forth, and I'm concerned that we're not emphasizing that. The bottom -- I may not differ from the bottom line where we're going. It's just that the signal may be that we have much more -- we have a better, more positive view of the study than we probably should have.

DR. DAVIS: As the clinician, and I'm not a study design person, it just seems to me we're not putting a stamp of approval that this is an ideal clinical study, but we are saying that this data, especially comparing it to the FC1, says that this is a safe and effective female condom. That's how I'm interpreting.

DR. D'AGOSTINO: Yeah, but I'm not arguing with the final vote, the way the final vote might go. I'm arguing with the sense that this study has more merit than it actually has, and getting that across is what I think we should need to do.

DR. CEDARS: Does the FDA understand our concerns about the quality of the data?

DR. WHANG: Yeah. Thank you for expressing that.

DR. CEDARS: If we can move to Question 3, and this has to do with the event rates for breakage, misdirection, invagination, and slippage. And the

question for the Panel is for each individual failure mode, the upper bound of confidence interval for the difference is less than 1.01. And our charge is to discuss whether the data provides reasonable assurance of FC2 safety and effectiveness when it's used as a barrier protection against pregnancy and sexual -- STIs. Dr. Gilliam? Dr. Katz?

DR. KATZ: I'm a little confused by the logic of this question.

UNIDENTIFIED FEMALE SPEAKER: I am, too.

DR. KATZ: Because we just voted yes on Question 1. And so if we vote yes on Question 1, then the Question 3 -- am I right?

DR. CEDARS: Well, I --

DR. KATZ: It hinges on is this statistically -- does this difference satisfy a certain threshold that is our standard for not being different.

DR. MARRAZZO: I mean, it also presumes that there is a direct and quantitatively direct relationship between what you're seeing here in these trends and the risk of acquiring STD, HIV, or getting pregnant, right? And so there's an assumption buried in the question that does get back to Question Number 1, which makes it a little difficult to interpret.

DR. KATZ: Yeah.

DR. CEDARS: Dr. Whang, could you clarify for us the specific intent, given Question 1 that we asserted, that a specific clinical study, clinical outcome other than failure rate study was not required, what the specific intent of this question was?

DR. WHANG: Right. So as I see the logic of these first three questions, in the first question, I think in your discussion, you've established that the failure modes study is reasonable, is acceptable. In the second question, you've established that some of the details of how this study were conducted are acceptable. And now in this third question, we're asking you to look specifically at the measurements in this study. And if you look at the numbers of what they got, where do you end up in terms of do we have a reasonable assurance of safety and effectiveness?

DR. CEDARS: Dr. D'Agostino?

DR. D'AGOSTINO: Yeah. I mean, I interpreted this that they want us to say 2 is the magic number for the confidence intervals, and these are all below 2, so we're happy. And I think, again, my feeling is that the study was not a great study,

realizing all the things that one has to go through to get it. These 1's are probably underestimates and so forth, but they're consistent, and, you know, this is what they are. But I don't think I'm going to -- I'd be willing to give you the fact that this is less than 2 in another study. But I would be willing to give you the fact that it's probably by any reasonable criteria not going to -- criterion you're not going to get a difference between FC1 and FC2.

DR. CEDARS: Dr. Padian?

DR. PADIAN: I don't understand the second part, but maybe it's not relevant because we just had a long discussion about not only in this study, but even in FC1, where we didn't have data on STIs. So, I mean, it seems like you're -- what I'm confused about is you're asking us, or it seems like you're asking us to infer or extrapolate in a way that we already had a discussion that wasn't even done for FC1. But maybe I'm misinterpreting it.

DR. GILLIAM: I was just going to say that it seems like we're looking at these outcomes as a surrogate marker for --

DR. PADIAN: For those. So --

DR. GILLIAM: -- prevention of STD/HIV, and how comfortable are we looking now at the actual

numbers, as opposed to sort of theoretic --

DR. PADIAN: I see.

DR. GILLIAM: I mean, that's how I'm taking it, but maybe I'm --

DR. D'AGOSTINO: Yeah, and they want it to be less than 2 by some magic criteria.

DR. CEDARS: So, I mean, the opportunity for discussion, given the answers to 1 and 2 for 3, are much more limited. Dr. Gilliam, did you have --

DR. GILLIAM: Well, I guess my concern is I see Question 3 as asking, one, about precision, and I think we've already said that this is imprecise because we don't trust that all events were captured.

UNIDENTIFIED MALE SPEAKER: Right.

DR. GILLIAM: We trust that they're comparable between FC1 and FC2, and so that's reassuring. And we're also reassured when we change the definition of slippage to that used by the Sponsor, that it's similar to other studies, so that's reassuring. But to come up with a number to say is the number that is -- is the true value less than 1.01 percent? I don't know what the true value is, but I can say that my bias is that these are okay.

And then we're also asked to make another

leap of faith because we were using indirect data to say whether it protects against sexually transmitted infection and pregnancy, and we said we could infer that. But now you're asking us to be specific about that. So I think we're asking for precision and --

UNIDENTIFIED FEMALE SPEAKER: Yeah.

DR. GILLIAM: -- being precise and making the final leap.

DR. CEDARS: I think this question does for the first time --

UNIDENTIFIED FEMALE SPEAKER: Right.

DR. CEDARS: -- specifically say pregnancy and STIs.

UNIDENTIFIED FEMALE SPEAKER: Yeah.

DR. CEDARS: Which Questions 1 and 2 did not.

UNIDENTIFIED FEMALE SPEAKER: Yeah.

DR. MARRAZZO: And it's also really asking more about a reasonable assurance of the degree of safety and effectiveness, right? Again, it's not the concept. It's looking at the --

DR. CEDARS: Whether it's a good enough surrogate to make that extrapolation.

DR. WHANG: Right, so in terms of the things we've just been saying, we're not asking you

to evaluate here if 1.01 percent is true. We're saying that's what was measured in this study, you know, with all the methods we've just talked about. Now, the proposed indication has to do with protecting against pregnancy and sexually transmitted infections. Knowing that's the proposed indication, do these data, do these results provide a reasonable assurance of safety and effectiveness?

DR. CEDARS: Dr. Zenilman?

DR. ZENILMAN: Actually, I had a question for Ralph, and that is on the first part, and then I want to address the second part. The first part, basically, we have so many questions of precision, but my interpretation, is it correct to say that, basically, the imprecision is actually randomly assigned to both groups and, therefore, when it looks like equivalent, that's a reasonable assumption?

DR. D'AGOSTINO: I kept pondering, you know, as we were going through the day, it's a double-blind study, but there's a seam on FC1.

DR. ZENILMAN: Um-hum.

DR. D'AGOSTINO: So they might know that. And that's probably the only thing that would bias it in favor of one versus the other, so it's probably a lot of randomness. But the trouble with this

statement that it's randomness in these non-inferiority sort of ruling out less than 2, the more randomness you have, the more likely it's going to go in this direction, you know --

DR. ZENILMAN: Right, right, right --

DR. D'AGOSTINO: If you're talking about superiority, then everything about randomness, if you still get superiority, you won the day, but if you get non-inferiority with a lot of randomness, it's just saying you may have had a very messy study, and that's my quandary.

DR. ZENILMAN: I'm struggling with the STI prevention issue.

UNIDENTIFIED FEMALE SPEAKER: Me, too.

UNIDENTIFIED MALE SPEAKER: Yeah.

DR. CEDARS: Well, but can we bring in the issue of the in vitro data because the in vitro data is fairly strong, and if the risk of --

UNIDENTIFIED MALE SPEAKER: Right.

DR. CEDARS: If the risk of either infection or pregnancy, because these are the two clinical outcomes in this question, if the risk of infection or pregnancy are -- if we agree that the substance is a barrier, then what I thought we were asking in Question 1 is, is the assumption that these

breakage/slippage, et cetera, failure rates --

DR. ZENILMAN: Would be surrogates --

DR. CEDARS: -- would be surrogates for that.

DR. ZENILMAN: Yeah, I think that's fair --

UNIDENTIFIED FEMALE SPEAKER: I think that's reasonable.

