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DEPARTMENT OF HEALTH AND HUMAN SERVICES

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FOOD AND DRUG ADMINISTRATION

+ + + + +

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

+ + + + +

CIRCULATORY SYSTEM DEVICES ADVISORY PANEL

+ + + + +

MEETING

+ + + + +

MONDAY, DECEMBER 4, 2000

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The Panel met at 10:00 a.m., in the Grand Ballroom of the Gaithersburg Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, Maryland, Dr. Cynthia M. Tracy, Acting Chairperson, presiding.

PRESENT:

CYNTHIA M. TRACY, M.D.	Acting Chairperson
SALIM AZIZ, M.D.	Consultant
MICHAEL D. CRITTENDEN, M.D.	Voting Member
ROBERT A. DACEY	Consumer Representative
MICHAEL J. DOMANSKI, M.D.	Consultant
RENEE S. HARTZ, M.D.	Voting Member
GARY J. JARVIS	Industry Representative

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PRESENT: (CONT.)

MITCHELL W. KRUCOFF, M.D.	Consultant
WARREN LASKEY, M.D.	Consultant
STEPHEN LI, Ph.D.	Consultant
TONY W. SIMMONS, M.D.	Consultant
MEGAN MOYNAHAN	Executive Secretary

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P-R-O-C-E-E-D-I-N-G-S

(10:03 a.m.)

1
2
3 ACTING CHAIRPERSON TRACY: I would like to
4 call to order this meeting of the Circulatory System
5 Devices Panel.

6 MS. MOYNAHAN: I would like to read the
7 conflict of interest statement.

8 The following announcement addresses
9 conflict of interest issues associated with this
10 meeting and is made part of the record to preclude
11 even the appearance of an impropriety.

12 The conflict of interest statutes prohibit
13 special government employees from participating in
14 matters that could affect their or their employers'
15 interests. Therefore, the agency reviewed the
16 submitted agenda for this meeting and all financial
17 interests reported by the committee participants to
18 determine if any conflict existed.

19 We would like to note for the record that
20 the agency took into consideration certain matters
21 regarding Doctors Cynthia Tracy, Warren Laskey,
22 Mitchell Krucoff and Stephen Li. These panelists

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1 reported interests in firms at issues but in matters
2 that are not related to today's agenda or have now
3 been completed. The agency has determined, therefore,
4 that they may participate fully in all discussions.

5 In the event that the discussions involve
6 any other products or firms not already on the agenda
7 for which an FDA participant has a financial interest,
8 the participants should excuse him- or herself from
9 such involvement, and the exclusion will be noted for
10 the record.

11 With respect to all other participants, we
12 ask, in the interest of fairness, that all persons
13 making statements or presentations disclose any
14 current or previous financial involvement with any
15 firm whose products they may wish to comment upon.

16 ACTING CHAIRPERSON TRACY: Could I ask the
17 panel members to please introduce themselves. We will
18 start over at that end.

19 MR. JARVIS: Gary Jarvis, the industry
20 representative.

21 DR. KRUCOFF: Mitch Krucoff,
22 interventional cardiologist from Duke University and

1 Director of Devices Clinical Trials at the Duke
2 Clinical Research Institute.

3 DR. DOMANSKI: Mike Domanski,
4 cardiologist, NHLBI.

5 DR. LASKEY: Warren Laskey, interventional
6 cardiologist, University of Maryland.

7 DR. HARTZ: CT surgeon, Tulane University.

8 MS. MOYNAHAN: Megan Moynahan, Executive
9 Secretary.

10 ACTING CHAIRPERSON TRACY: I am Cynthia
11 Tracy. I am from Georgetown University Hospital and
12 the Acting Chairperson for this session.

13 DR. CRITTENDEN: Michael Crittenden,
14 cardiac surgeon, Harvard University.

15 DR. AZIZ: Salim Aziz, cardiac surgeon,
16 University of Colorado, Denver.

17 DR. SIMMONS: Tony Simmons, Wake Forest
18 University School of Medicine, cardiac
19 electrophysiologist.

20 DR. LI: Stephen Li, Senior Scientist,
21 Department of Biomechanics and Biomaterials, Hospital
22 for Special Surgery in New York City.

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1 MR. DACEY: Robert Dacey, Longmont,
2 Colorado, consumer representative.

3 MR. DILLARD: Jim Dillard. I am the
4 Director of the Division of Cardiovascular and
5 Respiratory Devices at the Food and Drug
6 Administration in the Office of Device Evaluation.

7 MS. MOYNAHAN: I would like to read the
8 appointment of temporary voting status for today.

9 Pursuant to the authority granted under
10 the Medical Devices Advisory Committee charter dated
11 October 27, 1990, as amended April 18, 1999, I appoint
12 the following people as voting members of the
13 Circulatory System Devices Panel for this meeting on
14 December 4, 2000: Cynthia Tracy, Salim Aziz, Warren
15 Laskey, Tony Simmons, Mitchell Krucoff, Michael
16 Domanski and Stephen Li.

17 In addition, I appoint Dr. Cynthia Tracy
18 to act as temporary Chair for the duration of this
19 meeting.

20 For the record, these people are special
21 government employees and are consultants to the panel
22 under the Medical Devices Advisory Committee. They

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1 have undergone the customary conflict of interest
2 review and have reviewed the material to be considered
3 at this meeting.

4 It is signed David W. Feigal, Director of
5 the Center for Devices and Radiological Health.

6 ACTING CHAIRPERSON TRACY: At this time,
7 we are ready for our open public hearing, if there are
8 any members present in the audience who would like to
9 make a statement. Please identify yourself.

10 MS. LOW: Good morning. My name is
11 Bernadette Low, and I am with Guidant Vascular
12 Intervention in California. At this time, I would
13 just like to present guidance response to the petition
14 from Cook.

15 We would respectfully contend that the
16 reclassification of the PTCA catheters from Class III
17 to Class II at this time would not be in the best
18 interest of our ultimate customer, the patient, and we
19 would request that these devices remain as a Class III
20 regulated product.

21 Points to consider in support of this are:
22 That the primary concern has to be the safety of the

1 patient. We have been developing and manufacturing
2 these products over the past 15 years, and our
3 experience has shown a high level of control is
4 necessary to ensure the safety of these devices.

5 We may test between 1500 and 2000 units
6 during our validation studies prior to the release of
7 a new product. Reclassification of these catheters to
8 Class II would inevitably lead to an erosion of these
9 standards and ultimately, we believe, to a reduction
10 in the quality of the products seen by the physician
11 in patients.

12 Additionally, the proposal is heavily
13 based upon the fact that the PTCA catheters have now
14 been available for 20 years under the established data
15 on usage, performance, etcetera, etcetera. The
16 history being referred to, however, is based upon the
17 fact that these products have indeed been regulated as
18 Class III devices in the U.S. and, similarly,
19 internationally with the controls inherent in that
20 classification.

21 Another point we took into consideration
22 was the fact that these catheter systems now are used

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1 are used as delivery vehicles for stents. Thus, there
2 still needs to be a high degree of control over these
3 for the stent delivery application.

4 If the classification for the base
5 catheter is changed, this may additionally have an
6 impact on stent delivery system design and testing.

7 Furthermore, there's been increasing
8 concern in a number of countries in recent years over
9 the reuse of medical devices. At long last, even the
10 U.K. and France have published documentation
11 discouraging the practice.

12 FDA, additionally, has put forward a
13 proposal for controlling this for Class III devices
14 and also for 510(K) devices. However, the
15 reclassification of the PTCA catheter from Class III
16 to Class II would have two potential impacts on this
17 area within the U.S.

18 It would delay the timeline for the
19 product having to meet FDA's recent guidance and,
20 additionally, it would only necessitate the submission
21 of a 510(K) rather than a PMA. So the refurbisher
22 would then only need to establish substantial

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1 equivalence with predicate devices rather than having
2 to provide basic, valid scientific data establishing
3 the safety and effectiveness of the device.

4 Thank you.

5 MS. MOYNAHAN: I would like to mention for
6 the record that we also received two letters during
7 the comment period. The letters were forwarded to the
8 panel members this past week, and both the letters in
9 their entirety will become part of the public record
10 for the panel meeting today, and FDA will acknowledge
11 these comments in their presentation. But I wanted to
12 summarize for the record.

