anything directed at the high-risk end of a population, that we include this vague sense that, well, gee, maybe people who get this die more but maybe that is just because they are sicker. I think that is a difficult piece to communicate.

DR. HARRINGTON: Dr. Ellis.

DR. ELLIS: The question is asked there one or both. At this point of analysis, I am less inclined to include i3 than the New England Journal, Mangano. I am not sure that I am ready to include both but the i3 even less so at this point.

DR. HARRINGTON: Do you want to qualify that? Why is that?

DR. ELLIS: Because I think the analysis is less complete at this point. I think it is an administrative database which has not been prospectively collected. Granted, that in the JAMA article, data was not collected for this outcome specifically, but I just think it is methodologically so much stronger.

DR. HARRINGTON: So let me push you a little bit because, certainly, in the guidelines

world, for example in cardiology, observational information along the line of Steve's comments is being now included in guidelines in the sense that there is much more information coming from robust observational analyses.

Are we on a slippery slope here? Is some of it good enough? Some of it is not good enough?

DR. ELLIS: Well, perhaps. We saw the table of good information and good experimental design. I think the quality of the information in i3 is less robust.

DR. HARRINGTON: So you would ascribe to the notion that observational studies can be graded as to their quality and some measure of quality allows you, perhaps, to get into the label?

DR. ELLIS: Perhaps.

DR. HARRINGTON: Norm and then we will go to Dr. Neaton.

DR. KATO: My opinion is I can't tell which study is good or bad at the end of today. So I have to kind of throw my hands up. However, I also agree with Dr. Findlay that transparency and

full disclosure is really the way to go here. I think there is a way that we can legitimately caution the public. But I think to not do that would be to shirt our responsibility as a panel.

DR. HARRINGTON: Dr. Neaton, did you want to--

DR. NEATON: I will just maybe say it a little differently and maybe a little stronger. My concern is that any data we put would be just wrong. Because I am personally, in terms of i3 data, there are clearly missing kind of potential confounders that were shown to us in the first presentation this morning.

Some that were included are not measured precisely and so that is not going to be--they are not fully recovering the confounding. That is quite apart from the other issues that we heard about in terms of kind of looking at the propensity for choosing a treatment by center and across time which may be issues.

In the mortality data, which I again come back to, I have to say is a bit concerning. I am

very concerned about the follow up in that study. So that, if this was a trial, randomized, I think you would question it. And it is an observational study. I think we should be questioning it even more.

So, perhaps, some kind of general statement about some studies have shown and some studies haven't might work. But I just would be uncomfortable in citing that we have seen this morning, the specific statistics in the label.

DR. HARRINGTON: So let me push you. Do you feel that your comments are just germane to this particular set of studies or do you believe, I think as Henry suggested, that including observational data in package labeling like this is a slippery slope.

DR. NEATON: I think it is a very slippery slope.

DR. HARRINGTON: So we have Dr. Teerlink, then Emil.

DR. TEERLINK: So I now have to modify what I said before. So I agree it is potentially a

slippery slope. Reading the question more carefully, I actually would not describe the studies and go into in-depth detail. Rather a comment that there is a concern along these lines would be something that I would support and not get into the specifics of that, and perhaps reference the literature that is suggesting these things, but not saying it is a known concern, but it is a potential concern.

And it is in the spirit of full disclosure and giving physicians--they are having to make this risk-benefit decision for a specific patient and that is a way, I think, to do this middle way.

DR. HARRINGTON: So I think that is the comment that is coming in the corner over here, that there should be some language about the findings but not necessarily a description of the details of the findings. Emil.

DR. PAGANINI: I would jump on the bandwagon of those folks that are saying it is a slippery slope. I would not want to put this--because the data, I think, is flawed. We

have all seen the flawed data, why are you doing that. I am all for transparency but I am also against baffling them with a bunch of stuff.

DR. HARRINGTON: Dr. Jeevanandam.

DR. JEEVANANDAM: I guess I want a clarification. When we talk about this vote, this is not a black-box indication. This is just in the regular--

DR. HARRINGTON: This is included in the label.

DR. JEEVANANDAM: Just in the label so it is in small letters.

DR. HARRINGTON: I think that that would be part--I am going to look at my FDA colleagues, but that would be part of the negotiation as to where it belonged in the label, but we are saying in the label.