DR. CEDARS: Dr. Warner?

DR. WARNER: Well, I'm going to go the other way on that one because I think what this study says is that these two are similar on the types of problems that can occur when the condoms are used. It doesn't say how well the condom performs when it's used without these problems --

UNIDENTIFIED MALE SPEAKER: Right.

DR. WARNER: So I think you have to have -- does that --

DR. CEDARS: But that would be either from the in vitro data or a clinical study looking at those outcomes.

DR. WARNER: And you would have to use that data to supplement this answer is what I'm saying.

DR. CEDARS: So, in summary for the FDA, I think that there is some hesitancy because you've put the clinical outcomes into this question. There was

acceptance in Question 1 of the use of the surrogates of slippage and breakage rather than requiring a clinical study to look at outcomes of pregnancy and that, based on the data available to us, they would meet criteria for non-inferiority. There is still some hesitancy because you're then making a leap to effectiveness in terms of the two outcomes that you specifically ask us about, and so that requires the in vitro data and the assumption about FC1/FC2.

DR. PADIAN: Could I ask the group a quick question?

DR. CEDARS: Yeah.

DR. PADIAN: I'm just curious what you think about labeling with HIV with FC1.

UNIDENTIFIED MALE SPEAKER: Is that --

DR. PADIAN: Oh, I don't know. You had some -- yeah, I'll go for you.

UNIDENTIFIED MALE SPEAKER: I did have skepticism.

DR. PADIAN: Yeah.

DR. CEDARS: Well, the next question is specifically about labeling.

DR. PADIAN: Okay.

UNIDENTIFIED MALE SPEAKER: Okay.

DR. CEDARS: So if we can --

DR. PADIAN: Fair enough.

DR. CEDARS: I mean, I don't know that that's sort of a sum, but, Dr. Peterson?

DR. PETERSON: It's good that we're taking these in sequence, but when we get to the labeling, a lot of that's going to be related to the discussion we're having now and having trouble reaching closure on. And, as I understand it, the FDA, to approve the device, has to be able to say that there's reasonable assurance of safety and effectiveness for these outcomes. So if we can't get there, as I understand it, the FDA is hearing that we don't recommend approval.

And so part of the issue, I think, is going to come when we do look at the labeling because some of the discomfort is likely related to the lack of direct evidence for effectiveness during use. And we talked a little bit about history. So there was a time in our history where, for the male condom, we were inferring a lot based on the barrier protection properties in vitro and slippage and breakage rates. And then, ultimately, we had elegant and compelling studies in discordant couples with HIV infections. So we reached as close as we get to proof by any reasonable standard for effectiveness with consistent

correct use.

So we're not there with this device, clearly, and so I think a lot is going to come back to the labeling. And the question I think from the FDA is can we use the existing data on the FC1, which has some pregnancy prevention data, some STI --

UNIDENTIFIED FEMALE SPEAKER: But no HIV --

DR. PETERSON: No HIV. But has some data for pregnancy and sexually transmitted infections, and by induction, say, well, we think that there's sufficient data here for -- based on failure modes to say these devices are comparable and then infer the protection against pregnancy and STI. So I think that's why they probably walked us through each step. And then it might be that we can't get comfortable with three until we look at four and see what the bottom line is about what that leads to. But my understanding is that if we don't at least answer this question in the affirmative, that we're not recommending that it be approved. Is that correct?

DR. CEDARS: Well, I mean, that's a separate question. I mean, that motion hasn't been put to the Panel. These --

DR. PETERSON: Yeah, but I guess for the discussion now, we need to help us decide where we're

heading.

DR. D'AGOSTINO: I agree with what you just said, but let me make sure I'm understanding. I was under the impression that, and I may have misunderstood, but there was a feeling that if you do have a non-inferiority trial and it works on these particular -- breakage, slippage, and so forth, and it works on that, then the FDA has some comfort also saying that you can make -- you can infer it to the pregnancies and the STIs.

And the question before us, or the way I'm interpreting the question, are these confidence intervals tight enough or not including 2, or what have you, where we feel that even with all the faults in the study, these are still precise enough in showing that there's an equivalency. But once we say we thought there was an equivalency between them on these particular factors, then the rest has some sort of logic to it. Are we not dealing with that?

DR. PETERSON: Right. Yes.

DR. CEDARS: I mean, that's the way I understand it, yes.

DR. PADIAN: So then it's not on us to evaluate whether these are appropriate surrogates for those outcomes? It's just on us to evaluate whether

they're precise enough?

DR. CEDARS: Well, that's the point of Question 3. Question 1 was whether these were appropriate surrogates.

DR. PADIAN: Okay.

UNIDENTIFIED MALE SPEAKER: Yeah, exactly.

DR. CEDARS: So this just --

UNIDENTIFIED FEMALE SPEAKER: For pregnancy --

DR. CEDARS: -- whether having answered Question 1 affirmative, the question is, is the data presented and the numerical data, the statistical data, the confidence intervals, of such that we would accept that this is a successful non-inferiority trial.

DR. D'AGOSTINO: And just in terms of the answer I gave about if it's a sloppy study or lots of randomness, the intervals will tend to work in your favor in terms of saying they're equivalent, these are fairly tight --

UNIDENTIFIED FEMALE SPEAKER: They're pretty narrow.

DR. D'AGOSTINO: These are fairly tight intervals. So, you know, what usually happens that they're broad intervals. These are fairly tight

intervals. So even with the deficiencies, there's a lot of merit going on here.

DR. CEDARS: And so, then, I think in terms of the narrow question of whether or not this data shows non-inferiority, I think the answer would be yes to that narrow question. Are you comfortable with just our just addressing that narrow question and we'll go to the labeling, and then if you feel uncomfortable with that, we can come back, or do you want us to discuss that further?

DR. WHANG: So it sounds like you want to defer the issue as to whether this is reasonable assurance of safety and effectiveness for this proposed indication?

DR. CEDARS: For the two clinical outcomes.

DR. WHANG: Um-hum. Okay.

DR. CEDARS: Okay? The next, Question 4, has to do with labeling. And do we have a copy -- can you put up a copy of the current label for FC1? Oh, is it here? No, this is not it --

DR. STUBBLEFIELD: It's on the condom.

DR. CEDARS: Oh, it's on the packet.

DR. WHANG: I think it's on everybody's desk, or on the tables.

UNIDENTIFIED MALE SPEAKER: It's on FC1 --

DR. WHANG: It's this paper copy.

DR. CEDARS: So it's this, okay, because this is the one that has the four points that Mr. Pollard brought up earlier, which is:

"The latex condoms for men are highly effective at preventing STIs, including AIDS and HIV. If you are not going to use a latex male condom, you can use FC female condom to help protect yourself and your partner. FC female condom only works when you use it. Use it every time you have sex. Before you try FC female condom, be sure to read the directions and learn how to use it properly."

UNIDENTIFIED FEMALE SPEAKER: And then it says -- protects against --

DR. CEDARS: And then on the front, it says, "Intended to provide protection against pregnancy and STD, including AIDS/HIV infection.

So the question is, and this is for the current -- this is what's on FC1 currently. And so the proposal of the Sponsor was to keep the labeling the same for FC2. And so what information -- is there additional information that should be included in terms of failure modes, and then any other

comments regarding the labeling? Dr. Sharp?

DR. SHARP: I think there was also a question or a comment that there was going to be some instruction in terms of holding the outer ring in place, as to whether that ought to be on the label, and I think, I mean, I would certainly be in favor of that, to reduce the slippage and invagination.

DR. CEDARS: Dr. Katz?

DR. KATZ: Two things. On the front of this, it says the device is intended, not that it does prevent these adverse events, and on the back side it says to help protect yourself. It doesn't say it will protect you. It says it would help protect you.

DR. CEDARS: But I would wonder if a consumer would be savvy enough to get those subtleties.

