

Transcript

**Fifth Meeting of the
Secretary's Advisory Committee on Xenotransplantation,
U.S. Department of Health and Human Services**

Breakout Session: SACX Working Group on Informed Consent Issues in Xenotransplantation
Tuesday, February 4, 2003

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Agenda Item: Breakout Session--Working Group on Informed Consent Issues in Xenotransplantation

DR. SHAPIRO: So what I think we should do, unless people have a different idea, is to hit the important topics that are going to require more thought than wordsmithing. We'll get to the wordsmithing later.

DR. VANDERPOOL: Why don't we brainstorm over what those issues are.

DR. SHAPIRO: Yes, and I think it will help to refer people to yesterday's conversation, because I took some notes on it, and then everybody else should chime in. But one of the -- One of them, this is kind of in order of how they were mentioned, not necessarily in order of how important they were, but Dan brought up the whole issue, which is, um, on page 15 of the Consent Form about the informed consent, including what about if the studies ended early. And you'll remember the conversation about warning the participant that he or she may then have a lot of financial obligations not previously envisioned.

DR. VANDERPOOL: Okay, that is one issue.

DR. SHAPIRO: Okay. The second issue has to do with on page 14, on whether we want to, in that second paragraph, um, change our reference which we have sprinkled throughout the family members. I guess I would count that as perhaps not as important, but an issue that we can talk about.

A big one -- a third big one.

DR. COLLINS: Robin, I'm sorry, the second issue was taking the word "family members" out?

DR. SHAPIRO: Well, yeah --

DR. BERGER: It was replacing it with "intimate." Wasn't that it, Robin?

DR. SHAPIRO: Leave in "intimate," take out "family."

DR. BERGER: Leave in "family" and replace it with "intimate contacts."

DR. SHAPIRO: If people will think that is broad enough, if people will know that "intimate contacts" include family members.

DR. COLLINS: I think --

DR. SHAPIRO: Does "intimate contacts" include family members?

DR. MARTIN: No. Household contacts are defined separately.

DR. BLOOM: The intimate contacts actually includes -- where is it, it is in a box somewhere.

DR. SHAPIRO: On page 5.

DR. VANDERPOOL: It goes beyond taking something out. It has to do with clarifying, with being clear about what is required of both the education and the actual reporting of intimate contacts.

DR. SHAPIRO: Right. We talked about that.

DR. VANDERPOOL: That is why I put number two as first the study ending early, what happens; two,

clarify what is required of intimate contacts.

DR. SHAPIRO: Good.

DR. VANDERPOOL: Let's keep going with the issues we need to work on.

DR. SHAPIRO: Next listed issue was brought up, we need to talk about risks to fetuses and related to that contraception obligation. So I think we -- That is number three.

DR. VANDERPOOL: What?

DR. SHAPIRO: Risks to fetuses. Number four, and I don't know if we decided this yesterday or not, Harold, but I think we did, but Dr. Mendez' suggestion that we somehow document the understanding, or test the understanding of the informed consent dialogue.

DR. VANDERPOOL: You mean we have a tape recorder, or something like that in there?

DR. SHAPIRO: No, no, that he was suggesting --

DR. CRONE: He brought up what they do at their center is that they tell somebody about it, and then they have them fill out a test.

DR. VANDERPOOL: Yeah, that is a question of testing --

DR. BERGER: The issue is we do more for comprehension, is that what you mean?

DR. VANDERPOOL: For comprehension.

DR. SHAPIRO: To check.

DR. VANDERPOOL: And I remember that I called in question the whole -- the question of the whole deal. We can talk about it. I mean we can leave that as a question, okay.

MS. SHAPIRO: Sharon's points, which were good, about the incapacitated section, and about whether we mean that you have to have had a baseline that was a decision. So I guess the scope of the incapacitated patient to be eligible.

MR. VANDERPOOL: I'm still not right on it.

DR. SHAPIRO: Remember, Sharon said, well, what if we only enroll incapacitated people. Well, there is a likelihood they may regain capacity. What if they regain baseline, but baseline was never capacity.

DR. KIELY: Essentially it would be whether or not you would be excluding, and what I suggested is we be explicit about we are going to exclude individuals who don't have a certain, and I have no idea how you define that, mental capacity.

DR. SHAPIRO: Correct.

DR. KIELY: So the Down's syndrome adult, for example, or other somewhat limited intelligence individual.

DR. BERGER: There was also a recommendation, I think, from Dan that we just eliminate that group at the front end anyway.

DR. SHAPIRO: That is a question.

DR. KIELY: We have to discuss it. It is not clear in the document.

DR. BERGER: But -- right. To say maybe in the front end, what is the success rate.

DR. BLOOM: The advisory subcommittee also discussed not treating patients with behaviors that might be risky. That is certainly related.

DR. FINN: Dipram, when I was working with them, it was in the initial trial, they had something about if they had a disease, they wouldn't be eligible for the trial.

DR. KIELY: So you would be saying that would be an exclusion, so I think we need to establish exclusion criteria, explicit exclusion criteria.

DR. SHAPIRO: Around the incapacity issue. And the other piece of this is whether or not we are going to include them at all, the whole provision we had about the willingness of the surrogates to help with the compliance, which was very controversial.

DR. KING: Also the issue of whether we want to designate a surrogate, a legal guardian, or get into the issue of who is to say they are a surrogate, and all kinds of issues.

DR. VANDERPOOL: This is going to go with clarification of surrogacy, is that it, or recommendations?

DR. SHAPIRO: Part of it, yeah, about surrogacy.

DR. KING: Is an issue. If it is an issue, whether to include them.

DR. SHAPIRO: The other thing that is an issue brought up yesterday was whether the generic emergency exception for having to get a surrogate's consent should apply. So the emergency exception for incapacity.

DR. VANDERPOOL: I had some other issues. One is one that was talked about a bit by Megan, um, when she said, "Well do we need to," well, "other committee members, do we need the other Draconian measures regarding telling them what all they are going to have to do, and what all will happen with respect to reporting." And she said, "What about someone who has -- has some tissue that was in contact with mouse cells? Do they have to do the whole ball of wax like everyone else?" So that had to do with a section in the consent form. Remember when they wanted to soften this and say -- soften that section of it that we had in the consent form.

DR. SHAPIRO: That was about healthcare workers in particular.

DR. VANDERPOOL: Yeah. I don't know what we call that issue.

DR. SHAPIRO: Healthcare workers.

DR. BLOOM: It extends beyond healthcare workers, the issue does.

DR. SHAPIRO: She was most concerned about the healthcare workers.

DR. BLOOM: It extends even to the patients, the patient contacts.

DR. VANDERPOOL: Maybe it is really an issue of clarifying what is required of intimate contacts in regard to different types of xenotransplanted procedures, you know, the -- So there is going to be some differences here in terms of what procedures we are talking about. Another issue I had was --

DR. KING: -- kids.

DR. VANDERPOOL: Robyn, you and I talked about while we were talking this morning, should one of our recommendations be that there be changes in the public health laws to be able to enforce compliance?

DR. SHAPIRO: Yeah.

DR. VANDERPOOL: Let's talk about that as a recommendation, changes in public health laws. Excuse me one second. This raises the broader issue of what recommendations we want to make.

DR. CRONE: You also have the question about children, about not excluding, because this is written where children would be excluded, and Eda had brought up that, you know, that there is -- there we need to re-think that, there is really two edges.

DR. SHAPIRO: Then all the jobs we gave ourselves, and how maybe that was too self-serving, and some other body should be doing that.

DR. VANDERPOOL: Okay, right. So educational, do we really want to change that, or soften it, or whatever? Now any other comments from people about the issues that you see that we need to work on.

DR. KIELY: One was a general sense I got yesterday that some of the scientists took issue with us in comments, and what my sense of it was that it was more of a one size fits all approach to informed consent, which several, in fact I think that was actually the term that either Dan or Megan said that they had an issue with this about, because like the children, like several issues here that we are -- that are on this list, we have this one size fits all approach, and these procedures are not one size fits all, and so --

DR. BLOOM: We talked about that.

DR. KIELY: There has to be some latitude in the documents -- particularly the form, or maybe the directions for the form, so that researchers can adapt it within basic parameters that -- and suggestions that the committee makes. But not, you know, being -- and I think that was the issue about being Draconian, because in some circumstances that might be necessary, while in others it might truly be --

DR. CRONE: I think some of what the discussion was, I think, was that they recognize that this is, you know, kind of -- this informed consent is sort of an initial go at it, that, you know, as we know more, as you have more experience, that it will be modified, and I think that is kind of some of the things, at least I got the impression that some of the folks in the science kind of realized that.

DR. BLOOM: I think --

DR. CRONE: It is going to change.

DR. BLOOM: I think what Sharon is saying what I have been trying to say all along is you are not going to have the same safeguards for Epicel (phonetic) that you are going to have for a kidney, and maybe what you want to consider is a statement somewhere in here that acknowledges that there may be different levels of precautions, or of whatever you are putting in the consent form.

DR. SHAPIRO: Maybe more than that.

DR. VANDERPOOL: What we have now is on page 8, we have the statement, "Obviously the -- " at the end of that first paragraph on page 8, "Obviously the actual headings and specific content of a given consent form will vary from its generic format, depending on the particulars of a given xenotransplantation protocol." What we may want to do, rather than trying to specify how you are going to change it for kids, and how you are going to change it for people who had xenos in contact with human cells in contact with animal tissue, live animal cells, um, that we just expand that into a paragraph that talks about exceptions will obviously need to be made to the form which we have, which applies primarily to redefine what we take that form to apply to. So there will be certainly differences from this form. Because I think it is -- If we're not careful, we are going to end up in multiple, multiple suggestions about how to change forms for this, that, and the other thing, and we'll never cover all the contingencies that we can even identify.

DR. SHAPIRO: Yeah. I mean we could, in that expansion, we could give some examples in case people didn't realize, you know.

