

1 that can be attached to approvable with
2 conditions, so you can simply revise that,
3 please, to approvable with conditions.

4 MR. MORRISON: Mr. Chairman, I
5 revise my plea to approval with conditions.

6 DR. YANCY: Is there a second?

7 DR. JEEVANANDAM: Second.

8 DR. YANCY: There is a second.
9 Before we can vote on the motion, we now have
10 to separately put forward the conditions. And
11 then once all conditions have been placed and
12 approved, whichever conditions are approved,
13 we can then vote on the main motion.

14 The first condition, Dr. Normand.

15 DR. NORMAND: I -- the conditions
16 of post-approval study with a concurrent
17 control group.

18 DR. YANCY: Is there a second for -
19 -

20 DR. SOMBERG: Second.

21 DR. YANCY: There is a second for
22 this condition. Discussion for this first

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1 condition, which is a post-approval study with
2 a concurrent control group. This is
3 discussion?

4 DR. BRINKER: Yes.

5 DR. YANCY: Yes, please proceed.

6 DR. BRINKER: I would like to give
7 the FDA staff leeway deciding what kind of
8 post -- what kind of comparator is necessary
9 for the post-approval study, rather than
10 mandate a comparison group right now.

11 DR. SOMBERG: Are you saying that
12 there could not be a comparison group?

13 DR. BRINKER: No, I'm not saying
14 there could not be. I'd rather leave it up to
15 them to work out, than us mandate it.

16 DR. SOMBERG: Are you saying there
17 shouldn't -- are you saying there's a
18 possibility of having no comparator group?

19 DR. BRINKER: No simultaneous
20 comparison, which is what you asked for.
21 Right?

22 DR. NORMAND: Concurrent.

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1 DR. BRINKER: Concurrent. I'm
2 saying that there may not --

3 DR. YANCY: Additional discussion?
4 Dr. Morrison.

5 DR. MORRISON: Well, I think that
6 we would all agree it's not likely to be a
7 randomized comparison. And I think that once
8 we recognize that, and realize that when this
9 is released, the way we all have to practice
10 is to make a decision based on what's best for
11 our patients. We try to bias our patient's
12 outcome for the better, that's what we do.
13 And I think that for that reason, the historic
14 control of consecutive patients may be as
15 good, particularly if patients are well
16 characterized. I think practically, it's very
17 unlikely that we're going to get a concurrent
18 group that isn't very different based on the
19 way all operators decide to use these stents.

20 DR. NORMAND: Can I respond to
21 that? I actually -- I disagree, it's probably
22 not a surprise. So, first of all, the problem

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1 I think we have had typically in real world
2 when you use a historical control, we use an
3 outdated piece of information typically for
4 patients that are no longer like the patients
5 that are used going forward in time, and so
6 that's the risk. And you are correct in
7 saying that surely there's selection bias in
8 the real world; that is who gets -- I'm making
9 this up, a TAXUS versus the other types of
10 stents, that there is some selection to that.

11 But I would go out and bet you a dollar that
12 there's going to be less selection bias that
13 way, than there would be going back to a
14 historical control group, so that's the first
15 thing in terms of the selection bias issue.

16 The issue about the difficulty of
17 doing this, I also disagree with, because I do
18 this all the time. You can discharge - there
19 are ways to get data on the cheap, and you
20 just need to be innovative in your design, so
21 we do this, lots of other people do this. So
22 the fact that I disagree with the statement, I

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1 guess, that you cannot get concurrent
2 controls, and I also disagree with the
3 statement that the concurrent controls would
4 be more biased than a historical control
5 group.

6 DR. YANCY: Additional discussion?

7 Dr. Yaross.

8 DR. YAROSS: I think the
9 recommendation for a concurrent control group
10 was listed, in part, as to reduce risk to the
11 sponsor. And I would just posit that the
12 sponsor has the right to decide on that risk
13 burden balance.