DR. JEEVANANDAM: I think I agree that both those studies have significant flaws. I don't know--you talk about what is a good observational study. If there was a randomized controlled trial that came out that maybe showed this type of

problem, then you would certainly put it into the labeling.

DR. HARRINGTON: So you are in the slippery-slope camp.

DR. JEEVANANDAM: Yes.

DR. HARRINGTON: Let me go to Dr. Gillett, then Dr. Lincoff and then I would like to put it to a vote.

DR. GILLETT: Just to underline what Emil said, I agree about this being a slippery slope. I think the FDA did a good job of trying to elevate this through their reanalysis, but it started with a flawed system to begin with.

DR. HARRINGTON: Mike.

DR. LINCOFF: I want to go back on the other side because I do think we ought to be doing some description, small, but whatever these specific studies, just as oftentimes trials are described in the label.

It is not a slippery slope in terms of which studies you include. These three studies were basically the topic of one and half--I mean,

the last meeting and this meeting. They were the topic of a complete FDA statistical analysis.

There are a lot of studies in the literature but these three were the whole point of this entire meeting and most of the discussions that we are having here. So I think that you can justify using these three and not expanding it to the entire literature of every abstract that comes out, that you can make them relatively short discussions.

But I think it is relevant to say, in some summary form, that these were the findings subject to all the concerns and the doubts about all the covariates.

DR. HARRINGTON: Dr. Day and then Dr. Findlay.

DR. DAY: What has been the current practice in the last few years about including observational data in labels?

DR. RIEVES: I would like to offer one comment. In developing our labeling, we try to keep in mind that the labeling should include not

all the information--it shouldn't be a treatise, if you will. It should use some discretion. It should include the information that is important, and the key word is important. So it takes judgment there.

The key information that is important to safe and effective use of the drug; we try to avoid decoration, if you will, or airing anxieties within the label, so it does take some discretion and that is sort of the opinion we are hoping to get from the committee, a sense of the committee's judgment as to how important these data are.

DR. DAL PAN: We have, on occasion, put observational data. It is not very common, though.

DR. HARRINGTON: Steve.

DR. FINDLAY: So this slippery slope seems to be around being too specific, being too numerical, including too many numbers. I think I would concur and the remark just made underscores that, that it takes judgment. It is judgment. So I think, to clarify what I said before, it is some sense of the results of these very important

studies, which were confirmed upon a FDA analysis and I think we would all agree signals something pretty profound, need to be in the label.

DR. HARRINGTON: Dr. Heckbert.

DR. HECKBERT: One problem I have with including reference to these studies is that, for at least the Mangano study and the i3--first of all, the i3 Safety Study is not published; right? So the reader would have nothing to go to.

DR. HARRINGTON: But you had heard that they do have publication rights. But you are correct that it has not been published.

DR. HECKBERT: Right. And then the analysis that the FDA did with the Mangano data, I thought was quite excellent given what they had to work with. The reader wouldn't have access to that either.

I guess what I am getting at is I believe you can make judgments about the quality of observational studies and I think we do have a gradient here, and that the reanalyses that were done in two of the instances by the FDA are far

superior to the original analysis. I am not sure I want to refer the reader back to the--I don't know what i3 will publish, but I am not sure where that leaves the reader, if they want to go find out more.

DR. HARRINGTON: Fair enough. So let me read the question again, officially, into the record. Should these findings, one or both studies, be described in the product label. We will do the yeses first. So those people who believe yes, please raise your hand and leave them elevated.

[Show of hands.]

DR. HARRINGTON: So, Steve, again, we will start with you and go around the table.

DR. FINDLAY: Steve Findlay. Yes.

DR. TEERLINK: John Teerlink. Yes.

DR. LINCOFF: Mike Lincoff. Yes.

DR. LESAR: Timothy Lesar. Yes.

DR. CHEUNG: Alfred Cheung. Yes.

DR. KATO: Norman Kato. Yes.

DR. HARRINGTON: Next we will do the no's.

[Show of hands.]

DR. HARRINGTON: We will start with you, Dr. Day.

DR. DAY: Ruth Day. No--reluctantly.

DR. JEEVANANDAM: Val Jeevanandam. No.

DR. CRAWFORD: Stephanie Crawford. No.

DR. HARRINGTON: Robert Harrington. No--also reluctantly. I am not dismissing putting observational data in there, but these specific data.

DR. KASKEL: Rick Kaskel. No.

DR. NEATON: Jim Neaton. No.