DR. KATZ: Well, I think this gets into what are the requirements for specificity in the labeling of products, then. I mean, I don't find this labeling inconsistent with any of the uncertainties that we have debated today, you know, the biological uncertainties. It's just, you know, do we want to make -- I mean, we could certainly pose a more dire warning, but this isn't wrong.

DR. CEDARS: Dr. Peterson?

DR. PETERSON: Just as a point of clarification, could we ask the FDA, are we -- is re-labeling of the FC1 on the table now, or are we just talking about what in addition --

DR. CEDARS: No, this is labeling of the FC2 only.

DR. PETERSON: But we have to keep the FC1 labeling and add to it? Is that --

DR. CEDARS: No. The FC2 labeling could be -- the intent of the Sponsor was to keep the FC1 labeling. The labeling for FC2 I don't think has, other than the proposal, we're not sort of -- we don't have to keep that. We could recommend that that be modified. Dr. Mazzaro [sic]?

DR. MARRAZZO: It's Marrazzo.

DR. CEDARS: Marrazzo?

DR. MARRAZZO: That's correct.

DR. CEDARS: I keep getting my Z's and R's mixed up.

DR. MARRAZZO: No worries. So I guess I keep going back to the question I asked earlier about the original labeling and then the desire and impetus to do the Macaluso study and the results from that study not resulting in any change in the labeling,

and, to me, it's hard to imagine, again, as I think David said, why we -- how we could change the labeling based on that that labeling's been sustained on, you know, data that was supportive of those claims even though it's clearly not definitive.

I guess the question is whether there are concerning signals from the RHRU study that would mandate inclusion of some other cautions, that there might be things that women need to worry about because of these signals that we are sort of talking about, the invagination stuff primarily. And so I don't think with regard to the STI/HIV stuff and the pregnancy stuff there really should be any difference.

DR. CEDARS: Other comments? Dr. Gilliam?

DR. GILLIAM: Where does this come in? Does the patient receive this?

DR. CEDARS: Doctor --

DR. GILLIAM: They do?

DR. CEDARS: Yes, the patient receives --

DR. GILLIAM: Okay.

DR. CEDARS: -- this with the specimen [sic], with the --

(Laughter.)

DR. LEEPER: May I answer it?

DR. CEDARS: Can you answer that for us, please?

DR. GILLIAM: Yeah.

DR. LEEPER: Yes, sure, I'd be happy to. This is the official labeling, and, for instance, you go down to Rite Aid and you buy the female condom --

DR. GILLIAM: Right.

DR. LEEPER: They'll be in a box of five.

DR. GILLIAM: Oh, I see.

DR. LEEPER: There will be five female sachets in the box --

DR. GILLIAM: With this labeling --

DR. LEEPER: Along with this.

DR. GILLIAM: Okay.

DR. LEEPER: And I'd like to bring your attention to number five when you look at the instructions for use, and you can see that we are suggesting -- this issue about invagination has been the major failure mode, and we have from the get-go advised that the woman hold the device, the outer ring, to prevent that invagination.

DR. GILLIAM: Right, that was -- that was what my question was about. If they have this, and this says all of the other things we've --

DR. CEDARS: Thank you.

DR. GILLIAM: -- raised, do we need to put it on the outside of the packet.

DR. CEDARS: The comment about the holding that Dr. Sharp brought up --

DR. GILLIAM: Right --

DR. CEDARS: I would think -- well, that's open for discussion, but, I mean, I think we, you know, knowing that it's here, I wouldn't think that that would necessarily need to be on the outside of the packet --

DR. GILLIAM: Right.

DR. WHANG: Yeah. There may be some different, you know, families of information that you think should be on the paper insert that comes with each package as compared to the package labeling for the sealed package that, you know, the user opens every time and has a chance to read every time they're going to use the device.

DR. CEDARS: Ms. George?

MS. GEORGE: If I look at the package for the FC2, it does have the pictorials that do seem to line up with the numbers of the instructions as well, so it does seem to have some correlation. And I thought I heard them say they wanted to have this labeling on the packages as well because it was so

valuable to have it.

UNIDENTIFIED FEMALE SPEAKER: Right.

DR. CEDARS: So these pictures would be on it as well --

MS. GEORGE: Yeah. And then the second thing I wanted to point out is, is if you look at I guess it's the kind of the -- from the front, there's a section that actually talks about how it was tested and does mention things about the sexually transmitted diseases, as well as AIDS, how it was or was not tested, and it also talks about the whole pregnancy aspect. And if you look in the precautions, the very first item basically says if you don't use this, you're at a higher risk. It doesn't say that it prevents it. So --

DR. CEDARS: I think that's helpful, thank you, that the pictures are on the outside of the FC2 package labeling, but it also no longer has the four points that the FDA had talked about, which is to use -- the choice, the first choice should be a male condom.

MS. GEORGE: I think this is because --

DR. LEEPER: No --

MS. GEORGE: -- that's the European, non-U.S. version right now. They hadn't had -- they

wouldn't have the labeling for U.S. requirements on here yet.

DR. LEEPER: In your Panel pack -- sorry. In the Panel pack, we did lay out for you how we would put the pictures as well as the four key points on the sachet itself.

DR. CEDARS: Thank you.

DR. LEEPER: You're welcome.

DR. CEDARS: Dr. Hillard?

DR. HILLARD: My concern about looking at the pictures is that I can hardly see them. So this says to me it's designed --

DR. CEDARS: For young women --

DR. HILLARD: -- for young women and not --

(Laughter.)

DR. HILLARD: Maybe not menopausal women.

DR. CEDARS: Any other comment? Yes, Dr. Whang?

DR. WHANG: Can I bring your attention to Part A of the question here, and, in particular, the portion of the paper insert labeling that Ms. George highlighted, you know? It's common, you know, in their clinical study supporting a device that the labeling would include some description of the clinical study that demonstrate the safety and

effectiveness of this device. And you can see the information that's been used with FC1. So we would like the Panel's input as to whether there should be additional specific information about the failure modes study or not.

UNIDENTIFIED FEMALE SPEAKER: Can you direct us to where that is on this?

DR. WHANG: Yeah, if you look at the side that has the pink numbers, one, two, three, four, five, up to seven --

UNIDENTIFIED FEMALE SPEAKER: Um-hum.

DR. WHANG: On the left most panel, there's a precaution, and then the second panel, it says how FC female condom was tested.

UNIDENTIFIED FEMALE SPEAKER: Okay.

DR. WHANG: And then there it has the pregnancy rates and such.

DR. CEDARS: So the question the FDA is asking is, is if the information regarding breakage, misdirection, invagination, and slippage should be incorporated into that sheet, right? So, okay, so, thank you. So you're asking in Question A if the specifics, the percent occurrence, or the likelihood for each of the individual failure rates should be included in here?

DR. WHANG: Correct.

DR. CEDARS: So should there be a total? Should they each be included individually? Are there comments or thoughts from the Panel?

DR. MARRAZZO: Well, for it to be accurate, you'd have to have a complete methodologic description of how those things were assessed, which would be really challenging. I mean, not really complete, and I'm being a little facetious, but given the concerns about the accuracy of defining those outcomes, I think it could be tough. It would be a wide range for each of them.

DR. HILLARD: I think we're --

DR. CEDARS: Dr. Hillard?

DR. HILLARD: We're confused by this nomenclature. If you take many of our patients, they would be tremendously confused by it.

DR. CEDARS: What about a total failure rate? I mean, what does it say it -- or not failure rate, but --

DR. MARRAZZO: Failure mode rate.

UNIDENTIFIED FEMALE SPEAKER: Failure mode, failure mode --

DR. CEDARS: Failure mode rate. Not failure rate in terms of conception, but failure --

improper use of the -- yeah, something about -- would that -- so you wouldn't have to say specifically slippage, which might be nothing, likely would mean nothing to the consumer. But if you said, you know, even, you know, since one of the comments is that you should use it with every sex act, risk for improper use, or something, I mean. Would that be important, does anyone think? Dr. Thomas?

DR. THOMAS: I think that the, especially under Figure H in the information above, it just tells people to stop if they feel that things aren't proper with the use of the device. I think it would be very confusing. I mean, we spent a large portion of our day talking about the differences between slip-in, slip-off, clap-on, clap-off.