DR. BLOOM: We brought this issue many times to the FDA subcommittee as far as the different kinds of xenotransplantation procedures, rate, different levels of safety precautions, um, in our subcommittee. The only ones that they were willing to take a stand on, the last ones from a couple years ago, before you guys met, they had at that point less information than you do, was the scid cell, or the ex vivo contact perhaps required less stringent controls for example, than intimate contacts, might not need to defer from blood donation. For example, the regular follow-ups might not be required for xenotransplantation, but a patient ought to be counseled that if something peculiar comes up, they ought to see a physician. Other than that, they weren't willing to say, for example, that the implantation of a few pig cells was any less risky than the implantation of a pig kidney, because they just didn't know. So that was the one product they were willing to say perhaps required a lower level of concern. Um, the other thing we had asked them, is in regard to what you were saying earlier, perhaps you want a higher level of concern for certain patient groups for whom compliance would be a definite issue, such as substance abuse. They didn't touch the idea that you suggested, though, but that is something you may want to consider.

DR. VANDERPOOL: Are there any other issues, and we'll just take these one after the other. I just made this one size fits all issue to the point, and indicated we need to point out exceptions on page 18 to -- that will obviously need to be made made in the form.

DR. KING: Eight.

DR. KIELY: I think there was one other thing Megan mentioned about, that while the healthcare professionals that are mentioned in the document relate to those individuals who would be involved in the xenotransplant procedure, and part of the team of healthcare workers who are caring for the individual, but there is a wider range of healthcare professionals, and there should be some -- in -- Do they declare that they've had a xenotransplant, that it be clear to the patient that they -- this is something that they would divulge in a medical history, wouldn't necessarily be something that was asked. I don't think they're teaching medical students to ask about xenotransplants in the H and P these days, but --

DR. VANDERPOOL: So one size fit doesn't fit all for medical personnel.

DR. KIELY: Basically, that is fine, though.

DR. VANDERPOOL: What did you all get out of the discussion we had regarding how much medical professionals have to be informed? There, I -- I heard things to the effect that you didn't have to inform them about all these things, because they would already know about them.

DR. KIELY: How would they come to know about them?

DR. BLOOM: You mean the people doing the procedures.

DR. SHAPIRO: You mean as opposed to Megan's comment.

DR. KING: I think the consensus ended up being that it is probably good they are informed, but there was a question about that issue, in that do we need to, but the consensus came down to we should.

DR. VANDERPOOL: I heard the critical side, and you all heard the resolution.

DR. KING: Yes. I think it was Marion came down and said she thought it needed to be done, and she was pleased to see it come down.

DR. BLOOM: It is an educational thing. It's not the consent.

DR. VANDERPOOL: Okay. We'll just take a minute to go to one issue after another.

DR. SHAPIRO: Okay.

DR. VANDERPOOL: What shall we do? Why don't you -- You are doing the editorial work, right.

DR. SHUMAN: I am here to help you with the editorial types of changes to the document, so I am taking notes on the types of issues you want to address.

DR. VANDERPOOL: Do you have our document in there?

DR. SHUMAN: I didn't. I tried to get it, but I was not successful. I only have a hard copy.

DR. VANDERPOOL: When we talk, why don't we identify a page, if there is a page we are working off of, so Deborah can work our suggested changes into our document. And you and I can talk about some places where we never got some footnotes in, and some other things.

DR. SHUMAN: Sure.

DR. VANDERPOOL: Because we are actually -- I hope everyone feels good about what we came up with. I mean --

DR. KING: I'll say this has come a long way since I our last work group meeting. I was very impressed with how far it came, and how smooth it was. I think it was very good.

DR. VANDERPOOL: And we hammered away a lot. We have some more hammering to do this morning, but I certainly felt very good about how far along our report was. And I mean these minor little flips, we have to just --

DR. KING: Okay.

DR. VANDERPOOL: No, they did point out some significant things, they really did.

DR. BERGER: Are we also -- Harold, I assume we will need time at the end to put together our list of recommendations, when we are done with this.

DR. SHAPIRO: We tried to cull what we have, or what looked to me to be a recommendation, and I came up with 10 -- I'll get you all this stuff, too, but I think we should -- It doesn't include things we may want to do outside of what we really talk about here, and we should talk about that.

DR. VANDERPOOL: If we could possibly do it, we could raise -- we could have Robyn go through those 10 and see what we suggest.

DR. BERGER: Because that would be nice to present when we come back. Recommendations are probably as important, if not more important to present to the whole committee when we come back in session.

DR. SHAPIRO: True.

DR. BERGER: So it seems to me that we should make sure we have plenty of time to do that at the end.

DR. SHAPIRO: And a lot of this stuff will have a natural recommendation, so we should go quickly through this. So --

DR. KIELY: Excuse me, I'm sorry. I just remembered one last thing. We may not be able to discuss it here today, but we really do need to look into HIPAA, and how HIPAA affects the issue of future responsibilities of the individual. It's critical. It affects research directly. When you are talking about research, there is no way we can get around it.

DR. SHAPIRO: I just did a little research in HIPAA, which I'd be happy to provide.

DR. BLOOM: A little bit. HIPAA is a big book.

DR. SHAPIRO: It's a little book, a 30-page book. So I can get it for you.

DR. KIELY: Do you think it would be reasonable to include some statement related to that?

DR. SHAPIRO: Yes. I think it would be hard to get into it heavy duty. I don't want to provide legal advice, and all that, but I think we could pull out of this booklet a recommendation about how this is going to be yet another layer of regulations that researchers have to comply with.

DR. KIELY: Exactly. Perfect. Thanks.

DR. SHAPIRO: Number one, um, what about this thing on page 15 Dan discussed. I was not familiar with what he is saying is required elsewhere, which is these sponsors with insurance, or a bond, or something like that.

DR. BLOOM: I'm not aware of it either, actually, and the fault -- the long-term follow-up in gene therapy is only stringent for five years, and then you have a more loose follow-up. And we certainly have

had gene therapy sponsors that have withdrawn their IADs. We have had xenotransplantation sponsors that have gotten out of the business. So I am -- I have no idea what to tell you to recommend. It is a problem. It does happen.

DR. VANDERPOOL: Right, and we -- And part of the exchange I was having with Dan over this point is it may not seem fair, it may not be right, but we are responsible for informing the subjects what the lay of the land is.

DR. KING: When we wrote this, were we were not thinking about -- I heard them saying two different things. One is we are saying we have long-term follow-up, the company goes out of business, who is going to enforce that long-term follow-up? And I don't know that -- We're not trying to say that, but I think he was saying -- thinking we were complying, like Jim, for example, here the company is out of business, saying it is now up to you financially. You have to go and give the specimens. You have to pay for all this. I don't think we were saying that. I think what he was saying is any care they may have promised you they would cover, whatever that may be, that pays for other things besides the specimen, whatever.

DR. FINN: I believe my company said --

DR. SHAPIRO: We don't want to --

DR. KING: How can we mandate that that person has to go do that? That is the beyond the scope of this. But anything --

DR. SHAPIRO: We can't mandate it outside of this, if the company doesn't go out of business, we can't mandate it.

DR. KING: Right. So help me with this. What if the company goes out of business and the government is saying you have to provide these for the company. They go out of business, what is going to happen? The company is not going to go after the individual, or the government, to make them show the specimens, are they?

DR. BLOOM: That is right, we are not.

DR. SHAPIRO: We'd like continued monitoring of that person.

MS. KING: Right. So we are saying whatever comes, you will have to be responsible for that, but that is as far as we can take that.

DR. VANDERPOOL: So what we need to do is change the last sentence on that page 15. Perhaps the participants receiving life-long care from the sponsor could make the participant responsible for the healthcare cost. Dan was saying, "Well, it wouldn't make me responsible. I'd just quit altogether, I just wouldn't show up." You know, well what wording are we going to have?

DR. KING: I had reworded it already before this comment, because I didn't like it anyway. I had just said that we should explain to the subjects e.g., the participant's receipt of life-long care from the sponsor could be jeopardized, requiring the participant to be responsible for the healthcare cost arising from this research project. I don't know if that still gets to the point. We were talking about the subject would cover both.

DR. SHAPIRO: How about this. For example, early end of the study could mean that the participant,

rather than the sponsor, could be responsible for the healthcare costs deriving from this research project, implying that you have to -- they still have to do it.

DR. BERGER: Well, I -- Actually, I think the question, the -- the hazy point is that part of it may sound, and this was Dan's point, that the patient is responsible with life-long monitoring for the project, which is not the case.

DR. SHAPIRO: Right.

DR. BERGER: I don't think we're saying that, and as I said yesterday, I think it is any kind of health situations that occur because of it. I mean, for instance, someone has a kidney transplant, and they come up with a virus, you know, and the project is done, and where are they? They are going to have to cover any future healthcare costs because the company may not -- may be out of business. I mean it isn't health insurance. It is not monitoring. It is any situation that might arise later on with the company gone, and there is no one else to be responsible.

DR. KING: That is what I was thinking.

DR. BERGER: I mean maybe you'd give an example, and I agree here we don't want to, you know, add three or four paragraphs, but --

DR. VANDERPOOL: Well, I like -- take both wordings. I like your wording. I like part of what Karen said. I -- It seems to me that we need to take the word "requirement" out of this whole thing. They are morally obligated, something else. They are not --

DR. SHAPIRO: "Responsible," I think comes pretty close.

DR. VANDERPOOL: "Responsible" is a good word. They would be responsible for. So let's put your wording in there and see how it goes. Let's keep moving.

DR. SHAPIRO: Number two, okay. Oh -- oh, we dealt with this. The intimate -- The definition of "intimate contact," is it sufficient? So we can delete wherever "family members" appears on page 5 in the box.

MS. KING: It's on page 5 at the top.

DR. VANDERPOOL: I think it is -- I think we throw out "family members," I love family, you know, and family does -- So that is why it sneaked into the forum. But intimate contact is different.

DR. KING: So you are responsible for that.

DR. SHAPIRO: Great. The fetuses and contraception, what do we think about that?

DR. KING: That was in the section, too, right? We are saying they should refrain from. Were we saying we would add this in the same section. We didn't caution about these things. "You should be aware -- "

DR. BERGER: What section is that, Karren?

DR. KING: 14.

DR. CRONE: The "animal infection."

DR. BERGER: Page 15.

DR. KING: Is that 14? We are talking about the blood donation and all of this. But could this not play into that, in addition to caution, and then what not to think they can do, or this is something they ought to do.

DR. BLOOM: You might mention any behavioral modifications that the recipient -- I mean the generic term is behavioral modification. It goes beyond contraception and protection of the fetuses. They may want to stop sharing razors, or something they are already doing.