DR. HECKBERT: Susan Heckbert. No.

DR. BLACK: Henry Black. No.

DR. WARNER STEVENSON: Stevenson. No. I am not at all opposed to observational data. This data bothers me. I would suggest if we have to put something, language might be something like, questions have been raised from observation data regarding possible increased increase of MI, stroke and even death in a population of patients at high risk for these events.

DR. CHEUNG: Well, if there is an option, we are talking about--

DR. BLACK: We are saying yes or no.

DR. CHEUNG: That was not an option there.

DR. HARRINGTON: Let's finish voting. Then I will come back to it.

DR. GILLETT: James Gillett. No.

DR. PAGANINI: Emil Paganini. No.

DR. ELLIS: It is more a position of equipoise, but I abstain. John Ellis.

DR. HARRINGTON: Other abstentions?

DR. PHAN: We have 6 yes, 11 no and 1 abstain.

DR. HARRINGTON: Now let me open up for conversation. So, go ahead, Lynn. And then we will go to Dr. Cheung.

DR. WARNER STEVENSON: I would think, if we feel something should be included, that it might be along these lines; questions have been raised from observational data regarding possible increased incidence of MI, stroke and death in the a population at high risk for these events.

DR. HARRINGTON: Dr. Cheung.

DR. CHEUNG: That is what I have in mind. I didn't want to go into a lot of great detail about describing those studies but to alert people there is a possibility instead of people not knowing at all.

DR. HARRINGTON: Dr. Black.

DR. BLACK: If I could clarify my position about slippery slopes and all. I just think this particular data is so hard to interpret correctly that I think this would be an issue.

But I think we are just giving advice to the agency. If the agency chooses to put in a sentence, you don't have unanimity by any means or really consensus also. So I think if you think, when you put it all together that a sentence that doesn't have details, I would not object to something like that.

DR. HARRINGTON: Jim and then Emil.

DR. NEATON: I like Lynn's sentence except I would qualify it by saying, not all consistent.

DR. HARRINGTON: Emil and then Mike.

DR. PAGANINI: I didn't even want to market it but since you have it on the market and it is on a list, then I would have no problems at all with putting a statement in there about them. But I don't think that these observational studies should be detailed. But the conclusions that Lynn put out seem to be very, very reasonable as an alternative to putting in the studies.

DR. HARRINGTON: Dr. Lincoff.

DR. LINCOFF: I actually thought that that was the minimum. How could we be talking about restriction or anything else in the interim awaiting a clinical trial if we don't provide something in the label to say what we are worried about.

So I figured that was a minimum. If we are going to do it, of course, I think we should include the issue of renal failure. I am not sure that we have data that it is only in high-risk populations of patients.

DR. WARNER STEVENSON: I think that is already in there.

DR. LINCOFF: Maybe it did. Okay. And I am not sure we have the data we can stratify by risk who is at risk for these complications except, perhaps, the renal failure.

DR. HARRINGTON: Dr. Crawford.

DR. CRAWFORD: Thank you. I just wanted to go on the record of saying I am in agreement, absolutely, with the last series of comments that were made. Also, I never gave my personal opinion with respect to concerns about a slippery slope with observational data. I do not share that. It was specific to the question as it was asked and if such general language as people have just been discussing is considered by the agency, if Bayer had any concern with that, the quickest way, perhaps, to get such language removed if it were inserted is to come out with good data from well-designed studies.

DR. HARRINGTON: That is a very good point. So let me see if I can summarize the tone of the discussion. There was a very robust discussion about the value of including not just

these data but observational data in general in the label of drugs and specifically this drug.

I think the tone I am hearing is, including for myself, is that people who voted no were more concerned about the quality of these data than necessarily about including observational data. I sense a general agreement with Steve's initial point that we want there to be transparency in the process offered to both practitioners and consumers so that, from the Committee, you heard we like that idea but the people who voted no, I think, were reacting to the quality of these data.

Does anybody disagree with that remark?

DR. CHEUNG: So would it be fair to re-vote on what the tone might be because I am not sure those people's vote really means no.

DR. PAZDUR: I think we understand the comments here. Really, here, we are more interested in the comments than specific votes. We are looking, really, at what we are going to do and the general tone of the discussion.

DR. BLACK: I would have no problem with

observational data if they all said the same thing. I mean, we have a fair amount of discrepancy with tools that we don't think are all that good anyway. So it isn't observational data per se that I am objecting to. It is just this particular set, and there will be others like this. And I think there is a potential precedent problem which goes beyond--just goes beyond disclosure.