13 One letter came in from Boston Scientific.
14 In that letter, they agreed that there is substantial
15 clinical evidence to support the down-classification
16 of the devices. They believe that down-classification
17 should apply to standard PTCA catheters only and not
18 those with heated balloons or with cutting edges.

19 They have proposed -- or provided, rather,
20 additional comments on the guidance document that is
21 being proposed as a special control for these devices.

22 The other letter came from Spectranetics.

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1 The letter agreed with the proposed reclassification
2 of standard balloon PTCA catheters from Class III to
3 Class II. They believe that the definition of balloon
4 PTCA catheters should be developed that differentiates
5 standard balloon designs from those incorporating
6 other therapeutic features.

7 They have also provided additional
8 comments on the labeling, identified health risks in
9 the proposed guidance document.

10 ACTING CHAIRPERSON TRACY: I would like at
11 this point for Chris Sloan to take the microphone. He
12 is the Branch Chief for Interventional Cardiology at
13 the Device Panel.

14 MR. SLOAN: Good morning. I would like to
15 give you a brief update of two projects that you
16 recently reviewed at this panel.

17 The first one, the Cordis Checkmate
18 System, was reviewed at the June 19, 2000, panel.
19 This product, PMA number P990036, is an intervascular
20 brachytherapy system for the treatment of in-stent
21 restenosis.

22 The device is intended for the delivery of

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1 therapeutic doses of gamma radiation for the purpose
2 of reducing in-stent restenosis. The system is for
3 use in the treatment of native coronary arteries with
4 in-stent restenosis following percutaneous
5 revascularization using current interventional
6 techniques.

7 The system is for use in vessels 2.75 to
8 4 millimeters in diameter and for lesions up to and
9 including 45 millimeters in length.

10 On June 19, this panel made a
11 recommendation to approve the PMA with conditions.
12 The conditions included changes to the labeling,
13 modifications to the training program, and the need to
14 collect five-year clinical follow-up data on patients
15 treated with the device in PMA studies.

16 CDRH has concurred with the panel's
17 recommendations, and after the sponsor submitted
18 information satisfying the stated conditions, FDA
19 issued an approval order for this product on November
20 3, 2000.

21 On September 11, 2000, this panel
22 considered another intervascular brachytherapy system,

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1 the "Beta"Cath System from Novoste Corporation,
2 P000018. This system is intended to deliver Beta
3 radiation to the site of successful percutaneous
4 coronary intervention for the treatment of in-stent
5 restenosis in native coronary arteries with discrete
6 lesions treatable with a 20 millimeter balloon in a
7 reference vessel diameter ranging from 2.7 to 4
8 millimeters.

9 On September 11, this panel made a
10 recommendation to approve the PMA with conditions.
11 The conditions included the need for additional data
12 analysis, changes to the labeling, modifications to
13 the training program, the need to collect five-year
14 clinical follow-up data on patients treated with the
15 device in PMA studies, and the need for a prospective
16 post-approval study at new clinical sites to
17 demonstrate that modifications to the device and
18 instructions for use are adequate to reduce the
19 incidence of device failures and malfunctions.

20 CDRH has concurred with the panel's
21 recommendations, and after the sponsor submitted
22 information satisfying the stated conditions, FDA

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1 issued an approval order for this product on November
2 3, 2000. Thank you.

3 ACTING CHAIRPERSON TRACY: Okay, thank
4 you. At this point the FDA has some introductory
5 remarks regarding today's session.

6 MS. GABRIEL: Good morning. My name is
7 Lynette Gabriel, and I'm a reviewer in the Division of
8 Cardiovascular and Respiratory Devices at FDA.

9 Earlier this morning, you received
10 training in the procedures for reclassifying a medical
11 device. The purpose of today's meeting is to consider
12 a reclassification petition for percutaneous
13 transluminal coronary angioplasty or PTCA catheters.

14 Following these introductory remarks,
15 Cook, the sponsor of the petition, will give their
16 presentation. FDA will then present our questions to
17 the panel, and that will be followed by completion of
18 the reclassification questionnaires that you have in
19 front of you.

20 I would like to start by giving a brief
21 summary of the regulatory history and FDA's experience
22 with PTCA catheters.

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1 PTCA catheters are considered post-
2 amendments devices. This means that they were first
3 introduced into interstate commerce for commercial
4 distribution after May 28, 1976, which is the date of
5 the Medical Device Amendments regulation.

6 PTCA catheters are currently Class III
7 devices. The petition under consideration today
8 proposes down-classifying them to Class II.

9 The agency received its first pre-market
10 approval or PMA application for a PTCA catheter in
11 1979. That device was approved in 1980. Since then,
12 FDA has reviewed and approved 19 other original PMA
13 applications, the most recent in 1999, and
14 approximately 820 PMA supplements for PTCA catheters.

15 The majority of these supplements
16 represent device modifications and new catheter
17 models, which emphasizes the wide availability and use
18 of these devices.

19 During today's meeting, and as you listen
20 to the presentations, we ask that you keep in mind
21 that PTCA reclassification would apply only to those
22 devices described by the proposed definition or device

1 description presented on this slide. This will also
2 be discussed further during Cook's presentation.

3 Additionally, reclassification would only
4 apply to catheters with the proposed indication for
5 use, which is "intended for balloon dilatation of a
6 hemodynamically significant coronary artery or bypass
7 graft stenosis in patients evidencing coronary
8 ischemia for the purpose of improving myocardial
9 perfusion."

10 For example, stent delivery catheters do
11 not have this indication and, therefore, are not being
12 considered for reclassification as part of this
13 petition.

14 I would also like to point out that
15 reclassification applies to certain devices and not
16 necessarily an entire product code. The agency
17 maintains its ability to determine whether certain
18 device designs or modifications raise new questions of
19 safety and effectiveness or imply a new intended use.
20 If so, those particular devices may not be subject to
21 this reclassification.

22 As part of our review of the petition, FDA

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1 conducted a search of its manufacturer and user
2 facility device experience, or MAUDE, database. This
3 slide lists the most frequently reported adverse
4 events associated with PTCA catheters.

5 The search covers a time period from July
6 1996 through October 2000. This list, however, also
7 does include adverse events that are associated with
8 noncoronary PTCA, PTA procedures.

9 It has been our experience that the
10 product codes for those two devices are often
11 misidentified during reporting, making it difficult to
12 distinguish between them during our search. Overall,
13 approximately 40 manufacturers reported 3,316 adverse
14 events.

15 To conclude the introductory comments, I
16 would like to summarize the comments that we have
17 received to date regarding the reclassification
18 petition.

19 As of November 27, we received two letters
20 from individual manufacturers. Both companies agree
21 with the proposal to downclassify PTCA catheters, but
22 feel that the reclassification should apply only to

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1 standard devices.

2 One company expressed concern about the
3 use of PTCA catheters in the treatment of in-stent
4 restenosis and suggested that the device labeling
5 specifically address the fact that these devices have
6 never been studied for that indication.

7 Finally, both letters contained
8 suggestions regarding the revision and updating the
9 FDA current guidance document and device labeling
10 template. These suggestions and any others that we
11 receive will be taken into consideration as we move
12 forward with this project.

13 With that, I would like to turn the
14 meeting over to Cook for their presentation.

15 ACTING CHAIRPERSON TRACY: Before we do
16 that, I failed to close the open public hearing. Are
17 there anymore questions, comments, from the audience
18 before we move on to Cook's presentation? If not,
19 then the open session is cleared, and there will be
20 another open session at the end of the meeting today.

21 DR. FEARNOT: I am Neal Fearnot. I am the
22 President of MED Institute, which is a Cook company.

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1 I am responsible for science and regulatory issues.\

2 Cook, as a company, is perhaps the largest
3 private medical device company in the world and has
4 had a long history of these types of devices, and
5 brings to you this presentation really without any
6 products of its own in consideration. It's just our
7 feeling that, if reclassification is possible, it
8 would be to the advantage of FDA in terms of allotting
9 their resources to the most beneficial projects and
10 those being new technology.

