

But they don't specifically exclude wages. And therefore, I think it's at least possible to read it to include wages and I frankly would prefer that it include wages along with the CIRM, you know, the CIRM guidelines.

So even though I think frankly we are - I think we're going against the spirit of -- not the letter - but the spirit of 1260 by including wages. I think we should do it.

Henry Greely: Okay.

I'm not sure I agree with you that we're going against the spirit of it. But - because I think what the spirit of any legislative passage is, is often difficult to ascertain.

Elliot Dorff: Fair enough. Okay.

Henry Greely: It is the case, I know that I believe an earlier version of it did expressly exclude wages, that was removed but it wasn't removed and replaced for something that expressly included wages.

Elliot Dorff: I see. Okay.

Henry Greely: But I think legislative technique to punt the issue.

Elliot Dorff: Okay.

Henry Greely: Radhika?

Radhika Rao: I think on the interest of kind of consistency, we, you know, from one of the arguments that was made, both about SB 1260 and about CIRM was that permitting lost wages may be unfair because different people earn different amounts of money.

So if you have somebody who's in the highest paid job, they get - make $400 an hour, does that mean that they can be paid, you know, for however many hours they spend donating eggs versus somebody who's in a low-wage, minimum-waged job and spends so many hours.

So I don't know, I just thought perhaps we should think about that issue.

David Magnus: They're not getting paid for their eggs. You're just reimbursing them...

Radhika Rao: And for their...

David Magnus: ...for their expenses.

Radhika Rao: Right.

David Magnus: And that will mean that it will be different amounts and if people drive from further away, they'll have more in gas mileage. And if people take a cheap – if they take a taxi versus taking a bus, there'll be that difference.

It's just - you're not paying them to be oocyte donors, you're just reimbursing them for their expenses.

((Crosstalk))

Gregory Stock: Talking about lost wages if you're talking about a salaried individual, then they won't have lost wages. So I don't think you're going to have very huge amounts.

Henry Greely: Although even that may depend on whether they get (back the) vacation day, for example or a sick day that they otherwise might ultimately get paid for. I

think the actual on the grand implementation of this, may turn out to be a little tricky about what counts as actual lost wages but, you know, that's what we train law students to do, find all the possible ambiguities any of those terms.

Is there other discussion from the committee on whether or not we should adopt the CIRM version which includes expressly actual lost wages?

Okay? Let's move to the third of our reserve points. We'll get public comment before we do any voting on any of this. So let's move to the third of our reserve points.

And I think number - I can't remember which is, in which order but we'll take enforcement next.

Obviously, the department can't use the same enforcement mechanisms of cutting off money, that CIRM proposes in its regulation. There - at least two, maybe three different questions.

The bigger one is do we think – do we want to recommend any enforcement provisions or not? Because they'd be pure - should they be guidelines that are not mandatory, not required other than whatever moral course it would have which I think frankly, would be significant particularly to the extent they're consistent with the CIRM guidelines, or should we recommend guidelines that have some enforcement provision leaving, as I think we probably need to given our ignorance about what the department's authority is, leaving what's precisely - what precise enforcement mechanisms the department might impose largely up to the department.

David?

David Magnus: SB 1260 certainly seems to - in some parts of it, suggest that these are not just guidelines, certain aspects of the things that we would want to have in terms of review, some ESCRO review and so on are actually mandated in SB 1260.

And it's says that - as – although some of the languages is ambiguous than others.

So I would recommend that on this issue that we punt this to the Department of Health to devise whatever compliance mechanisms are appropriate for what they usually do, given the statutory requirements of not just 322 but 1260.

Henry Greely: If it's not (unintelligible).

Woman: Positioned.

Henry Greely: Right. Okay.

There's also the possible further complication of it. There maybe some mandatory - some of our regulation - some of our recommendations for guidelines will track things that are required by (1260 if 1260) is signed.

Some of them will deal with things that aren't necessarily required by 1260.

David Magnus: Right.

Henry Greely: So we can't fall back and say, everything we do would be required by 1260 if signed.

David Magnus: Okay.

Henry Greely: Plus I don't think 1260 itself really has talked about enforcement mechanisms...

Radhika Rao: It doesn’t.

Henry Greely: …which...

David Magnus: Yeah.

Henry Greely: ...is kind of interesting.

David Magnus: It just says these things shall not be done...

((Crosstalk))

Radhika Rao: Yeah.

Henry Greely: But on the big issue, David, you're in favor of enforcement mechanism.

David Magnus: I'm in favor of punting that issue to...

((Crosstalk))

Henry Greely: But you're in favor of the idea that there should be enforcement mechanisms but would punt what they would be to the department.

David Magnus: Correct.

Gregory Stock: Greg Stock.

It seems to me if we do not put in place enforcement mechanisms, then the department already would have the ability to sit - to put in place enforcement mechanisms if the guidelines are not followed, just as statutory measures could do the same.

So it seems to me that especially if all we're going to do is punt, then it doesn't seem an appropriate thing to do to include enforcement measures.

Henry Greely: Well so, not to include specific enforcement measures, Greg, but I'm not - do you think that these guidelines should be enforced or should they be purely recommended?

Radhika Rao: Hortatory.

Henry Greely: Hortatory.

Hortatory guidelines.

Gregory Stock: I think that they should be hortatory in the sense that they are what we believe would be is appropriate methodologies, procedures to follow and then it's - there are many other mechanisms and situations where enforcement can be developed, both statutory in the example of 1260 or other measures or in terms of funding, measures can be passing if the guidelines are not followed, then funding does not occur.

But what we're creating is a document that is - represents what should be done.

Henry Greely: Okay.

So what we're creating is (second) to a recommendation to the Department of (unintelligible) guidelines they should put out. It sounds to me like there's a difference between you and David.

David Magnus: I don't think so. I think it actually - I think we're saying the same sense - I think this issue we don't have to take a stand-on. We're going to put out some guidelines for what we think should happen.

How to interpret what - whether that's something that should - there needs to be compliance measures and if so, what they are, I think is not something that we should address.

Henry Greely: Okay. So you don't think we should even recommend to the department that it should have enforcement mechanisms without specifying what those mechanisms would be?

David Magnus: Correct.

Radhika Rao: I disagree. I think that we should recommend that the - that the - they not be purely hortatory but that they actually be some enforcement mechanisms...

Henry Greely: Whatever the Department...

Radhika Rao: Whatever the Department (unintelligible) and feel is authorized under the mandate that created us and SB1260 and so forth.

Henry Greely: Can I ask the Department whether it has (unintelligible) the current representative who I'm sure are not fully authorized to speak in every respect for the Department.

So with that caveat understood, what do you guys think about whether there - whether you would normally have enforcement mechanisms for guidelines like this?

Shabbir Ahmad: I think of - for this we have to go toward legal folks…

Henry Greely: Okay.

Shabbir Ahmad: …to give - I cannot say anything at this moment.

Henry Greely: That's fair.

Gregory Stock: Can I ask a question? Is the recommendation that we would include the enforcement suggestions within the guidelines themselves or that we would wrap the guidelines with a suggestion that the department come up with whatever enforcement measures it feels are appropriate? Because if it's the latter, I certainly would agree.

((Crosstalk))

Henry Greely: ...too ignorant of….

Man: Yeah.

Henry Greely: …what the Department authority and normal appropriate, what would be an appropriate mechanism would be to make a recommendation of that (fast).

So it would be the latter Greg.

Gregory Stock: Oh then, I'm in agreement with that.

David Magnus: I don't think that's (unintelligible).

Henry Greely: Okay?

Radhika Rao: I'm in agreement with that too (unintelligible), so…

Henry Greely: How many angels are on this – okay.

((Crosstalk))

Man: (Unintelligible).

Henry Greely: All right. Other comments on this?

I think I understand where we are and that takes me to the fourth and I think last of the reserve issues on this non-clinical trial section and that is the part of 100,030, sub-section F, Page 5, Line 17 in the documents of the regulations as you got them, the transfer to a uterus of a genetically modified human embryo.

The CIRM says, that's not eligible for (unintelligible) that's not eligible for CIRM funding. If we translate all six of those prohibitions of CIRM funding into recommended guidelines for prohibited practices, we would also be prohibiting (that).

It seems to be our general understanding that that's neither required by any of the California statutes nor was it required we think of CIRM by Prop. 71, nor is it addressed by the NAS. So this report...

Man: In that...

Henry Greely: ...although if you view that as being a prohibition on germ line gene therapy, then as David points out, it has been widely condemned in a variety of circumstances.

But I think Radhika's question, what does that term mean throws some doubt on whether it means the product of germ line gene therapy or not. So let me throw that open for suggestion or - for a discussion.

David Magnus: Is there a definition of genetically modified in the CIRM regulations?

Radhika Rao: Genetically modified embryo.

((Crosstalk))

Geoff Lomax: We did not define it and all the other (unintelligible) I might make you aware of, was that this point was also addressed in the ISSCR (unintelligible) research guidelines. I don't have (unintelligible) that language handy, but if it's handy to your committee, they modeled this provision (unintelligible).

Henry Greely: But they use the same – they reached the same conclusion.

David Magnus: Which is almost an argument against doing it, so.

((Crosstalk))

Henry Greely: Strike that.

David Magnus: Yeah.

Henry Greely: Radhika?

Radhika Rao: Question. It just seems to me if we're about embryonic stem cell research, the coverage - extending it beyond embryonic stem cell research in humans cell lines that aren't necessarily embryonic seems one thing.

But then to go beyond it, to genetically modify the embryos if there isn't a connection to stem cells, seems to me to go further afield from our mandate and I'm not sure given the questions regarding what a genetically modified embryo is, whether we want to be venturing that far.

Henry Greely: So - go ahead, (unintelligible).

Margaret McLean: And to go another step further and transfer to a user, you know, whereas the other things that we're talking about that is not there. So – I mean I think this pushes us well beyond...

Henry Greely: I think it's fair to say that nobody here is saying, boy it's a great idea that...

((Crosstalk))

Woman: (Unintelligible).

Henry Greely: ...genetically modified embryos to human uteruses, uteri. But if we...

((Crosstalk))

Henry Greely: ...don't incorporate that, then we're not necessarily - we should make it clear that we're not saying it's a good idea, we just think that that goes well beyond

any recommendations about stem cells. It could make - arguably one could have raised the same point at the CIRM but, I certainly can understand a funding agency wanting to be much clearer about what is not going to find, or CIRM could also arguably, as said, we're not going to fund anti-trust violations, we’re not going to fund burglary.

Woman: Uh-huh.

Henry Greely: We're not going to fund all sorts of other bad things, but, you know, I won't argue with their decision to include this, but I do think the point that the distance from our essential mandate is stronger here. It's good reason for us to not include it.

David Magnus: There's only one possible exception I could think and that is whether or not genetically modified was intended not to mean right. Well I interpret it to mean, which is basically germ line gene transfer, but rather to include something related to what happens if you put - might take place to actually using embryonic stem cells and putting them into human embryos, or something like that during the first clinical trials in which case those…

Henry Greely: Covered.

David Magnus: ...clinical trials regulations that we’re already are going to discuss.

Henry Greely: So it seems to me possible that we're going to end up recommending to the Department that they have guidelines that are on almost every respect identical to the CIRM guidelines with the technical differences needed to make them sensible in a non-CIRM context with the sole exception of we're not going to make a recommendation that you should ban implantation of genetically-modified embryos into human uteruses.

I'm happy to do that if that's what we want and I actually think it's probably what I want. But I want to make it clear and I think we all probably want to make it clear that in so doing, we are in no way endorsing germ line gene therapy.

Woman: Right.

Henry Greely: We're just saying it's not our issue, it's not before us. It's not a stem cell issue if – it were before I suspect that we would all – I think we would all at this time say that would be inappropriate.

But let's stress that, I don't want any misunderstanding. We're not saying that germ line - if we do this, we're not saying germ line gene therapy is a great idea. Let's go for it.

Oto Martinez-Maza: Right.

This doesn't state germ line gene therapy it's...

((Crosstalk))

Oto Martinez-Maza: ...very vague...

David Magnus: Very vague.

((Crosstalk))

Woman: Well that's, I thought, yeah, yeah.

Henry Greely: Okay.

Margaret McLean: I think it's the vagueness of it that troubles me.

Henry Greely: Okay.

So, I think we've come to the end of the flagged items with respect to the non-clinical trial aspects of CIRM (regs).

I think I know where the committee wants to go on those, but before calling for a vote on that, let me ask if there is public discussion on the non-clinical trial aspects of our recommendation.

Anybody present in the room want to speak?

Yes. Mr. Reed.

Don Reed: Let me think. First of all, on the...

Henry Greely: Well, could you come closer so we could make sure we capture for posterity and history your comments?

Don Reed: First off I'm not sure (unintelligible)(the 28th is a large) meeting on the oocytes issue and...

Henry Greely: Nobody did.

Don Reed: Okay.

Henry Greely: (So good).

Don Reed: And I wonder if that (affects) you in any way, and your recommendations in any way. I'm not sure it would or should, but I just thought I'd mention that.

Henry Greely: Fair point.

Don Reed: Secondly on the oocytes, I know it's not compensation but to lose a day during which one provides for one's family financially is a loss which I feel should be replaced.

Henry Greely: Okay.

Don Reed: So it would be my hope that that would be recognized as such.

Henry Greely: Okay. Thank you.