DR. CRONE: I think specifically --

DR. BLOOM: And give examples.

DR. BERGER: Is there some wording that the FDA uses, or has used in something we can just adopt?

DR. BLOOM: In the PHS guidelines.

DR. BERGER: For this same kind of thing, for adding things on contraception, or pregnancy, or --

DR. CRONE: Or warning that you don't know what the --

DR. BLOOM: Yes. It doesn't specifically say a warning to the fetus. Actually, England, unfortunately, I don't think the gentleman from the UK is here today. But they had a big hubbub there because they were being accused of telling people they couldn't get pregnant.

DR. KING: Yeah.

DR. BLOOM: Life, liberty and the pursuit of whatever.

DR. KING: My question is do we know for a fact that all the individuals who would get a xeno product would be told they should not become pregnant when they are beginning. By saying that we are assuming that is true. Is that true?

DR. BLOOM: We actually had, this goes back to the children, we had one child where we found out retrospectively it was a xenotransplantation trial because it was an ex vivo contact, the cells that were being implanted had been grown up in mice. And the patients were children, and one of the investigators flatly refused to tell their children "For the rest of their lives, they're going to have to use contraception." And at that point in time, we kept them on hold because of that. But, on the other hand, I don't think it's realistic to expect, especially given the kind of exposure, that the people need to adhere to that, that the patients will need to even -- will adhere to it, but even need to adhere to it in 25 years, when they become pregnant.

DR. KING: I remember the days of just regular kidney transplantation, when we would suggest people should not be pregnant, because we didn't know the long-term effects of the drug. That is not true anymore. We used to totally advise people in the same way, so I don't know if we can say that in this document. Should it be something we say we should encourage them to discuss with their physician or with their research people, whomever, in this?

DR. BLOOM: The issues are different, because with the kidney transplant patient, it was considered to be a risk to the patient's health, right?

DR. CRONE: Also to the fetus.

DR. KING: Also to the fetus. It would go beyond a kidney at that point. We didn't know about that. I mean I'm just saying your point is well taken.

DR. VANDERPOOL: Sorry. In the FDA -- In the Guidance for Industry, this is the guidebook.

DR. BLOOM: You have it marked up.

DR. VANDERPOOL: Slightly. Look at that.

DR. BLOOM: It bled to death.

DR. VANDERPOOL: In the Guidance for Industry, to speak to your point. It says "The recipient should be counseled regarding other behavioral modifications, the behavioral modification that had been discussed is that of not donating blood, um, although some sperm, and so forth." At that point, not only the participant recipient, but the contact should be deferred from donations, and so on. That is the specific direct statement about the contact. And then back to the recipients. "You should be counseled regarding other behavioral modifications." Advised on the use of barriers to transmission of sexual disease during sexual activities and use of proper precautions for nonsexual contact." So that is no more specific than barriers for sexual activities, so I assume that is --

DR. KING: This is what I think.

DR. BLOOM: We should get more specific. We can do that.

DR. SHAPIRO: We don't really know what the impact would be. What I think we should do is on 14 add a sentence about how, in addition, there may be a risk of transmission to the fetus. And on page 16, the responsibility section, um, that they should, you know, consider the fact that there may be risk of transmission to the fetus, and put it in their hands.

MR. RAJAD: I'm Jeff Rajad (phonetic) from NIAD, and I have been asked to represent some of the collective NIH comments, and I think one of the additional places that this could be included is in the exclusion criteria, because it is quite frequent in our transplantation trials to have one of the criteria excluding pregnant women or sexually active persons who are unable or unwilling to practice birth control.

DR. SHAPIRO: But do we want to go that far? That is the question. Do we think that the nature of the risk is that big, that anyone who is not going to agree to never have children should be excluded.

DR. BLOOM: That is what happened in England. The problem is, is when you have such a broad spectrum of products also. You know, that is unfortunately a caveat that this document has to deal with.

MR. RAJAD: If you put it in the exclusion criteria, then it pertains only to the term of the study.

DR. BLOOM: Then you have to say that for some studies this should be an exclusion, because the term of the study is 50 years.

DR. KIELY: Right, a lifetime.

DR. BLOOM: It should be --

DR. BERGER: I mean you could make a general statement that exclusions would be for people that wouldn't -- would be deemed not responsible to follow the surveillance practices, or the -- or the monitoring practices, and just leave it as a sentence. I'm not sure we want to list all of the exclusions that might be there. And I am not even sure of the dangers to the fetus or pregnancy. It seems to me it is assumed if you say "contraception," whether the patient's a woman or a man, that that pretty well says it all.

DR. KING: That is what we were just saying, Allan. We are saying what does this mean? That is already in there, restricting behavior with a partner. Does that not mean contraception? Doesn't that then mean protecting the partner? But you are not going to become pregnant if you are doing this. So why does that not cover it?

DR. BERGER: I think it does. I think it is fully covered, and for the exclusion, I think anyone would be excluded that would be deemed incapable of following the monitoring practices. And I think that would be assumed, don't you?

MR. RAJAD: Well --

DR. BERGER: Rather than having to be so specific, and I mean we're not writing an informed consent form that somebody takes and uses. It is just a guidance, a guideline.

DR. SHAPIRO: How about if we say "protection should be made with intimate partners in order to protect against risk of transmission of infectious disease to partners and possibly fetus."

MS. SHUMAN: Do you mind just repeating that so I can --

DR. SHAPIRO: Sure. I'll give it to you.

MS. SHUMAN: If you give it to me, that would be fine.

DR. BLOOM: It's going to be a lot, more than you bargained for.

DR. VANDERPOOL: Sometimes you can read what she has written, sometimes. If I were writing it, you for sure couldn't read what I wrote.

DR. SHAPIRO: Oh, right. Worst hand writing in the world.

DR. VANDERPOOL: Robyn's writing is considerably better than mine.

DR. SHAPIRO: So maybe we have that kind of under control. Why don't we move to four, testing for comprehension in -- comprehension, testing of the recipient of the informed consent disclosure.

DR. KING: What do we say at this point, comprehension?

DR. VANDERPOOL: After reading an incredible amount of material on the subject, and listening to a lot of people, I don't think we should call for testing of comprehension. I mean to test Jim -- to give Jim a three hundred point test on the consent form he was given before he could have the procedure would be a

perfect example of forced coercion and undue influence.

DR. CRONE: Also realistically when you think of the past, or, you know, when you take a test, you can take a test, not really understand the material, but just be good at remembering the facts. That does not guarantee that you really understand, so I don't think it has a place. I think that is why we had said -- why we had done all the focus on process, to try to -- I mean it is not going to be it is an imperfect process. But we tried to add that section to try to facilitate things that we thought could facilitate, you know, greater comprehension of what they are going to be facing.

DR. VANDERPOOL: I couldn't agree more, and I think that to that effect, we might want to put -- I have to find the paragraph, in our statement, that it may belong under the question about difficulty of informed consent for the bottom of page 4 --

DR. BERGER: Comprehension is on four. But, you know, it also seems to me, I would agree, I don't think we want to say something specifically about that, that you have to take a test, or show a video, or anything, however, I do think we are missing one sentence here. To say that, um, that the team has to do whatever possible to assure themselves that the patient clearly comprehends all the information, or comprehends to a certain level. We haven't quite said that. We said the process, and all the things we have to do without saying that. At some point, you know, whoever is making this -- this decision has to feel that the patient adequately understands, or comprehends the information to the level appropriate to make a decision. And we actually haven't said that. And maybe that fits in the middle with what Bob was recommending, without making specific suggestions. I mean maybe that is understood, that maybe we need to say that.

DR. VANDERPOOL: Maybe we should find a place to say that, Allan.

DR. BERGER: It would fit into that.

DR. VANDERPOOL: And I also think that -- that this discussion means that page -- that page 4, the last paragraph, should be reworded, because we have the words "when risks are high, when certain procedures are complex and when patients are desperate, researchers should make an effort to determine whether they have in fact comprehended." And I don't think "determine" is the word to use. Should make an effort -- extra effort to --

DR. SHAPIRO: Assure.

DR. VANDERPOOL: Assure.

DR. BERGER: Yeah.

DR. VANDERPOOL: Or to assist --

DR. SHAPIRO: Assure. Assure that --

DR. VANDERPOOL: Assure -- ensure comprehension, or assist in, then, should be the word used for the team. Maybe we could find a place to say "assist," really would help people comprehend.

DR. BERGER: Brad, what do you do with patients? I mean obviously you have to get to a point where you are -- where you feel comfortable that a patient comprehends the informed consent.

DR. COLLINS: You know, Allan, it -- the more I --

DR. BERGER: You know, I'm not going to like your answer, I could see that right away.

DR. VANDERPOOL: Don't say it, because he is not going to like it.

DR. COLLINS: The more I meet with the committee, the more I realize I am pretty sure I am not truly getting informed consent, and I will tell you this when we meet a patient who needs a liver transplant with chronic liver disease, and we get to know them over a year or two years through the process of my meetings with them, I can feel pretty comfortable that I've discussed the risks, the possibility of dying, and those sorts of things, and give them an opportunity to ask questions, and that sort of thing. I don't -- There are no checkpoints that I check off, or anything like that. In a situation where a patient, for instance, comes in for a kidney transplant, I've never met them before, although it is not really an emergency situation, um, that -- that whole process is shortened, and I do give them an opportunity to ask questions, but I don't, in my mind, I don't think about whether they really understood what I've said. You know what I mean. It is not -- I need to do better with that. Thank you very much, sir.

DR. VANDERPOOL: Page 6 in the middle of the first paragraph under "Participants." We have the wording "In addition, the group, or consent team, should evaluate the subject's comprehension of the information given by encouraging discussion and raising open-ended questions about the xenotransplant procedure." And then "Furthermore, the consent team should use the discussions to determine whether the individual is voluntarily entering the study." I think that is a fair statement to know that it is voluntary. But the statement just before that, maybe we should say "In addition to the group, the consent team should evaluate -- should -- " We've talked about assistance, really, in much of this, but maybe should -- I don't know. That is -- That is where -- That is where this subject comes to discussion in the process. And I don't know that we need to change anything there.

DR. CRONE: I don't think -- You mean in regards to what Allan was saying?