11 As you can see, I am going to be using
12 slides behind you there. The first part of our
13 presentation will be a review of the history of
14 angioplasty, the evolution of the PTCA balloon
15 catheter, and labeling information that is needed by
16 a physician from a clinical perspective.

17 We are really honored today to have to
18 present to you one of the fathers of angioplasty, Dr.
19 Cass Pinkerton from Indianapolis. Dr. Pinkerton
20 himself has been involved in close to 20,000
21 angioplasty procedures.

22 He has started with the very first

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1 catheters, and we felt like a person with this
2 perspective and this experience could provide the
3 panel with an excellent overview of angioplasty.

4 So without any further ado, please welcome
5 to the podium Dr. Cass Pinkerton, interventional
6 cardiologist, Indianapolis, Indiana.

7 ACTING CHAIRPERSON TRACY: Can I ask just
8 that speakers who come to the microphone please
9 identify themselves and state any conflict of interest
10 you might have.

11 DR. PINKERTON: Good morning. I am Cass
12 Pinkerton from Indianapolis. I work at St. Vincent's
13 Hospital. I have no conflict of interest at this
14 time. I previously was involved with a variety of
15 different device companies, but I am no longer on any
16 panels or advisory committees at this time.

17 What I would like to do is spend just a
18 very few minutes talking about the history of
19 angioplasty and some of the problems we have had to
20 occur, and then discuss the labeling issues, the
21 composition of the balloon materials, and what are the
22 important factors that a physician must have at their

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1 knowledge so that they can do a safe procedure.

2 I would like to begin with a little bit of
3 history. As a matter of fact, in 1929 Dr. Forssmann
4 performed the first cardiac catheterization in 1929 on
5 himself, and a full 30 years later he shared the Nobel
6 Prize with Dr. Cournand.

7 He made the statement that the cardiac
8 catheter was the key in the lock. I think that we
9 certainly all can agree that, with the advent of
10 cardiac catheterization and balloon angioplasty, the
11 change in the treatment of patients with cardiac
12 disease has gone under a complete change within the
13 past 20 years.

14 In the 1950s Dr. Cesare Gianturco designed
15 some catheters with the thought that he could open up
16 arteries that were obstructed mainly in the peripheral
17 vessels. In the 1960s Charles Dotter and Dr. Melvin
18 Judkins, who is responsible for the Judkins catheter
19 that is used for diagnostic catheterization even
20 today, began working on a series of catheters to open
21 up blocked coronary arteries mainly in the iliac
22 arteries and in the periphery.

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1 In 1964 Dr. Dotter and Judkins in
2 California performed the first iliac angioplasty by
3 using larger and larger catheters to open these
4 arteries in the iliac arteries with good clinical
5 results.

6 In the 1970s Dr. Andreas Gruentzig
7 developed a balloon catheter that he initially used in
8 the peripheral arteries. He performed the first
9 peripheral human balloon angioplasty in 1974.
10 Subsequently, he did renal artery dilatations, and
11 eventually got the catheter small enough so that he
12 could move it into the coronary arteries.

13 Now the first coronary angioplasty was
14 actually done during surgery in San Francisco. A
15 balloon was blown up during surgery, and a filter was
16 used to see if there was any material that escaped and
17 could damage the heart muscle, and they found there
18 that was not. In 1977 he performed the first cath lab
19 PTCA on a conscious patient in Zurich, Switzerland.

20 This is an angiogram of that first
21 patient. On the left you can see the pre-stenosis
22 before he blew up the balloon. The second picture is

1 the one that occurred directly after, and the
2 following picture is at six months.

3 So from 1977, the development of balloon
4 catheters continued, and the description of a balloon
5 catheter is as follows: A PTCA balloon catheter has
6 a single or double lumen shaft with a balloon near the
7 distal tip. The catheter typically features a
8 minimally compliant balloon constructed by a high
9 density polymer.

10 The balloon is designed to expand
11 uniformly to a specified diameter and length at a
12 specified pressure as labeled, with acceptable rates
13 of inflation and deflation and acceptable burst
14 pressure. The device generally features a type of
15 radiographic marker to facilitate fluoroscopic
16 visualization of the balloon during use.

17 Now we are going to go over a couple of
18 these points, mainly rated burst pressure and
19 compliance, and first I would like to talk about the
20 types of balloons that are available.

21 Now the first balloon that was made was a
22 fixed wire catheter. So there was not a moveable wire

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1 So it was fairly difficult to access a lot of areas of
2 the coronary anatomy. These are still used, but to a
3 much less frequent usage at present day, but they are
4 still available.

5 Finally or secondly, there was an over-
6 the-wire catheter which allowed a moveable coronary
7 guide wire to be placed in the coronary anatomy, and
8 this provided the physician with the ability to access
9 many different vessels and overcome certain problems
10 of the coronary anatomy.

11 Lastly, the Rapid Exchange catheter is a
12 catheter that goes alongside a wire, over a part of
13 the wire into the coronary anatomy, and this improves
14 the speed of the procedure and also makes it much
15 easier to change balloon catheters during the
16 procedure itself.

17 Here's some examples of balloon catheters
18 that are currently available. I'm not going to go
19 over these in detail, just to give you a list. There
20 are many PTCA catheters available. As a matter of
21 fact, over 200 have been approved for use in the
22 United States, and these are just some of the current

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1 catheters that are now on the market.

2 Now the problem that we've had is that
3 we're dealing with different kinds of coronary
4 lesions, varying from a soft, young lesion with smooth
5 muscle cell dominance on the left, all the way to
6 severe calcification.

7 So during the past 20 years, we've had to
8 develop balloon material that is able to attack these
9 catheters -- My battery is fully charged. Well,
10 that's good to know. I sure wish I could get rid of
11 that. I've never used one of these mouses before.

12 So we've had a great deal of difficulty
13 developing the materials that could approach these
14 difficult types of lesions, and for that reason over
15 a long period of time, there has been changes in
16 materials that we have used to approach these clinical
17 problems.

18 Excuse me. Now here we are on complete
19 standby.

20 ACTING CHAIRPERSON TRACY: While they are
21 working on that, I will just take this opportunity to
22 entertain you by remarking that any other speakers who

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1 come up, please state whether or not your travels were
2 paid or if you are receiving any kind of compensation.

3 DR. PINKERTON: Actually, I can make that
4 statement right now. My travels were paid for, and
5 I'm not receiving any compensation.

6 Back in the early 1980s, the earliest
7 balloons were made of polyvinyl chloride, and that's
8 when I began doing angioplasty in 1979. The highest
9 atmosphere of pressure that we go to at that time was
10 about four atmospheres.

11 Usually, we broke at least one balloon a
12 week. It didn't seem to have any negative effects on
13 a coronary artery if a balloon wasn't too large, but
14 it was obvious that balloon materials had to be
15 developed to approach the differing kinds of coronary
16 lesions that we encountered in the clinical
17 population.

18 Over the next ten years or 15 years,
19 polyethylene was used to maintain a fixed diameter of
20 balloons through a wide variety of pressures. At this
21 time, most balloons are made of some variance of nylon
22 or PTE. Some balloons have been developed to take

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1 very high pressures, at least 20 atmospheres; whereas,
2 in the early 1980s we could only go to four.

3 So these balloons maintain their same
4 diameter with a much higher pressure, so that we can
5 attack different kinds of coronary lesions that are
6 present now.

7 The labeling information that really is
8 needed by the clinician I am going to go over on this
9 slide. The balloon length is really important,
10 because you don't want to use too long of a balloon to
11 dilate a coronary artery and damage the normal vessel
12 walls. So you want to pick a balloon length that is
13 appropriate to a lesion that you are trying to treat.

14 The diameter of the balloon also is very
15 important. Picking too large a balloon may overextend
16 the vessel and damage the vessel, causing a coronary
17 dissection. So you want to pick an appropriate size
18 balloon, and that must be on the label.

19 The shaft length should be noted. There
20 are a couple of types of lengths of shafts. There are
21 some long catheters that are 145 sonometers. Those
22 are relatively unusual, but this also should be on the

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1 label.

2 The balloon catheter lumen diameter should
3 be noted. Basically, that falls into two areas, in
4 14,000th and 18,000th wire lumen diameter, and most
5 frequently 14,000ths is used in the year 2000.