If we were really disclosing how we feel, I think we would just throw our hands up and say it is futile with what we currently have to be able to make a definitive statement or even definitive advice.

So I think we ought to just leave it as it is and leave it to you guys to work on how you say it.

DR. HARRINGTON: Go ahead, Steve.

DR. FINDLAY: I would just like to go on record saying that I think, from the discussion today, I will go on record in saying that I thought that this observational data reached the level of warranting the kind of statement that Lynn put

forward and that be included in the label.

DR. HARRINGTON: Let me read the last question and then we will have some discussion and then we will vote. Do you regard the performance of additional clinical studies to more thoroughly assess Trasylol safety particularly with respect to mortality as a prerequisite to continued market authorization and, if yes, discuss the most important design considerations. For example, should the study be powered sufficiently to rule out a certain increase in mortality risk where Trasylol is compared to no antifibrinolytic therapy or to placebo or to both antifibrinolytic therapy and placebo.

So I will open--

DR. HECKBERT: Isn't the premise of the question in doubt because we just established that they can't require--I mean, it can't be a prerequisite to continued marketing authorization.

DR. HARRINGTON: We voted to continue market authorization. Perhaps--and Mimi has told me that we can tweak the question. The question,

perhaps, is better, do you believe that there are continued additional--or additional clinical studies which ought to be done to better understand the risks and benefits of Trasylol.

Would that fit better?

DR. HECKBERT: Yes. I think that is more practical. I wish we could do No. 3 the way it is written but I don't think we can.

DR. BLACK: I really like your rewording of that. I think that is exactly what I would agree with. Requiring a mortality study may be just an impossibility and it would be dead on arrival. We would never be able to mount that in time.

We have only had one hypertension study where we ever showed benefit in mortality, and that was HDFP.

DR. HECKBERT: Actually, I was not referring to the difficulty of getting a mortality endpoint. I was referring to the fact that the FDA doesn't have the authority to require a clinical trial.

DR. HARRINGTON: Let me go to Emil.

DR. PAGANINI: I would be consistent with the original way the thing was and say yes to that original one. But I would also say yes to the altered question as it is there since the original question has morphed.

With regards to the study design or a thought process behind that, I think there would have to probably not be a placebo controlled because that is not the population you are going to deal with. We have heard that from our surgeons and I know our own folks probably wouldn't want to get involved in it as well. So it would have to be an alternate drug to this drug.

The second thing would be a better definition of the patient population of the target population and that would have to be clearly defined in the study, well defined from either observational or other RCTs to define what population you are dealing with exactly.

Then the third is expanded datapoint collections to include a variety of variables

associated with or without the use of aprotinin for specific outcome. In there, I would specifically point to renal dysfunction after open-heart surgery as one of those major variables.

DR. HARRINGTON: Do you believe that mortality has to be in the equation?

DR. PAGANINI: I think that is an impossibility. I honestly, sincerely, believe that it is so difficult to come up with mortality statistics based on the use of one drug at one time in a long-term effect other than the secondary effect of mortality for secondary issues that were caused by the original drug example.

If the drug causes acute kidney dysfunction and then they get an infection and then they die from the infection, was that caused by the drug? Was it caused by the kidney failure? Was it caused by an infection? It is very difficult to do that.

Second, the number, as we have heard before, of mortalities that might be associated with this drug would be so small that the

population to capture that would have to be so large that it would really be an impossibility on anybody to try to find that.

So I would say mortality probably shouldn't be in it.

DR. HARRINGTON: I think we have Dr. Lincoff then Dr. Teerlink

DR. LINCOFF: I respectfully disagree with most of what Dr. Paganini has said. First of all, I think the FDA wants to hear our discussion. Our discussion, I think we have already had in terms of although you can't, in a regulatory means, actually require a trial, I think you understand our intent is that we would want to monitor the trial, et cetera, to really--this is serious.

From the standpoint of trial structure, I agree that I think it should be against the active control and I think that the label--my understanding of the label of Amicar is that it is vague enough that it probably would be an acceptable control. But, again, I believe that that would be within your domain to say yes, we

would accept that.