Don Reed: Thank you also finally - on the - I support your trend of leaving the germ line situation as beyond the scope of today's discussion. It seems to me that the CIRM made such a huge issue on that we're 100% opposed to reproductive cloning which is basically using the technology developed to grow new babies, that that would be automatically a no-go anyway.

So I think that people are pretty much - everyone's in the same page in that I believe. Thank you.

Henry Greely: Thank you.

Other comments from people in the room? And those of you on the phone I'll get to next.

Jesse Reynolds: Thank you.

Henry Greely: Identify yourself again, please.

Jesse Reynolds: Oh sure. Sure.

I'm Jesse Reynolds from the Center for Genetics and Society. Thanks for the chance to make a comment. I just want to add a little something around this topic of germ line modification and perhaps stimulate you to reconsider some of your thinking.

I think the prohibition on the implantation of genetically-modified embryo should be included although I certainly think there's room for some clarification around definition about what either is or is not a genetically-modified embryo.

I mean it seems there's consensus that this is a) a very profound issue and b) there's an emerging social consensus against germ line intervention and that's encouraging.

So I would assert that there is a technological connection between germ line modifications, stem cell research – in the same way that stem cell research provides a technical building block for reproductive cloning, and thus, stem cell builds off in mammary productive cloning.

It also builds a technical block for germ line modification. More blocks are required, but it is a key building block. And I think that's probably the logic behind the ISSCR prohibition on that which I'm not familiar in, might be that official to look at.

So given those circumstances, I would encourage you to adopt sort of a precautionary attitude and so, circumstances warrant otherwise to include that as a prohibition.

It also has the advantage of increasing consistency with the CIR and with ISSCR.

Okay? Thanks.

Henry Greely: Thank you.

Next.

Ellen Auriti: Hi, Ellen Auriti (unintelligible) from University of California. I had two comments.

One is that I think you started out by commenting on the goal of promoting consistency. And I wanted to note that the - in the preface you note that there's still an IRB review requirement that's duplicative actually of the ESCRO review requirement.

Henry Greely: That's my understanding. I might be wrong.

Ellen Auriti: I - my understanding was that (1260) was intended to eliminate that duplicative burden on institutions and to recognize that there’s been a development in thinking that ESCRO committees are the more appropriate body and I’m wondering if this group might consider making a recommendation to that effect – that the ESCRO committees are the more appropriate body and that to the extent that you have any authority to make a recommendation in that area that’s something that would be welcome…

David Magnus: Are you saying, you don't think there should be IRB review…

Ellen Auriti: No, no, no. IRB approval and review should absolutely be required when there's human subjects involved. I think that what's happened in 1260 of the things, in 1260 is that they have replaced the old SB 322 and SB…

Well it should have…

Henry Greely: I don't think they replaced (253). I think that was the problem.

Ellen Auriti: (253) right. I think that…

Henry Greely: I think that's right.

Ellen Auriti: Not been the intent. So I think it would be helpful if this body of experts would make a recommendation in that area.

Henry Greely: So to be clear it is that when it's not human subject research and is not – would not otherwise require IRB approval under federal regulations, then IRB approval – then the State of California shouldn't require IRB approval.

Ellen Auriti: Correct.

Henry Greely: There is - let me ask you a follow up on that. Limitations on IRB coverage are really two in nature.

One is whether it's human subjects research or not;

The other's whether you have an appropriate access and appropriate connection with the federal government.

So the IRB requirement only applies to research done with federal money, or research done subject to an (IND) from the FDA ,or research done by an institution which like your institution and my institution and every other significant research enterprise, non-commercial research enterprise, is given an assurance to the federal government.

It wouldn't necessarily cover a pharmaceutical company before it was doing anything with human subjects that would require an (IND). So pre-clinical work by a private biotech or pharmaceutical wouldn't be covered, but then it's not likely to be human subjects research.

Is there any human subjects research they could do that wouldn't require an (IND)?

David Magnus: You could do some pre-clinical…

((Crosstalk))

Henry Greely: …with personally identifiable material, that's not clinical trial. So I think there maybe…

((Crosstalk))

Ellen Auriti: I'm wondering if perhaps you could address that and how the recommendation is worded. You know, if it were to involve a human subject as defined under the federal regulations, it should require IRB.

Henry Greely: David and then Radhika.

David Magnus: Can I actually ask a question? So practice because I can't imagine that at Stanford that we wouldn't have the IRB review anything that the ESCRO reviews. Just almost as a matter of form and course that our IRB would always want to be involved in any ESCRO case in terms of the way we've got everything set up procedurally.

Is that not the case?

Ellen Auriti: Our institutions are trying to figure out which bodies should be responsible for which level of review and we don't think or at least at some campuses, there's concern that we not burden both bodies with doing the same review.

So if the scientific efficacy and the justification are being considered by one body, that might not require the full review of the other body.

David Magnus: I mean that makes it easier for the job, but we do this all the time with things that (GCRC)s do and that cancer – conferences (unintelligible) do. We have multiple committees doing different things and it makes life easier for the other committees because they don't have to do certain things, but I guess I don't see why this is a special problem for this area rather than other kinds of areas.

Oto Martinez-Maza: You – one could imagine for instance doing research with human embryonic stem lines, purely in vitro, learning how to culture them better for instance that now has to go through IRB which really seems kind of redundant if you're not going to involve human subjects that are identifiable or place these into a clinical trial, it's an extra burden.

David Magnus: But this is different because those actually don't require ESCRO review. Those only require ESCRO notification.

Henry Greely: And some ESCRO oversight.

((Crosstalk))

Henry Greely: The institution has to assure that the stem cells involved were appropriate-were ethically derived, (unintelligible)…

((Crosstalk))

Oto Martinez-Maza: …At UCLA I'm on our ESCRO and we're definitely reviewing those and those are also being reviewed by IRB as well, so.

Henry Greely: I mean historically I think what happened was when 253 was passed in 2002, escrows were companies that dealt with title transfers.

Nobody had any idea these ESCRO committees. They had IRBs where the handy things and so the legislature kind of stuck this responsibility on IRBs, even though it wasn't in some cases human subject research.

And frankly I think some of the IRBs didn't know what they were supposed to do with it, because it wasn't the kind of stuff they dealt with. The development of the ESCRO concept, thanks to the National Academy, and now it's incorporation in state law both through the CIRM proposed regulation and through (SB 1260) if it passes, does render that the IRB requirement of 253 redundant in some cases.

And it may be, Ellen, that you're right in that maybe either I'm missing something in the text of 1260, that specifically repeals (125) (115) or maybe a court would say, it implicitly repealed it.

It certainly does push ESCROs rather than IRBs, but it would have been cleaner if it had expressly repealed it.

Ellen Auriti: To the extent that your analysis is correct here, I just think it will be very helpful to have this committee included in set of recommendation, the recommendation that ESCROs should be the (body in charge) of doing...

Henry Greely: Or at least there shouldn't be overlapping redundant review when it serves no purpose.

Ellen Auriti: Definitely.

Henry Greely: That sounds like nothing. Most of us can agree on.

Oto Martinez-Maza: Would that conflict with the CIRM regulations? (Unintelligible)

Ellen Auriti: (Unintelligible) but my understanding is that the CIRM regulations only require IRB review when there's human subject research involved. So in other words, if it is something that falls under the federal.

Henry Greely: Right. Because under Prop. 71 the CIRM is exempt from (SB 253) and (322 and 1260), for that matter should it be signed.

Radhika, you've been waiting patiently.

Radhika Rao: Just - no actually I was wondering whether you were recommending that we make a recommendation to the legislator to change (SB1260). But I now understand it seems to me that you're not asking for that but simply that we make it clear in our guidelines that we recommend that there not be duplicative (unintelligible).

Ellen Auriti: Well, it may be a little of both of that…

Henry Greely: Yeah.

Ellen Auriti: …because to the extent that Hank is correct in the analysis here, it seems that there is something that's still on the books that I think is leftover from a previous kind regime of how reviews should take place.

Radhika Rao: Well but it seems to me it's too late for us. To amend…

(Crosstalk))

Ellen Auriti: …as the 1260 but I think the extent that the state and policymakers are looking to this group as a group of experts convened on how stem cell research should appropriately be reviewed in California.

Radhika Rao: Yeah.

Henry Greely: So just as we made recommendations to the legislature about proposed amendments to (1260)…

Radhika Rao: Right.

Henry Greely: This wouldn't necessarily be part of our recommendation for – to the Department for guidelines but would be an additional separate recommendation anybody who is interested in listening…

Ellen Auriti: (Unintelligible).

Henry Greely: To clean up this (unintelligible) appendix with stem cell oversight.

David Magnus: On (SB 253).

Henry Greely: On (SB) – that's left over from (SB 253).

So I would hate to have my not completely informed view of this be taken as evidence that it still is alive.

So I'm not saying that it's clearly still alive, but I think - I'm afraid that (125115) is still alive.

((Crosstalk))

Henry Greely: Because then our guideline, if in fact I'm right about that, then our guidelines would be inconsistent with the statute.

Radhika Rao: Oh, with the statute.

Henry Greely: Yeah. With (253).

Ellen Auriti: Thank you.

Henry Greely: Thank you.

Bertram Lubin: I - at our site, we have both of these committees. There's no way we're going to get away without both committees. And maybe there'll be some redundancy but right now there's such anxiety that something's…

Henry Greely: Yeah.

Bertram Lubin: …going to be done wrong, somebody's going to be pointed out, we got to go – we're going to do, we're going to make a mistake and then the whole institution…

Woman: Right.

Bertram Lubin: is going to fall apart, that there's – that that's the way it's going to be. And I think for a while, it's going to be like that. I don't think that's bad.

David Magnus: Yeah I think so too. I don't think this matters very much. In fact, I can't imagine any place that's in the IRB that isn't looking at (unintelligible).

Henry Greely: Well, you know, this…

David Magnus: And watching what the ESCROs doing…

Bertram Lubin: We can't get to the IRB without going through ESCRO first.

Henry Greely: This fits nicely though with agenda item 5 or so…

((Crosstalk))

Ellen Auriti: I have one more comment, which is a completely different topic.

I just wanted to point out that under section 100060 of the…

Henry Greely: Uh-huh.

Ellen Auriti: …CIRM (reg), we have - it's another aspect of the issue of compensation, when these regulations were out for public comments, we had submitted a concern that it sets up an inequity between the ability of the members of the ESCRO committee to get paid depending on whether they're scientist members or non-scientist members of the public. Currently on our campus (IRBs), we're able to and many of our campuses do provide a (stipend) to the public member who's serving on the (IRB) in recognition of their service. And unfortunately, the way this is written - the way that we read it, it would prevent the non-scientist member who serves on the ESCRO from receiving remuneration from the research institution.

Henry Greely: So you're looking at…

((Crosstalk))

Henry Greely: …100060A.

Ellen Auriti: Correct.

Henry Greely: A SCRO Committee shall include at least one non-scientist member of the public who is not employed by appointed to or remunerated by the relevant research institution and not a family member. Any member of SCRO committee member… typo there, Geoff.

Any member of a SCRO committee member may be reimbursed for reasonable out of pocket expenses for attending the meeting not including lost wages there.

Ellen Auriti: So if we have a nurse or some other person serving on our ESCRO committee as a public member where unfortunately I think if these regs go into effect broadly never going to be able to compensate them in the way that the scientist member doesn't lose their wages by losing a day or two or however many it takes.

Henry Greely: Presumably you could reimburse them through out of pocket expenses. I'm not sure that would be considered remuneration but you certainly can't reimburse them their lost wages…

Ellen Auriti: Right.

Henry Greely: …under the language of this regulation.

Ellen Auriti: So I just wanted to put that out there for your consideration?

Henry Greely: So the question would - on all these, we have sort of double edged question. One is do we think that's right or not and the other is do we want to deviate from CIRM on it and then if we think the CIRM is wrong on it. But I think that's another good point to discuss.

Radhika Rao: Do we want to discuss this point?

Henry Greely: I think we should.

Radhika Rao: If we deviate then, you know, and we allow payments but CIRM doesn't allow payments then…

Henry Greely: Right.

Radhika Rao: …the institutions would have to have two committees.

Henry Greely: Right. They won't have…

((Crosstalk))]

Henry Greely: Yeah. I think you're right.

David Magnus: I think it's - there's no - we haven't had any problem and I don't know of any other institutions who's had any problem recruiting these members these people from the public to serve on the committee. And I do think the extra added thing, there's no money being paid to these people, helps for public confidence in the functioning of our committee. So if it doesn't stop us from being able to recruit people and it's not - and it has an extra added value there. I think those are good…

Henry Greely: But it is just loss wages. I mean one way to read this would be just to say take out the no lost wages part and you might argue that this potentially restricts the set of people who you could choose to be a public member because for some people…

Radhika Rao: Yeah.

Henry Greely: …those lost wages might be significant enough to prevent them from taking part. It seems to me that if I'd had my druthers, I would compensate for lost wages.

Radhika Rao: Yeah.

Henry Greely: But I think Radhika's point about the impossibility of effectively varying here since every institution will want it's ESCRO to meet the CIRM requirements because they want Geoff's money. I'm sorry, because they want the tax payer funded research money will require them to make their ESCRO CIRM compliant. But I do think that on fairness grounds and also on possible restriction of who can serve grounds. You got a good point it seems to me.

Radhika Rao: Yeah.