(Laughter.)

DR. THOMAS: I think because of that, I think this is probably more than enough without bringing in another element of confusion.

DR. CEDARS: Dr. Gilliam and then Dr. Zenilman.

DR. GILLIAM: Since from the data that we have it doesn't seem as if FC2 is different than FC1, I'm not sure why we would introduce new labeling in terms of slippage mode. And just wearing my clinical

hat, my bias is to scare people less about contraception because at the end of the day, that's the biggest issue is that --

DR. CEDARS: Anything is better than nothing.

UNIDENTIFIED MALE SPEAKER: Right.

DR. GILLIAM: People say, oh, I'm not going to use it because this is going to happen.

DR. CEDARS: Dr. Zenilman?

DR. ZENILMAN: Yeah, I want to echo Melissa's points, which I agree. But, also, I had some concerns because this is phrased very carefully. And the website, though, says, if you go to the home page of the company, they said the FC female condom has high acceptability among both men and women in many countries and provides dual protection against the transmission of STIs, including HIV/AIDS, and unintended pregnancy, which is a much stronger statement.

DR. CEDARS: Unfortunately, we don't have control over the website --

DR. ZENILMAN: Okay.

DR. CEDARS: Just what's in front of us. Dr. Marrazzo?

DR. MARRAZZO: Yeah, sorry, I just wanted

to point out that there is actually a fairly extensive section, problem using female condom. I mean, they actually --

DR. CEDARS: Right.

DR. MARRAZZO: -- talk about some women have reported problems. One of the problems is the outer ring can be pushed inside. Some have reported penis slipped to the side, other problems, difficulty, yada, yada, yada. So, to me, if anything, there are -- to my mind, this is adequate, and I would not feel compelled to expand on it.

DR. CEDARS: Yeah, I don't think, to just clarify, I don't the FDA was specifically asking or stating we should, but it was more of a question. So I think those points are well taken. Dr. Padian, and then we can wrap this up.

DR. PADIAN: Okay. But maybe this is completely obvious. It is going to say, however, how this was tested, right, which was this was tested for whatever -- in comparison to FC1? It's not going to just lift the FC1 data, knowing that they are comparable, then use those data, right?

DR. WHANG: We can take that as your recommendation.

DR. PADIAN: Well, I think you have to be

truthful about --

DR. WHANG: That's certainly, yes --

DR. PADIAN: -- about what was done.

DR. CEDARS: Well, I mean, so you're talking about a statement that because this talks about pregnancy outcome that FC2 has not -- there's no clinical data available but was found to have a similar failure rate --

DR. PADIAN: Well, I don't know that you need to say it that way. Maybe you can say that through lab -- I'm not wordsmithing, but it's comparable to FC1, which was, and then what was shown with FC1, something like that.

DR. WHANG: We could follow up on that sort of concept.

DR. PADIAN: Okay.

DR. CEDARS: Okay. So I think the consensus is that no real change in labeling over what is currently in place. So, given that, does anyone want to go back to Question 3 just briefly, and are we comfortable given the data that we have, given the FC1 data, given our comments regarding Question 1 and Question 2, how comfortable are we with the conclusion of safety and effectiveness barrier protection against pregnancy and STI?

DR. STUBBLEFIELD: Enough.

DR. CEDARS: Enough? Yes?

UNIDENTIFIED FEMALE SPEAKER: Good enough, I'd say.

UNIDENTIFIED FEMALE SPEAKER: Yeah, good enough.

DR. CEDARS: Some dis-ease, but good enough?

UNIDENTIFIED FEMALE SPEAKER: Good enough.

UNIDENTIFIED FEMALE SPEAKER: Well, I have dis-ease with male condom also.

DR. CEDARS: Okay. Question 5 has to do with the postmarket plan, proposing postmarket approval requirements, including quality release, corrections, removals, and this lists the standard postmarket expectations of the FDA. And so the question is, is there anything else that you would request of the Sponsor postmarket other than the standard reporting requirements. Hearing none, then I would suggest the answer to that -- Dr. Stubblefield?

DR. STUBBLEFIELD: I wouldn't request it --

DR. CEDARS: I'm sorry?

DR. STUBBLEFIELD: I wouldn't request it, but I would hope that what might happen is what

happened after FC1; the FDA director might twist the arm over at the NIH to get them to spend some money in this direction.

DR. CEDARS: We can certainly share that with the FDA -- let them share that with NIH.

DR. STUBBLEFIELD: Christmas gift.

DR. CEDARS: Okay. What I would like to do is take -- oh, I'm sorry, Dr. Peterson?

DR. PETERSON: Just following up on that point, because I would concur that we don't want to ask the Sponsor to be responsible for that. I think that it's almost now, speak or forever hold our peace on the female condom effectiveness, and that what we have, having been involved with the CDC and WHO studies, whether they'll be without some -- further studies on the effectiveness of the female condom, now the FC2, is unclear. So what we've got is assumptions on assumptions on assumptions on assumptions. And the question is, will we ever see the train get to the other end. And I think there is a serious reason to question whether that will ever happen.

DR. CEDARS: But I think we can't really recommend a postmarket study that would be another --

DR. PETERSON: Right, right, right.

DR. CEDARS: I mean, we can't --

DR. PETERSON: And that's why I wanted to say from the outset that I'm not recommending that, but I do think that Phil's point is very important. And if the rest of the group concurs that there be some sentiment expressed that further studies for the public good would be helpful.

DR. CEDARS: Dr. Marrazzo, did you --

DR. MARRAZZO: Yeah, I don't want to belabor the point. I just want to say there are plenty of interventions that compliant, and consistent uptake depend on patient preference and willingness to adopt the intervention. And so there's a lot of precedent for doing studies where it is not the perfect, wholly, triply blessed randomized double-blind trial where you do -- you know, people know what they want. They take that and you go with that, and that might be something that we need to think about in terms of really studying this. So it's doable. It's just challenging, and no one knows that better than many of the people on the Panel.

DR. CEDARS: Dr. Hillard for the final comment for this.

DR. HILLARD: Just very briefly to add on

to Dr. Stubblefield's comment in terms of any studies that would be done in the future. I think some of us have made these comments to the FDA in the past. But in terms of the individuals who are included in studies, I would make a plea to include adolescents and other groups that are not traditionally studied in the studies that we've seen in the past.

DR. CEDARS: Thank you. So we will end the discussion here. We will take a ten-minute break and then return for the second open public hearing. So return at 4:00.

(Off the record.)

(On the record.)

DR. CEDARS: 4:00, and we're now going to resume the meeting, and we'll now proceed with the second open public hearing. Prior to the meeting, we received formal requests to speak during today's open public sessions. Our first speaker is Dr. Diana Zuckerman, if you'd please come forward to the microphone. And, again, if I could remind the speakers this afternoon, as stated earlier this morning, if you would let us know your name and your affiliation and any potential conflicts of interest.

MS. ALLINA: Is this where you want me, or you're pointing you want me somewhere else?

DR. CEDARS: No, right there, perfect.

MS. ALLINA: Okay. So I'm not Diana Zuckerman. I'm Amy Allina, but Diana was -- had a medical emergency that made it impossible for her to come speak, and I'm just going to make a very brief statement on her behalf.

So Diana is the president of the National Research Center for Women and Families. The center does not accept financial support from pharmaceutical companies or medical device manufacturers and has no conflicts of interest with the matters before the Committee today. And in the interest of time and because the Committee has had such a full discussion at this point, I'm just going to say that Diana was recommending that the Committee, was urging that the Committee recommend approval. And she really agreed with many of the points that the Committee discussed regarding the data, both in terms of what some of the concerns are but also how to put those concerns in context of the decisions before you today.

So her summary was that she believes the data are persuasive that the new female condom is comparable to the previously approved female condom in terms of safety and effectiveness and that this product is greatly needed and has the potential to

save lives. And she urged the Advisory Panel to recommend the FDA to approve the new female condom.