6 The minimum guiding catheter lumen should
7 also be noted. This is what size of catheter the
8 balloon will fit through. Most catheters that are now
9 available will fit through a six inch guide that are
10 now available from most manufacturers.

11 I'd like to spend a little bit of time on
12 compliance and also on rated burst pressure, and I
13 think that these are very important labeling
14 information that is needed by the doctor to perform a
15 safe procedure.

16 Talking a little bit about compliance,
17 what we've done here is draw a graph. What we mean,
18 with increasing pressure a compliant balloon, even
19 though it is, say, at the same size, will increase
20 more versus a less compliant balloon that will
21 maintain relatively the same size over a large area of
22 pressure.

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1 Now here is some examples of what's
2 currently available. Here is something I would like
3 to point out that I think is relatively important.
4 Most balloons are what we call semi-compliant. In
5 other words, the balloon diameter increases a certain
6 amount over a range of pressure. However, there have
7 been some high pressure balloons developed, and a
8 semi-compliant balloon -- this is the Solaris balloon
9 -- even though it will go over 20 atmospheres and not
10 burst, will tend to grow slightly, much more so than
11 PTE which has a relatively flat compliance curve.

12 I think this is relatively important for
13 the doctor to know what kind of balloon compliance
14 pressures he is using.

15 Now as far as compliance, the balloon
16 diameter tends to grow, increasing pressure, no matter
17 what kind of material you use. Most balloon catheters
18 that are used now reach their nominal size at
19 approximately eight atmospheres of pressure. I think
20 that is important to be on the label so the doctor
21 knows what pressure he can go to, so the balloon will
22 reach the stated size.

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1 Now rate of burst pressure is very --
2 Usually, a general rule is the larger the balloon, the
3 lower the rate of burst pressure, and I think that
4 this should be on the label as well. There may be
5 some small change in reference to length, but I think
6 the physician needs to know this to perform a safe
7 procedure.

8 In concluding remarks, PTCA catheters have
9 evolved a great deal over the last two decades, the
10 past 20 years. Since I've been performing
11 angioplasty, I mean, it's just night and day. I think
12 that there is a lot of experience.

13 Although the PTCA catheters are a mature
14 technology, I think they will continue to improve, and
15 mainly with decreasing profile and materials that may
16 even go to higher pressures, although I'm not sure
17 that that ever is going to be needed.

18 The risks are known, although the
19 incidence of each risk may vary, obviously, to many
20 clinical and angiographic factors, and should be taken
21 into account by the physician. Interventionalists
22 need the labeling information to decrease the

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1 potential for these risks.

2 I'd like to thank you very much. Dr.
3 Fearnot will continue on with his presentation,
4 talking about the use and status of special controls,
5 currently labeling requirements, guidances,
6 regulations, post-market information and industry
7 perspective.

8 DR. FEARNOT: Thank you, Dr. Pinkerton.
9 What I would like to do is give you three segments of
10 information that I feel would be valuable to you in
11 your consideration. The first are the reasons why we
12 feel like reclassification makes sense.

13 Secondly, we would like to talk about the
14 special controls, guidance documents, etcetera, that
15 we feel could be adjusted and updated to provide a
16 level of safety and review and information equal to or
17 better than what is presently available for these
18 catheters.

19 Then the third group of information I'd
20 like to go through are the actual risks associated
21 with the PTCA procedure and show how the special
22 controls relate to each of those risks.

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1 So with that as an overview, I want to say
2 that this is a collection of 30 or so different IFUs
3 that I've reviewed, and it is really somewhat
4 rewarding to find out that the information in these
5 IFUs is very consistent from manufacturer to
6 manufacturer. In fact, even though there are a number
7 of manufacturers here, they seem to already be using
8 the FDA guidance to a large degree.

9 Some of the wording itself changes a
10 little bit here and there between the different
11 manufacturers, but in general I can tell you that the
12 basic same information is in most of these. I think
13 that, if the guidance is updated and it is
14 downclassified, we can actually get better consistency
15 between the different IFUs.

16 Let me start by a little bit of
17 information on why we believe that reclassification is
18 important at this time or it would be an advantage.

19 First of all, we do know after 20 years
20 that there are a couple of advantages to the PTCA
21 procedure. First, it is a minimally invasive
22 technique. Secondly, in most cases, it is less

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1 traumatic and less expensive than the alternative
2 bypass surgery, and in that way it's a real benefit to
3 the patients.

4 There are three indications for use I
5 would like to show you, the first of which you saw in
6 the earlier presentation by FDA. But I wanted to make
7 you aware of the other two indications that have been
8 approved for PTCA catheters.

9 The Percutaneous Transluminal Coronary
10 Angioplasty Dilatation Catheter is indicated, first,
11 for dilatation of stenoses in coronary artery or a
12 bypass graft stenosis for the purpose of improving
13 myocardial perfusion. This involves both de novo and
14 restenotic lesions in those two locations.

15 The second indication that has been
16 approved for PTCA balloon catheters relates to using
17 a PTCA catheter in an acute myocardial infarction
18 case. In this situation, balloon dilatation is used
19 for coronary artery occlusion for the purpose of
20 restoring coronary flow in patients with ST-segment
21 elevation myocardial infarction.

22 Finally, there is one PTCA catheter at

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1 least that is approved for dilatation of stents after
2 implantation of the coronary stent.

3 Being one who stood before a previous
4 panel like this to ask for the approval of the first
5 coronary stent, it's a privilege to be at this
6 position today after millions of uses of stents.

7 Let's look at the history of
8 angioplasties. We can see that since 1980 the number
9 of angioplasties has grown consistently over time. At
10 this point in time, there are 400,000-plus procedures
11 in the U.S., and there are over a million in the
12 world. This is a well known procedure, and by some
13 measures, it is the most common medical intervention
14 worldwide.

15 There are a number of manufacturers that
16 your decision on reclassification will affect, and
17 these manufacturers have over many years provided a
18 number of angioplasty catheters which, as previously
19 spoken, is greater than 200-250.

20 There have been a number of clinical
21 trials looking at the outcome of PTCA procedures.
22 These that I have listed for you are early studies.

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1 Since that time, there have been many additional
2 studies.

3 Most often now, the clinical studies on
4 PTCA's are as a control group for a new intervention
5 such as coronary stenting or atherectomy or something
6 like that. So they are still being acquired in well
7 controlled clinical studies on angioplasty.

8 We feel like at this point in time there's
9 a real good understanding of the outcome of these
10 procedures, measured in terms typically in the
11 published literature as MACE or Major Adverse Cardiac
12 Events, and these include, as you see on this slide,
13 surgery, myocardial infarctions, death, repeat
14 angioplasty.

15 There also have been studied in clinical
16 trials the access site complications which include
17 pseudo-aneurysm, A-V fistula, surgery repair,
18 infection, bleeding, things such as those. So I would
19 submit to you that the adequate clinical trials have
20 been run on angioplasty catheters at this time.

21 While looking at the number of procedures,
22 the number of manufacturers who have provided balloons

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1 and who do have history in making good balloons, let
2 me summarize the rationale that led us to come to FDA
3 and to you today to recommend and suggest that
4 reclassification is reasonable.

5 First, the risks associated with PTCA
6 catheters are well known at this time. Secondly, the
7 risks are similar across many different models.
8 Thirdly, the probability of discovering a new risk at
9 this point is really extremely low.

10 I think, with the experience of the
11 manufacturers that will be providing these balloons,
12 they do have the experience to understand when a
13 catheter deviates from the standard PTCA balloon and
14 when it would require additional studies.

15 Requiring a specific study for each and
16 every individual catheter at this point really offers
17 very little additional information.

18 We believe that special controls at this
19 point with an updated guidance would adequately
20 address the risks of a standard PTCA catheter, and I
21 will go into the risks and the special controls a
22 little later.

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1 Finally, reclassification would allow FDA
2 to review PTCA catheters as Class II devices under a
3 510(k) process, saving some of the resources.

4 There are a couple of issues with
5 reclassification that have been raised by FDA that we
6 want to address. First, is the device description
7 complete? Secondly, are the clinical risks fully
8 described? Thirdly, are special controls adequate to
9 control for those risks?