Henry Greely: Mr. Lomax, your name having been taking in (vain)

((Crosstalk))

Geoff Lomax: …because this is was actually a comment we received considerable public comment on along the lines of the comment that was just made and if it's one note as a funding agency, we have other options we may pursue we would do it in a public format pursuant to our public process. For example, CIRM may have the ability to provide stipends to those public members as an option because the intent of provision was to neutralize any conflict of interest…

Henry Greely: Right.

Geoff Lomax: …that may result from the payments originating from the institutions.

Radhika Rao: Huh.

Geoff Lomax: Given the level of public comment we have received, we have gone back and began just sort of think about coming back to this provision in future deliberations. And again I offer an example of - in would it be satisfactory for - would we accomplish the goal of neutralizing the conflict of interest if we allowed CIRM to provide for example a stipend to that member because it has been identified as a hardship in terms of recruitment of the expertise required to do the (deliberations). So again, this might be one unique place where the ability of the funding agency to remedy and address an issue is different than what you accomplish through a (state law) which is a hard and fast restriction so I just offer that as sort of continuation of the thinking and what we've learned from public comment on this particular provision.

Thank you.

Henry Greely: Other comments from the public on the non-clinical trials portion? Anybody else in the room who wants to speak?

Okay. Anybody on the telephone, member of the public? And I think as far as I know that’s just Susan who wants to speak on this section of the agenda.

Anybody still on the phone?

Hello.

Man: Hello.

((Crosstalk))

Woman: Elliot.

Henry Greely: Elliot, are you guys still there?

Elliot Dorff: Elliot's is here.

((Crosstalk))

Henry Greely: Okay. So if I don't hear from anybody on the phone in about 30 seconds I'm going to say there's no public comment coming in from the phone.

It didn't work.

Okay. Thank you.

So I think at this point - and we're getting close to what would be a very break time but we're also getting close to open a very logical break time.

I think the committee is probably in position to vote on our recommendation. It sounds to me -- if I'm readng the committee correctly --that basically we want to go with the CIRM regulations accept as technically required to deviate.

On all of the points we discussed, the broader definition, the lost wages for-as direct reimbursement for the (oocyte) donors, the - and even I think ultimately the reimbursement for the public member of the SCRO. Those three we want to go with some on the enforcement issue. We obviously have to - we can't recommend their enforcement mechanisms, but it sounds like we want to say department think about how you think this should be enforced. We recommend that you think about enforcement mechanisms without us trying

to presume to tell you either what's legal or what's appropriate. And on this issue of the genetic modification, it sounds to me like we want to drop that while being very, very clear that that is not in any way our endorsement of germ-line gene therapy or the other implantation of genetically modified human embryos into human or non-human uteruses. But that we don't think it is. We're a little concerned about how- what it means and then we don't really understand what it means and it's sufficiently far though not, now I think the public comment is saying these technologies are connected has some merit to it. But it's (sufficiently) far from the core of our concerns that we want to drop it. So I would look for a motion saying, "I think all of that."

Is there - I heard it so moved and I heard a second now we're open for discussion, right? I think Elliot moved and David seconded it.

Elliot Dorff: Right.

Henry Greely: Anybody want to discuss further these points?

I see and hear no effort in which case I think I'm going to call for a vote.

So all of those in favor of the motion which I won't try to (restate) but which I think we all understand. Signify by saying aye.

Man: Aye.

Woman: Aye.

((Crosstalk))

Henry Greely: All opposed say nay.

All abstaining say (abstention).

I believe the motion has passed unanimously. It looks like there's coffee here.

Elliot and Greg you're on your own for coffee, but I think we'll take a 10 minute break and then reconvene. So thank you for your attention in the first part of this meeting. We still end five but my 3 o'clock…

((Crosstalk))

Henry Greely: Thanks.

((Crosstalk))

Henry Greely: Okay.

So, I'd like to call our meeting back in session. We are now on the fourth item in the agenda which is the recommendations with respect to clinical trials.

Now, the CIRM proposed regulations don't - I think even say the word clinical trial that I recall, but they do have a little bit of relevance to this in their 100,070 SCRO committee review and notification down at (70F) on Page 13. (CIRM) funded research introducing stem cells from (covered cell lines) into a live born human may not commence without a SCRO committee review and approval. And it requires several things from the SCRO committee.

It is -- four things, acceptable scientific rationale, assurances that acceptable derivation of stem cell lines, evaluation of (probable) patterns affects the

differentiation and integration and documentation of compliance with required review by an IRB, (IBC) or other mandated review.

And I think it's fair to say that that's the only thing in the regulations that really go directly to the issue of clinical trials or that they would be relevant particularly to clinical trials, understandably, because, as I said earlier, I don't think CIRM expects to fund clinical trials immediately.

And so we've identified at our last meeting that this was an area where we might make some really quite useful contribution given the absence of substantial CIRM language, and the fact that there are some California entities that – including as we heard at our last meeting Geron, that anticipate doing clinical trials with human embryonic stem cells or their derivatives before very long. Geron's vice president I think told us next summer was their hope, was it?

((Crosstalk))

David Magnus: Yeah.

Henry Greely: Recollections, right?

So, David Magnus led the working group and I think was the working group.

((Crosstalk))

Man: Okay.

Henry Greely: That did most of this that did come up with these recommendations we have. Again, recommendations to the Department for it's guideline, and I will turn

the table over to David to say a word about those proposed guidelines (to create) from Line 80 on Page 2 to Line 133 on Page 3 of the document that we have. So, David?

David Magnus: Sure.

So our subcommittee before our last meeting met and at the last meeting you may recall, we had a very crude rough draft of the guidelines that we put forward for discussions for the group.

This is the result of revisions based on all the feedback we got at that meeting which was pretty clear guidance about what to include, what to drop, what to revise. And so that's what we've got here is really based on that discussion that we had at our last meeting.

Obviously, there need to be integration since we've just approved the section that Hank just alluded to in the CIRM regulations as part of our guidelines.

We'll need to make sure that that's integrated with this.

Henry Greely: But (I'm right) in thinking there are no principle conflicts to stay there.

David Magnus: Not at all, not at all.

In fact, in some ways, all that's happening is there might be one or two things that are included in the CIRM guidelines that we would want to make sure are still included but they're spelling out some of the other kinds of considerations that in particular (Bernie) identified that would need to be covered.

And basically, it comes - falls into two different categories. Obviously, the CIRM guidelines require an SCRO review and we think that's really the most important thing is at least any clinical trials should have ESCRO review.

And then, there are number of requirements for what sorts of things need to be taken into account for really knowing both - when an institution is ready, when a field is ready and when it is appropriate to go forward under those circumstances.

Then, second thing was that there was a lot of discussion about the issue about the language of embryo, although I will note that since we just agreed with the CIRM language and they used the word embryo. But Irv Weissman and a number of other people objected to that term to refer to ex vivo fertilized things that wind up going out to blastocyst stage or things that are the product of somatic cell nuclear transfer.

So, we decided to avoid having to have a debate about that by wording languages such a way that it was - could not specify the terms to be used so that presumably local ESCROs could decide what language should be used.

It's simply just requires that informed consent means that anybody who is going to have the product of (HESC) placed into them are entitled to know where the materials come from and how they were produced. And then the details of the language used. It's something that's going to be a local problem.

And then, of course, the requirements that no (HESC) should be placed in human embryos that are going to be used with intent to create an infant. I would just add that given our earlier discussion, we might add to this, a requirement that neuroprogenitor stem cells should require ESCRO review as

a (fourth) that uses of neuroprogenitors stem cells in human clinical trials should require an ESCRO review might be a fourth thing.

Henry Greely: So, would that be a Number 4 for this or would that be an amendment to the Number 1 that says all clinical trials involving the use of human embryonic stem cells or materials derived from human embryonic stem cells (we could add) or human neuroprogenitor stem cell?

That would be - that would satisfy…

David Magnus: Absolutely.

((Crosstalk))

David Magnus: Absolutely.

Bertram Lubin: You're (talking about) cells that were derived from neural tissues initially?

David Magnus: Yeah, like (fetal stem cell tissues) that are going to then be placed in human brains in clinical trials.

Henry Greely: Brain stem cells, fetal brain stem cells, for example.

Oto Martinez-Maza: What about (autologous) stem cells?

Henry Greely: Good question.

Bertram Lubin: I thought we were - I mean, I want to stick on that as well, but I thought we were focusing this on embryonic.

David Magnus: Right.

Bertram Lubin: So you're saying that embryonic definition is broad?

David Magnus: No, we have said before that we were going to make our recommendations broader than embryonic. And in the CIRM guidelines, there are some requirements that are exceptions about using neuroprogenitors stem cells in (chimeras) even though they're not covered stem cells.

I'm suggesting that we should - I think it would be a good idea.

And this certainly reflected some of the things that Bernie suggested that first in human (uses) of neuroprogenitor stem cells that are placed into human brain…

Man: Uh-huh.

David Magnus: …should get ESCRO review and not merely IRB review because IRBs don't have necessarily the expertise to do these appropriate kinds of evaluations that we required.

Henry Greely: You're specifically worried about neuroprogenitors because of the particular sensitivity of the brain?

David Magnus: Correct.

Henry Greely: And the central nervous system?

David Magnus: Correct.

Bertram Lubin: And what about autologous?

David Magnus: I don't have anything to say about that. I mean, I am nervous about going too far down - I'll be able to do an argument whether you think ESCRO evaluation would be needed for that.

Henry Greely: So, we obviously we can't be talking about autologous embryonic stem cells.

David Magnus: Right.

Henry Greely: At least.

David Magnus: Right.

Henry Greely: Unless we get to the (blastomere) biopsy -- 20 years from now.

David Magnus: (ACT).

Henry Greely: Right.

So, we're only talking here about the things that aren't embryonic stem cells. And we can actually have autologous, fetal tissue…

((Crosstalk))

Henry Greely: But you could have autologous cord blood or autologous adult cells if we were able to…

((Crosstalk))

Henry Greely: …isolate and purify brain stem cells from adults. Do you think that they exist although they're hard to find.

Then, should those be subject to ESCRO review. That's your question, right Oto?

Oto Martinez-Maza: Correct. I mean, analogous and hematopoetic (unintelligible).

Henry Greely: Right.

David Magnus: Yeah, I'm torn because so far, they are analogous to (hematopoetic) stem cells and then I would think not.

Bertram Lubin: I would say not.

David Magnus: Yeah.

Bertram Lubin: But I'm asking since you're broadening this.

David Magnus: Yes. So, I guess I would say I don't - I would need some convincing…

((Crosstalk))

Bertram Lubin: …like autologous cord blood for example.

David Magnus: Yeah.

Bertram Lubin: For a neurological problem.

David Magnus: Yeah.

((Crosstalk))

David Magnus: I wouldn't think…

((Crosstalk))

David Magnus: So what I have in mind here is more like the (Battens) trial.

Bertram Lubin: Yeah. I understand

David Magnus: And that sort of thing I think should directly (unintelligible).

((Crosstalk))

David Magnus: Yeah. That sort of thing should have an ESCRO review…

Henry Greely: So, I forget. What's the opposite of autologous - heterologous?

Radhika Rao: I thought weren't we also including in our definition -- outside the definition covered cell line the possibility that pluripotent stem cells could be created from…

((Crosstalk))

Henry Greely: …autologous.

Woman: Yeah.

Radhika Rao: Those could be autologous…

David Magnus: But those are already covered…

((Crosstalk))

Henry Greely: …those are pluripotent and we would be concerned about them because of their pluripotency.

Radhika Rao: Their pluripotency not because of the - but if you say heterologous, then…

Henry Greely: And you say it fast three times.

Radhika Rao: Then you don't -- the clinical trial in this situation. You don't have the (regs) apply in the situation of…

Henry Greely: Right.

((Crosstalk))

David Magnus: We should make sure that it includes pluripotent

Henry Greely: Which it would given our…

((Crosstalk))

David Magnus: Well, we could. I didn't put that…

((Crosstalk))

Henry Greely: Right. Right, right.

David Magnus: So we should add to the language of this human embryonic stem cells, pluripotent cells or…

Henry Greely: Well, no, we just need to say from covered cell lines.

Radhika Rao: Covered cell lines.

Henry Greely: Because we've…

David Magnus: Okay.

Henry Greely: Plus the neuroprogenitors which are not part of covered cell lines.

((Crosstalk))

Henry Greely: And then we've still got this lingering question about what about autologous neuroprogenitors which don't yet exist as a feasible possibility, but it might.

David Magnus: Which I think we don't need to worry about.

Henry Greely: Oto?

((Crosstalk))

Oto Martinez-Maza: Not yet, perhaps, but I mean I don't know. I don't see the rationale for that.

((Crosstalk))

Oto Martinez-Maza: Autologous - partially differentiate...

((Crosstalk))

Henry Greely: Do we need ESCRO review for autologous stem cell transplants?

Okay.

Well then, why don't we say non-autologous, it's a heck of a lot easier than heterologous.

David Magnus: So non-autologous neuroprogenitor stem cells that are placed in the brain

Henry Greely: Right.

Right.

Woman: Yeah.

Henry Greely: That still leaves open the question- the remote possibility of getting autologous (pluripotent) cells.

But there, I think, if it's something that has gone through whatever the de-differentiation process would be necessary.

It's not like putting somebody's own cells back in. It's putting in their own cells after they've been much more than minimally manipulated and some special concern about that pluripotency.