From the standpoint of endpoints, though, I agree that all the different renal endpoints may be important and collect as many as you can in a large-scale trial but I strongly believe this should be a mortality trial. And I believe it should be a mortality trial of mid-range mortality, six months, maybe a year, maybe--somewhere in there that would take in the influence of that renal failure that was pneumonia that died because that is a result of the drug.

I think that if you accept the reasonable range for a definition of non-inferiority, you may be able to get away with an 8,000- to 10,000-patient trial which, if you can do a 3,000-patient trial prior to all this interest with Trasylol and now they are the topic of two FDA advisory panels and a revised label and a whole lot of concern, I think there should be enough motivation, enough equipoise, out there to be able to roll out to enough sites to accomplish this sort of trial. It is an important question and they

were pointing out how many blood transfusions are involved, how many people are involved year by year. It is important enough to answer the question in a definitive way.

DR. HARRINGTON: So let's go to Lynn, John, Dr. Ellis.

DR. WARNER STEVENSON: I am actually going to disagree with you in turn. First of all, I think BART will be incredibly informative and it will change whatever we decide today. However, I don't think it will be possible to do a trial powered on mortality. I think it would be not possible to randomize those patients in terms of real life. You will get a very odd group of people that the surgeons are willing to put into a trial, surgeons who currently feel strongly.

I think the option would be to define high risk exceedingly narrowly such that you have then a intermediate-risk group in which it would, hopefully, be possible for the surgeons to reach equipoise and be willing to randomize within that group and then that would inform you there.

You are never going to be informed on that highest-risk group for bleeding.

DR. HARRINGTON: John Teerlink and then Dr. Ellis.

DR. TEERLINK: So this is unusual because usually I always agree with Lynn. But I will respectfully disagree with her this time. I do strongly support--actually, I would have voted yes to No. 3 as it was written.

My vote yes to the No. 1 was contingent upon finding a way to actually give this trial some teeth. And I would encourage the FDA to do whatever they can to ensure that this trial gets done using whatever powers you have including pulling it off the market until this trial is done.

So, hopefully, that is clear enough from my standpoint that you can hear that.

I do think that BART will provide some useful insight. I think it will provide insight into actually helping to plan the trial. So, if you wish to wait until those results come along, that's fine. It would be nice if there were some

opportunity cost to that because I think there are still issues that need to be resolved.

I would check for 6- to 12-month mortality as well and would recommend a noninferiority design. This is the advantage of having the data from BART is it should give you some sense of what the comparator to placebo rates are for these different studies which will give you some info.

DR. HARRINGTON: Dr. Ellis.

DR. ELLIS: I agree with Lynn in my concern. I believe that, in an ideal world, it would be nice to do the 8,000-patient study that is probably of adequate power. I just don't think that is going to be feasible.

I think, given anecdotal reports that BART is having enrollment difficulties at this point, I am not convinced that that study would be able to be done.

DR. HARRINGTON: Dr. Cheung.

DR. CHEUNG: I am still questioning why does it have to be an 8,000-people trial if this is really limited to very high-risk patients. That is

what we are proposing the label to be; right?

DR. HARRINGTON: So that was, I think, at least part of Lynn's point is that one could decide what the population is and one can figure the sample size around that. Let me go to Dr. Gillett, then Dr. Neaton, Dr. Black.

DR. GILLETT: I would just hope that they could somehow return to this idea of--one of the purposes of this is not only to spare blood products from having to be given but to spare the patient from the problems that were alluded to by the transfusion of blood products by the time in surgery, time on the machine and other issues like this that they are trying to avoid by taking these steps.

I am not a surgeon and I can't express these fully but I would like to see those 90 or 95 or 97 or 98 percent of the people who survive have a good quality of life for their trouble and the surgeon be rewarded by having a person who feels really good about having had the surgery.

DR. HARRINGTON: Dr. Neaton, then Dr.

Black.

DR. NEATON: I guess I was going to say I support looking at mortality outcome here. I think the current trial might inform it. But the best it is going to have is 30 days. I remain concerned about the long-term impacts of renal dysfunction.

Based upon the Mangano data, roughly 10 percent of people are dead in a year. So you need about 300 deaths to rule out a 25 percent, 30 percent, reduction of the hazard. So I don't think we are talking about gigantic numbers. It is feasible.

DR. HARRINGTON: Dr. Black.

DR. BLACK: There are only two things that I think we have to have which is an active control study and a very clearly defined high-risk group. I think exactly what it is, whether we include renal death as an outcome or whether we talk about double the serum creatinine, something like that, we could work out. But it is going to have to be practical and feasible or we are not going to get anywhere.