14 DR. YANCY: Additional discussion?

15 Dr. Somberg.

16 DR. SOMBERG: Yes, but without that
17 you get a lot of data that may not be useful
18 to the patient, so there's the other part of
19 that coin. And the patient is more important
20 than the sponsor.

21 DR. YANCY: If there's no further
22 discussion on this motion, then we need to

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1 vote on the motion. Dr. Normand, will you
2 restate your motion, please, your condition.

3 DR. NORMAND: Conditional on a
4 post-market study that includes a concurrent
5 control group.

6 DR. YANCY: Those that are in
7 favor, please raise your hand. Keep it
8 elevated so that your name can be recorded by
9 Mr. Swink. There are five. Those that are
10 opposed? There are five. The Chair has to
11 vote, and I would be opposed. That motion
12 dies. We are looking now for another
13 condition. Dr. Page.

14 DR. PAGE: I move that there be a
15 post-market approval study, the details of
16 which to be determined later.

17 DR. YANCY: Is there a second for
18 this new motion? Here is a second by Dr.
19 Brinker. Discussion on this new motion?

20 DR. BRINKER: Historically, I think
21 that these things work out quite well when FDA
22 and the sponsor get together and look at the

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1 big picture, and I'm sure they'll be motivated
2 to come up with an acceptable post-market
3 study.

4 DR. NORMAND: I think historically
5 it has not worked out very well. I mean, I'm
6 trying to recall the data at the December
7 meeting to say what are the concurrent
8 comparison groups, and that was our problem.
9 So I guess in terms of your statement,
10 historically worked out well, we probably need
11 -- it's me hating adjectives - trying to
12 figure out sort of why we think --

13 DR. BRINKER: Well, that's unfair,
14 because the historical issues have changed.
15 There was no issue with the expectation of
16 late stent thrombosis when the original stents
17 came up to approval; therefore, the post-
18 market studies were the best that were thought
19 to be necessary. I think now, given the
20 questions that are being asked, which are
21 different, they can come up with between --

22 DR. NORMAND: I don't think, unless

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1 I'm recalling incorrectly, which is a
2 possibility, is that many of the post-market
3 studies were never conducted, so we have that
4 issue. Then we have the issue that in terms
5 of bringing things back, when we had asked
6 them, they were very long in getting data back
7 to us, so I'm just not talking about the
8 control group.

9 DR. BRINKER: But that's -- let me
10 just say that that's another issue, whether
11 the sponsor complies with what we mandate now,
12 or whether they respond to and comply with
13 what they work out with the FDA, is a problem
14 because of the traditional leverage that the
15 FDA has in making sure that there's
16 compliance. But they're more likely to comply
17 fully with a study that can be done, that can
18 be straight-away, than they are with something
19 that's mandated, that's hard for them.

20 DR. NORMAND: But you're presuming
21 that's hard -- I mean --

22 DR. BRINKER: But if it's easy for

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1 them to do, they'll agree to it, and that will
2 be that.

3 DR. YANCY: Dr. Zuckerman.

4 DR. ZUCKERMAN: Yes. I just want to
5 underline that you're both right. While Dr.
6 Normand is reflecting a reality that post-
7 approval studies in the past, really in the
8 very near past, have not been done with the
9 diligence that one might expect, the landscape
10 has changed significantly. I would remind
11 everyone that the first presentation today was
12 from our Office of Post-Market Surveillance.
13 Before we sign off on PMAs these days, we have
14 to have a good idea of what the post-market
15 study design is. We would not hesitate to
16 employ an expert like Dr. Normand post-panel
17 if we felt that we still had issues, et
18 cetera. So the general construct, while may
19 not have been working well in the past, we're
20 committed to changing it right now. And I
21 wouldn't worry so much that the post-market
22 study won't be completed.

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1 DR. YANCY: Dr. Somberg.