((Crosstalk))

Henry Greely: …I'm spinning my wheels here but trying to figure out do we need to exclude autologous transplant from the covered cell lines that are not just human embryonic, since we've picked up the broader covered cell line language from CIRM. Then I guess I think we don't.

Man: Yeah.

Man: Yes. That's right.

Henry Greely: But I think you're right, Oto, we probably should exclude it from the neuroprogenitor.

David Magnus: Right.

Oto Martinez-Maza: Partially differentiated it seems that, that we're entering a differentiation slippery slope.

David Magnus: Yeah, I agree.

Oto Martinez-Maza: Go too far down.

David Magnus: I agree.

Henry Greely: And they're from…

Yeah. And presumably they are things that are actually in the patient that you just purified and are putting backing in the patient.

David Magnus: I wouldn't mind if (we specify fetal).

Henry Greely: (Fetal)?

David Magnus: Neuroprogenitor cells.

Henry Greely: I think we'd be better off going broader to adult non-autologous, to encompass adult non-autologous at least at this stage for a variety of reasons, including not wanting to appear to be singling out any one particular company or technology.

Not only not wanting to appear to, but not wanting to.

Okay. So I think these provisions are open for debate and discussion.

And note they really fall into three categories, requirements for SCRO review on some clinical trials. Requirements for IRB review on some clinical trials, and then the thing about, shouldn't be placed in human embryos.

Although, refresh, I can't remember right now, there is a CIRM variant on that isn't there? That we have already just adopted?

Doesn't CIRM say something about not funding stuff where you put (bowels into) human embryos -- 100030 C? The introduction of any stem cells whether human or non-human into human embryos. That cover what you just proposed?

David Magnus: Uh-huh.

Henry Greely: Okay.

David did not have the luxury of this nice compendium of the CIRM regs when he wrote this up so it's not shocking that there'd be overlap.

So we arguably don't need that number three in our proposal.

David Magnus: Yes, it's covered, although, again from an organizational point of view, there's advantages to having this all fall under the clinical trial issues, because this is- I'm thinking about the analogy with germ line, gene therapy, as a restriction on…

((Crosstalk))

Henry Greely: …so one argument would be that if it's redundant it's not necessarily a bad thing to have it in both. I mean we could make it technically non redundant by saying this.

Radhika Rao: Actually, David's provision is different from CIRM because it says with the intent to create an infant and the CIRM provision says the induction of any stem cells whether human or non-human into human embryos.

Henry Greely: True but the CIRM would encompass David's…

((Crosstalk))

Henry Greely: …regardless of intent. They are different but the CIRM is broader which is we've already adapted.

Radhika Rao: Right. Yeah.

Henry Greely: All right, we'll flag that, to see if we want to keep it in or not.

I guess it kind of moved me back to what the heck.

It's probably no harm in keeping it in as an additional provision with respect to the clinical trials part. But now to the substance of the clinical trial thing, you know. What we're recommending here, although we talked about in June, is non-trivial the SCRO committee shall assure that adequate scientific and ethical reviews taking place.

Well that's not a big deal or a new thing, and that's part of the small section dealing with putting them into live born human that CIRM has but it shall require to establish that there is sufficient institutional strength in the field to justify conducting such research particularly with respect -- R-E-S-P-E-C-T to the trials involving the first time particular kinds of cells are being transplanted into humans for particular diseases or in particular organ systems.

Three particulars in one sentence maybe a record. And I would note. I - that's my fault. That's not David's language.

((Crosstalk))

Henry Greely: …and I was trying to spin out what first in human use meant…

David Magnus: I wasn't trying to do that in a separate, put that in a definition section rather than put that in here.

Radhika Rao: It was a bit cumbersome.

Henry Greely: Establish, so institutional fields, institutional strength in the field. Number two is sufficient knowledge for the risk invested associated with the proposed

intervention that it's reasonable to proceed human population. So this is to say, do we know enough about the risk and benefits to do it all in people?

First one is, is the field strong enough that we're confident it can go in people? Do we know enough about this intervention that we're confident it should go in people?

Number three is provide justification to risk to the trials have been minimized and are reasonable in relations to the anticipated benefit of the trials included benefits from the (generalizable) knowledge to be gained.

That's saying - so even if there's enough field strength and even if we know enough about the intervention to be happy with the risks in general in this context, in this risk benefit assessment, are we happy with it and have those risks been reasonably minimized.

David Magnus: Also - this also means that this is sort of consideration that normally IRBs could use in their evaluation.

Henry Greely: Right.

David Magnus: Which we're saying that the ESCRO should take sort of take a look at that different expertise than IRB.

Henry Greely: So number three is really an IRB requirement transplanted into the ESCRO. One and two are not with the - expressed IRB requirements.

And number four is the justice issue, diversity of research subject population. So sufficient saying clear and justification of why they're not included if they are included. They are included. Right.

So that's, and then the last one about safety reasons requiring testing or screening of donors that seems to be not…

((Crosstalk))

David Magnus: …lo article that's (pointed out) that the FDAs - a good chance that the FDA is going to require other kinds of testing. In this way, this will flag it, because it's one things that would be useful for researchers to know that they are (anonymizing) the material which a lot of people are doing because it makes the confidentiality issue easier to deal with, that's the materials that they derive and the cell lines they derive probably won't be able to be used in the clinical trials later on.

Henry Greely: May not be able to be used.

David Magnus: May not be able, so this flags that.

Henry Greely: So I think the big deals here are B1 and 2, those are new. C to some extent although I don't think C should be very controversial. Comments on any of these first recommendation…

Elliot Dorff: This is Elliot.

This is just in response to, I forgot who made the point before we had a break of not being overly - let's just say - overly burdensome. I think I like the draft actually in lot of ways.

But I think we might want to say at the very beginning that in order to fulfill our social responsibilities to make sure that this is being done ethically, but at

the same time, not to overburden institutions, but what we are doing here is suggesting that there be these reviews each, very specifically spelled out for their expertise.

In other words, the SCRO would be looking for things for its expertise and the IRB for its expertise but hopefully not, not being redundant one with the other.

I think we just had some kind of explanatory paragraph that from what I understand is that there is our intention. At least I would hope it would be our intention that that would be good.

Henry Greely: Bert.

Bertram Lubin: So we have a couple of committees here that are not these two but this kind of thing comes up a research committee, the medical staff and the IRB. They review all the NIH, non-NIH grants with they can go through another peer review, and we have a member of the IRB on the research committee.

And the research committee on the IRB so that we facilitate some of these things instead of doing everything all over again.

I don’t know whether we can say something like it but it seems to me that if there was a possibility of having somebody on ESCRO that was on the IRB, somewhat 1 person , the other way around as well, then it might be a good way to facilitate communications prevent duplication.

David Magnus: It might but do we want to require that?

Bertram Lubin: I don’t know. I'm just throwing that out.

David Magnus: Sounds like a good idea but I'm not sure we should require it.

Henry Greely: Especially since CIRM has it. I think we could encourage communications back and forth between the two.

Bertram Lubin: I think some mechanisms for communications…

((Crosstalk))

Bertram Lubin: …redundancy and duplicity…

((Crosstalk))

Henry Greely: So, and this actually isn't so much about the clinical trial section this interplay between the IRBs and SCROs that Elliot pointed out and that you point out applied through out this.

Bertram Lubin: Right.

Henry Greely: I did a little bit of this in that preface statement on the second page of line 63 through 67.

We thus consider the respective strength of those institutions, SCROs and IRBs, recommending the duties of each, the SCRO committees that would likely to have more expertise on stem cell research more expertise in stem cell research than the IRBs which cover a very broad range of research, and so have assigned blah, blah, blah.

Bertram Lubin: Okay.

Henry Greely: Now, Elliot, I like your point, and could easily build that in there, that we recognize two institutions, don't want to overburden people, but they're somewhat separate with different expertises.

Elliot Dorff: Uh-huh.

David Magnus: And also, Bert, your point about as would be it's really good so that we communicate well with each other…

Radhika Rao: And it will (unintelligible).

Henry Greely: And it's one of way of doing that might include (overlapping) memberships.

Bertram Lubin: Yeah, I guess, I think, at least the way we do with the other one, this is about -- is this something we want to have done at this point? And the next one, are the subjects protected? Do they understand what the research is? Do they know the risks and benefits?

So when that comes up, and the second one, we say, "We already discussed that in the other one.

David Magnus: Right.

Bertram Lubin: That isn't what we're here to discuss."

David Magnus: Right.

Bertram Lubin: And vice versa.

David Magnus: Which is why we have systems laid out the way it is, so the consent issues are under - the IRB is a number two, right under the first one.

Henry Greely: Other comments on number one on (SCROs)? Institutional strengths in the field -- everybody is happy with that?

Oto Martinez-Maza: Not entirely. I'm not sure really what that means.

David Magnus: Again, we can have the definition section, but the concept of institutional field strength is in the surgical literature, surgical innovation. It's a way of evaluating when doing sort of first in human surgical procedures. So, the first time somebody does a face transplant, the first time that anybody tried to use a liver lobe for transplant.

So this is the concept that was developed about 10 or 15 years ago as a way of evaluating when it's appropriate to move forward with these sort of different kinds of surgical innovations or - which often fall outside of the regulatory system.

Bertram Lubin: So does this restrict the places that have expertise 'cause they've done several?(unintelligible)…

David Magnus: Or they have - it means - there's a couple of different dimensions to it, but it means that they've got enough personnel, you've got people with enough relevant experience. You wouldn't want to have a place doing a first in human clinical trial with embryonic stem cell trial at a place that has minimal resources, minimal expertise in clinical trials, doesn't have all the things that you would want to have to really be able to manage a difficult clinical trial.

They may - so, you know, you talked about maybe even requiring a (GCRC) (unintelligible) that might be too much, but there needs to be enough resources that they can handle difficult challenging cases like this in terms of regulatory, every aspect of what it takes to do a difficult person/human clinical trial.

Henry Greely: And what this specifically does is says the (ESCRO) has to be convinced that they're institution...

David Magnus: Right.

Henry Greely: …before it approves it. And after the (ESCRO) the theory that the (ESCRO) more than the IRB will know things about stem cells, the stem cell field that they'll be in a better position to make that assessment (unintelligible) IRB.

Gregory Stock: I have a question on two of the points. (Greg) Stock here.

Item 3, in terms of the reasonableness related to the anticipated benefits of the trial, how is that determined, one's evaluation of reasonableness if there is really true informed consent and judgments are being made about that, is, you know, is that a significant impediment to certain areas of research and…

Henry Greely: That's the IRB standard, what IRBs are required to do.

David Magnus: Right. This is the one area that I thought it was reasonable to have overlaps because it is kind of a quasi (unintelligible) review. I thought it was appropriate for (SCROs) to do that same evaluation.

Henry Greely: On your broader question on whether that holds back research, I - by, you know, potentially preventing an intelligent, confident adult from being a

research subject in situations where she says, “I want to be research subject here.” And the IRB says, “No, it’s too risky, you can’t.”

That’s the system we've got right now. It’s not a fully libertarian system. The IRB will not or it should not allow to allow research to go forward if it finds that the risks outweigh the benefits.

And I haven’t heard enormous complaints about the application of that standard by IRBs. Although from time to time there are concerns.

Gregory Stock: Well, one wouldn’t because it probably - it doesn’t get to that point, I would guess, if it’s an issue.

David Magnus: Well, then, it’s a (unintelligible) evaluation. There are times when for example the choice is subject population, it seems too risky to do a certain trial in that certain population, and so you take a different population to change the risk-benefit ratio. And things like that happen all the time.

Gregory Stock: And is it the same thing as the representation in terms of the diversity, is that pretty much standard now? Item 4?

David Magnus: Four came from the public comment period at our last meeting. That’s something that we ought to strive to make a point of attempting to do. You're right though that that is something that the FDA now does require in general, but I think this is something that we should highlight.

Henry Greely: Geoff, can I ask you if the CIRM has thought about inclusion of minorities and other under-represented groups in research -- as part of your regs or discussions so far?

Geoff Lomax: It is a major topic within the plans that organizations may develop. (Till now) we've refered to existing (unintelligible) model after the (unintelligible) regulations.

Henry Greely: So I think it's fair to say that this little (4) on diversity is not currently something IRBs are required to consider but something that research institutions and researchers in lots of different ways at the state and federal and FDA levels are highlyencouraged to do.

Gregory Stock: Uh-huh.

Henry Greely: So this would be - that's why I said I didn't think this would be a controversial recommendation. This is kind of conventional wisdom, just adding our voice to it in the guidelines.

David Magnus: In this particular area, it might be more important than the general though just because insofar as a lot of the cell lines might be derived from excess IVF embryos that is a relatively homogenous population that is being derived from and if they wind up being matching issues, that might be a reason why you might expect clinical trials, so that adds a similar narrow focus…

((Crosstalk))

Henry Greely: Be all white I think is what David is dancing around.

Gregory Stock: But if you're saying that that would - that one might expect that for purposes related to the donor population and there are a variety of issues of terms of whether or not it will be challenging to get the donors in many situations, then perhaps adding this is less appropriate in this realm than it would be in other realms.

Henry Greely: Except that what it says is just address the issue.

Gregory Stock: Okay.

David Magnus: It doesn't say that it's required, it says it needs to be thought about, because it's like - more likely to be a problem. It's good to have people be aware of it and address it and maybe people can come up with some innovative solutions to it that way.

Gregory Stock: Uh-huh.