DR. CEDARS: Thank you very much. The next speaker is Jeff Spieler.

MR. SPIELER: Thank you. I'm Jeff Spieler. I am from USAID. I'm the Senior Technical Advisor for Science and Technology in Population and Reproductive Health. I have no financial interests or gain from this company, no conflict of interest. My colleague, Mark Rilling, spoke this morning. And our only relationship with the company is that we buy their product right now. So USAID is purchasing their product, which you heard this morning.

And I'm the person that Mary Ann Leeper referred to as the one who said you better make it cheaper and we need a less expensive product. And I'm here because of what Colin Pollard told the group, and that is that we're about public health impact, and the international perspective in this product is particularly important, and that's the perspective that I represent. And I have 40 years of work in reproductive health. I started when the mouse was invented I found out yesterday. And I've had a lot of work with WHO, I work there, and I continue to advise there, including advice on female

condoms.

USAID has supported research on female condoms since the beginning of the female condom and we supported the pivotal study that result -- through FHI and CONRAD that resulted in the PMA for FC1 Reality. And we did that not because we thought it was a blockbuster in the United States, but we did it for the greater public good, and it also would permit USAID, who at the time would only by products that were approved by the FDA, by policy not by law, and we wanted it approved so that we could consider purchasing it.

And I should tell you that in the early years, from '93 to '97, we bought female condoms primarily for research. We weren't buying them to supply our field missions and programs. And we set up a research agenda, and we had critical questions that we wanted answered. And it wasn't until about -- and we were answering some of those questions. And a lot of them had to do with targeting and use and appropriate use. And while we didn't answer all those questions, we changed our mind about providing the product before all the answers to the research were in because of the pandemic, because we felt there was a great need for

that product. And we started providing female condoms in larger volumes starting around 2004. And you heard from Mark that we're now buying 8 to 10 million, and globally, there's about 140 million of them that have been sold so far.

The Reproductive Health and Research Unit in Johannesburg and Durban I know quite well. I was involved in doing a visioning exercise for them in 1999 and 2000. I visited Mags' facility. And I can tell you that their reputation for research, particularly the Durban group, is stellar. While we may have some problems with data, and I can tell you I've never met a study that I couldn't analyze and find some fault with, and while there are some faults, I think you've done a marvelous job in your discussions today addressing some of the issues and not necessarily letting those issue interfere with your discussion on how to answer those questions.

One of the things that I feel relatively strongly about is that when we do research on the female condom, when we did the reality trial, we actually studied that product in the totally wrong population. Why? Because they couldn't be at risk of STIs, it was a contraceptive trial, and the people who were in that study aren't the people who would

really be out there wanting to buy that product. While it can be used for dual purpose and it is, when used correctly and consistently, is highly effective for both contraception and I think for HIV, for STI prevention, the average kind of user would be more like the users that we saw in Durban.

Commercial sex workers. We're trying to target this product for the people who need it the most. That's commercial sex workers and bridge populations. And we want to have those people in our clinical trials. And, in fact, the Reproductive Health Drugs Division insists that now there be a broad range of the kinds of clients and trials that represent the people who would really use it. So I'm pleased with what you decided that another pivotal clinical trial was not necessary for approval of this PMA because if it were, what would that population look like? And it would look like a very different population than those who would actually be using it, and I don't think you would have -- as you said, you would not have gotten very important information from that trial that would change your decisions.

I really adjusted what I was going to say based on the fact of what I heard today. And I just wanted the prerogative of speaking in the event that

I was a little uncomfortable. But I think your decisions have really been very thoughtful.

I wanted to say that I'm really pleased that Colin brought this to the Panel because he told us that the PMA doesn't fit the current paradigm. And I was really pleased to hear that just because you make a decision that this product in that class doesn't need a contraceptive trial doesn't necessarily mean that all products in that class would get that by. I think it's a very wise choice.

And I want to talk a little bit about biological plausibility, something that we talked about all the time when we don't get results like we would like to have. People don't always behave in the manner which gives us the kind of results we would like to have. And the biological plausibility for the male condom to be highly effective against secretion-based STDs was part of the reason why we did so much more research after our 2000 meeting because, at that time, if you remember, all we could say was effective for HIV and gonorrhea in men, when all of us said it's crazy. If you use it and it's a good barrier, it's got to be effective in preventing gonorrhea in women, chlamydia and gonorrhea in women. And we went on to do more studies.

So we need more studies. Who is going to fund them is another issue. I think we would like to have, and I'm glad that you spoke to that, but I think the biological plausibility for the strength and the continuity of the product, that if people use it correctly and consistently, it will provide a high degree of protection.

From a personal point of view, I've tried just about every method I've ever worked on excepting female sterilization. My wife has been a willing, sometimes not so willing, compliant spouse in trying the things that I've worked on. So as soon as we had the female condom, we were using it. I had a pipe dream, and Lee knows this very well, that I wanted to work on inventing a male condom and work with condom manufacturers that made sex better with it than without. It would then be an easy sell. And I think -- I'm not very successful in doing that, but what comes closest to it is the male use of the female condom. And I can tell you right now that if I had to be a condom user, I would prefer to use a female condom with me donning it because I can tell you that with me donning it, I can insert it, and it stays in place after it's been inserted, and it is a much more pleasurable product, as far as I'm

concerned. And that sample of one, I think, anecdotally, is a sample of many.

So it's a highly --

DR. CEDARS: So if you could just sum up please?

MR. SPIELER: Okay. I will sum up. So for USAID and for the world to be able to take full advantage of the Female Condom 2 and the reduction in cost --

UNIDENTIFIED MALE SPEAKER: I think you're being paged. You're being paged.

MR. SPIELER: That's okay. Cut that part from the tape. The reduction in cost, which I understand there's break points, if we could actually -- if they could actually be selling 120 million units in a year, we might get it down to 25 cents. That cost reduction will result in a geometric, not an arithmetic, increase in the use because the price is actually a major factor. It ought not be, but it is. So a lower cost product will result in much more public health benefit, much more protected acts of sex, primarily for prevention of HIV and STIs. Thank you.

DR. CEDARS: Okay. And if I can just remind the Panel that cost is not an issue in your

final decision. The next speaker is Anna Forbes.

MS. FORBES: Hi. I was worried about bringing a personal perspective to my statement until I heard Jeff. Not worried anymore.

(Laughter.)

MS. FORBES: I'm the deputy director for the Global Campaign for Microbicides. We're a broad-based international coalition of organizations working to accelerate access to new prevention options especially for women. We do not fund or develop any products nor do we receive any corporate funding. We are simply advocates working with -- in collaboration with hundreds of NGOs worldwide.

I have cut out most of my statement because, A, I think you've heard it all already and, B, I think that you have reached very wise conclusions and don't need to hear it. But I did want to share this one piece with you. I had the very good fortune to travel through four countries in Eastern Africa earlier this year and meet with the staff of 27 NGOs in the region. And we heard over and over there that while there are acceptability issues around the female condom, these are far outweighed by the unmet demand for them in the region.

People have had limited experience with this prevention tool in the region as a result of the first acceptability trials that were done there in the 1990s. But after those acceptability trials were over, female condoms in many, many areas basically just disappeared and since then have been consistently either unavailable or unaffordable to women and to the NGOs who serve them. The NGO staff we met with told us that there are many women who want to use the female condom but either can't find it on the shelves or can't find it at a price they can afford even when it is there.

Let's see. Your decision to approve the FC2 condom offers us one important additional advantage that has been discussed somewhat today but not a whole lot. There's a general consensus, I think, in the field that insufficient introductory work actually went -- combined with provider bias really inhibited uptake of the FC1 when it first appeared in the 1990s, certainly in the U.S. and Europe and also probably in other areas of the world. So the introduction of the FC2 on the market, if we're able to do that, provides an opportunity to sort of reintroduce the female condom as a method of contraception and HIV prevention and promote the next

generation version of that as a product that may address some of the acceptability problems identified with the FC1. And we all know from watching television in the evening, or whatever, that there's nothing that the market likes better than new or better, more improved.