10 Let me talk about the special controls.
11 Special controls include guidance documents, labeling,
12 and two additional areas, design validation testing
13 and post-market surveillance. I'd like to go through
14 each of these and try to describe to you just in a
15 snapshot what is available today.

16 Guidances do exist and have been used as
17 draft guidances, not fully issued. This gives us an
18 opportunity at this time to update those guidances and
19 process them through good guidance practices such that
20 comments can be obtained and the guidances can be
21 brought up to date and adequately control this
22 situation.

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1 The first guidance I'd like to draw your
2 attention to is the Guidance For Submission of
3 Research and Marketing Applications for Interventional
4 Cardiology Devices, which includes, as you will see,
5 PTCA catheters along with atherectomy, laser and other
6 devices.

7 The second guidance available is a
8 guidance on the Percutaneous Transluminal Coronary
9 Angioplasty Package Insert Template. This guidance
10 guides the labeling for PTCA catheters, such that the
11 labeling is consistent and complete and includes the
12 information Dr. Pinkerton discussed earlier that is
13 necessary for the physician.

14 Finally, there is a guidance related to
15 the wire guide, and it is entitled Coronary and
16 Cerebrovascular Guidewire Guidance.

17 Let me describe to you quickly what the
18 content of these guidances are. Guidance that talks
19 about the labeling requires that the label -- the
20 instructions for use in the package labels include a
21 device description, indications for use,
22 contraindications, warnings, precautions, adverse

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1 effects, clinical and laboratory data, if applicable,
2 from a clinical trial, detailed instructions for use -
3 - you will see how later that is important --
4 references.

5 So this guidance actually has, I believe,
6 been used for several years voluntarily by
7 manufacturers to make sure that the IFUs contain the
8 information that is valuable to physicians. I know
9 from our company's standpoint that we use these
10 guidances extensively, and really appreciate them,
11 because they take an error of uncertainty out of the
12 process of putting a label together.

13 I also think, when physicians see common
14 labeling, they can quickly get the information they
15 need.

16 The first guidance I showed you related to
17 interventional devices lists -- I'm sorry, this is the
18 labeling guidance -- lists the potential adverse
19 effects, to include but are not limited to a large
20 list, which I will quickly go through: Acute vessel
21 closure, total occlusion; coronary artery dissection,
22 perforation, rupture or injury; myocardial infarction;

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1 conduction disturbances of several kinds, including
2 arrhythmias, fibrillation, etcetera; embolism; hypo or
3 hypertension; drug reactions, including allergy to
4 contrast agents, reactions to the anti-platelet/anti-
5 thrombus or anti-spasmodic type drugs; vascular access
6 site complications, which include A-V fistulas,
7 infection, pain, bleeding, pseudoaneurysm; coronary
8 artery spasm; unstable angina; restenosis; and death.

9 All of these are in some way or another
10 listed among the potential adverse effects in the
11 labeling for various angioplasty catheters. I would
12 like to, during this talk, add a few extras to that
13 that we have seen since that guidance was put
14 together, but these are the basic adverse events.

15 The guidance on interventional devices
16 talks about several types of information that are
17 required of manufacturers, and this information must
18 be obtained through testing today, and it would be
19 after reclassification as well.

20 This information also must be reported to
21 FDA to allow their review of these devices. It also
22 plays a major role in the labeling. So this includes:

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1 uniformity of the balloon catheter along its length;
2 several dimensional measurements, diameter of the
3 balloon, diameter of the catheters, other dimensions;
4 compliance issues such as diameter versus pressure
5 that Dr. Pinkerton talked about.

6 Angioplasties are used multiple times. So
7 the guidance suggests that repeatability tests are
8 performed, inflation and deflation times are measured,
9 torqueability of the catheter is measured, bond
10 strengths of any bond areas in the catheter be
11 measured, and tip conformity be measured.

12 Now as a manufacturer, the physical
13 testing that actually goes on is probably a little bit
14 more detailed than this guidance, and the guidance
15 could be updated. It includes minimum burst strength,
16 a complete compliance chart, inflation and deflation
17 performance, balloon fatigue measures, bond strengths,
18 catheter diameter and balloon profile, tip pull
19 testing to ensure that the catheter has integrity,
20 over-the-arch torque strength tests which are
21 applicable to fixed wire catheters, over-the-arch
22 torque response testing --this basically is to ensure

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1 that after the catheter is bent over the aortic arch
2 that twisting or turning of the catheter will result
3 in a movement at the tip of the catheter and not
4 destruction of the device -- balloon preparation
5 testing, catheter body burst pressure, contrast medium
6 flow rates, and pressure monitoring.

7 The guidance also, in addition to the long
8 list of bench testing that is required for these
9 catheters, talks about the use of animal studies and
10 states. The animal studies of PTCA balloon catheters
11 are only necessary if the design of the catheter or
12 mode of angioplasty differs from that of standard
13 balloon catheters that are presently approved for
14 marketing.

15 When the animal studies are performed, and
16 the animal studies that were performed many years ago
17 looked at maneuverability of the device in anatomical
18 situations, performance of the balloon during the
19 actual angioplasty procedure, and provided pathology
20 which has been well published at this time.

21 There are two other special controls in
22 addition to the guidance documents and the labeling

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1 that I would like to talk about. First, the Federal
2 regulations now require that manufacturers during
3 their design process of medical devices go through the
4 following steps, and this is a regulation I've just
5 laid out the outline of:

6 Design control regulations, which are
7 relatively new for manufacturers, require that there
8 be a written process for designing and developing new
9 medical devices or modifying existing ones. This
10 procedure includes procedures for obtaining inputs
11 from physicians or other requirements such as higher
12 pressures, larger diameters.

13 Whatever the change in the requirement for
14 the device would be, manufacturers are required to
15 have written procedures and maintain files on the
16 gathering of those inputs.

17 They are also required to have written
18 procedures and maintain files discussing how those
19 inputs from physicians or other engineering
20 requirements are translated into a design that would
21 meet those requirements.

22 They are required to have design reviews

1 with the major people throughout the company to make
2 sure that all aspects involved in the manufacturing
3 and distribution of a medical device such as the PTCA
4 catheter is all coordinated properly and none of the
5 steps are left out.

6 There are required now verification
7 procedures, such that if a PTCA catheter were
8 modified, one would have to certify through a
9 certifying process controlled by a written procedure
10 that, in fact, the final balloon that was produced
11 did, in fact, meet the design outputs, the design
12 inputs, that the procedure was followed correctly.

13 In addition to that, validation procedures
14 are required to control and to demonstrate that the
15 actual balloon produced really does meet the clinical
16 need and meets the requirements for the clinical
17 situation.

18 There are also requirements that control
19 the transfer from design to manufacturing so that the
20 manufactured catheter is equivalent to what was
21 expected to be manufactured, and change controls so if
22 there are any modifications, there is a documented

1 process for changing those.

2 These were not available back in '76.
3 These are only recently introduced in the legislation.
4 So I believe they provide an additional measure of
5 security for people using PTCA catheters, and all
6 manufacturers are now required to comply with these.
7 They are inspected by FDA.

8 Finally, post-market reporting is
9 mandatory, and it does gives us a snapshot with regard
10 to complications to go back and check and see if the
11 expected or potential adverse effects are, in fact,
12 the ones that are occurring.

13 We have done a search, as the FDA did.
14 There are 7500 procedures dating back to '85, and
15 there are over 3 million procedures. I think FDA
16 talked about the reasons for these.

17 In our estimation, our analysis of this,
18 the procedural problems that we are seeing in this
19 database are, in fact, reflected in the list of
20 adverse events. There are no brand new adverse events
21 that we could pick up in looking at these data and
22 comparing these results in MDR reported events to the

1 list that I showed you.

2 So I feel like it is a very mature
3 technology in terms of expected adverse events.

4 Lastly, I would like to go through the
5 adverse events and talk about the special controls
6 that we believe are in place and how the special
7 controls relate back to each of those adverse events.

8 Potential risks are listed here. As I
9 told you earlier, I have added a few on top of the
10 guidance, and these include coagulopathy, stroke,
11 balloon rupture -- although balloon rupture itself is
12 not a medical complication, it does occur -- it's a
13 device complication -- guidewire complications, and
14 failed procedures.