2 DR. SOMBERG: Dr. Brinker, I think
3 you said to the effect that it was unfair
4 because we didn't know that stent thrombosis
5 was going to be a problem. And I hear you on
6 that, but we never know what may come about,
7 and what may be the concern. And five years
8 later, I think the whole scene is going to
9 change, the antiplatelet therapy is going to
10 be very different, a whole host of things. So
11 not having a concomitant control will be
12 devastating. I mean, what happens if you're
13 on -- if the difference is just mediated by
14 having a more potent antiplatelet drug, and
15 you're comparing it an historic control there,
16 or you have data?

17 We have had several meetings, and
18 we're going to have meetings of this panel
19 when you have a performance criteria based on
20 something that's assumed to be correct, and
21 then you just miss it, or it doesn't sound
22 good. And then what are we supposed to do?

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1 So to do it without some sort of comparator
2 is, to me, Russian roulette in the research
3 area.

4 DR. BRINKER: I've not proposed
5 that. I've proposed that the FDA and the
6 company work it out. And I think that rather
7 than give them a marching order, or suggestion
8 for one, I think they could do the job.

9 DR. YANCY: And I think the
10 important statement that Dr. Zuckerman made is
11 that whatever the plan happens to be, has to
12 be approved by FDA before it can go forward.

13 Any further discussion on the
14 motion proposed by Dr. Page? Seeing none,
15 it's time to vote on that motion. Dr. Page,
16 would you restate the condition, please?

17 DR. PAGE: I recommended that the
18 condition be that a post-approval study be
19 undertaken, the details of which will be
20 worked out at a later date by the FDA.

21 DR. YANCY: All in favor, signify
22 by raising your hand, and leave it elevated

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1 until your name is recorded. That's ten
2 votes, so the first condition passes, and it's
3 unanimous. For those opposed? Please leave
4 your hand up until your name is recorded.

5 (Laughter.)

6 DR. YANCY: The motion passes, not
7 unanimously, but 9-1.

8 We now have one condition. Is
9 there a second condition for approvable with
10 conditions? Dr. Morrison, you were making
11 some other comments when you first started.

12 DR. MORRISON: Thank you, Mr.
13 Chairman. I would propose the condition that
14 labeling with regard to antiplatelet therapy
15 be consistent with guidelines of the College
16 and the Society, and that be consistent with
17 what the FDA has recommended for previous
18 drug-eluting stents.

19 DR. YANCY: Is there a second?
20 It's been seconded by Dr. Hirshfeld.
21 Discussion for this motion? Seeing none,
22 we'll take a vote. All in favor of -- did I

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1 not see you again? Did you have a comment?
2 I'm sorry. I'm serious. Okay. All in favor,
3 please raise your hand, and leave it elevated
4 so your name can be recorded. It's unanimous,
5 depending on the peace sign.

6 We have two conditions now,
7 approval with condition. The first relates to
8 a post-approval study, and the second relates
9 to language with regards to dual antiplatelet
10 therapy that is consistent with guidelines.
11 Do you have another condition?

12 DR. SOMBERG: A third condition I
13 propose is that SPIRIT III be completed before
14 approval.

15 DR. YANCY: I'm sorry. Please
16 restate that.

17 DR. SOMBERG: SPIRIT III be
18 completed, being completed means filling in
19 the data for 12 to 24 months before approval.

20 DR. YANCY: So this is a third
21 condition that's been proposed, that before
22 approval is granted, that the outstanding data

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1 from SPIRIT III for long-term follow-up at two
2 years - I assume that's what you mean, Dr.
3 Somberg? So beyond 12 months be acquired. Is
4 there a second for this? Seeing no second,
5 the motion dies. Is there another condition
6 referable to approvable with conditions?
7 There is a comment that Dr. Laskey wanted to
8 make about our last vote.

9 DR. LASKEY: A trivial point, but
10 to revise the aspirin recommendation for
11 lifelong since it's not reflected in the
12 Societal guidelines.