Margaret McLean: But this doesn't address the donor. This addresses the research subject.

David Magnus: Right, because but that's the worry, is that it's - because HLA matching or some other reasons, it might wind up leading to a similar bias from the donor sources on the (clinical trial line).

Henry Greely: So for example, if you have 100 (cell lines) that might be used for the trial and 99 of them are from people of European ancestry and 1 is from somebody of Sub-Saharan African ancestry, you might say, "Well, lets" - and you're only going to use five of them in your trial, and say, "Well, if we can, let's make sure we use that African-American line, so we - if there is an HLA matching issue, we can actually have some African-American subjects as part of the trial."

David Magnus: Right.

Henry Greely: That would be…

David Magnus: Right.

Henry Greely: …one thing an (ESCRO) might think about as a way to deal with this issue.

Other comments on number one? Then let's move to number two.

"All clinical trials involved in the use of." And here, you know, again I think we need - we're going to have to modify - say covered (cell lines) (unintelligible) we've now broadened to.

"Shall be reviewed and approved by an IRB. Shall require an informed consent for any clinical trials involving HESCs and the derivatives involving covered (cell lines) and the derivatives, would like that to come back to the derivatives points.

Include information where the materials originated from and how they were produced. IRB shall ensure that the language used in the informed consent are early-phase clinical trials blah, blah do not convey an unrealistic impression of the direct benefit of trial participation.

Sub 1, the expression "therapeutic cloning" shall not be used to describe any Phase 1 clinical trials. And then, number three, IRB shall require that any clinical trials involving HESCs and their derivatives shall have a data safety monitoring board."

David Magnus: Right…

Henry Greely: So, three, you know, sort of specific and innovative recommendations.

David Magnus: The third one we didn't have agreement on last time, we said we'll talk about it later, so that's - so that's for now.

And the, obviously, A should be a no-brainer. That means that if some people opposed to embryonic stem cell research, that we are to put the stuff into people, they deserve to know where it's from. It would be very bad if somebody who was in the clinical trial later found out that the material came from something that they found moral objectionable…

Henry Greely: Desperately, I will do anything to save my life except that. And maybe some people who…

((Crosstalk))

David Magnus: Yeah, I'll take the (unintelligible) who are desperately…

Henry Greely: And say that.

Margaret McLean: And say that, uh-huh.

Man: (Unintelligible).

Henry Greely: So is there any controversy about A? I agree with David; I think this is - should not be a controversial.

B, on the other hand, is a little stronger than what we normally see.

David Magnus: It's a little bit - you may recall that in the last time, one of the recommendations have been that IRBs should not assume any prospect of

direct benefit. And then there was a lot of talk and objections. And so this is a modified version based on the conversations we had about that point.

So rather than making - because the real core issue was a concern that we don't want the problems that have plagued gene transfer research to plague this area of research. And there have been a lot of studies that have been done of consent forms for gene transfer research that have shown misleading language used over and over again, and that conveyed a false impression. We want to make sure that that doesn't happen in this case.

Hence, the requirements that - rather than simply state that there should be no assumption of prospect of direct benefit, it simply leaves to the IRBs to make sure that the informed consent forms are reasonable and don't convey anything.

And this is flagged before them because obviously the studies that (Nancy Kane) and others have done on informed consent form, those all got approved by IRB. So on gene transfer research, IRBs are actually at the present time doing kind of a lousy job.

So given that this is another important area, flagging for this, that's for them I think will be useful, and in particular, asking that they not use this misleading language which has plagued also gene transfer research, I think is worth doing.

Radhika Rao: One small thing, should you - the language used does not convey, right, not the language you do not convey.

David Magnus: Correct.

Henry Greely: That's a no-brainer.

Man: Yeah.

Woman: Yeah.

David Magnus: And then the DSMB issue. Given how quickly…

Henry Greely: Hold on.

David Magnus: Sorry.

Henry Greely: So anything else on this? People are happy with…

((Crosstalk))

Henry Greely: …the therapeutic cloning part in particular which is an unusual level of detail to say, "Don't let this language be used."

Gregory Stock: Right. Yeah. My feeling is that the B is good but that the expressed prohibition of therapeutic cloning is a little bit excessive, a little bit too narrow in my view. I mean, why not go through and do a variety of other terms as well. Therapeutic cloning in many instances has a negative connotation associated with it as well.

David Magnus: (Unintelligible) I'll say that I think it's a risk -- it's a particular risk because it has been commonly used, and I will just note having reviewed the informed consent protocols for the South Korean research. They did use the terminology of therapeutic cloning and we flagged that in our science paper

precisely for that reason. So I'm very worried that in fact we will see this language creeping up in informed consent forms if it's not strictly prohibited.

Gregory Stock: Well, you might. But to take the South Korean situation, there were so many egregious problems with that. I mean….

David Magnus: No, I agree…

Gregory Stock: …therapeutic cloning is the least of it.

David Magnus: I'm saying I think this a good chance for it to happen. Why not just flag it to say that we can't use this language if it's something that everybody has agreed that is misleading.

Henry Greely: Other comment on this point, 2BI?

Radhika Rao: Not 2BI but just 2B. Might as well…

Henry Greely: Or not. Sorry.

((Crosstalk))

Radhika Rao: My understanding, David, of that is that if the informed consent form says that there may not be any direct benefit to you from engaging this clinical trial, that is considered to be unduly misleading because it suggests that there may be…

David Magnus: So - no, not necessarily.

So if you look at the literature that looks in gene transfer trials and informed consent, I mean if you - give you examples. But what you typically have happen that's seen as problematic is an informed consent form that will have some (unintelligible) contentless assertion that this may or may not benefit you. That's why itself isn't necessarily that, it doesn't sound good, it's not sufficient, but it's contentless, but then it's also often accompanied by a description of what's going to take place that actually directly states that what you're getting is something that's therapeutic, like, what we are going to try to do in this is put a gene into - that you're missing in these cells. The goal of this is so that people like you who lack this gene will be able to have this gene and be able to be cured by it. And then there'll be this contentless assertion that may or may not benefit you. Nobody could see those two things and not conclude that the goal of this is to benefit you.

I mean, there are problems in about half of the gene transfer trials. So there's a couple of big studies in informed consent forms of gene transfer trials. And they both found that about 50% of Phase 1 gene transfer trials are extremely misleading.

So I think given that problem and that history and some of the similarities that I think are going to arise between frontier area of research like stem cell research and gene transfer research, I think it behooves us to flag this as an area of concern, in particular so that institutions should be careful about it.

Gregory Stock: But when you say no direct benefit, in fact that doesn't cover what you just stated because that the goal of the research is ultimately might be beneficial is often the case, it's that they don't receive direct benefit in that trial which it sounds - in other words, it sounds to me like the problem is much broader and more general, and to address it in this way is fine, but let me ask you a question. What fraction of the sort of false conveyance of an unrealistic

impression of benefit would be with therapeutic cloning or with anything specific? You know, isn't it a general concern that you have that is best addressed by the IRB?

David Magnus: That's why we have flagged it in these. So we say, this is what IRB should do. IRB should make sure that they don't - that this doesn't happen. I - so that's why B is there.

(Unintelligible) the specific thing, it's just - that's a likely source of a problem, why not just get rid of it?

Henry Greely: Yeah, and you know, it is true. I don't know how much you looked through this, Greg, but the whole gene therapy stuff, the whole thing with human trials of gene therapy today, it has (unintelligible) of a lot of us that people are talking about gene therapy.

Woman: Uh-huh.

Henry Greely: And it's research that they hope may lead to a therapy. The very name is to encourage, and if you talk about therapeutic cloning or stem cell, you know, presumably you also would be offended appropriately. We'd be concerned if people said, we want you to sign upfor this stem cell therapy trial.

Elliot Dorff: So why don't we just - why don't we do, after the end of B, for example, the expressions "therapeutic cloning," "stem cell therapy," and "gene therapy" shall not be used to describe any Phase 1 clinical trials?

Woman: Yes.

Man: Perfect.

Woman: Good.

Man: Okay.

Oto Martinez-Maza: Then it's not appropriate if you described (unintelligible).

Henry Greely: And so you could say shall, you could say should, which has that wonderful fuzziness of whether it's…

Man: Fine. Okay.

Woman: (Unintelligible).

Henry Greely: Or you could say it's not appropriate to which is I think a longer…

Gregory Stock: Or convey that impression -- or convey an impression or something.

Henry Greely: Oto, I interrupted you, I'm sorry.

Oto Martinez-Maza: It's more of a suggestion that indicates specifically that you should (unintelligible).

David Magnus: I'm happy with this appropriate.

Man: Okay.

((Crosstalk))

Oto Martinez-Maza: I agree wholeheartedly…

Man: Then…

Radhika Rao: So do we have that down?

Henry Greely: I think we have either to say it's good or to say it's not appropriate.

Radhika Rao: And the three examples. I like this better than…

Henry Greely: The three examples…

((Crosstalk))

Radhika Rao: …cloning, stem cell therapy, and gene therapy.

Man: Yes.

Radhika Rao: Yeah. For example. Or for example, the term therapeutic cloning.

Man: Okay (unintelligible).

Henry Greely: DSMB, Data Safety Monitoring Board, comments on this? This also breaks new grounds. So it follows DSMBs are common in clinical trials, they're not - they don't exist in every clinical trial.

David Magnus: I mean these are probably going to be large multi-institutional trial.

Bertram Lubin: And actually, almost every clinical trial…

((Crosstalk))

Bertram Lubin: We used to have very few, but now it's like if you have a DSMB, if you don't, (unintelligible) all the clinical research centers…

David Magnus: Right.

Bertram Lubin: …DSMB, so.

((Crosstalk))

Bertram Lubin: So it's not rare.

David Magnus: I think now - I think this is a requirement that almost anybody who's going to do this, and I think any place that has sufficient institutional field strength will have a DSMB in place. But I thought it was important enough that it should be something that is just a requirement…

Man: Right.

David Magnus: …just to make sure that there isn't a small place that once we do this, it doesn't have that.

Henry Greely: I mean, I suppose we could imagine really trivial on a clinical trial of stem cell research.

Man: Right.

Man: Yeah, I can.

Henry Greely: (Unintelligible) skin on the tip of your finger. But even that actually…

Woman: Yeah.

Henry Greely: …suppose…

((Crosstalk))

Henry Greely: As long as you're using pluripotent cells, I think you've got to be worried. Okay, I withdraw my (half baked) idea.

So any other comments on 2?

Oto Martinez-Maza: I have a question that's come up since we discussed 2A.

Henry Greely: Uh-huh.

Oto Martinez-Maza: So I'd like to go back to that for a second.

What specific information do you want people to have (unintelligible)?

David Magnus: So, again, avoiding the language issue that the - that things that some people consider embryos may have been destroyed in the production of the cell…

Oto Martinez-Maza: So where doesn't mean Cleveland or…

David Magnus: No.

Oto Martinez-Maza: …or England…

David Magnus: No.

((Crosstalk))

Woman: Yeah.

David Magnus: I just try to…

((Crosstalk))

David Magnus: …actually to be honest, I would have been - felt comfortable in the initial version that we had simply said that people have a right to know that this - that embryonic stem cells come from embryos.

Woman: Right.

David Magnus: But Irv felt very strongly that we should never refer to ex vivo embryos.

Henry Greely: (Though he) was happy to keep talking about human embryonic stem cell research.

David Magnus: Correct.

Henry Greely: But they didn't come from embryos.

David Magnus: So I know it’s a little vague in the language, but that’s really what this is, trying to put it in such a way that did not make a commitment about what language should be most appropriate for describing the things would find objectionable…

((Crosstalk))

Oto Martinez-Maza: Okay. Because, you know…

David Magnus: …and would want to just point it out.

Oto Martinez-Maza: …SCROs are spending a lot of time discussing (unintelligible) and cell line…

David Magnus: Correct.

((Crosstalk))

Radhika Rao: …that we should be specific here because we don't want guidelines to confuse people, think that they need to provide…

((Crosstalk))

Radhika Rao: …information about it came from…

David Magnus: Okay. I just follow the instructions from our last meeting which was to fuzz it up, so I'm happy to… That was the sense of…

Henry Greely: What do we substitute for the word “where”?

Gregory Stock: You could just say from the origin of the material.

Henry Greely: The origin of the material.

Margaret McLean: Yeah, yeah.

Woman: Well, the origin of the material and how they…

Woman: Yeah, that is…

Gregory Stock: …to production or something like that.

Man: Exactly.

Woman: (Unintelligible)…

Henry Greely: I tell you what, we'll fix it.

David Magnus: Yeah, I know. So I mean, can I ask questions - I mean I know Irv isn't here, and expressed very strongly his believe that these are not embryos. But CIRM uses the language of embryos throughout and we just adopted those. Can I just ask, can we use the word "embryo"?

Woman: Yes.

David Magnus: It would make life a lot easier to explain especially the point of some people…

Henry Greely: Although, I have a different objection than Irv's, and that is maybe some of the things some of these are coming from for some purposes aren't embryos...

Radhika Rao: Aren't technically embryos.

Henry Greely: So maybe part…

((Crosstalk))

Henry Greely: …shouldn't be considered embryos.

Radhika Rao: Yeah.

Gregory Stock: So you could put the biological source of the materials and biological…

((Crosstalk))

Margaret McLean: There we go.

Henry Greely: Bingo.

Margaret McLean: There we go.