DR. VANDERPOOL: Uh-huh.

DR. CRONE: Actually, what I would say, if you want to put it somewhere, put it somewhere early on in this informed consent process piece, or under the comprehension piece that you want to make, if you want to make a statement about, you know, what is the team's responsibility. We are kind of trying to take a baseball bat to the people and kind of say, you know, by the way, this is your responsibility, so you might want to put it somewhere early on, some comment. I don't know. It could either be worked into that first paragraph -- a couple paragraphs in the informed consent process before you get to the points to convey, or something about the comprehension. Because it is just emphasizing, kind of, how much onus we are putting on the researchers. This is a responsibility that they carry.

DR. KIELY: If I could say one thing, so we don't lose what we have agreed to. We don't support testing, and for the reasons we don't support the testing, might be at the end of that first paragraph under "Comprehension," just say "While we don't support testing" for whatever reasons Harold eloquently said, "we do the other piece, the -- about the responsibilities of the team." We do see that there is a responsibility of the consent team to continually assess comprehension throughout the process.

DR. KING: We are --

DR. KIELY: Something along those lines, because I think, while testing is out there, some people do testing. Um, we have deliberated about it, and I think we should say here that while we thought this through, and have decided for these reasons not to endorse testing, we do expect, like Katherine said, the -- this would fall to the responsibility of the consent team to have some sense of the -- of -- you are

better at saying it than I am.

DR. KING: It doesn't assess comprehension as well as that they signed a form. And that is like --

DR. KIELY: That goes on in the next paragraph there, that is why I felt we could fit it in there.

DR. KING: That was the other thing.

DR. KIELY: The next paragraph is about the form, and so it clearly states that that is not the issue.

DR. KING: We are just making sure that they understood, which is I guess the consent piece, I mean I thank that that is ridiculous.

DR. CRONE: I think that is part of why the process was put forth in the form.

DR. KING: It was.

DR. CRONE: It was because of that, was to say we're not just focusing on this. We have it in the sentence in the early, early part of the informed consent process. But the process itself is a real work to kind of focus your eye on the fact that the informed consent process is not merely an official record, sort of shift the focus of that form.

DR. VANDERPOOL: Where is Robyn?

DR. COLLINS: She stepped out one second.

DR. VANDERPOOL: Um, on page 6, that first paragraph "In addition, the group or consent team should -- " We could change that to say, and this is right up -- We could change that to say "The consent team should do all it can to enable the subject to comprehend the information given by encouraging discussion, raising open-ended questions about the xenotransplant project." Does that make sense?

DR. CRONE: Yes.

DR. VANDERPOOL: That former sentence says about evaluate the subject's comprehension, and it shouldn't be there anyway, so I think we should -- I'll give Robyn that wording.

DR. KING: She's added a sentence here to the end of this comprehension that I think she thought was going to cover as well, excuse me. The first paragraph under comprehension, page four, very last sentence.

DR. VANDERPOOL: What does she say?

DR. KING: "And for the researcher to assure the prospective participant has comprehended the disclosed information. So it says "This informed consent process should provide ample time and opportunities with respect to research participants -- "

DR. VANDERPOOL: Is that the first paragraph or the second?

DR. KING: First paragraph, and what I am reading from now is already in the document, so what she has added to the sentence, the original sentence she has "This informed consent process should provide ample time and opportunities for the prospective research participant to ask questions about the details of

the trial, and about his or her physical, emotional, social and spiritual concern related to the trial, and" this is the part she's added "for the researcher to assure the prospective participant has comprehended the disclosed information." That is what she wrote. Does that cover –

DR. VANDERPOOL: I don't know, I am -- I think that that sentence was pretty nice just the way it is. And it would be better to go ahead and change the one later on.

DR. KING: Should we take that off?

DR. VANDERPOOL: Where we leave that, and why don't we add in the manuscript, Karren, the middle of page -- the paragraph on page 6, scratch "in addition, the group or," and just begin with "the consent team."

DR. KIELY: Where are you, Harold, on page 6?

DR. VANDERPOOL: In the middle of the first paragraph under "Participants in the process."

DR. KIELY: Okay.

DR. VANDERPOOL: "The consent team should do all it can to ensure the subject's comprehension -- "

DR. KING: Not evaluate.

DR. VANDERPOOL: Right. Scratch "evaluate." "Assure the subject's comprehension of the information given by encouraging the discussion raising open-ended questions.

DR. BERGER: I actually think the consent team has to go further than that. It is not just -- You can provide all kinds of information, and "evaluate" is not the right word, but maybe -- Maybe "assured" isn't either, but maybe "feel comfortable." The consent team has to feel comfortable that the participant comprehends the disclosed information. Somewhere there -- It is just not enough to provide the information. Somehow the consent team has to feel that that patient has comprehended to the level necessary to make an informed decision.

DR. KING: The sentence, as it was, doesn't make sense, now that I look at it, because you are saying you need to evaluate their comprehension by giving them time to answer open-ended questions. To me that is facilitating their comprehension by doing these things. That is not evaluating.

DR. VANDERPOOL: That is not evaluating anyway. Right.

MS. KING: It is not even --

DR. VANDERPOOL: Well, maybe "to facilitate" would be better than "to ensure," or you like "ensure"?

DR. KING: "Facilitate" to me goes with what we are saying there, but that doesn't get at the issue of evaluation.

DR. VANDERPOOL: We could go on and say -- We could say "To facilitate subject's comprehension." We could add a separate sentence.

DR. BERGER: It's kind of like dealing with children. At some point you have to feel that they

understand what you are -- what you are saying to them, I mean, and I think, I mean I know this is similar in some ways, I mean, you are going to -- You are going to perform a procedure that has, and the thing about xenotransplantation, is we have a third-party at risk, and, boy, I'd sure want to make sure that they comprehend the situation before they would be able to sign an informed consent form.

DR. KING: What they are trying to say here, because I worked with Katherine on this, that one way to assess comprehension is to allow the participant --

DR. BERGER: I don't think we have to set up specific guidelines, you have to do this, this, and this. We are trying to get away from testing. I don't know why we can't just say it, that they have to feel comfortable, they have to assure themselves, they have to feel something to feel that with the information they have provided, that the participant, at some reasonable level, understands it.

DR. VANDERPOOL: But, Allan, see, I have a problem with that, like I have in a written test. I mean I think if, again, to refer to Jim, if I had been part of a consent team, and they said, "Well, do you think he understands the consent form so we can proceed with this procedure?" My answer, in light of what Jim would say is "No. I think you got to go in there and work with him for four more hours." So, see, I am not sure a criteria should be that the consent team should be comfortable with the notion that this person really understands everything. You've tried hard, you've given them the consent form. You see, one thing about informed consent is I can say to Dr. Crone, "Dr. Crone, I don't want to hear anymore. I've read the form. I trust it. I have tried to understand it the best I can. I want you to go ahead." You say, "Well, are there other things you need to understand?" "I don't want to understand anything else." Um, "I think I understand it, but don't give me an exam, I am ready to go." Well, is that all right?

DR. BERGER: Well, you know, Harold --

DR. VANDERPOOL: Are we going to force people to understand --

DR. CRONE: You can never --

DR. VANDERPOOL: -- to pass the -- a C level of comprehension, or --

DR. CRONE: You could never fully ensure, I mean, we, you know, because you could tell the person the information over and over and over again, and I am sure, Brad, you know this with patients, that you can, and you really kind of come away where you open end it, where you give them a chance to ask questions, where you spoke with the family, and you'll have these patients who, you know, who you may get to actually know over time, and yet something comes up afterwards, "I didn't know," and it's just like, you know, so it's not foolproof. There is no -- there is nothing in here for us to say it is foolproof. But there is sort of like a responsibility that the team has to, at least in the best, you know, in good faith, try to, you know, provide the best shot that someone really understands what they are getting into.

DR. KIELY: Go ahead.

DR. BERGER: No, well, you know, what I was going to say, in this case, I mean this is a public health risk situation, and I'd go as far as to say if a patient can't comprehend this, if that consent team feels that that patient really doesn't comprehend this informed consent process, which includes life-long monitoring, they are not a patient for a xenotransplant. They should not qualify for it, period.

DR. VANDERPOOL: Oh, I agree with that.

DR. BERGER: So I think we ought to be able to say that. I think it is a different criteria.

DR. VANDERPOOL: What about knowing all the procedures, knowing all the immunosuppressives -- See, the thing about it is --

DR. BERGER: Well, you have two sides about it, one is the patient knowing what they are getting into just from a medical procedure. But, you know, when we were doing this, we were saying, "Okay, what is different about xenotransplantation?" And so I'm saying what is different is that they need to comprehend to actually qualify to be a patient for this project, because there are responsibilities that they have to do, because it's not just them that is at risk. I am at risk. You are at risk. The public is at risk.

DR. KING: Even with that, to play the double advocate, even assuring they comprehend it, doesn't assure adherence.

DR. BERGER: Well, I mean, you know, of course right.

DR. KIELY: This actually hinges on a topic that we've -- it is going to take a long of time to discuss related to incapacity and mental capacity. And comprehension, as one of the components of informed consent, there has to be some nod to comprehension, I think we all agree with that. But I think what we haven't addressed in the first sentence there, we do sort of address the fact that we have to give the information in a way that, um, understands the person's level of education, their, what else do we say here, mental capacities, language skills, et cetera. So what we might use here is recognizing that all of these things will affect their level of comprehension. But I agree with Allan, in the sense that, and that would be an exclusion, and tell me if I'm wrong. At our institution, at least, if the individual, you know, doesn't understand that they are going to need to be on life-long immunosuppressives for a kidney transplant, well, they don't get that kidney transplant, or they are unwilling to come back for follow-up, well, that is a precious resource that would go to somebody else, and people are denied the transplant on the basis of their lack of comprehension/willingness to proceed with the protocol. And so I think this section, you know, with just a couple more words, could address that.

DR. VANDERPOOL: I think we may need to add a section that -- under the process. Maybe it should follow the sentence we have been working on, that the team needs to be assured that subjects comprehend the responsibility of life-long surveillance, and needs to comprehend the responsibilities that go with protecting the public health. What about adding something like that? Needs to take special -- Needs to take special -- Needs to be assured that the person understands the responsibilities related to the public health. And we might also -- I want you to add something like that.