DR. HARRINGTON: Some themes emerging for

sure. Dr. Kaskel.

DR. KASKEL: As commented last year when this was reviewed, I think for any randomized controlled trial we need specific measurements of kidney function over time. And they exist, more than the serum creatinine.

DR. JEEVANANDAM: I think there are a couple of things. First of all, I agree that this would have to probably be compared to antifibrinolytic drug and not placebo. If you look at all the Bayer randomized controlled trials, there were trends but they were never statistically significant.

There were trends towards worse renal failure or trends towards high incidence of MI but never significant. I think you need to power it so or have a large enough trial that you can actually see if there is a difference and if those trends really map out into something that is clinically significant.

I guess my question is, you know the BART trial already has enrolled a significant amount of

patients. I mean, would we be satisfied with that BART trial because the patient population that they have included in the BART trial is very similar to the patient population that is currently probably using aprotinin.

Aprotinin, as it stands right now where you just have the "high-risk" CABG is really antiquated. We use it for valve patients or multiple valve patients or multiple reoperations. So I don't know. Is there a role of just increasing the BART trial to power it or to actually follow those patients for a longer period of time to get the mortality data.

DR. HARRINGTON: Dr. Lincoff.

DR. LINCOFF: I think that is a very good idea, maybe not just--but to design a companion trial to be able to combine and maybe extend BART to longer-term here. We can send the patients to longer-term follow up to get at least mortality and maybe not waste the data but actually design a trial as there have been examples in the past that it is a companion and that it is prospectively

designed to combine the sample sizes.

DR. HARRINGTON: I am going to make one comment and then take the vote, that I believe, absolutely, that additional studies need to be done including randomized clinical trials. Dr. Smith and others pointed out from the time the original trials were done, the patient population is different. The concomitant medications are different. The surgical procedure, itself, is different.

To think that we know enough about the therapy that was studied 15 years ago, I think we are fooling ourselves and they absolutely need to provide us with contemporary data in a contemporary setting.

People I know need to get on the road. I am going to read, at Dr. Heckbert's request, a revision question and see if people agree with this tone before it is the official question.

Do you believe that there should be additional clinical studies including randomized clinical trials to further assess the risk and

benefit of Trasylol.

Does anybody disagree with that being the question? Okay. Do I need to officially read it now? Okay. Now I need to officially read that. So we are going to vote again, yeses first, no's and then the abstaining.

Do you believe that there should be additional clinical studies including randomized clinical trials to further assess the risk and benefit of Trasylol. Raise your hand and leave them raised if it is yes.

[Show of hands.]

So, Dr. Day, we will start with you again.

DR. DAY: Ruth Day. Yes.

DR. FINDLAY: Steve Findlay. Yes.

DR. ELLIS: John Ellis. Yes.

DR. JEEVANANDAM: Val Jeevanandam. Yes.

DR. CRAWFORD: Stephanie Crawford. Yes.

DR. TEERLINK: John Teerlink. Yes.

DR. LINCOFF: Mike Lincoff. Yes.

DR. HARRINGTON: Robert Harrington. Yes.

DR. KASKEL: Rick Kaskel. Yes.

DR. LESAR: Timothy Lesar. Yes.

DR. NEATON: Jim Neaton. Yes.

DR. HECKBERT: Susan Heckbert. Yes.

DR. BLACK: Henry Black. Yes.

DR. CHEUNG: Albert Cheung. Yes.

DR. KATO: Norman Kato. Yes.

DR. WARNER STEVENSON: Lynn Stevenson. Yes.

DR. GILLETT: James Gillett. Yes.

DR. HARRINGTON: Any no votes?

[No response.]

DR. HARRINGTON: Any abstaining?

[No response.]

DR. PHAN: We have 17 yes, no no, and no abstains.

DR. HARRINGTON: So I will look at FDA. Did you get the tenor of the discussion around this?

DR. PAZDUR: Yes.

DR. HARRINGTON: Are we done? We are ending. I spared you 15 minutes in your day. I want to thank the panel members, thank the

presenters, thank the sponsors and thanks to the FDA.

Dr. Rieves, do you have any final words?

DR. RIEVES: No. Just thank you. It was very useful.

DR. HARRINGTON: Thank you.

[Whereupon, at 4:45 p.m., the meeting was adjourned.]

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