So I think that we will have an opportunity, if we make good use of it this time, especially in the developing world where the rates of HIV are so high, to present the product in a new light, to present it to broader audiences, to really focus attention on it and clarify misconceptions that may exist around it. And with all due respect to all of my colleagues here, I don't necessarily see it as something that's just for use by sex workers or even primarily for sex workers. We heard a great deal of interest in it expressed among women, particularly among women who are not sure what their partner's HIV status is and who may not have the power in their relationship to insist that he have an HIV test, women who really want to protect themselves who may have no other risk than their married partner, or their long-term partner, but know that they need something just in case.

I heard a wonderful expression by one

Rwandan woman we were working with who said, "Just tell him if you don't put on yours, I'll put on mine."

I also heard a very sad story from another Rwandan service provider who pointed out to me that she was doing presentations on the female condom in her population that she served, even though she had never seen one herself. She thought that the possibility of it was so important that people needed to know about it. But she had no access to them.

We heard other stories of educators who showed the two or three female condoms they had, again, because they thought that the people they served deserved to know that this existed. But when people asked them afterwards if they could have that female condom, they had to say, "No, this is the only one we have. We can't get it to you."

So anything that increases supply I think will be very, very welcome. I want to close with the words of a colleague, Lucas Maquizu (ph.), whom I met in Tanzania. In Tanzania, in the hardest hit areas of Tanzania, the rate of HIV infection among women of reproductive age goes as high as 24 percent. We asked Mr. Maquizu, among other things, how he thought that the men he worked with would feel about

increased access to female condoms because some people had raised the concern of, oh, our men won't like it, we can't use it. He said most families have been affected by HIV. People want to avoid death. So there is a possibility of change of attitude. But there must be education and access going together.

Mr. Maquizu's organization and dozens of others like it very much want to have male -- female as well as male condoms to distribute into the communities they serve. They are ready and willing to do the education and promotion, but they need help getting the female condom into their hands. So I congratulate you on your deliberations today. I was very gratified to hear some of your conclusions. And the Global Campaign for Microbicides and our many partners thank you for your efforts.

DR. CEDARS: Thank you. Does someone have questions for -- no? And the final speaker for the second public open hearing is Beth Jordan.

DR. JORDAN: Good afternoon. My name is Beth Jordan. I am an internist formally of the Mayo Clinic, and I currently serve as the medical director of the Association of Reproductive Health Professionals, ARHP.

For nearly 50 years, ARHP has established

itself as the leading source of trusted medical education and information on reproductive and sexual health matters. We advocate for evidence-based clinical education, provider training, and patient counseling to ensure the best quality patient care and healthcare outcomes. Our membership is composed of 11,000 professionals who provide reproductive health services or education, conduct research, or influence reproductive health policy.

Because everyone's needs are unique and different, ARHP supports the availability of as many safe and effective contraceptive methods as possible. We believe this is of critical importance for good healthcare globally. I am here to express ARHP's support for any and all safe and effective contraceptive methods for the prevention of pregnancy as well as STIs, including HIV/AIDS. ARHP is pleased at the potential for a new and more cost-effective version of the female condom.

The female condom offers numerous benefits. Its use does not rely on the assistance of a healthcare provider. It is immediately reversible and has few or no side effects. Like any contraceptive method, with solid education from a healthcare provider or another trusted source, a

female condom can be used very effectively. Because it remains the only female-controlled HIV prevention tool, women who cannot negotiate condom use with their male partners will especially benefit from the availability of a female condom.

Making new safe and effective contraceptive technologies available and prioritizing provider training and patient education on these methods is paramount in helping women and men plan their families. Because everyone's contraceptive needs are unique, we support the availability of all safe and effective options. Thank you.

DR. CEDARS: Thank you. Are there any questions for Dr. Jordan?

(No response.)

DR. CEDARS: If not, then it is time to close the open public hearing, and we'll now proceed to the FDA and Sponsor summaries. Are there any further comments or clarifications from the FDA?

DR. WHANG: No.

DR. CEDARS: If not, is there any further comment or clarification from the Sponsor?

DR. LEEPER: I was going to summarize what we've just been talking about for eight hours, and I don't think that that's necessary except first to

tell you that FC1 has been on the market for 16 years, and it does a good job. It offers a good option for women. We have not, in the 16 years, we have 60 -- total complete total -- 63 comments that we have gotten in terms of side effects. Sixty-three in 16 years. And the majority, 90 some percent of them are minor irritation. So I think that's an important piece for you to go back and think about, you know? FDA agrees, you know, FC2 is comparable, is non -- has been found non-inferior to FC1, and I want you to feel comfortable about FC1.

And now I want to thank FDA for the hard work that they have done to evaluate our data and spend the time that they have spent working. Elaine and I, back and forth, questions, scrubbing the data, and trying to probe all of the aspects of the data, and I think we have had a very successful and productive experience over the last three years in doing that. And I want to thank you all for the time that you've spent in reviewing that Panel pack, not a easy job, and probing the issues and discussing them this afternoon and this morning. And so thank you all very much. And I'll be eager to hear what happens next. Thanks.

DR. CEDARS: Thank you. We are now ready

to vote on the Panel's recommendation to the FDA for this PMA. And Dr. Bailey will now read the Panel recommendation options for a premarket approval application. Dr. Bailey?

DR. BAILEY: The medical device amendments to the Federal Food, Drug and Cosmetic Act, as amended by the Safe Medical Devices Act of 1990, allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on designated medical device premarket approval applications that are filed with the Agency. The PMA must stand on its own merits, and a recommendation must be supported by safety and effectiveness data in the application or by applicable, publicly available information.

The definitions of safety, effectiveness, and valid scientific evidence are as follows:

Safety: There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks.

Effectiveness: There is reasonable

assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.

Valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of safety and effectiveness of a device under its conditions of use. Isolated case reports, random experience, reports lacking sufficient detail to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.

Your recommendation options for the vote are as follows:

Approval: If there are no conditions

attached.

Approvable with conditions: The Panel may recommend that the PMA be found approvable subject to specified conditions, such as physician or patient education, labeling changes, or a further analysis of existing data. Prior to voting, all of the conditions should be discussed by the Panel

Not approvable: The Panel may recommend that the PMA is not approvable if the data do not provide a reasonable assurance that the device is safe or the data do not provide a reasonable assurance that the device is effective under the conditions prescribed, recommended, or suggested in the proposed labeling.

Following the voting, the Chair will ask each Panel member to present a brief statement outlining the reason for his or her vote.

Dr. Cedars?

DR. CEDARS: Are there any questions from the Panel regarding these voting options before I ask for a motion?

(No response.)

DR. CEDARS: Seeing none, do I have a motion regarding the approvability of this PMA? Dr. Peterson?

DR. PETERSON: Motion for approval.

DR. CEDARS: Is there a second? Dr. Hillard? So this motion has now been first -- we've now had a first and a second on the motion of approvability. Is there any discussion regarding this motion? Dr. Davis?

DR. DAVIS: We earlier discussed the concept that if you don't speak now, you may forever not be heard, and although we discussed it briefly, if there -- and maybe this isn't an addendum to it, but I do feel strongly that it would really be nice to encourage the NIH/HIV section to consider studies on the female condom. And I don't know how we make that recommendation. But, I mean, this is something if we will never really get the eloquent data that we got on the male condoms if we don't encourage that. And if there is a way to -- we have to formally say that, that we strongly recommend that they consider or is that just an informal thing that -- recommendations.

DR. CEDARS: Well, a conditional approval is a different motion than approvable.

DR. DAVIS: Okay.

DR. CEDARS: And the kinds of statements that you're making would not be something that would

be returned to the Sponsor.

DR. DAVIS: Okay.

DR. CEDARS: So whether or not that's information that the FDA can take to the NIH, it's not something that we can add on to the process --

DR. DAVIS: Okay. All right. But as a group I think --

DR. CEDARS: It's been stated by several people.

DR. DAVIS: Yes.