DR. CRONE: You realize that we talked about some of this early on the informed consent process in that first paragraph, we had brought up some of the fact that while some of -- In the sentence, it is sort of the middle to the latter part of that first paragraph, about sort of the whole informed consent issue, and some of the risks. "While some of these concerns are yet not unique to clinical research regarding xenotransplantation, the complicated nature of this procedure and possible attendant public health risks require careful consideration of the informed consent process, including" da, da, da -- It goes on from there. I mean we -- Do you wouldn't to put something more explicit there about the fact that -- I mean because part of what we are saying is that is sort of the comment about what makes this unique, why is this -- Why are we being so picky?

DR. VANDERPOOL: Well, that is -- It seems to me that is a perfect setup sentence for an additional sentence under "Participants" in the research process to say, after we say the consent team should do all it can to facilitate comprehension, the team should ensure -- should also ensure comprehension of -- of the responsibilities that accompany public health risk.

DR. KIELY: Uh-huh.

DR. VANDERPOOL: That make sense to add that there.

DR. KING: Yes.

DR. VANDERPOOL: You are right. You really do forecast that as a unique problem, and then when we actually talk about what the team needs to be sure of, then to nail that one down here. Does that make sense to you?

DR. KING: To make sure I understand, the sentence that we changed right prior to that, it says "The consent team to do all it can to facilitate the subject's comprehension," and the sentence goes on as it is written. Is that correct?

DR. VANDERPOOL: Uh-huh.

DR. KING: And what did you add right after that? That is where you are adding this new one?

DR. VANDERPOOL: "The team should also -- "

DR. SHUMAN: "The team needs to be assured that subjects comprehend the responsibilities of life-long surveillance and others that go along with protecting the public health.

DR. VANDERPOOL: Perfect.

DR. KING: She already has it? Do I need to add it to our notes?

DR. COLLINS: She is not working off the hard copy.

DR. VANDERPOOL: Read it again.

DR. SHUMAN: "The team needs to be assured that subjects comprehend the responsibilities of life-long surveillance and others that go along with protecting the public health. That go along with, or that accompany protecting the public health."

DR. KIELY: "Other measures," probably.

DR. SHUMAN: "Other measures that accompany."

DR. VANDERPOOL: Okay, I've got it loaded now. We have been doctoring it up. What about on page 11, under who cannot enroll, should we add under "B," um, we have now those who are unwilling to comply, should we add those who cannot comprehend, or are unwilling to comply?

DR. BERGER: You could say "Those who are unwilling or incapable of complying." That covers kind of a wide variety of things.

DR. VANDERPOOL: I like that. What do you all think?

DR. KIELY: Incapable –

DR. VANDERPOOL: We are at page 11 under who cannot enroll.

DR. KIELY: As an individual, so this would affect our surrogate issue.

DR. BERGER: Right. Sure, why not.

DR. CRONE: We have to discuss something about that.

DR. VANDERPOOL: It will, but --

DR. BERGER: Incapable, that could include surrogates easily, because it is a broad statement.

DR. KIELY: Capability might be supported by the surrogate.

DR. VANDERPOOL: We will have said that this consent form is not for every contingency.

DR. KIELY: Right.

DR. VANDERPOOL: So when we later on talk about surrogacy, that is going to call for some changes in the consent form. We might even want to say that under -- But right now, we are talking for ordinary comprehension, you know, people who can comprehend. So I like that. "That those who are unwilling or incapable."

DR. BERGER: "Or incapable of complying."

DR. VANDERPOOL: "Unwilling to, or incapable of complying." I like that. Did you get that?

DR. SHAPIRO: No, because I'm having a problem with what you did. I'll tell you why. We make this great big deal about re-looking at informed consent across the board, what grounds it, why it is important, um, and a big piece of that should be not so that you and I are protected from the person who could be infectious, but so that they get what they are getting into themselves, not only about their responsibilities to protect you and me, but about what they are getting into. And this sentence is much more narrowly focused than that, than your sentence. We want to assure that they comprehend what they are getting into for their benefit, as well as the public health.

DR. VANDERPOOL: Now what sentence are you talking about?

DR. KING: The one we just added, where we are basically saying we, as a team, need to assure they understand the responsibility for life-long surveillance.

DR. SHAPIRO: Comprehension is a lot broader than that.

DR. BERGER: I would agree. We made that too narrow. There are two sides to it. There is the public and the individual themselves.

DR. SHAPIRO: That cuts out the whole piece of what we've done.

DR. BERGER: I agree with that.

DR. KIELY: I'm lost.

DR. BERGER: We are going back to the sentence that we had provided, and Robyn's point is that we

just narrowly focused it to life-long monitoring.

DR. SHAPIRO: We only care if they comprehend one thing.

DR. BERGER: But we do want them to comprehend the whole thing.

DR. SHUMAN: So how do you want to change that sentence, or are you taking it out?

DR. BERGER: You can say "comprehend all aspects of the informed consent process." I'm not sure you need to say "including," just leave it broadly.

DR. SHUMAN: How do you want to change it?

DR. KING: It would be "the team needs to be assured the subjects comprehend -- "

DR. VANDERPOOL: We just argued that one out.

DR. KING: I thought you just said that. Isn't that what you just read to me?

DR. KIELY: Yeah. Also that "the team needs to be assured that the subject comprehends the responsibilities -- "

DR. KING: " -- of life-long surveillance and other measures that accompany the protection of the public health." But we are just saying we want to alter the last part of that, correct? And say --

DR. KIELY: Yes.

DR. KING: This is back to assessing comprehension, and we narrowed it down, right? Blah, blah, blah is gone. Now we want to go on more specifically to life-long surveillance is what we were concerned they comprehend. Now we are saying that is too narrow.

DR. VANDERPOOL: Kathy and I are concerned about this assurance business of comprehending everything. The team can't be ensured that there is comprehension, but they can give it the best shot they've got.

DR. KING: The sentence we just added that you read back to me, right, I am just reading back what I thought we all agreed that was added. We changed the -- We changed one sentence to say "the consent team should do all it can to facilitate the subject's comprehension," and then that sentence ended, and then we added what you had said --

DR. SHUMAN: Right.

DR. KING: -- that we had said. "The team needs to be assured -- "

DR. CRONE: "Facilitate comprehension."

DR. SHAPIRO: It's too narrow.

DR. KIELY: It is an also statement, Robyn, so I mean the second one was an also statement, that was meant to be additive, not subtract from, so maybe we could make a change in the sentence that precedes it, because the -- the conversation that occurred a minute ago was really related to the fact that if they

really -- if they don't understand and comprehend, that that could be an exclusion criteria. That is what this is hinging on.

DR. VANDERPOOL: If they don't understand that they are going to have to take these surveillance methods --

DR. SHAPIRO: Well, my point is that if we really believe in informed consent, including the three elements, then they should be excluded if they don't comprehend a lot more than just that. If you really believe in what we are saying, you know, we make this great big deal about why is informed consent important, and what are its elements, and one of the three critical, irreplaceable components is comprehension, so now we are saying, "But if you don't comprehend, it is really okay, unless you don't comprehend about this little piece of it, which is for your protection, not mine."

DR. SHUMAN: May I just clarify? Is your issue with this sentence just the fact that it focuses on surveillance and other measures? Do you just want to broaden it to include everything that is involved --

DR. SHAPIRO: But I hear people saying, and this is a good point, how do you commit the team to assuring comprehension about anything?

DR. CRONE: They can't.

DR. VANDERPOOL: Before we get to the actual wording, my reply to you is we're making a big deal out of comprehension. We make it throughout. It's sustained. But -- And so you do every effort to understand. What I am opposed to, and I think what most of us are opposed to is the test.

DR. SHAPIRO: Right. Then you shouldn't --

DR. VANDERPOOL: A three hundred page test. So the idea of guaranteeing or ensuring comprehension is a problem. You -- You do everything -- The whole team is meeting and doing everything possible, but -- and this person will end up comprehending a lot, but we don't know how much. Now --

DR. SHAPIRO: The juxtaposition --

DR. VANDERPOOL: What Allan brought up was don't you think they ought to comprehend the responsibilities they have, vis-a-vis protecting the public? And it seems to me it made sense.

DR. SHAPIRO: See, for me the juxtaposition of the sentences just smacks of self-serving stuff. And I would rather see an exclusion criteria the way we have it, which is if somebody says they are just not going to do it, not focus on the comprehension, because if we do, I think, given what we've said before, we are obligated to focus on assuring comprehension about everything we are telling them. If they, for whatever reason, and it could be lack of comprehension, but if they indicate that they won't accept these responsibilities --

DR. VANDERPOOL: They are unwilling to comply.

DR. SHAPIRO: Yeah. So I'd rather not put it in the comprehension thing, at least not juxtapose. We are going to help you understand everything, and we hope you do. But we are going to exclude you if you don't understand this one piece.

DR. VANDERPOOL: Okay, I am -- I agree with that, I mean --

DR. KING: Could we exchange number 2B -- 2B and another 2B, back under 11?

DR. CRONE: What you are saying? In the informed consent?

DR. KING: "Those who are unwilling or unable." Would that cover it? Because if you don't comprehend, you are unable to comply.

DR. VANDERPOOL: That will cover it, "unwilling or unable."

DR. KING: You said the first one, not the second. Unwilling or unable. To me that covers. That gets into the idea of comprehending.

DR. KIELY: That is incapable of. That is what we said before.

DR. VANDERPOOL: We do keep the changes in the sentence about facilitating. I mean that is a better sentence now.

DR. SHAPIRO: And take this one added one out.

DR. SHUMAN: Now we are going to omit this sentence that we had decided to add?

DR. VANDERPOOL: Yeah, but to add that -- unwilling or unable to comply.

DR. SHUMAN: Got that.

DR. VANDERPOOL: Moving right along.

DR. SHAPIRO: Okay. Well, we are on five, which is the mental capacity. How much really, I think is what do we want to do with this whole section?

DR. VANDERPOOL: Do we want to do the others first and come back to that?

DR. SHAPIRO: Okay.

DR. VANDERPOOL: I'm not saying we should, but that is such a -- I'm afraid -- I think there are some things we are ready to change and get at, and almost complete this thing, except for maybe an argument on that, so why don't we move to the others first.