15 These may or may not need to be listed as
16 clinical events, but I wanted to talk about them
17 today, because I think they are important in
18 understanding balloon catheters.

19 The first of those is acute vessel
20 closure, and this is really caused by thrombus in the
21 area of the stenosis, dissection or spasm. Thrombus
22 and spasm are dealt with in terms of pharmacological

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1 agents. Dissection is related to the device in
2 general. So I tried to split that out.

3 The practice of medicine involves
4 technique by the interventionalist as well as use of
5 pharmacological agents and other devices to deal with
6 these issues. The balloon catheter, though, itself as
7 it relates to vessel closure is controlled by these
8 guidances.

9 Dissection can occur for several reasons.
10 It can occur when the wrong balloon catheter is
11 chosen, the diameter is too large, or it is inflated
12 to too high of a pressure. So in the guidances it is
13 important to obtain the data during the testing period
14 on compliance, burst pressure, dimensions, and then in
15 the labeling provide these to the clinician so they
16 can have a choice and correctly choose the balloon
17 catheter, thereby minimizing dissection.

18 Physician training in interventional
19 procedures is a requirement in the labeling for PTCA
20 balloons. The PTCA labeling itself says that
21 cardiologists using this balloon must have specific
22 training in interventional procedures, which includes

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1 the practice of medicine issues listed.

2 Dissection, perforation, rupture of a
3 coronary artery is due to trauma during the inflation
4 of the balloon. It can be due to a balloon being too
5 large for the vessel, the balloon rupturing, the
6 balloon being moved during its inflated state, or an
7 expansion of an intramural hematoma within the wall of
8 the coronary artery.

9 The precautions that are listed in IFUs
10 are here, and the clinician is instructed to choose
11 appropriate catheter, not to exceed the burst
12 pressure, advance the guide carefully, do not advance
13 it while it is inflated.

14 Then in terms of managing this clinical
15 situation, if it should occur, use of stents,
16 embolization or surgery are also included.

17 The guidance provides the data -- The
18 guidance for testing provides the data that addresses
19 the size of the balloon, the rupture pressure of the
20 balloon. Also the instructions for use and labeling
21 suggest do not use excessive force, do not advance it
22 while it is inflated, and also instruct the physicians

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1 on other issues in the instruction portion on exactly
2 how to use the balloon.

3 Acute myocardial infarction and unstable
4 angina, which are two different events but can occur
5 during the balloon inflation by the fracturing of the
6 plaque or atherosclerotic material, can cause failure
7 -- or be caused by failure of the procedure, thrombus,
8 spasm or dissection.

9 Spasm, thrombus, again, are medically
10 treated, dissection, and failure of the procedure is
11 often related to the device. Careful use of the
12 interventional technique, fractionation of the
13 expansion of the balloon based on SD segment
14 elevation, care in patient selection and monitoring
15 are precautions.

16 In this case, the practice of medicine
17 addresses technique issues, pharmacological agents
18 used to deal with spasm and thrombus. Guidances deal
19 with providing the data related to the angioplasty
20 procedure again for dissection, and several warnings
21 and precautions related to avoiding failure of the
22 procedure.

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1 Arrhythmia can occur during balloon
2 expansion. Arrhythmias can be caused by myocardial
3 ischemia during the balloon inflation, hypoxia,
4 stimulation of myocardium with guide catheters, vagal
5 stimulation and ICD.

6 Precautions to avoid this include:
7 Avoiding unnecessary stimulation and poking of the
8 coronary vessels with the guide wire and catheters;
9 fractionating the inflation if there is real
10 dependence on that vessel for blood flow; and then
11 adequate pharmaceuticals to deal with some of these
12 other medically related issues.

13 The guidance documents deal with labeling
14 or include labeling that addresses inflating the
15 balloon to the proper diameter for a short period of
16 time, and also to limit the inflation period based on
17 angina and EKG tracings.

18 The stimulation of the myocardium with the
19 wire guide is addressed as well in the labeling.
20 Hypoxia, ICDs and vagal stimulation are left to the
21 practice of medicine.

22 One of the outcomes that has occurred in

1 especially early procedures and sometimes now includes
2 embolization of the thrombotic material, distally or
3 even proximally.

4 This is caused by fracture of the plaque,
5 expansion of the balloon in thrombus, or
6 atherosclerotic material being freed by the expansion
7 of the balloon or the insertion or removal of the
8 balloon catheter.

9 In cases where there is fractured plaque
10 in the lumen, stents can be placed or the material can
11 be aspirated.

12 The labeling addresses this in terms of
13 providing data on the balloon and providing
14 instructions and, in particular, precautions against
15 trying to do placement of these and manipulation of
16 these catheters in a thrombotic, heavily thrombotic,
17 vessel. I think this is one area that could be
18 improved in the present guidance on labeling.

19 Air embolism can occur from a balloon
20 catheter in a number of ways: Incomplete aspiration
21 of the guiding catheter before placement of the
22 balloon catheter; balloon rupture, if the balloon is

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1 filled with air; air that enters into the guiding
2 catheter when the balloon catheter is inserted into
3 the guiding catheter; and structural failure of some
4 or all of the equipment.

5 It is common in angioplasty. It is also
6 listed in the labeling regarding the proper
7 preparation of these devices. This includes pre-
8 flushing the lumens of the catheters, guiding
9 catheters. It also includes pre-filling the balloon
10 itself, lumen to the balloon, and using negative
11 preparation, filling it with contrast media
12 appropriate to inflation.

13 There are some practice of medicine issues
14 in terms of techniques for preparing each of these
15 devices. They are in labeling, listed here for each
16 of the manufacturers.

17 I think the guidance can do a better job
18 with this, but I think, clearly, that is an area that
19 has been overcome with most of the training for
20 interventional cardiologists.

21 Hypotension and hypertension is a
22 possibility, given that there is access to the heart.

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1 It can be caused by bleeding. It can be caused by
2 several of the medications. It can be caused by pain
3 or inadequate peripheral perfusion.

4 Close monitoring of the hemodynamic status
5 of the patient is typical during an angioplasty
6 procedure, and it is used as one of the indicators
7 when to deflate the balloon and allow blood flow to be
8 restored to the distal myocardium.

9 During these procedures, vasodilators are
10 used to control blood pressure. Nitrates are used to
11 expand the arteries, and there are antispasmodic
12 consequences as well as blood pressure consequences.

13 I think this is a well understood area.
14 Most of it is technique and pharmacological agents.
15 There are some labeling that is in each of the IFUs
16 that talks about precautions that physicians should
17 take in watching and treating hyper- or hypotension.

18 Stroke can occur in a situation where the
19 balloon catheter drags some of the atherosclerotic
20 material back up into the aortic arch and freeing it
21 for access to the carotids, etcetera. It can be
22 caused by air embolism, thrombus, and it can be a

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1 result or associated with either hypo- or
2 hypertension.

3 Clearly, this occurs very seldom, and in
4 fact, in many cases it is not listed as a
5 complication. I am putting it up here, because it has
6 occurred rarely.

7 One can monitor for thrombus in the area.
8 It is visible angiographically. One can treat
9 hypertension to avoid hemorrhagic stroke, and this is
10 basically part of the training of physicians in
11 interventional cardiology. It relates to technique in
12 using the balloon catheter, also the pharmacologic
13 agents in terms of controlling blood pressure.

14 The guidance doesn't address this at this
15 point in time, but it certainly could. Proper use of
16 the angioplasty balloon and integrity of the balloon
17 minimizes the trauma to the area, and also would
18 minimize the possibility of dragging thrombotic
19 material or atherosclerotic material up into the
20 aorta.

21 There are some reactions to contrast
22 media. These are rare. They are more problematic in

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1 patients with renal insufficiency and some other
2 conditions that are medically being treated at the
3 time of the angioplasty.

4 The precautions, clearly, are to make sure
5 that we understand a thorough medical history; that we
6 use a consider the proper use of the various contrast
7 media, especially in the high risk patients -- there
8 are several types of media, some of which have lower
9 risk profiles for these patients; have proper IV
10 hydration; and minimize the use of contrast agent.