David Magnus: There we go.

Henry Greely: You win.

Margaret McLean: Perfect.

Man: Ding-ding.

Henry Greely: You get all the money and free parking.

Parking time, whatever that is.

Okay, so - oh, and then on three, we danced around this a little bit. It sounds to me like…

Radhika Rao: It was just the biological (source of) materials or and how they were produced.

Henry Greely: And how they were produced.

Radhika Rao: And how they were produced. Biologic (source of) materials and how they…

David Magnus: Some people object to cloning, and not this…

Man: Right.

Radhika Rao: Right.

Man: Right.

Henry Greely: So on 3 no HESCs shall be placed in human embryos that are going to be used with the intent to create an infant…

((Crosstalk))

Henry Greely: We think it's probably redundant but it may not be a bad idea to say it. Reactions to that?

It's certainly I think falls within a prohibition that already exists in the CIRM regs which we've adopted. It's smaller than that. It's more focused. In the clinical trial area, it may have some more force. I don't think it's essential, I also don't think it's harmful whatever people want to do with it.

(Unintelligible)…

Woman: Leave it.

Henry Greely: Leave it?

Woman: Yeah, just leave it.

Henry Greely: Anything else on the clinical trial side?

((Crosstalk))

David Magnus: No, that's what I had in mind…

((Crosstalk))

Gregory Stock: This is - number three is for clinical trials? One can imagine a clinical trial using - where it’s placed into human embryos that are going to be used with intent to create an infant?

David Magnus: Yes. And again, this doesn’t necessarily mean only ex-vivo embryos.

Henry Greely: So it would be like gene - it would be akin to gene therapy in an embryo…

David Magnus: Exactly -- that's exactly what I have in mind.

Henry Greely: Actually do you want to say embryo?

Woman: Yeah.

Henry Greely: Do you want to say embryo or fetus?

Woman: Fetal, yeah. Yeah.

Man: Yeah.

Margaret McLean: Yeah. Fetal surgery.

David Magnus: That's right.

Woman: Yeah.

Gregory Stock: Wouldn't though - wouldn't that kind of clinical as a trial that would be pretty difficult to get through on a lot of other grounds?

Radhika Rao: But then you should say, into human embryos that are going to used with the intent to create an infant or fetuses, or just to say, no human embryo - stem cell should be placed with the human embryos or fetuses, and cut out the, with the intent to create…

Henry Greely: (Unintelligible) well, with the intent to create an infant, it makes it a clinical trial.

David Magnus: Right.

Radhika Rao: Right.

Henry Greely: Arguably although query whether it's a clinical trial, if the thing you're doing it to is not a human person for purposes of the common rule but they are fetuses, are covered for some - and fetuses for the common rule I think includes anything that's implanted. It's not those 56A definition we're familiar with for other purposes.

Gregory Stock: Actually I have a further comment reflecting on that. It seems to me that if you think in the short term of early trials being done in this way, that it seems rather extraordinary and one would not imagine that occurring. But if you were to think decades from now, after therapies were - assuming that therapies were actually - lots of demonstrations had been made and there were actually treatments that existed in adults, one could certainly imagine trials of this order. I mean what you're saying is that one could never imagine…

David Magnus: No, I'm saying this is a good rule now, any of these regulations we are putting in place, I mean maybe 30 years from now, no one will think ESCROs - we need ESCROs anymore. But for the - all regulations and guidelines are bounded by a particular period of time.

Gregory Stock: So - but you have various requirements that are for safety that a review in terms of the risks and benefits and such, it seems to me that at this time right now, those with - this would be so far beyond the realm of anything that could pass those other criteria that by singling that out, it’s unnecessary. And the only way it would come up would be sometime way down the line. And we can see what a momentum regulations have to them and how hard it is to change them.

David Magnus: I felt this… I don’t necessarily agree. I think this is something that I have a hard time imagining anybody doing. It was expressed on our subcommittee that analogous to the gene transferred. I mean, there are a lot of guidelines that prohibit germ line gene transfer from taking place. Including apparent, possibly (upon) have interpretation including essentially the CIRM regulation. Nobody is proposing doing any of those sorts of things for exactly the same analogous statements but there are all these statements about that. So in the group, somebody expressed the view that we should have something analogous to that and that's why this is here.

I don't feel - I mean if people don't want it, it is covered by something else, I'm happy to take it out. So I don't care.

Henry Greely: I do think that preparatory, you've pointed out usefully, that I think the preparatory language to these recommendations should point out that they are recommendations for guidelines for now based on what we currently know, and in the future as our knowledge (unintelligible) mechanisms and research changes, the guidelines may need to be changed.

Man: Right.

Henry Greely: So I think it expresses acknowledgement of the idea that these are not eternal (unintelligible). This is not necessarily…

Gregory Stock: So that's easy to say, but I would suggest that from our experience with just the way we have adopted other guidelines, that in fact it creates a significant hurdle to make that alteration.

Henry Greely: It sounds like nobody's arguing strongly in defense of this, Greg, you're arguing strongly against it. Anybody really want to go to - and remember this is redundant with…

David Magnus: Yeah.

Henry Greely: …the earlier provision we all ready adopted in the CIRM regs about not putting…

David Magnus: Right.

Henry Greely: …embryonic stem cells into human embryos.

David Magnus: That would be our response to Greg though. Greg, this is already explicitly prohibited in the regulations whether we have it here or not.

Gregory Stock: Okay. It just feels to me that you're…

Henry Greely: It sounds like we're going to drop this, I think.

Radhika Rao: One question about the CIRM regulations. The CIRM regulations only spoke of embryos, not fetuses.

Henry Greely: True.

Radhika Rao: I mean we just talked about fetuses. Does that mean that its allowed to do it with fetuses or do we just want to leave ourselves in the same (unintelligible)as CIRM?

Henry Greely: Dr. Lomax would you care to address that?

((Crosstalk))

Geoff Lomax: …(unintelligible) face value it says embryo.

Radhika Rao: Embryos, embryo, so.

David Magnus: So I guess that…

Geoff Lomax: I think this is - well this is…

Man: So I guess probably…

Geoff Lomax: I think this is just - well, this is a…

((Crosstalk))

Geoff Lomax: I think, looking at our records there's a - the close - what this is a living piece of work we've got to file and we need to get…

David Magnus: So, do we want so many assets, so three (instead) since embryos are covered; do we want to include a restriction on fetal embryonic stem cell research - transferring…

Radhika Rao: Human embryonic stem cells.

David Magnus: …human embryonic cells into…

((Crosstalk))

Henry Greely: Perhaps specifically modified here within - at this time.

Gregory Stock: Well, do you feel - I would ask - a question is -- the reason for including is a philosophical issue, which primarily it is with the - a lot of the other prohibition and/or is it - in other words if you could in fact meet the criteria of safety and benefit and such that would be - that would operate with adults, do you feel that it should still be excluded?

David Magnus: I guess the only other question is whether or not there's going to be anything that would be analogous to (germ line) worry. So one of the worries in

transfer research is whether or not it's going to have any implications for future germ line - germ cells.

And so, is there anything like that could happen with stem cell interventions early on?

Well if there are, then that's the reason for flagging, it's something that needs to be either prohibited or at least considered.

Gregory Stock: Well - and certainly, it would have to be considered. I mean, there's no way once - that's - and clearly that's the intent of the prior clauses where you talked how could one look at this and not be looking at safety issues such as you're talking about now.

David Magnus: …generation issues that doesn't occur in most clinical trials and hence the reason for flagging it.

So I still think that that's an issue that needs to be flagged. This language may not be the right language for capturing that; but I think we still need to say something about potential early stem cell.

Henry Greely: Yeah, there is interestingly different because unless the introduced stem cells contributes to the (gametes)…

Man: Uh-huh.

Henry Greely: …(it isn't multi generation).

Man: Yeah. And then if we…

Gregory Stock: So one might then, if you wish - I would have no objections to putting in a clause that if human - if there were human embryonic stem cells were placed in human embryos or fetal - or fetuses that there would be expressed consideration of whatever those issues are, they should - in my view, be considered in any event.

But, you know, it seems to me a prohibition is not a good way of dealing with the concern that you're expressing right now.

Man: Yeah.

David Magnus: I think that - it makes sense. It's exclusively prohibited in any case for the embryos by other regulations that we've already approved. So I'm not sure it matters that much unless intervention in - at a fetal level could have a germ line implication.

Henry Greely: Can we come to closure on this or not? I'm not sure that we're - either have a consensus emerging or have attention spans that are up to and on this point. But I'd like to get closure on this Number 3.

I think - well, let me go around the table and ask people. Put them on the spot.

And I'll start with myself in all fairness. I guess I think there's a minor advantage to including this here. I'm not troubled by (Greg's) concern about possibly if it becomes safe in the future because I'm happy that either overall prefatory language or prefatory language in the senset about at this time. But I don't think it's a big deal. I'm not going to…

Margaret McLean: I think there are some advantages to having it explicit under clinical trials so that, you know, you're not trying just to brag the concept over from another set of regulations or they're regulating something different. Although, I'm not interested in going to the mat for this language either. But I think there is some advantage to having it here.

Henry Greely: Bert?

Bertram Lubin: Though I was - I started thinking about this when you mention, David, in (utero) surgery or any utero intervention…

David Magnus: Uh-huh.

Bertram Lubin: …so you detect the child if - I think in an experiment and there are some embryonic stem cell way to induce that need to grow do we exclude that clinical trial? Or as a whole in the mark or has some other structural things or maybe embryonic stem cells could be of value.

((Crosstalk))

David Magnus: I think actually I am happier about just that the language of - any IRB looking at that should have to take into account the germ line implications.

Bertram Lubin: Yes, I don't have a problem.

David Magnus: But I'm happy with changing the language to be that the germ line enters implication…

((Crosstalk))

David Magnus: …multigenerational.

Henry Greely: I mean the germ line aspect is really is the multigenerational aspect, right?

David Magnus: Right.

Woman: Uh-huh.

Henry Greely: Extending past the generation of the person or embryo or fetus into which they are transplanted…

((Crosstalk))

Radhika Rao: Which would presumably be the main thing that would differentiate it from other kinds of…

((Crosstalk))

David Magnus: So putting something like that, that should be taken into account by the IRBs I think that - I think that's official to my point of view.

Oto Martinez-Maza: I agree with that. I think it would be a mistake to prohibit…

Henry Greely: Radhika?

Radhika Rao: I think I'm coming to that since we're doing it.

Henry Greely: Elliot, how about you?

Elliot Dorff: I think the decision is a good idea.

Henry Greely: Greg?

Gregory Stock: Yeah. And I may - to consider that multigenerational issues I think is a very good solution.

Henry Greely: Okay.

Woman: Uh-huh.

((Crosstalk))

Man: Yeah.

Henry Greely: Okay, I think we've got consensus on that. Let me then open it for public discussion because I think we're close to being able to vote on this part of our recommended guidelines.

Any members of the public in the room wish to speak?

((Crosstalk))

Ellen Auriti: …question for you about the intent in using the word "derivatives" in Number 2…

Henry Greely: We were going to talk about that I forgot, thank you.

Ellen Auriti: …A and C that so the requirement that you have is that IRBs will review any clinical trials involving human embryonic stem cells and their derivatives and IRBs shall require that any clinical trials involving human embryonic stem

cells and their derivatives shall have a data safety monitoring board. This issue has come up for us from a couple of our campuses because of the federal NIH rules…

Henry Greely: Right.

Ellen Auriti: …about federal funding of non registry stem cell lines and their derivatives. And the question has come up about how many generations do you go if you have stem cells that produce a chemical or antigen and then there's three things down, are you still requiring a DSMB for that?

Henry Greely: I actually it started to deal with that and did not follow through consistently. If you look at the language in two, initially and this is – playing around with David's language without his permission.

Involving the use of human embryonic stem cells or cells differentiated from human embryonic stem cells. But then later on I went back to the derivative language because it might arguably be proteins or factors or other things.

So what I think makes most sense is cells derived from - cells differentiated from which is most likely to be used in clinical trials. Anyway, I think most of the clinical trials won't use straight HESC cells; but will use as a dermomesenchymal cells or cardiomyocites or the things differentiated from. But it still seems to me that we'd want both the (ESCRO) and the IRB.

Ellen Auriti: I actually noticed that there's also the use of the word "derived" in Number 1. I hadn't noticed that before. All (ESCROs) should review…

Henry Greely: Yes.

Ellen Auriti: …clinical trials…

Henry Greely: Yeah, actually so - I managed to have three different contradictory versions.

That one says embryonic stem cells or materials derived from human embryonic stem cells through cell differentiation or otherwise.

Ellen Auriti: Yeah.

Henry Greely: So, at the very least, its inconsistent drafting to which I plead guilty. So what do we think we should do here?

It seems to me that at least the cells differentiated from HES…

((Crosstalk))

David Magnus: That clearly was intended - and Bernie who says clearly as multi that that was their intent in the CIRM guidelines. Well, I have to say, one problem I think with the way the CIRM regulations are written is that if you took them on their face value, you could argue that anything that doesn't involve actually putting in embryonic stem cells that only differentiate itself doesn't actually fall under some of those regulations.

But clinical trial section in particular that we just said we're adopting - you could argue that the Geron trial that they proposed which would differentiate itself, both derived from federally registered embryonic stem cell lines would not therefore trigger…

Ellen Auriti: Uh-huh.