13 DR. YANCY: My sense is that we
14 don't need to vote on that. Great. So we now
15 have approvable with conditions, with two
16 conditions that have passed. The first
17 condition deals with the post-marketing study,
18 the second condition deals with specific
19 language on dual antiplatelet therapy. Are
20 there any other conditions? We're ready to
21 vote for the main motion, then.

22 It's been moved and seconded that

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1 the Abbott Vascular PMA application P070015
2 for the XIENCE V Everolimus-eluting coronary
3 stent system is found approved with the
4 conditions the panel has just voted on. We
5 will now vote on the main motion. With a show
6 of hands, please indicate if you concur with
7 the recommendation that the above-named PMA be
8 found approvable with conditions. Please keep
9 your hands raised until we can record all
10 names.

11 For the benefit of the record,
12 those voting in favor, Drs. Brinker,
13 Hirshfeld, Kato, Laskey, Page, Blackstone,
14 Normand, Jeevanandam, and Morrison. Thank
15 you.

16 If you are opposed to approval with
17 conditions, please raise your hand so that
18 your name can be read into the record. Dr.
19 Somberg.

20 It is the recommendation then of
21 the panel to the FDA that the Abbott Vascular
22 Application P070015 for the XIENCE V

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1 Everolimus-eluting Coronary Stent System is
2 approved with the previously voted upon
3 conditions. The conditions are, number one,
4 an appropriately designed post-marketing
5 survey or study that will be determined in
6 conjunction with the FDA, and approved by the
7 FDA prior to it being commenced. And number
8 two, that the language that appears within the
9 application referable to the use of dual
10 antiplatelet therapy is consistent with
11 guideline statements, and indicates lifelong
12 use of aspirin. I'd like to thank the panel.

13 I will now ask each panel member to
14 state the reason for his or her vote, starting
15 with Dr. Brinker.

16 DR. BRINKER: Well, I think that
17 the device has been shown to be reasonably
18 safe and effective. I think that on the basis
19 of the data that they have, and some of the
20 structural design that went into the study,
21 that interventionalists be enthusiastic to use
22 it, and it deserved approval.

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1 DR. YANCY: Dr. Hirshfeld.

2 DR. HIRSHFELD: I would agree with
3 Dr. Brinker. I think it looks like it will
4 prove to be a very nice adjunct to our
5 armamentarium. I am going to pay very careful
6 attention to the forthcoming follow-up data,
7 and the post-market data to continue to
8 examine the question of whether or not there
9 may possibly be a safety issue.

10 DR. YANCY: Dr. Kato.

11 DR. KATO: I voted for approvable
12 with conditions, although I had some
13 reluctance because of the small data size.
14 However, considering that we limited our
15 comments to safety for the first 12 months, I
16 can agree with that.

17 I think that the design of this
18 stent is very encouraging, and I am, again,
19 cautiously optimistic that going forward, the
20 data will support what we've seen in the first
21 12 months.

22 DR. YANCY: Dr. Normand.

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1 DR. NORMAND: I voted for approval
2 with conditions, because the sponsor showed
3 effectiveness with a reasonable sample size
4 for the clinical endpoint. The late loss was
5 based on a much smaller sample size, and so I
6 rested more of my weight towards the clinical
7 endpoint.

8 With regard to safety, I had no
9 prior reason to believe there would be a
10 safety issue. The data that were demonstrated
11 did not show there was a safety issue, and
12 hence, my reason for voting for approvable
13 with conditions.

14 DR. YANCY: Dr. Somberg.

15 DR. SOMBERG: Well, I voted against
16 approval. I thought the safety data in the 12
17 to 24 months was inadequate, and it was a bad
18 precedent to establish, and I thought with the
19 pivotal study only contributing, or having not
20 been fully evaluated, and only contributing 35
21 percent to the numbers, it was of concern to
22 me in that with the recent tumult about late

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1 stent thrombosis, which may or may not be a
2 real issue, to have inadequate data leaves
3 this issue really unaddressed for many years
4 to resolve.