DR. CEDARS: And I think that there is general interest that the FDA take this to the NIH as an important area for study.

DR. WHANG: Yes, we can do that.

DR. CEDARS: Thank you. Any further discussion?

DR. WARNER: I had one question.

DR. CEDARS: Dr. Warner?

DR. WARNER: Is the question whether we're approving as is with the current labeling as is?

DR. CEDARS: If this is approvable without conditions, then, yes, it's labeling as is. If there was a choice to change the labeling, then we would have -- it would be approvable with conditions. So the motion on the table is for approvable with no

conditions. Dr. Padian?

DR. PADIAN: Then I'm a little confused because I thought we had a little discussion that you at least have to be honest about how this was tested.

DR. WARNER: Exactly.

DR. PADIAN: And you seemed to say that that was fine and you would do that. So now do we have to build that into the approval?

DR. CEDARS: Well, what you would say then is that if you wanted to change the labeling, then this would be not -- this would be approvable with conditions, which would be -- so you would vote this motion down if that was what you wanted. This is approvable with no conditions.

DR. PADIAN: But then you would be saying this was tested in a way that it wasn't tested because --

DR. CEDARS: Right. But you can choose not -- you can not support this motion.

DR. PADIAN: Okay. Well, then I guess I actually would support it with being honest about the labeling.

DR. CEDARS: Okay. But that right now is not the motion.

DR. PADIAN: Okay. Sorry.

DR. CEDARS: So that may be -- so we will vote on the motion for approvable --

DR. PADIAN: With no changes whatsoever.

DR. CEDARS: With no changes whatsoever, which is the motion that's on the table. So are there other --

DR. STUBBLEFIELD: Can I just --

DR. CEDARS: Dr. Stubblefield?

DR. STUBBLEFIELD: Just clarify the existing pamphlet is going to be used with --

DR. CEDARS: Correct.

DR. STUBBLEFIELD: -- FC2?

DR. CEDARS: Correct.

DR. STUBBLEFIELD: Which has the labeling as done for FC1. That's going to carry forward. And we discussed the fact that the instructions deal with most of the concerns that might lead to a failure?

DR. CEDARS: Correct.

DR. STUBBLEFIELD: And that's given that that's going to happen. So we don't need to specify that.

DR. CEDARS: Well, that's part of the discussion is whether or not there is an issue about the labeling.

DR. PADIAN: No, sorry. I think I might have confused things. In the bit here where it says how the female condom was tested, is that considered part of the labeling?

DR. CEDARS: This is patient labeling --

DR. STUBBLEFIELD: Yes.

DR. CEDARS: This is patient information, yes?

DR. PADIAN: Oh.

DR. CEDARS: Okay. Dr. Warner, did you have a comment about this?

DR. WARNER: So this is part of the labeling?

DR. CEDARS: Yes.

DR. WARNER: So if we wanted to have a clarification on what was tested that lead to these results, it would have to be --

DR. PADIAN: Changed.

DR. WARNER: -- changed, right.

DR. CEDARS: Any further discussion on this motion?

(No response.)

DR. CEDARS: So we've had a first and a second for a motion for approvable. And if I could ask the voting members who concur with the statement

that the PMA is approvable, if I could ask for a show of hands for those who support this motion. Dr. Peterson?

DR. PETERSON: I would be willing to withdraw the motion with the clarification so that we don't have to go through that process if you're agreeable.

DR. CEDARS: Then the second would also have to agree.

DR. HILLARD: I'm fine with that.

DR. CEDARS: Okay. So the motion has been withdrawn. Do we have another motion?

DR. PADIAN: I'm going to say it wrong.

DR. CEDARS: Dr. Padian?

DR. PADIAN: I'm not going to use --

DR. CEDARS: Approvable with conditions?

DR. PADIAN: Yes, thank you.

DR. CEDARS: Do we have a second?

DR. DAVIS: Second.

DR. CEDARS: Dr. Davis. So we have a first and a second approvable with conditions. So we go to -- we need to discuss the conditions. So does anyone want to recommend a condition. Dr. Davis?

DR. DAVIS: We need to change the wording on the labeling that says the FC condom was only

tested in humans for its ability to prevent pregnancy because this one wasn't. So change it to reflect what the studies were. Do we have to be specific what we want it today? All right.

UNIDENTIFIED MALE SPEAKER: Well, the concept.

DR. CEDARS: The concept.

DR. WHANG: Yes.

DR. CEDARS: So that the FDA -- so is the concept, do you want it to say that F --

DR. DAVIS: To be --

DR. CEDARS: I'm sorry. Go ahead, tell me what --

DR. DAVIS: Want it to be truthful that this condom was not tested but its predecessor was, or something like that.

DR. CEDARS: Is that sufficient information for you to address?

DR. WHANG: Yes.

DR. PADIAN: And you could say that it was deemed -- I don't want to say it confusing in a way the public would understand it, to be non-inferior to one that was tested, something to that effect.

UNIDENTIFIED FEMALE SPEAKER: Yes, absolutely.

DR. CEDARS: And is there a second to that condition? Dr. Katz? Any further discussion about that condition, that there be a change in labeling that acknowledged that the FC1 was tested but not the FC2, and we'll leave to the FDA that change? Any further discussion?

(No response.)

DR. CEDARS: Then if we can vote on that condition, we'll have a vote on that condition. If I can have a show of hands all in favor of the condition that the labeling may change to reflect that only FC1 was tested. So Dr. Hillard, Dr. Warner, Dr. Davis, Dr. Katz, Dr. Thomas, Dr. D'Agostino, Dr. Padian, Dr. Sharp, Dr. Ramin, Dr. Stubblefield, Dr. Zenilman, Dr. Gilliam, Dr. Marrazzo, and Dr. Peterson. So since that was all of the Committee members, then that condition passes. Are there any other conditions?

(No response.)

DR. CEDARS: A motion for additional conditions?

(No response.)

DR. CEDARS: If not, then we would move to a second vote, which is a vote approvable with conditions or a motion -- or no, I think we go

straight to the vote.

UNIDENTIFIED MALE SPEAKER: Page 21.

DR. CEDARS: Yeah. It's been moved and seconded that the Female Health Company PMA application P08002 for FC2 Female Condom be approved with one condition about which the Panel has just voted. We will now take a vote on the main motion, which is approvable with conditions, and with a show of hands, please indicate if you concur with the recommendation that the above named PMA be approvable with conditions. So, again, if I can ask everyone who supports the motion that this is approvable with a single condition about a change in labeling -- show of hands? Dr. Peterson -- okay -- this --

DR. DAVIS: Can I ask a point of clarification?

DR. CEDARS: Certainly.

DR. DAVIS: Does this include the outside labeling that was mentioned earlier about number five was mentioned that should that be on the outside label, about making sure that the outer ring was properly placed, because that was recommended by the study, as I understood it.

DR. CEDARS: But I think that we discussed that it was actually already in here in the

instructions --

DR. DAVIS: But can we also ask --

DR. CEDARS: -- and that the pictures were --

DR. DAVIS: Okay. So we don't want it on the outside of this? Okay.

DR. CEDARS: You can make a motion if you --

DR. DAVIS: No, I'm just asking.

UNIDENTIFIED FEMALE SPEAKER: We have a motion on the floor so --

DR. DAVIS: Okay. Yeah.

DR. CEDARS: So the motion on the floor is for approval with the single condition for the change in labeling regarding what was tested, FC1 versus FC2. Can I see a show of hands for all of those who concur with that motion? And that is unanimous.

It is recommended by the Panel to the FDA that the Female Health Condom PMA application P08002 for the FC2 Female Condom be approved with the previously voted upon one condition. I will now ask each Panel member to state the reason for his or her voting. If we can start with Dr. Peterson.

DR. PETERSON: Well, we had evidence to address the comparability of the FC2 to the FC1 in

addition to the in vitro testing of the bearer properties and the integrity of the material per se. We had a clinical study that looked at failure modes as an endpoint. There have been some questions about the methodology. I think it was said that every study can be criticized. I actually think this was -- study had substantial methodologic strengths and balance that it showed that the FC2 is not inferior to the FC1.