David Magnus: …those part of the CIRM guidelines.

So that's why we wanted to explicitly say something about derivatives and I think it's going to be really important especially in clinical trial context that we capture that.

And I think it's not - it's not going to be enough to just say that these cells are differentiated from them. There may also be some immediate product - that could be derived from them, that could be used both as well.

But I also agree with you that you can't - can't go on forever. And so, there needs to be a definition of whatever term that we use that - reasonable way of cutting it off or alternatively allows the local (ESCROs), maybe some boundary that they have to include, you know, cells immediately derived from differentiated from embryonic stem cells

But beyond that, the local (ESCROs) should determine what counts as a derivative.

Henry Greely: So as a process suggestion it does seem to me this might be an area where definitional term could make sense. So defining derivatives for purposes of these (regs) rather than trying to make sure we use the same extended language…

Radhika Rao: Yeah.

Henry Greely: …everywhere.

That still of course leaves open the substantive question of what do we define them as. I would argue strongly that all cells differentiated from them should count at least for now…

Ellen Auriti: Yeah. I would…

((Crosstalk))

Ellen Auriti: …caution that as far as we know from our preliminary research, there is not a definition that's being used now…

((Crosstalk))

Ellen Auriti: …to interpretation…

Henry Greely: …co-writing a paper on, exactly that point, and I agree with you.

Ellen Auriti: Then I'll leave it to you.

Henry Greely: But no, but we still need to decide - this committee still needs to decide what we think should be encompassed in the concept of derivatives, self-differentiated from I think are easy, proteins and other factors derived from maybe, maybe not. So you have less safety concern about - not that you have no safety concern; but you've got less concern about putting a protein into a person than putting cells into a person especially pluripotent cells or stem cells of some sort.

It's less - it's more self-limiting in many ways than the cell therapies would be. How far do we want to go? Not to mention Ellen's point about a number (unintelligible) over time this becomes more routine.

David Magnus: I'm happy to leave it as differentiated cells should be included and everything else should be decided by the local…

Margaret McLean: I think in 2A particularly where someone may…

Henry Greely: Right.

Margaret McLean: …have an objection to…

((Crosstalk))

Henry Greely: I don't want a (protein) put in that was derived from murdered babies…

((Crosstalk))

Woman: Yes.

Margaret McLean: …we do hear this now about…

Woman: Yes.

Margaret McLean: …certain vaccines that, have you know, 50 years ago were derived from embryos and you still have people who will object to those vaccines because 50 years ago an embryo was used in the initial…

((Crosstalk))

Radhika Rao: So the informed consents may need to be broader.

((Crosstalk))

Henry Greely: Whereas 2C the (DSMBs)…

Woman: Maybe…

Henry Greely: May just be the differentiated cells.

Woman: Yeah.

Margaret McLean: So, I think you may not be able to have a single definition of what counts as a derivative. I also think that we might want to - we might want to think about whether or not in (A and C) whether or not we want and/or language rather than only and - so, (HESCs) and/or their…

Henry Greely: Okay.

Margaret McLean: …whatever it is…

((Crosstalk))

Margaret McLean: …as compared to just…

Henry Greely: Right.

((Crosstalk))

Henry Greely: That clearly was intended as an inclusive and.

Woman: Yeah.

Henry Greely: There's an ambiguity there…

((Crosstalk))

Woman: Yeah.

Henry Greely: Okay. Here's what I propose.

I think we can rewrite 1 and 2C, rewrite them or just refer - yeah, so I just refer to (HESC), the cells differentiated from (HESCs); but for 2A, the informed consent one, have derived from…

Woman: Yeah.

Henry Greely: …and factors derived from.

And then, the only question I guess would be with non-cell factors derived from HESCs would we think those should go through ESCRO review necessarily? I'm not sure I see a big argument for that since they're not cells. It's the cellishness of the stem cells that I think requires the expertise of the SCRO.

Woman: Yeah.

Margaret McLean: So only IRB...

Henry Greely: So, it would only be in the informed consent side of the IRBs to make sure that we are not offending the sensibilities of people…

((Crosstalk))

David Magnus: …so for everywhere in this we'll replace the derivatives with and differentiated…

Henry Greely: Cell differentiated…

((Crosstalk))

David Magnus: …and with the exception of 2A where you use the (unintelligible) derivatives.

Henry Greely: Derivatives.

Okay.

Thank you. That was a very productive question.

Woman: Yes.

Henry Greely: Next.

((Crosstalk))

Don Reed: Don Reed, California for Cures. As somebody who's been deeply involved in the battle for language, the cloning issue comes up again and again and again.

In the attacks on Proposition 71, one ad had the word clone and kill 17 times. And in fact that is how they refer to Proposition 71. I get about 300 or 400 emails that I subscribed to the service, and anything that has to do with Prop. 71, stem cells, etc.…

Now, the opposition has pretty much got their language set. (The pope) recently said that cloning is more destructive than weapons of mass destruction.

Woman: Uh-huh.

Don Reed: Okay.

So - but we also, you know, Gerald Ford, Jimmy Carter and Nancy Reagan - all using the word therapeutic cloning in official recommended language, okay?

So, it can be dealt with. I would urge you strongly not to forbid people to use the word therapeutic cloning. The way I usually use it is I say somatic cell nuclear transfer, advanced stem cell research sometimes referred to as therapeutic cloning. That shows we're not hiding something.

As soon as you say, don't use it…

Man: Uh-huh.

Don Reed: …here's how it would be played out.

California, an elite group of administrators is attempting to hide the truth from you they're cloning…

Man: Yeah.

David Magnus: But the therapeutic part is misleading. (Unintelligible) it's not therapeutic…

((Crosstalk))

Don Reed: So given the negative connotations of the language…

Man: Yes.

Don Reed: …use that term with care. Something like that will be fine.

Man: Yeah.

Don Reed: But don't forbid it.

David Magnus: …we should not - some people - if you call it therapeutic cloning, the people are going to believe that it's therapeutic.

((Crosstalk))

Gregory Stock: David, this is Greg - comment on that. When I first read your - I thought it was - negative associations with it, because with gene therapy, you only have therapy which admittedly has very positive association. With cloning. I would say by and large cloning is quite negatively viewed.

So I think what the question that was just raised is an important one that we should think about the idea of obscuring negative rather than what your intent was to avoid unnecessarily mentioning therapeutic.

David Magnus: The new language that has been revised, now says that - that what's inappropriate is using therapeutic cloning, stem cell therapy or gene therapy. I think that's putting it out in that context, I think makes it even clearer.

Don Reed: It may make it clearer to you; but how it will be used is against you. It will come out that you're trying to hide something.

And this will be combed through by language experts and any kind of lawyer lie that can be told about it will be told.

Henry Greely: (Lawyer lie)?

Don Reed: Lawyer lie.

It's like - there was - there's an old lawyer lie joke about the Russians had a competition with America in which we won. The official statement, the spin doctors said Russian team got - magnificently finished a strong second, American team comes in next to last.

The opposition is experts at using this all the time. So just be careful that's all I would say to you.

Henry Greely: That maybe this has been a very productive and enlightening meeting for me; but that joke may be the single best thing. I like that a lot.

Well, thank you, that's…

Woman: Yeah.

Henry Greely: …I think that requires some thought.

Other comments from the public?

Susan Fogel: This is Susan Fogel on the phone. I'm sorry I had to step out for a little while.

Henry Greely: Sure, no problem. Go ahead.

Susan Fogel: But, with all due respect to Mr. Reed, his comments are, you know, may be true but that's about politics and it seems to me that your responsibility really is quality of research and subject protection.

And I do think that the words therapeutic are misleading and we would very much support keeping that prohibition in place because I think it has been - it has been used in ways to hype the science and I know you've all spoken about how you disapprove of any kind of hyping of science and so we would recommend that that we try to get those words out of the language and this seems to be a really good way to do it by actually putting it in guidelines, you really raise consciousness about so it's not only the actual practical application of it, but it's also raising consciousness that this language is misleading and shouldn't be used generally.

Henry Greely: There may be a way to square this circle.

Radhika Rao: Yes.

Henry Greely: And…

Radhika Rao: Couldn't you say that the impression of therapeutic, you know, we don't…

Henry Greely: It's the therapeutic…

Gregory Stock: I agree.

Radhika Rao: …so put the emphasis on them - they, you know…

Henry Greely: So Don, maybe in response to your concern, we can say, you shouldn't say therapeutic cloning; but we're not prohibiting you from saying what some people described as cloning.

Gregory Stock: Then you could…

Henry Greely: In a way to avoid - if an IRB or if an investigator wanted to preemptively avoid the idea that they're hiding the fact that some people think this is cloning.

Don Reed: I think there is value on every side of this issue. I will just say to avoid anything like it sounds like we're prescribing language or prohibiting language because it will look like a (cover up). Remember what got Nixon down was not what he did, but he covered up. If we even look like we're covering up, this will be a whole new ballgame.

David Magnus: We're not covering up, we're trying to make sure that the language is not misleading, and I think in this context where it says therapeutic cloning - stem cell therapy, gene therapy, I think that's extremely clear.

For political reasons, somebody wants to say that we're misleading- I don't care. I mean, as opposed to…

((Crosstalk))

Gregory Stock: The example - the suggestion was including the use of such words like therapy or therapeutic which has the same effect and certainly can't - very difficult to misinterpret.

Henry Greely: I think the circle is at least rectangularized, if not square.

Other public comments? Susan, is that it for you?

Susan Fogel: Yes, thank you.

Henry Greely: Thank you.

Geoff?

Geoff Lomax: Geoff Lomax, CIRM. To go back to that Point 1, where you were talking about the (neuroprogenitors) and coupling it with stem cells and this comment may be irrelevant, I actually didn't quite follow the - and how that conversation ended up.

And I also want to caveat it with saying I - this is a very eloquent presentation of the issues, and I hate to make a comment sort of suggest adding sort of words to something that's very eloquent and streamlined to begin with.

But, with that said…

Henry Greely: You will.

Geoff Lomax: I just - it's - my understanding is you sort of coupled two concepts. And with the (pluripotent) cells, it seems the issue is, (it's the) inherit potential of the (cell) that's of a concern, so it serves as a very useful sort of construct and I sort of (learned this to) in trying to draft - it gets - it's sort of the anatomy of regulation.

When you talk about - but then when you isolate out a particular type of cell, the (neuroprogenitor) the issue is, it doesn't have the same potential except in a very narrow circumstance.

And so you're - so the example that comes to mind that I'm just cautioning you of, when you have a (neuroprogenitor) cell that may be incidental to a matrix or medium that's being used in a therapeutic context and Bert, correct me if I'm right or wrong, but you could say, an example I think, kind of like using (cord) blood really to deliver to get enzymatic activity in the brain because it permeates the blood brain barrier, but that material, that (progenitor) cell is incidental to that medium.

If you're not careful, you've potentially regulated something that is completely irrelevant to the therapy.

So some - I mentioned earlier on the neuorprogenitors - I characterized it as an exceptional circumstance and sometimes it's quite inelegant in a sort of in the regulation that takes away from that kind of - but we did sort of pull it out and just – place it in a special circumstance and we did that because we didn't want to sort of introduce an unintended regulation to something.

So that's kind of a long statement not really a comment and it's just as a word of caution that I - not knowing exactly how you ended up on that point. Just be careful to get what you want there and not go too far.

Henry Greely: So I think neuroprogenitor cells are going to be inserted in both one and two here in terms of IRBs should review and ESCROs should review.

Geoff Lomax: Is it their use or their - because again, we use the language implantation to the brain - it's a very specific location of those materials…

((Crosstalk))

Henry Greely: …Although implantation to the brain or to the central nervous system which includes the spinal cord?

((Crosstalk))

Geoff Lomax: I offer that as a comment.

Henry Greely: Dr. Lubin is the doctor here.

((Crosstalk))

Bertram Lubin: …don't exclude spinal cord, because (she's been involved) in spinal cord injury and that's (unintelligible), so…

((Crosstalk))

Henry Greely: So we make more specific…

((Crosstalk))

Geoff Lomax: Thank you.

Henry Greely: Other comments from the public?

Jesse Reynolds: Thanks, I'm Jesse Reynolds from the Center for Genetics and Society.

I just have one quick comment here about the occasionally contentious item 2B but not 2B1.

The language here says shall ensure that the language used in informed consent for early phase. And I'm going to highlight early phase of clinical trials - dot-dot-dot - should not convey an unrealistic impression. And I'm assuming you don't want to convey an unrealistic impression at any phase of the clinical trials.

At the different phases, the language that is appropriate will differ in perhaps Phase 3, the word therapeutic might be appropriate.

((Crosstalk))

Jesse Reynolds: So I would…

Henry Greely: Since we're particularly worried about the early phase…

Jesse Reynolds: I would recommend removing the early phrase from B; but perhaps including it in the - which I believe one is now a for example clause.

Radhika Rao: Right.

Jesse Reynolds: Early might be appropriate and for example but not in the general statement.

Henry Greely: Or we might say this may be a particular issue - should be watched particularly closely in early phase.

You're certainly right. We are not intending to endorse unrealistic expectation.

Jesse Reynolds: And that's the implication right now and that's a danger at all phases of clinical trials.

Radhika Rao: Yeah.

Henry Greely: That's very helpful.

Other comments from the public?

Okay well, I think we're ready to vote.