DR. SHAPIRO: Maybe we should also put on the back burner for the moment the children thing.

DR. VANDERPOOL: Yeah.

DR. SHAPIRO: The changes, one of our recommendations being changes in public health laws.

DR. CRONE: Three and four are out.

DR. VANDERPOOL: We are going to write "wait" on those recommendations.

DR. SHAPIRO: I want to talk about how we need to complete our careful study of where it is we believe it may be deficient, and hopefully have suggestions with grappling with the issue of the

non-compliance.

DR. VANDERPOOL: Did you all hear that?

DR. SHAPIRO: The study first, an in-depth study of public health laws, the capability to.

DR. KIELY: That would be undertaken by this committee?

DR. SHAPIRO: Yeah.

DR. KIELY: Or someone recommending PHS look at it?

DR. VANDERPOOL: Robyn already had the discussion -- We already had the discussion that that there -- We can't get any leverage on these people, but we need to make a comment in that discussion that public health laws need to address this problem.

DR. SHAPIRO: Yeah.

DR. VANDERPOOL: Then, in the recommendation, we flesh that out. So why don't we put somewhere in your text, when you talk about problem --

DR. BERGER: Either 18 or 19.

DR. VANDERPOOL: It may already be there.

DR. SHAPIRO: Yeah, on 19.

DR. BERGER: 19.

DR. SHAPIRO: The paragraph above "Issues."

DR. SHUMAN: What page are you on, please?

DR. SHAPIRO: 19.

DR. BERGER: You can do it under that last paragraph, "Public health laws," "mandatory public health monitoring would likely not be possible." You can add a sentence literally right after that.

DR. SHUMAN: I'm sorry, which paragraph are you referring to?

DR. COLLINS: Second complete paragraph.

DR. BERGER: Nineteen. I was saying the second full paragraph, but the third paragraph, right in the middle, it says "Under current public health laws," Robyn makes that statement that it doesn't seem possible.

DR. SHAPIRO: The whole rest of the paragraph, I think, is in line with what we are talking about now. If we just add at the end "and recommendations for modifications or amendments of those laws would be forthcoming."

DR. VANDERPOOL: Right, good. I like that. So we have dealt with changes in public laws, and we are going to make it a later in "Recommendations."

DR. CRONE: You have a thing on eight.

DR. VANDERPOOL: The two questions we have are exclusion and --

DR. SHAPIRO: No, eight.

DR. VANDERPOOL: Oh, eight. I forgot about that. SACX education role. I thought that was so good. I thought we were all just going to educate the world.

DR. BERGER: Actually all you need to do is just at SACX, or some other, or -- I mean some other --

DR. SHAPIRO: Some other representative.

DR. BLOOM: Or appropriate.

DR. BERGER: Right. So that is all you have to do is just add a few words, that SACX --

DR. VANDERPOOL: I love the way Allan's thinking took care of that. What do you think, Eda?

(Discussion off the record).

DR. KING: I had a hard time, before we had a discussion at the meeting yesterday, visualizing how the first little dot and the fourth and the fifth one actually fit into the informed consent document.

DR. KIELY: What page is this, please?

DR. KING: 21 and 22, right where we were. Same place.

DR. SHAPIRO: About -- It's about --

DR. KING: I need you to explain why. Maybe it is clear in here. I mean to me it was a stretch to say --

DR. SHAPIRO: We try to say -- I mean what I tried to do is say we need to involve the community. We could do it this way. If this doesn't work this way, if this doesn't work this way, is the only thing that seems to work in terms of compliance.

DR. KING: But to me, saying why SACX needs to do these things, we need to be, for example, aware of the protocols that are there, that will help us inform, because to me we are talking about informing the community, and then we are saying: No. Other activities, SACX has to do.

DR. VANDERPOOL: Karen has a good point. We need to make a transition between informed consent for prospective subjects, and educating the public. And what we can say is, to that effect, is that better understanding of these -- of the informed consent issues for patients is predicated on better understanding generally in the public.

DR. KING: Because to me --

DR. VANDERPOOL: And then -- And then move into who is responsible, how the education can occur.

DR. KING: We are saying people need to be educated. SACX is going to do that. The bullets two and three, to me, are talking about methods to be used to do that, brochures, forms, whatever, but to me the first one is what we would do to get information to help us inform in a brochure.

DR. BLOOM: That is already in the charter.

DR. KIELY: Yeah, it is not in our --

DR. BLOOM: The first point is in the charter.

DR. KING: And the fourth little bullet, the fourth dot, whatever, we go into making recommendations to the secretary. How does -- Help me understand how that fits in. It didn't fit in, to me.

DR. CRONE: It doesn't, you are right.

DR. KING: The last one, developing closer collaborative efforts with these agency, to me the fifth one and the first one are what we at SACX need to do to make sure we are informed so we can do the second and third bullets.

DR. BLOOM: The first one is already in the charter. It actually says "keep informed."

DR. KING: The fourth one, to me, didn't fit into informed consent or educating the public at all. Now we want to educate the secretary on policies.

DR. SHAPIRO: To the extent the secretary is going to make policy about what is going to happen to the community, then we can help communicate back to the secretary what that should be, so in terms of giving consent --

DR. VANDERPOOL: Maybe that should be moved to our recommendation section?

DR. BERGER: Yeah, actually I'd take the whole community part and put it at the end, because it doesn't fit right here, and just make a statement about the community, and you are right, you can see, in light of the shortcomings at the expenses of the public, this committee suggests that -- that the SACX or an appropriate government agency should continue, blah blah blah, and just ending that sentence "clinical research, period," and the rest of this should be in a recommendation. A couple should be taken out, because there already are mandated rules. You could see in the recommendation, in addition to the role already chartered for SACX, we would recommend that SACX should, and whatever those few things are that we are adding, and that shouldn't be in a recommendation, just pull it out of here altogether. Too many changes, huh?

DR. BLOOM: Sounds good to me.

DR. SHAPIRO: We want to educate the public and have an exchange with the public when we want to gather all our information.

DR. BERGER: But this whole thing on the community, in the middle of these informed consent issues, maybe that should be outside of it, kind of in a separate section.

DR. VANDERPOOL: My thinking is, is that discussion --

DR. KIELY: Community consent.

DR. VANDERPOOL: -- about the problems of community education, I think that is beautiful, I mean I think it needs to be brought out.

DR. BERGER: I'm not arguing that it shouldn't be. I am saying to separate it out.

DR. VANDERPOOL: You are arguing that separating out that --

DR. BERGER: Just put it at the end, put this whole community section, but take these recommendations, and put it in "Recommendations" at the end, get it out of here, and then you limit it. I think Eda's point is some of these are in our charter, so what you are recommending is in addition to our charter.

MS. SHAPIRO: Here is something. I went through this, and this isn't the only place where there are recommendations embedded in this thing. I think if it is part of this conversation, I don't know if it is here, because I think that it needs to be reworked in light of these comments, but if it is, I'd do it both. I mean I think we should pull out all the recommendations and reiterate them in bullet points at the end of the whole thing.

DR. VANDERPOOL: That is going to happen with the other report, too. I mean I could find 30 recommendations there.

DR. SHAPIRO: If you save every piece of advice you have for those bullet points, you lose the context of why you came up with it in the first place.

DR. KIELY: I don't think it fits here, because it is community consent. It is an issue that involves a third party, which is defined in this way, so it just may need to be, like Robyn said, maybe part of it should be moved to another section. But I think the issue of community consent is a real one when you are doing -- dealing with informed consent.

DR. VANDERPOOL: I completely agree.

DR. SHAPIRO: Of all the areas that are controversial, I think, this is area number one.

DR. CRONE: It fits, I mean it is also the way you formatted this thing, about issues involving third parties. You went from the circle right around the patient, to bigger, to broader, to broader, and this fits.

DR. VANDERPOOL: So are we clear about what we are going to do?

DR. SHUMAN: I am not.

DR. KIELY: We need clarification, Robyn.

DR. SHAPIRO: Yes.

DR. KING: She needs a little clarification.

DR. SHUMAN: I want to make sure I know what --

DR. SHAPIRO: I am going to be sending this to you, so don't worry about it. I have to look at it and see it, but then I'll get it to you.

DR. SHUMAN: Okay.

DR. VANDERPOOL: So, Deborah, you get as much as you can, and Robyn is going to rescue you. She says it. Please send me an e-mail if it doesn't happen.

Are we taking -- The SACX deal was taken care of by one statement by Allan, so let's move on.

One size fits all on the consent form. That is where we need to expand out, it seems to me, um, just before we start this model consent form, page 8, end of that first paragraph on page 8. Obviously the actual heading and specific content of the consent form will vary from this -- I don't think we need to call it generic form, but from this format, and depending on the particulars of a given xenotransplant protocol. I don't know whether we want that long and laborious sentence. So what else do we need to add that needs to be a paragraph? What else do we need to add? Do we need to say a "for example" here?

DR. SHAPIRO: Yes.

DR. VANDERPOOL: In order to take our science of -- state of the science colleagues into consideration? For example, "The consent form for so-and-so for a person who received such and such would vary significantly from the following"?

DR. BLOOM: We could say "For example, a patient who has received human skin cells that have been grown on a mouse feeder layers might be substantially different." You could even refer to the subcommittee meeting.

DR. VANDERPOOL: For example --

DR. BLOOM: You might want to refer to human skin cells that have been grown --

DR. VANDERPOOL: An individual who had received human stem cells --

DR. BLOOM: Skin cells. Skin cells.

DR. VANDERPOOL: Yes, skin cells. Stem cells are off limits, aren't they? That is not supposed to be mentioned here. You know, human skin cells that have been grown off a mouse feeder layers.

DR. BLOOM: Cells. And then we look at "For example, individuals may not need, or their contacts may not need to comply with every single aspect set forth in these guidelines." Something to that effect. And then you can refer back to an FDA panel, I think it was January 13th of 2000, and it is on the Internet, where a product such as this was discussed, and the panel at that point came to the conclusion that this product may not present all of the concerns that other xenotransplantation products might. You were on that panel. John was. Dan was.

DR. VANDERPOOL: Right. I just remember we thought that some of the -- some of the surveillance procedures and other things could be modified, depending on the actual exposure level and so on.