DR. CEDARS: Thank you. Dr. Marrazzo?

DR. MARRAZZO: I would say that the data aren't perfect, but consistent trends support that FC1 probably does protect against some unintended pregnancy, STDs and HIV, and that the failure study that we discussed today as the pivotal trial was really generally consistent in supporting that those two condoms are equivalent. And then, finally, that the need is just very great for women to have a female-controlled method and an additive way to protect themselves and that the benefits far outweigh the risks in my estimation.

DR. CEDARS: Dr. Gilliam?

DR. GILLIAM: I would agree. I think the in vitro data are very strong. I think the clinical data are -- there are some difficult aspects to it,

but, overall, I think the study has many, many strong elements and is a very difficult study to do. And so I think while we have questions and questions about some of the quality of the coital logs, I also congratulate the investigators on research in this population and providing important data. And, overall, I think the risks are greatly outweighed by the benefits.

DR. CEDARS: Dr. Zenilman?

DR. ZENILMAN: I take a more narrow approach. I think the condom is actually very -- the FC2 is very comparable in terms of physical properties to the FC1. And I also agree that the side effect profile is actually very favorable. I still have some issue with the STI efficacy studies that were presented, and I think we are where we were with the male condom eight, nine years ago. I think it needs to be studied further, but those reservations are not enough for me to withhold approval.

DR. CEDARS: Thank you. Dr. Stubblefield?

DR. STUBBLEFIELD: I think that the evidence presented and our discussion shows the essential points that the new one is certainly not inferior to the first one and that there is evidence

that it is safe and efficacious. And more that we've heard from everyone presenting at this meeting about the potential and enormous importance of the female condom in the world. If it can be made cheap enough and it's accessible, then we have a real chance to reduce the number of acts of intercourse that are unprotected.

DR. CEDARS: Thank you. Dr. Ramin?

DR. RAMIN: Ditto all the comments that have been made. In particular, number one, the in vitro data is very reassuring. We have no evidence that it's not safe. I mean, there have been no deaths. There's no allergic reaction. And so I think as far as safety, it appears to be quite safe. And then the data that's been presented today, FC2 is comparable to FC1. And then the obvious need that we need worldwide for a female condom.

DR. CEDARS: Thank you. Dr. Sharp?

DR. SHARP: I think there has been precedent that we can use surrogate endpoints for good studies. I think this is a good study. I feel very comfortable that the surrogate endpoints do show that the FC1 and the FC2 are equivalent or at least not inferior with the FC2. I would also just say that not my primary decision, but I am certainly

moved by the global need and the local need for a condom as such.

DR. CEDARS: Thank you. Dr. Padian?

DR. PADIAN: I think the data that we reviewed, both the clinical data and the in vitro data, are consistent with a larger body of evidence that would lead one to say that it makes sense to approve it, that it's not inferior to FC1. And I think, certainly, especially for women who can use nothing and have nothing, not in a position to negotiate male condoms, that this fills that niche.

DR. CEDARS: Thank you. Dr. D'Agostino?

DR. D'AGOSTINO: Yeah, I believe there is a need, and the case was well presented, I believe, by some of the open public hearing presentations. I believe the device is safe. I think the in vitro data is very good. The clinical trial, no one was more critical of it than I have been. I think that it reflects somewhat the field itself. And even with all the concerns that were raised and thoroughly discussed, I think that the data has a compellingness to it that the new condom is not inferior to the first generation.

And I think the surrogate endpoints are more than just plain surrogates because they sort of

direct all the mechanism. A lot of times with a surrogate you're looking at something that goes on in the blood and you're hoping that you can extrapolate. Here you're talking about how would you prevent the possible transmission. So I think the surrogates have a compellingness to it, to the transmission of the sexually transmitted infections and also for pregnancy. So I was very comfortable in voting positive.

DR. CEDARS: Thank you. Dr. Thomas?

DR. THOMAS: I think that, as was said, the in vitro data is very compelling. I think the study had some issues particularly when it relates to the issue of bias, but over time probably does even itself out. But I think because women purchase -- the majority of the market is from female patients, and I think this will allow them to -- allow women in general to take even more control over their ability to protect themselves against sexually transmitted diseases and pregnancy. And I felt that this was definitely needed in the United States as well as globally.

DR. CEDARS: Thank you. Dr. Katz?

DR. KATZ: Thank you to the FDA for your comprehensive due diligence and to all the presenters

today, from the Sponsor and from the public sector, to help inform us about the benefits and the likelihood of those benefits in relation to the risks. I'm very comfortable in voting in favor of this. I think the evidence is more than adequate to demonstrate the equivalency of, the non-inferiority of this device. And I think there's additional evidence, mechanistic evidence, that one could use in support of this, and I look forward to further studies with this device in the spirit of what was done with the male condom.

DR. CEDARS: Thank you. Dr. Davis?

DR. DAVIS: I, too, was very -- would ditto everyone's remark that certainly the in vitro data was compelling. The clinical study had some minor imperfections. However, I think that it certainly is reassuring to me. And the last thing I'll say is that it was really moving to me to see how many groups and organizations really are working hard out there to support at-risk women both in the U.S. and internationally. And, hopefully, this will help this problem.

DR. CEDARS: Thank you. Dr. Warner.

DR. WARNER: I say there's a clear need for female-controlled barrier products, and I thought it

was a good demonstration that the products were equivalent. These are very hard studies to conduct whether it's with a male condom or female condom, and I think this study, albeit it had some imperfections, is a clever way to attack that problem. That being said, I would encourage folks to keep doing research looking for other surrogate endpoints, including biomarkers, as well as other creative epilogic designs that can further assess how effective the condom is. Thank you.

DR. CEDARS: Thank you. Dr. Hillard?

DR. HILLARD: So I would just echo what others have said regarding the pluses and minuses of the study. I am convinced of the safety and effectiveness and non-inferiority of the Female Condom 2. In addition, I applaud the company for developing a product that has the real potential to be more accessible to women in the U.S. and worldwide, and in addition, I'm impressed by the potential benefits of the new female condom that appears to be at least as acceptable and perhaps more acceptable than the first version of the product, which would then potentially enable more women to -- empower more women to protect themselves worldwide.

DR. CEDARS: Thank you. Ms. George, do you

have any comments?

MS. GEORGE: Sure. I just had a couple of very quick things to say. First, I wanted to thank the Sponsor and the FDA for all of their hard work to actually get us here to have an opportunity to evaluate the product. And I want to say that I was pleased to listen to all of you guys trying to address something that -- a PMA that was a little different than kind of the average PMA that's brought to Panel because usually it is nice clean data and with clear endpoints, and this really was a manufacturing process change and a material change. So it was very engaging and thoughtful to listen to all of this. And having been a industry rep for the past four years, I want to say that I hope the FDA keeps these kind of panels going because it's great for the Sponsor to have an opportunity to work with industry, another industry rep to work with the FDA, to work with all of you to bring some innovative products to the market. So that's it.

DR. CEDARS: Thank you. And I would just like echo the comments. I'd like to thank the FDA for their hard work in interpreting these studies for us, thank the Sponsor for their presentation and their work in this very vital area, particularly

thank the public hearing speakers for not only their comments today but their hard work globally. Do you have any final comments, Dr. Whang?

DR. WHANG: Sure. I'd like to thank the Panel members as well for your efforts preparing for today's meeting and for the very constructive discussion. And I'd like to thank the members of the public who've attended who have spoken today. We appreciate your interest in these devices and in the FDA review process. And, finally, a big thank you to Dr. Cedars for leading our meeting today.

DR. CEDARS: Thank you. And I'd like to extend my thanks to all the Panel members for taking time from their busy lives to come help us with this decision. And, with that, Day 1 of this meeting of the Obstetrics and Gynecology Devices Panel is now adjourned.

(Whereupon, at 4:45 p.m., the meeting was concluded.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

OBSTETRICS AND GYNECOLOGY PANEL

December 11, 2008

Gaithersburg, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

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Official Reporter