11 There is a description in the labeling
12 guidance as well as in most of these IFUs suggesting
13 minimum use of contrast media as well as the type of
14 media to be used in the inflation of the balloon.

15 Coagulopathy is a problem, given that
16 these patients -- could be a problem, given these
17 patients are on anti-platelets, on heparin, and on
18 other medications as well. Care has to be taken in
19 the level of heparinization.

20 This is really well controlled by training
21 for interventional cardiologists. It requires close
22 monitoring of the patient as well as standard

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1 procedures in the hospital.

2 The labeling does relate to the use of
3 heparinization and its need, and that adequate
4 heparinization should be obtained before angioplasty
5 is conducted.

6 Aneurysms can form, although the incidence
7 is very rare. It can occur due to damage to the
8 coronary vessel with subsequent dilatation over time.
9 Careful interventional technique, not to over-inflate
10 a vessel will minimize that.

11 The labeling suggests to avoid over-
12 inflation. The guidance document suggests to avoid
13 over-inflation, and the testing that is required by
14 the guidance provides the physician the data to avoid
15 over-expansion, all of which should minimize the
16 formation of aneurysms.

17 There are several vascular access site
18 complications. These include hematoma, A-V fistula,
19 infection, pseudoaneurysm, in addition to that a few
20 retroperitoneal bleeds and other situations such as
21 that.

22 There are several causes. Excessive use

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1 of force when doing the initial stick. Difficult
2 device placement requires manipulation of more
3 catheters, which aggravates the vascular site.
4 Simultaneous puncture of adjacent artery and vein can
5 lead to A-V fistula. Inadequate aseptic techniques or
6 a decreased host defenses can all lead or exacerbate
7 vascular access complications.

8 These are very well understood, though, at
9 this time. Meticulous interventional and sterile
10 techniques are required. Adequate pressure on the
11 groin site and adequate technique for obtaining access
12 are important. Use of vascular sealing devices can
13 help, and placement of stents can also help.

14 There is in the instruction for use a
15 detailed description of how to do the access site
16 preparation and Seldinger technique for obtaining
17 access to the femoral arteries, and I think that is
18 very, very well trained. I don't think that presents
19 risks as far as labeling today, but it is included
20 both in the labeling that I have here as well as the
21 guidance.

22 Restenosis is an occurrence that we all

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1 know is associated with angioplasty. Its causes are
2 fibrocellular proliferation at the site of PTCA in the
3 vessel wall or inadequate dilatation of the artery by
4 PTCA.

5 The proper labeling allows physicians to
6 use an appropriate balloon catheter. I think the
7 correction of restenosis in most cases following a
8 successful angioplasty is another issue, not really
9 attributable to or treatable by the balloon catheter
10 itself.

11 So what I am talking about here are
12 restenoses due to failure mostly of the angioplasty
13 catheter to obtain an adequate lumen.

14 The labeling talks about choosing an
15 appropriate type of catheter, appropriate pressure
16 compliance profile for the catheter for the particular
17 lesion. Dr. Pinkerton raised the issue of the various
18 types of plaque. The various different types of
19 plaque require different types of balloons to address
20 them. Higher pressures are required for more
21 calcified lesions.

22 So I think today the interventional

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1 training is adequate for physicians to choose the
2 right catheter. The labeling instructions provide the
3 data to those clinicians to be able to choose the
4 right catheter, and at this point in time there are
5 very few failed procedures.

6 Emergency bypass surgery is really a
7 result of some other previously discussed
8 complications. It is really the treatment in the case
9 of a rupture or one of the other catastrophic events.
10 It is very, very rare today.

11 What minimizes that is meticulous use of
12 interventional techniques and careful patient
13 selection.

14 The labeling does address emergency bypass
15 as a complication or as a potential adverse effect,
16 and in this case I think the clinicians are well
17 trained on when to provide their patient to surgery --
18 send their patient to surgery.

19 Death has been a result of PTCA
20 procedures, rarely due to rupture, sometimes due to
21 bleeding complications, including retroperitoneal
22 bleeding. Acute myocardial infarction, failure of the

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1 procedure, arrhythmia, and emergency bypass have all
2 resulted or been associated with death. It is very
3 rare today to have death as a result of angioplasty
4 procedure.

5 Careful operative technique, promptly
6 intervening in the case of complications, monitoring
7 the patient closely and anticipating the need for
8 surgical intervention with a surgical team on alert
9 are all precautions.

10 Labeling today, including the guidance
11 labeling, does require or suggest that for each
12 angioplasty that there be a surgical team available
13 during the angioplasty. The advent of stents has
14 minimized the use of surgery, because many of the
15 complications in early angioplasty can now be
16 addressed using stenting.

17 So the labeling does actually provide or
18 address the issue -- several issues that minimize the
19 likelihood or risk of death.

20 ACTING CHAIRPERSON TRACY: Neal, I want to
21 point out that you have about an hour for your
22 presentation. You have about five minutes left.

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1 DR. FEARNOT: I will be done in about
2 three.

3 Balloon rupture is really not a clinical
4 complication, in a way. It is one, though, that I
5 wanted to bring up. It can occur from over-
6 pressurization of the balloon, a defect in the
7 balloon, calcification in the lesion with a real sharp
8 calcified spicule, and inappropriate use of an
9 inflation medium.

10 Proper pressure monitoring is the method
11 of minimizing this complication, and today
12 angioplasties are done with a pressure monitor. Not
13 only that, but labeling does talk about pressure in a
14 number of different ways. It does recommend using a
15 pressure monitor for the inflation pressure. It gives
16 the compliance chart, which gives diameter versus
17 inflation pressure, and there are warnings not to
18 exceed the burst pressure.

19 So I think, in terms of balloon rupture,
20 the uncontrollable area is the inflation of a balloon
21 against a calcified spicule or sharp plaque.

22 Wire guides still today, though very, very

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1 rarely, do break and are a result of trying to advance
2 a balloon catheter over a bent wire guide where the
3 wire guide gets twisted, and someone tries to advance
4 the balloon over that wire guide, and it does fracture
5 the wire guide.

6 It can also entrap them in thrombus or in
7 a spasmodic section of coronary vessel. This occurs
8 very seldom. There are ways to address it. In the
9 case of the fractured wire guide, surgery is required
10 in general, although some of them are retracted with
11 retractors.

12 In the case of a wire being in a spasmodic
13 area, anti-spasmodic medication works. Thrombus
14 around a wire has caught the wire before an anti-
15 thrombotic medication can address that. Basically,
16 though, caution during the angioplasty procedure is
17 sufficient to avoid these complications, and they are
18 extremely rare. Most cardiologists have had one, two
19 or three of these in their lifetime.

20 The labeling does address proper use of
21 the balloon, the need for careful advancement, the
22 need for fluoroscopy during advancement so that the

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1 physician can adequately see the wire guide and the
2 balloon catheter during any movement, which minimizes
3 this occurrence.

4 Finally, the failed procedure: In this
5 case, what I am talking about is the inability to get
6 one of these balloons into the lesion, the inability
7 to expand the balloon in the lesion and properly crack
8 the plaque, and inadequate balloon pressure or balloon
9 rupture.

10 Physicians are properly trained in
11 techniques for reaching difficult lesions, though
12 today not all lesions can be accessed, and there is a
13 training process for new interventionalists.

14 The labeling warns against several of
15 these issues. The guidance provides information on
16 accessing lesions, crossing lesions, proper inflation
17 of lesions, and instructs use of adequate pressure as
18 well as providing the burst pressures to avoid balloon
19 rupture.

20 Now in my concluding remarks, what I would
21 say is that we have gone through a number of these
22 IFUs, millions of procedures, and it is my feeling

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1 that it would be at this time possible to update the
2 guidances and special controls and that they would be
3 adequate for reclassifying.

4 The risk of PTCA balloon catheters are
5 known. Although the balloon material may be
6 continuing to improve, the improvement of balloon
7 materials really has not raised any new risks.

8 Secondly, the evolution of the practice of
9 medicine, pharmaceutical usage and adjunct devices
10 really have presented balloons with a minimum
11 likelihood of any new major risks for PTCA.