DR. BLOOM: That is a very much broader statement, and you didn't say that. You were unwilling to say that.

DR. VANDERPOOL: We don't want to say that here.

DR. BLOOM: Because that is much broader. Then you could say ex vivo perfusion with liver cells is a short-term contact, so we don't have to worry about that.

DR. VANDERPOOL: I am trying to recall the committees' discussion. We said exceptions could be made under --

DR. BLOOM: -- certain limited circumstances. It was very limited.

DR. VANDERPOOL: Let's find the wording for it.

DR. BLOOM: There is also --

DR. VANDERPOOL: What else do we want to say in this paragraph? I think the "for example -- " Eda, can you --

DR. BLOOM: Well, you know, it was actually -- The summary of that meeting was published Hugh Akenclaus (phonetic) and Gail DePalito (phonetic) offered publication in the "Journal of Xenotransplantation" that came out later in 2000. It is a nice, concise summary of that.

DR. VANDERPOOL: We could find the reference.

DR. BLOOM: Yeah.

DR. VANDERPOOL: "For example -- " what do you have, Deborah, down?

DR. SHUMAN: "For example, a patient who received human skin cells grown on mouse feeder layers, or the contacts of such a patient, may not need to comply with every aspect set forth in these guidelines." I'm not sure where that is going.

DR. VANDERPOOL: With every element of --

DR. SHUMAN: Okay.

DR. VANDERPOOL: With every --

DR. SHUMAN: -- element of compliance.

DR. SHAPIRO: How about "all of the consent requirements in the following form may not be applicable to an individual who will receive human skin cells grown off mouse feeder layer cells or his or her intimate contact."

DR. VANDERPOOL: That's good.

COURT REPORTER: Can you repeat that? I couldn't even hear it.

DR. BERGER: Such as.

DR. VANDERPOOL: Read it again.

DR. BERGER: Such as.

DR. SHAPIRO: Well, you tell me how to do it. "For example, all of the consent requirements in the following form may not be applicable to an individual who will receive human skin cells grown off

mouse feeder layer cells."

DR. BERGER: I would have just said "to an individual such as," or "for example." That is all I meant.

DR. SHAPIRO: Okay.

DR. VANDERPOOL: Read it again.

DR. BLOOM: Instead of "requirements," I would suggest "elements."

DR. SHAPIRO: Okay. I had that first and then I changed it.

DR. VANDERPOOL: So read it again.

DR. BLOOM: That is where I got it from.

DR. SHAPIRO: "For example, all of the consent elements in the following form may not be applicable to an individual, such as one who will receive skin cells grown off mouse feeder layer cells, or his or her intimate contacts.

DR. BLOOM: It's grown on, not grown off.

DR. SHAPIRO: On.

DR. VANDERPOOL: Deborah will offer us refined wording, but that is real close, Robyn. The initial sentence should read, instead of what we now have, drop the word "obviously" on page 8. "The actual headings and specific content of a given consent form will vary from this format, depending -- depending on the particulars of a given xenotransplantation protocol. For example -- " do we want to have another example? I don't think we need a lot of examples.

DR. SHAPIRO: No.

DR. CRONE: No.

DR. VANDERPOOL: So we have taken care of number nine, one size fits all. What about --

DR. SHAPIRO: Wait. I have a question on that. Um, do we want to make that disclaimer only about the form, or about the process?

DR. BLOOM: You are right.

DR. SHAPIRO: On page 5 we kind of carve out some exceptions. We say "the following recommendations are aimed at interactions involving adults/individuals who are mentally competent to provide informed consent considering the moment," blah, blah, blah. And we say "If it is urgent, it may be different." We may also want to build in some exceptions to the rather rigorous process that we otherwise would require.

DR. VANDERPOOL: Don't we want -- Most of what we have in the process would apply to everyone, in terms of the group of people, the repeated meetings, and so on.

DR. BLOOM: Except you already have the urgency, if it is urgent, but it is already in here.

DR. SHAPIRO: Do you have to add the whole thing for the mouse cell?

DR. COLLINS: Robyn, I think you do. When the protocols first start, I think you do, because of the unknown of the whole xeno process. I think that as more experience is gained years down the road, we may not need that much detail. I think early on you do.

DR. BLOOM: It is likely within this country, before the end of this year, I shouldn't say it is likely. These cells are already for sale. It is likely they will have an improved mechanism to do that. So it's --

DR. VANDERPOOL: We could say at the bottom of -- I think the process section, I think Robyn is getting to something. The process section was written on the model of there being an almost organ recipient, so --

DR. CRONE: Not even that. I don't think so.

DR. VANDERPOOL: Okay. Not really. Mouse organ cells --

DR. CRONE: It's more having to do with a xeno cell being transplanted.

DR. BLOOM: Most cases -- the more common approach --

DR. VANDERPOOL: I think the process --

DR. SHAPIRO: If you think that --

DR. VANDERPOOL: See on page five, the middle paragraph, "The following recommendations are aimed," this is in the process section, at interactions involving adults who are mentally competent to sign an informed consent and who are considering enrollment in xenotransplants, both in nonurgent situations. Now that would be nice. In the event the subjects need to be considered on an urgent base, modification to the consent process will be necessary." At that point, do we want to say anything about modifications for other -- for mouse --

DR. SHAPIRO: That is the question.

DR. VANDERPOOL: For example, the mouse cell example, again?

DR. BLOOM: You know, I don't know if you want to get that specific here. I wonder if you'll want to say --

DR. VANDERPOOL: Let's keep the mouse cells for later, but do we need to say anything here?

DR. BLOOM: Right. Um, or other -- "on an urgent basis, or for other," I don't know if you want to go here, but for other justifiable medically and scientifically justifiable reasons. But I don't know if you want to do that.

DR. CRONE: I don't know if you want to do that. It starts to get really --

DR. BLOOM: It is kind of open, especially when you get to medically justifiable.

DR. CRONE: Because you just made that point, you know, I don't know if I would do that.

DR. VANDERPOOL: I think we're okay.

DR. BLOOM: If the science group wants to change it, they will.

DR. SHAPIRO: Okay, let's leave it there, as is.

DR. VANDERPOOL: Are we are okay?

DR. SHAPIRO: Yeah.

DR. VANDERPOOL: So we are done with nine. That takes us to 10. Okay, 10, one size doesn't fit all for medical personnel.

DR. SHAPIRO: Page 20, what I did do already on this was to just suggest the following sentence after the first sentence. So "Healthcare workers who come in contact with xenotransplantation recipients also face the risk of xenogeneic infections, accordingly, the informed consent process for xenotransplantation research should include a component that informs the recipient of his or her responsibility to inform healthcare providers, his or her health care providers, about his or her receipt of xenotransplant products." That got to Megan's point, I think. And then in the new paragraph, I think, we can get into the healthcare professionals involved in the procedure itself, and what we want to require them to know.

So the next sentence -- then the next paragraph starts, "In addition, with respect to healthcare providers involved in the xenotransplantation procedure, comma, as is true of the recipient's intimate contacts, comma," and then the rest of the sentence goes on about being informed of the procedure.

DR. VANDERPOOL: Any comments to --

DR. SHAPIRO: I don't know. I mean we do have these recommendations out there already. And what I heard was a suggestion that we should say we don't like them for the pre and post exposure, but I kind of do like them.

DR. VANDERPOOL: Kind of what?

DR. SHAPIRO: I do like them.

DR. VANDERPOOL: The regs?

DR. SHAPIRO: Yeah.

DR. VANDERPOOL: All right. Me too.

DR. BERGER: I mean I don't see where there is such a problem with this.

DR. SHAPIRO: I don't either.

DR. KIELY: I think what, at least, because I -- it was a thought I had when I read it, um, first, and it ties to the responsibilities in the informed consent, and we say that they need to have regular checkups and these other things. Um, they have to educate their family members, that list of eight things on page 15, um, donations and what have you. But, you know, people move, people travel, um, they end up in emergency rooms that don't do xenotransplants, or don't do any transplant. And so I think the point that

she mentioned, and the thing that I want to get to in this regard relates to them relating this in terms of their history, in being aware that this is something they do need to be -- to divulge, um, you know, to other healthcare workers.

DR. VANDERPOOL: Okay, let me just -- Let me go to -- to scripture, okay. Um, and in this case the scripture is the PHS guideline. It speaks very clearly in two paragraphs on what needs to happen with healthcare workers. First paragraph says there is some risk there, but it is undefined. Then under "Education," there are two paragraphs. One is -- has to do with, um, education of healthcare workers. "All centers where xenotransplantation procedures are performed should develop appropriate xenotransplantation procedure-specific educational materials for their staff. These materials should be -- should describe the xenotransplantation procedures, the known and potential risks and researcher health activities that may pose a greater risk of infection or of nosocomial transmission of xenotic and other infectious diseases and safety precautions. The education program should detail the circumstances under which the use of standard precautions and other isolated precautions are recommended," you know, and it mentions gloves are worn and so on. That is very specific about what needs to be done with respect to education. Now, healthcare worker surveillance. The sponsor and the occupational health service in each clinical center should develop protocols for monitoring healthcare personnel. These protocols should describe methods for storage and retrieval of personal records, and collection of serologic specimens from workers. Baseline sera should be collected, um, and should be compared on a basis, um -- baseline sera can be compared to sera collected following occupational exposure. Such baseline sera should be maintained for 50 years from the time of collection."

DR. BLOOM: Yep.

DR. VANDERPOOL: "The activities of the occupational health service should be coordinated with a lifetime control program." Um, and then finally, under "Post exposure evaluation and management of healthcare workers," "written protocol should be -- protocols should be in place for evaluation of healthcare workers who experience an exposure where there is a risk of transmission. The post exposure protocols describe the information be recorded through the daily nature of the exposure, and so on." Um --

DR. SHAPIRO: So we adopt those and say that.

DR. VANDERPOOL: Yeah. So the point is that -- that I think -- Have we summarized that well enough? I know --

DR. SHAPIRO: Yeah. We lifted it and cited it as such.