5 DR. YANCY: Dr. Laskey.

6 DR. LASKEY: I voted for approval.

7 The study met it's pre-specified endpoints on
8 both counts out to one year in terms of
9 safety. We discussed that, so the condition
10 for approval reflects that with prolonged
11 follow-up, and a post-approval registry. And,
12 finally, there's something very gratifying
13 about returning to an earlier form of
14 technology which works very well, which is the
15 thin strut. The data was always there before,
16 and it's nice to see it reflected again.

17 DR. YANCY: Dr. Page.

18 DR. PAGE: I voted in favor of
19 approvable with the conditions as outlined. I
20 feel that reasonable assurance of safety was
21 demonstrated, as well as reasonable assurance
22 of effectiveness, and even advantage. And I

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1 think this represents a step forward for
2 interventional cardiology, and for our
3 patients.

4 DR. YANCY: Dr. Blackstone.

5 DR. BLACKSTONE: I voted approvable
6 with conditions. I was convinced that the
7 efficacy data was there. I thought that the
8 safety data, especially for the first 12
9 months, also showed the device was safe.
10 There was encouraging information, especially
11 about late restenosis that may well offset my
12 concern about the long-term data that may come
13 about thrombosis.

14 DR. YANCY: Dr. Jeevanandam.

15 DR. JEEVANANDAM: I voted for
16 approvable with conditions. I think in their
17 12-month endpoint, they're showing efficacy of
18 this device. I think at least for 12 months
19 they've shown safety, and with the post-market
20 approval, I think we'll look at the long-term
21 effects of this device.

22 DR. YANCY: Dr. Morrison.

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1 DR. MORRISON: I think I probably
2 have kept the committee long enough with my
3 review. I trust everyone knows why I voted for
4 approval.

5 DR. YANCY: Dr. Yaross.

6 DR. YAROSS: I would just like to
7 congratulate the sponsor on their development
8 program, and on their very clear presentation
9 today, and thank the panel for a balanced
10 discussion of the issues.

11 DR. YANCY: Ms. Rue.

12 MS. RUE: I would just like to have
13 everyone remain cognizant of the client's
14 ability or inability to pay for the dual
15 antiplatelet therapy, which is so important.
16 And if they need, get them referred to
17 resources, rather than exclude them from the
18 program all together.

19 DR. YANCY: Thank you for your
20 input. The Chair would similarly have voted
21 for approvable with conditions, with some
22 hesitancy, because of the less than robust

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1 safety data set, but the very significant, and
2 very effective evidence of efficacy that the
3 investigators brought forward. And I, too,
4 congratulate the investigators for completing
5 a series of clinical trials in a very
6 important arena, under some arduous
7 circumstances given the recent concerns about
8 safety.

9 I trust that the post-marketing
10 study will assuage the rest of our concerns,
11 and I have every reason to believe that those
12 persons that are involved with this will
13 exercise the correct due diligence to make
14 that happen. But I do think that there are
15 some residual concerns, and I agree with
16 others. Certainly, the early safety data are
17 reassuring, and beyond that, we simply need
18 more information. It's not a negative, we
19 just need more information, and I hope that we
20 make a good faith effort to get that.

21 I'd like to thank the panel
22 members. I think today's discussion was

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1 relevant, was deep. I agree with what Dr.
2 Yaross said, it was balanced, and I appreciate
3 the exchange.

4 Before we can adjourn, we need to
5 give the sponsor an opportunity to make a
6 final statement, should you have such.

7 MR. JOHNSON: We have none. Thank
8 you.

9 DR. YANCY: The FDA, Dr. Zuckerman?

10 DR. ZUCKERMAN: I'd like to again
11 thank the panel members for a very good day of
12 work today.

13 DR. YANCY: The meeting of the
14 Circulatory Systems Device Panel is now
15 adjourned. Thank you very much.

16 (Whereupon, the proceedings went
17 off the record at 5:46:59 p.m.)

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