Now, this is a little more challenging as a motion that the other one. But I think what we are - I think where we are on this is we are in pretty general agreement with respect to one, the main change we need to make in the first part of one is to include neuroprogenitor cells when they are being transplanted into the central nervous system.

((Crosstalk))

Henry Greely: …Covered cell lines, that's right. That's throughout.

And then on B, we may want to explain a little more what we mean by institutional field strength.

David just used the term institutional field strength. I tried to spin it out not very effectively either here or in a definition.

David Magnus: I'm happy to provide definitions from literature, there's very clear definitions…

((Crosstalk))

Radhika Rao: We may need a definitional section on the derivatives…

David Magnus: Right, that's right.

((Crosstalk))

Henry Greely: And then there's - oh, and with respect to one we also want to say (HESC) and cells differentiated from (HESCs).

With respect to - and I don't think we may have any changes in C - 1C, right?

In 2, again, we need to change to covered cell lines and neuroprogenitor cells when used to transplantation and here I think we want to say, right.

In A, we want to have the broad differentiated from a derivative or derivatives language, the broadest language for that. And we need to change the where to biological source. B, we changed due to those - I think something about to take out the idea that we're encouraging false hope in late-phase trials.

Say something about particularly concerning an early-phase trials, broaden the example with the focus on therapy or therapeutic.

On C, I think C is okay, except rather than derivatives there we just want the cells differentiated from.

And I think that's it on 2 and on 3, what did we end up doing on 3?

Radhika Rao: Embryo 4…

Henry Greely: Oh, we kept that, right?

Radhika Rao: …and we're going to - they said…

((Crosstalk))

Henry Greely: …multi generational.

((Crosstalk))

Radhika Rao: …those consequences that should be considered.

Henry Greely: Okay. So do I have a motion to approve all that?

Radhika Rao: One more thing. In the preface…

Henry Greely: Oh, right and in the…

((Crosstalk))

Radhika Rao: …in these two structures are not meant to be not necessarily…

((Crosstalk))

Henry Greely: And in the preface, what I thought I would do is make it accurate which would be nice.

Radhika Rao: Right.

Henry Greely: And shorter which would also be nice, the preface I've got here. But have some sort of explanation of what we're doing? Why we're doing it? What we think?

((Crosstalk))

Henry Greely: So, do I have a motion that encompasses all of that which undoubtedly would violate Robert's rules of order…

((Crosstalk))

Henry Greely: The (dread) parliamentarist Roberts is not here.

((Crosstalk))

Henry Greely: Okay, is there discussion on that motion?

All in favor signify by saying aye.

Man: Aye.

Henry Greely: Opposed say nay.

Abstention say (blah).

That was a laugh right…

((Crosstalk))

Elliot Dorff: That was a laugh, yes.

Henry Greely: Motion passes unanimously.

So I think we're done with the guts of our work but there are a couple of agenda items left.

One is, are there other recommendations we want to make?

And I personally liked Ellen Auriti's suggestion of saying, you know, we really - if 253's IRB requirements for non-human subjects research is still there, when things that wouldn't be human subjects that would not be covered by IRBs because you're not in appropriate relationship. But it's because it's not human subjects research - we want to get rid of it.

I think that make sense. It's something to tell the department or the legislature or somebody, we think there may have been –an inadvertant oversight in drafting 1260.

Anybody have concerns with that? People in favor of me trying to send a letter to somebody saying that?

Elliot Dorff: Uh-huh. Yes.

Man: Yes.

Henry Greely: All in favor say Aye.

Man: Aye.

Henry Greely: Opposed, abstention?

I'd ask for a motion to second. But I'm not going to.

Other things you think we should recommend?

Let me jump ahead here. Later on, I think the very last agenda time, is next meeting.

Dr. (Ahmad) and I were talking about this a little bit. And this may be relevant with the other things we think we should talk about recommending.

Obviously, the long term future of this committee is in some significant doubt. Whatever happens with 1260, there won't be a legislative mandate for it. I'm assured by our DHS representatives - that DHS values us and would love to have us. And will try, but funding is funding, and you never know.

We do think and I'm told that the department would very much like to put our recommendations out for public comment. Even before, they become recommendations to them for guidelines which presumably they would put out for public comments.

He thinks public comments can be done in 30 days, 45 days, something like that, in which case it may be useful for us to have one more meeting sometime between Thanksgiving and the middle of December and before the holidays kick in too strongly for some of us after our classes are over. In that wonderful little window of sanity.

So we may have another meeting. I think it's actually fairly plausible that we'll have another meeting. Before that meeting though, we're going to turn

what these motions into a document which the department will put out for comments.

It would be my intent to circulate that documents via email to you for typos, proofreading and “Oh my God, you can't possibly do that” comments. But anything short of that, you know, I think we voted on and taken care of today. So, it’s sort of a quality check.

Woman: Yeah.

Henry Greely: But not an intent to reopen new comments and with apologies to our absent members. You’re not here, you don’t vote.

So I would propose that we redraft this in line with the motions today circulated for quality control, comments, issues only. Given to Dr. Ahmad for the department to circulate it for public comment with the expectation that probably we can discuss the public comments.

It may be that there no public comments or the only public comments are from the people who commented publicly here. And it’s possible that they might not say anything new.

So the mere fact that it’s circulated for public comment might not entail another meeting. But it also may well.

If that doesn’t happen until after January 1, it is conceivable but less likely that we would have another meeting.

But unclear – David, you’ve been trying to say something?

((Crosstalk))

David Magnus: I was going to ask, after we put this together – does this get reviewed by the lawyers, for the Department before it gets submitted public comments?

Shabbir Ahmad: It can go as such for public comment and simultaneously being reviewed by the Department…

Henry Greely: So, having said that about next meeting, this is now a time when anybody can say it, "Oh my God. More meetings, I've already invested, way too much time and effort in this."

But also it is relevant to the issue of are there other things we think - it would be nice for us to take on if we continue to exist? David?

David Magnus: One thing I would have liked to have had in our regulations that wasn't I don't know how to put this in. Mildred and I made a plea for distinguish- that IRBs and SCROs should distinguish research donors from research subjects.

It's actually I think that's very helpful. And in fact, I've now become more convinced of it - because it concerns that - I'm not going to say who but I believe that there maybe a researcher who's under the misunderstanding that he could pay bone marrow donors for their bone marrow, for research purposes without realizing that if he transfers that into living person that it's a (NOTA) violation.

And that by conceptualizing…

Henry Greely: National Organ Transplant Act.

David Magnus: …as research subjects rather than as donors, just wasn't taking that into account, and that may be – have been a problem with their IRB.

Henry Greely: Does bone marrow count as an organ for NOTA?

David Magnus: It does. And so, if it's in vitro research it's not a NOTA violation…

((Crosstalk))

David Magnus: …transferred to anybody, then that would be a violation.

Henry Greely: So the things that are exempt tend to be renewable things like…

((Crosstalk))

Henry Greely: …sperm, hair, blood. But bone marrow is not?

((Crosstalk))

Henry Greely: Okay.

David Magnus: It is included in - explicitly in…

Henry Greely: Okay.

David Magnus: And the point I'm making is there are a number of - actually a number of different reasons why research donors are challenging, capturing the relationship between that person and the physician responsible for doing the egg procurement.

It's very difficult to see what the nature of their relationship is because they're not really subject – investigators, they're not really patient, physician. It really needs a separate category to understand. And so I would urge that- we actually recognize that.

Henry Greely: And it's particularly significant to stem cell research.

So, I think if we have another meeting and depending what the future of the committee looks like, at that next meeting that maybe something to discuss as an amendment to our recommendations with respect to guidelines.

I don't think it's something we can do right now. But…

Gregory Stock: About the other meeting, if you have another meeting, I would suggest that you tentatively try to schedule it and perhaps shorten the period of public comment because it would be relatively easy to cancel. But if you're moving towards later in the year to try and schedule it at a later point, I think will be exceedingly difficult.

I know that I certainly would have difficulty at that time. So…

Henry Greely: So try to get the email out, blocking out dates soon.

Gregory Stock: Right. Pick out some dates, tentatively schedule a meeting, and if it isn't necessary, then we can just scratch it.

Henry Greely: I think that's good advice.

Other thoughts?

Henry Greely: Public comment (Bob)?

Actually I think the plan was for…

((Crosstalk))

Henry Greely: You two keep doing that (unintelligible).

Ellen Auriti: Ellen Auriti. I'm just not sure whether there's anything formally on the table for the continuance of this committee. But I just wanted to express our appreciation for the work of this committee and perhaps I should direct it to Dr. Ahmad.

I think it's very useful and dynamic fields like stem cell research that is so significant and that there's so many ethical and public concerns to have a committee of experts like this in a continuing role. So, I just wanted to put that on a public record.

Henry Greely: Thank you.

I'll send you the check soon.

Jesse Reynolds: Jesse Reynolds Center for Genetics and Society. I would like to take this opportunity to draw your attention to not one but three upcoming events regarding stem cell research in California here in the Bay Area.

The Institute of Medicine day long scientific session on assessing the health risks to oocyte donors is Thursday in San Francisco. Unfortunately coincidentally on Thursday and Friday - Friday is not the problem but Thursday is.

Henry Greely: We should (say) Thursday of next week.

((Crosstalk))

Jesse Reynolds: Thursday of next week. As in nine, eight days from now if my math is right, it's the 28.

Radhika Rao: Twenty-eight.

Jesse Reynolds: On Thursday and Friday, there is a brief conference at UC Berkeley, I'm not sure…

Radhika Rao: And UCSF.

Jesse Reynolds: …and UCSF.

Henry Greely: So is it physically at both?

((Crosstalk))

Radhika Rao: Thursday September 28 at Berkeley. Friday, September 29 at UCSF the same conference occurring…

Ethical world of stem cell medicine.

Jesse Reynolds: Thank you. Thank you.

And third is a topic that was brought up a little earlier here. This toward (Fare Cures) Integrating the Benefits of Diversity of California Stem Cell Research

Program. Not only are two of my colleagues from the Center for Genetics and Society speaking but at least one other person sitting here at the table will be presenting that day as well. So, and also I'd like to note that Children's Hospital Oakland Research Institute is one of the presenters and I believe it's occurring in this room. And that's October 14 which is a Saturday but it's not all that long -- it's 9:30 to 4 so thank you. Hope you can make it.

Henry Greely: Thanks for the notices.

Other comments?

((Crosstalk))

Geoff Lomax: Geoff Lomax.

Again, to second (Ellen's) comments it's been tremendously useful. (We have been) members of the committee the past eight months to get your comments and input and just have another deliberative body out there thinking about some of these things, so thanks and again, sort of our pitch to those that be that it is always, two heads are better than one based on these issues.

Secondly - and again, this - to sort of further that 1260 does talk about reporting issues on health outcomes and I can think of no agency other than the Department of Health Services with the capacity to do that type of work correctly if we are going to be tracking health events related to egg donation in the future and I think that needs to be thought through very carefully if we move in that direction and again. I think some (compensation)…

((Crosstalk))

Geoff Lomax: … and deliberation in this area is critical. (Capturing) the type of information is only as good as the system you have in place. At the moment there is a vague and imprecise mandate and I think that needs to be thought through very carefully or we are liable to end up with information that is incomplete.

((Crosstalk))

Henry Greely: …epidemiology is not good.

Radhika Rao: Yeah.

((Crosstalk))

Radhika Rao: That brings one last issue that another (unintelligible) article talks about shortages of eggs in states that have prohibited compensations for egg donors as a problem in stem cell research and so if perhaps, you know, if these statistics are being considered that's another thing that should also be considered along with the health risks…

Henry Greeley: Okay.

Radhika Rao: …are also the implications.

Henry Greeley: And so if this committee where to extend indefinitely in the future these set of issues that's how we should go about, how the department should go about looking at healthy risks, what the effects of the compensation limitations seem to be are questions on which the department of no doubt would be interested in expert advice.

Well it will - I'm not going to say anything valedictory because I think we'll have one more meeting…

((Crosstalk))

Henry Greeley: And I hope we'll have a lot more meetings but I want to thank you for your time and effort today and in preparing for this meeting and also thank the public spokespeople who were extraordinarily helpful.

Woman: Yeah.

Henry Greeley: All of you contributed very usefully to this process including Susan on the phone. So I see Shabbir's hand…

Shabbir Ahmad: We want to thank the Children's…

Henry Greeley: Oh yes.

Shabbir Ahmad: …Hospital for hosting this meeting completely. For providing the lunch, and coffee and the refreshments. Thank you very much.

And on behalf of the Department of Health Services, I want to thank you for your volunteer services, time providing this highly, highly technical advice to the department.

Henry Greeley: And of course, again, and I said I don't want to be valedictory but for your work this time, thanks to the Department of Health Services staff, Dr. Ahmad and the others Heidi and Cindy and other folks who worked on it so hard.

Bert.

Bertram Lubin: I'd like to thank Hank for his leadership…

((Crosstalk))

Elliot Dorff: Here, here, yes.

((Crosstalk))

Radhika Rao: And David for his hard work…

Man: Yes.

Radhika Rao: …for the clinical (unintelligible).

Henry Greeley: So I'd like to – see if we could combine motion to thank everybody for everything.

And at 4:15, 42 seconds to adjourn…

((Crosstalk))

Henry Greeley: …if there's such a motion.

((Crosstalk))

Henry Greeley: Second.

All in favor to leave?

((Crosstalk))

Henry Greeley: Thank you all.

END