DR. KIELY: Doesn't that really relate to centers that are doing this work, and not to a community hospital that wouldn't know anything about xenotransplantation, much less know how to deal with a needle stick with it, or I -- The issue is not the centers that have the protocol with the IRB in place where their occupational health department is on, you know, board, and knows what these issues are about. What I am really thinking about are the hundreds of other hospitals and healthcare workers that interface with these patients more frequently after the procedure possibly than even these people. So again, our focus is very narrow on a well-protected group of individuals, and we aren't really contemplating in terms of third parties, you know, the fact that they'll go to another state, another place, maybe be in a motor vehicle accident, show up in an emergency room, and what have you. And so that is what I am getting at in that regard, and when we talk about education of the public, it might be in that way that we raise the bar of understanding about this as a procedure, and as an occupational risk. I'm not sure where it goes, but I felt that we did not adequately address it.

DR. VANDERPOOL: That we adequately addressed the -- what needs to happen vis-a-vis not informed consent, but education for healthcare workers in the, quote, centers where xenotransplantation procedures are performed. So you want to --

DR. KIELY: They probably have it all wrapped up. I'm not worried about that. They better be following the guidelines. My concern, rather, is the small community hospitals, the visiting nurse associations that will make home visits to people, you know, what have you else. And so there is a whole circle of healthcare workers that are going to be in a much larger circle, really, um, that will be interfacing with this population as the procedures develop and the population grows.

DR. SHAPIRO: So we have two steps. One is that they know, so we addressed that in this added sentence. And the other is who is going to provide whatever help they may need, if there is a needle stick or something.

DR. KIELY: But I think the first line of defense, and I think the healthcare workers, and there is some standard educational base, and what have you, for first responders, like EEDs and PCPs, like Robert was saying. He has these patients who have had xenotransplants. The blood banking system, for example. Making the individual -- Making a responsibility of the recipient, like doing all these other things, like not donating sperm would be to declare that they've had a xenotransplant in their medical history on appearance to the emergency room, you know, because again, the health system is going to have to catch up with this, and as I said earlier, kind of tongue in cheek, the medical schools aren't asking students to ask this question. You know, they might say "Have you had surgery?" You might get to it that way.

DR. VANDERPOOL: There are so few right now.

DR. KIELY: The responsibility of the individual.

DR. VANDERPOOL: This is an extension of that worry that xenotourism is going to be xenotourism in the United States, where somebody gets a xenotransplant in Pittsburgh and moves to Nacogdoches.

DR. KIELY: Right. And I think from a regulatory standpoint we really protected the healthcare workers that are doing these procedures, and are involved with caring for these patients, but in terms of advising the Secretary, I think we have fallen short in making a recommendation about the greater first responder community, in particular, and potentially the blood banking system. I mean we need to think about that.

DR. VANDERPOOL: It seems to me that your point, Sharon, is very important for a recommendation, namely, that presently there are press policies and recommendations for the centers where xenotransplantation procedures are being done. Further thought and guidance needs to be given to all the healthcare centers and clinics that are likely to deal with, or likely to treat, um, persons who have received xenotransplantation products.

DR. KIELY: The point that Louisa made earlier today about there is this system, and you find something unusual, you report it to your department of health and all this, and, you know, in the real world, um, you treat these things for a period of time, until you recognize that the cat's out of the bag. Um, and, you know, it is -- it is unusual that that process is followed seamlessly, and so it would be important, as a recommendation, to do this education of departments of -- I mean many departments of health wouldn't know what to do with a call about a person with a xenotransplant. They'd be calling you, Harold.

DR. BLOOM: That is true.

DR. BERGER: Right. But, Sharon, don't we already have procedures, I think as was mentioned before, with HIV. So for instance, if you get a new patient that comes in that is HIV positive, um, who you haven't seen before, who just moved into the area, wouldn't there be some basic procedures, or some education you'd have within your own --

DR. COLLINS: HIV has been around so long, that is pretty standard. All the local hospitals will know there is prophylaxis to give, and that sort of thing. But xenotransplantation, as Sharon said, the onus is on the patient to inform them. I think the center or the primary healthcare, not the primary, but the investigator should have some responsibility for if a healthcare worker in an outside hospital is stuck, the study center should in some way assist in facilitating the process of testing, and that sort of thing. Because for HIV, I mean everyone knows that throughout all the healthcare systems, and that sort of thing. Xenotransplantation is different. I get all kinds of phone calls from patients who go to local hospitals for a problem, the first thing the doctor does is calls the transplant center, and says "We're sending them," so I am just thinking that perhaps the major center could assist in that.

DR. BERGER: And I'm just suggesting we follow a similar process, because HIV is out there already. Although some things might be different, it is similar in a way. And maybe the process should be the same.

DR. COLLINS: The process, right.

DR. KIELY: Ultimately I think it might be likely.

DR. VANDERPOOL: Now would be the perfect time to mention that Adrian, is that -- Adrian --

UNIDENTIFIED FEMALE PARTICIPANT: Adrian.

DR. VANDERPOOL: -- came to talk to me right after this morning's meeting saying that she gets all kinds, and she is working with the -- with CBER Office of Communication, she gets all kinds of questions about various health service concerns, but none about xeno. And so the word isn't out there yet about xeno. It may not need to be right now. But -- And she suggested that perhaps we encourage the secretary to make a public health service announcement at some time so that this alert will occur. So the alert, the education is associated with the general community hospitals having some information about how to deal with this. How does it affect the document, Robyn?

DR. SHAPIRO: Karren came up with a great suggestion. On page 16, under "Responsibilities" we should say "Exposure to future healthcare providers following the individuals after receipt of a xenotransplantation product." In addition to that other sentence that we added in the -- in the healthcare providers section.

DR. KIELY: Could you say that again, exposures agreement to --

DR. SHAPIRO: To inform.

DR. KIELY: To inform, or to --

DR. SHAPIRO: Where are we?

DR. KIELY: You said on page 16.

DR. SHAPIRO: Yeah, disclosure. So this is one of the responsibilities -- enumerated responsibilities.

Exposure to future healthcare providers about the individual's receipt, um, of a xenotransplantation product. And then that other sentence on page 20.

DR. KIELY: Okay. I think that covers it. And then it will go in as a recommendation to the Secretary. That is good.

DR. COLLINS: I agree.

DR. VANDERPOOL: We were supposed to be done by 11:50, is that it?

DR. BERGER: Supposed to be back here to start the next session.

DR. VANDERPOOL: We are 15 minutes late. Let's see. We've done this. Now what about the mention of H-I-P-P-A?

DR. COLLINS: Did I spell it wrong?

DR. KIELY: We're going to read Robyn's book.

DR. BERGER: They have to buy it first, don't they? Recommend they buy it first, an autographed copy.

DR. KIELY: That might be extra, but --

DR. KING: That is as to children and surrogates.

DR. VANDERPOOL: We have to brainstorm "Recommendation." Okay, so, Robyn, well, why don't you read yours right quick, and let's hit them quickly, um --

DR. SHAPIRO: Well, yeah. I mean I am not going to read the whole thing, because these are just pulled out, and they have to do with everything that we said. One would be --

DR. VANDERPOOL: Let's double star the ones we really like. Read through them all first.

DR. KIELY: Can I ask a point -- Are we not going to deal with the other issues now because of time?

DR. SHAPIRO: I really think we should.

DR. KING: The surrogate and the children.

DR. KIELY: We should, but we can't. I'm getting --

DR. SHAPIRO: We have to. I think we have to, because these are just rehashing what we already know we need to work on, putting them in order.

DR. VANDERPOOL: You think it is more important to go to the --

DR. SHAPIRO: I do.

DR. BERGER: Why don't we trade those after the meeting by e-mail, just send them around for comment after the meeting.

DR. SHAPIRO: Yeah, I will have these put in legible form and e-mail them.

DR. VANDERPOOL: We need to all give our recommendations we have, too.

DR. BERGER: That is what we can do.

DR. VANDERPOOL: Everyone send your recommendations to Robyn.

DR. KIELY: Insofar as discussing those other populations, um, how are we going to do that? I mean we have run out of time.

DR. VANDERPOOL: We are not, not today.

DR. BERGER: Eda, did you have recommendations, because you are the one that really brought it up about how to deal with children.

DR. BLOOM: The problem with children is you have different products, and, you know, I can understand Dan's point, and perhaps with diabetes, you could -- you can use adults first. Um --

DR. BERGER: So what are things that would be specific for children that are already being done right now?

DR. SHAPIRO: Can I read a sentence I did based on your note, and see if it sounds right. This would be on page 24, right after first sentence. As a general matter, we don't want to do it. There may be special circumstances where the possibility of benefit to a child from a xenotransplant procedure is applied, given the available opportunities, parenthesis, e.g., porcine islets for a child --

DR. BLOOM: I'd take that part out. Take out the e.g.

DR. SHAPIRO: Okay. "And in these situations should be considered on a case-by-case basis."

DR. BLOOM: I think that is fine. Leave out the example.

DR. KIELY: Yeah, no example.

DR. VANDERPOOL: Can we deal with this, this way, that is those of you who are particularly concerned about these areas and children, send suggested recommendations to Robyn so that Robyn can develop that section, make a few changes, get it back to all of us.

Now, group, what I am thinking is that we can have a finished product when?

DR. BERGER: If we finish it, we'll have one more draft to go to everyone via e-mail to do a final comment. I would say a couple months, two months. The end of March, end of the quarter?

DR. VANDERPOOL: I think April Fool's Day is pretty good.

DR. BERGER: April Fool's Day, we'll do that. That is probably true.

DR. VANDERPOOL: We will have a completed draft for circulation to the group by April Fool's Day, and then we will all have our comments back to Mary. Mary is going to be the source, and Deborah. And we'll have all that done so that we will have a completed -- I think within a month we can have our --

have a draft to the entire committee set out. We can make our changes in --

DR. KIELY: I just have some concerns that while we put off these two topics, which were of significance to the group at large, that we haven't really, and I am just concerned that we are going to come back on April 1st, and --

DR. COLLINS: Conference call.

DR. KIELY: -- have that not really teased out.

DR. CRONE: We can do a conference call.

DR. SHAPIRO: A conference call.

DR. KIELY: We need to have some communication.

DR. VANDERPOOL: Right, we need a conference call.

DR. KIELY: That is my recommendation. I am not comfortable just leaving it.

DR. VANDERPOOL: We need a conference call before April Fool's Day. We need a conference call in the next few days while the anvil is still pretty hot.

DR. KIELY: Good. Okay. Thank you.