12 We have the advent of stents in
13 atherectomy and laser and Rotablator and several
14 others, and yet with all of those new technologies, we
15 have not seen new risks associated with the balloon
16 catheter. So it is really unlikely, in my view, that
17 we will see any new risks that we would miss by
18 avoiding some of the clinical trials that we have done
19 for many years.

20 I believe that special controls have been
21 identified to address and minimize each of these
22 potential risks.

1 So with those remarks, I appreciate your
2 attention. I know it is somewhat long and laborious
3 to go through this list, but I felt it was necessary
4 to be absolutely sure that in downclassifying this
5 device we have addressed all of the risks and have
6 taken an adequate responsibility in reviewing the
7 risks to see if, by downclassifying, there might be
8 any safety issues that arise to the patient.

9 It is my view, in the way and experience
10 that the FDA reviews these devices, that there are no
11 additional risks that we will be avoiding or not
12 finding, and that the safety of the patient will be
13 maintained, even though it is downclassified.

14 Thank you very much.

15 ACTING CHAIRPERSON TRACY: Thank you. At
16 this time, I'd like to ask the FDA to read their
17 questions to the panel, please.

18 MS. GABRIEL: First, I would like to thank
19 Doctors Fearnot and Pinkerton for their informative
20 presentation.

21 As Cook identified, the proposed device
22 description is as follows: A PTCA balloon catheter

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1 has a single or double lumen shaft with a balloon near
2 the distal tip. The catheter typically features a
3 minimally compliant balloon constructed from a high
4 density polymer. The balloon is designed to uniformly
5 expand to a specified diameter and length at a
6 specific pressure as labeled, with acceptable rates of
7 inflation and deflation and acceptable burst pressure.
8 The device generally features a type of radiographic
9 marker to facilitate fluoroscopic visualization of the
10 balloon during use.

11 Our question to the panel is: Does the
12 proposed classification description sufficiently
13 describe PTCA catheters?

14 This slide outlines the risks to health
15 that have been identified in the petition. Our
16 question for the panel is: Have the health risks
17 associated with PTCA catheters been adequately
18 identified? If not, what are the additional risks
19 that should be described?

20 Finally, in order to reclassify a device
21 from Class III to Class II, adequate special controls
22 must be identified which can address the risks to

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1 health associated with that device.

2 The FDA guidance document and device
3 labeling have been proposed as special controls for
4 the reclassification of PTCA catheters.

5 Have the appropriate special controls been
6 identified to adequately address the risks to health
7 specific to PTCA catheters? If not, what additional
8 special controls are necessary to reclassify PTCA
9 catheters?

10 Thank you.

11 ACTING CHAIRPERSON TRACY: Since we are
12 running a little bit ahead of time, I would like to
13 open up the committee discussion, and the two lead
14 reviewers for this were Doctors Krucoff and Domanski,
15 and we will begin with Dr. Krucoff.

16 DR. KRUCOFF: Is it okay if I direct my
17 remarks to wherever? Dr. Fearnot, I would like to
18 also thank you and Cases for coming before the
19 committee and the panel. I do have a couple of
20 questions.

21 ACTING CHAIRPERSON TRACY: The sponsor can
22 sit at the table at the front.

1 DR. KRUCOFF: I apologize for my voice,
2 but I will try and get them out.

3 I am very interested to have Cook, of all
4 companies, step forward in the interventional
5 community to initiate this petition, and I understand,
6 if I heard your comments correctly, that one of your
7 goals in this was to free up FDA resources so that
8 they could be applied to other areas of more novel or
9 new innovation.

10 DR. FEARNOT: That is correct.

11 DR. KRUCOFF: And I wonder exactly how you
12 see that working. Specifically, one of the things
13 that you mentioned is that currently only balloons
14 require new -- as a Class III product would require
15 new clinical trials to be done. In fact, that is not
16 the case.

17 A modification of an existing balloon
18 platform, in fact, is a -- can be essentially a bench
19 process through FDA. So I wonder if you could help me
20 understand how you think this would really free up FDA
21 resources.

22 DR. FEARNOT: That is a good question. We

1 have been active for sometime in trying to
2 downclassify a number of devices and have taken a
3 role, first, in trying to exempt many of the Class I
4 and some of the Class II devices.

5 We believe, and I think the data shows,
6 that that has freed up resources. I think it is also
7 wise to look at devices that have been available in
8 the marketplace for which manufacturers have
9 significant expertise, and the affected community of
10 physicians has a clear understanding.

11 With the proper guidances in place, it
12 uses more of the company resources and relies on their
13 responsibility for conducting those tests to provide
14 the data on the device that is needed by the
15 physician.

16 I believe that the annual reporting and
17 other parts that are associated -- or expenses or, if
18 you will, use of resources that are associated with a
19 PMA supplement of a well understood device aren't
20 really justified any longer.

21 So we felt like PTCA balloon catheters
22 were in that category where manufacturers understand

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1 methodology. The methodology is available for doing
2 the testing.

3 The guidances could be updated and
4 actually made more consistent among manufacturers, and
5 that given that there is consistent testing and
6 consistent reporting, we felt like that would be an
7 improvement in providing information to the physician
8 as well as reducing the burden on manufacturers and to
9 generate and reviewers to review each of those
10 submissions that are required.

11 DR. KRUCOFF: Okay. I am also sort of
12 intrigued by your decision to go forward with an
13 application just for balloon catheters as opposed to
14 other components in the system, guide wires or other,
15 say, simpler or more simply constructed pieces of the
16 many components that go together in doing these
17 procedures.

18 Can you tell us about that?

19 DR. FEARNOT: Well, perhaps if the
20 balloons are reclassified, we can move on from there
21 to other devices, but we figured that balloons were a
22 good start.

1 DR. KRUCOFF: Okay. Cases, I have to ask
2 you, because I sit here and I think about this as
3 anything but a well understood procedure, anything but
4 highly controlled after all these years. As we flash
5 a list of all of the different balloon platforms that
6 have emerged even over the past few years, much less
7 if we went back to the ACS Pinkerton balloon, you
8 know, I don't see this as a stable picture.

9 I see this as an evolving picture with
10 continuous innovation and really a changing profile
11 ultimately in clinical outcomes to patients. Is it
12 your feeling that balloons are such a stable platform
13 that they should be reclassified?

14 DR. PINKERTON: Yes. I think that in
15 reference to the materials that are used in balloons
16 and the amount of pressure that we deliver to the
17 coronary anatomy over the millions of procedures that
18 have been done, it doesn't appear -- For example,
19 there was an article written by Geoff Hartzler back in
20 1988 where 88 percent of all balloon -- of all the
21 atherosclotic plaque opened at seven atmospheres of
22 pressure.

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1 So, I mean, I think that the clinical
2 situation with arteriosclerotic plaque -- I don't
3 think that is going to change, as far as the patients
4 we are going to have to deal with. I think the
5 developing a balloon with a different material to go
6 to higher pressure is probably not going to be
7 necessary, and I haven't seen that happen.

8 What I have seen happen is that the
9 balloons are being made with lower and lower profiles.
10 So they are smaller and smaller, so that they are
11 easier to use and so that we can use smaller and
12 smaller guiding catheters, so that we decrease the
13 amount of -- the size of the arterial stick in the
14 femoral artery.

15 DR. KRUCOFF: Okay. Last two questions
16 for both you gentlemen: Of the many design elements
17 that there are guidance for now in a balloon system,
18 there seem to me to be quite a few that there are not,
19 and some of these have to do with the many
20 simultaneous decisions that are made, for instance, to
21 reduce the diameter of a catheter where engineers or
22 where individual product manufacturers decide to

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1 create that space, whether they shrink a lumen here or
2 a diameter there, produce a lot of novel elements for
3 which I in this list don't see a lot of guidance
4 coverage.

5 For instance, tip contour, tip
6 construction -- ultimately how much pressure before a
7 balloon shaft begins to accordion? There are a number
8 of elements that particularly, as the moving target
9 gets into -- of the clinical application gets into
10 more complex lesions or more complex patients or more
11 complex interactions with existing stent struts or
12 whatever.

13 I take it from your presentation that you
14 do feel comfortable that these are elements that are
15 straightforward, stable, definable, and somehow that
16 our current guidances either measure at the bench
17 before we get into patients? Is that understanding
18 correct?

19 DR. FEARNOT: If the design validation and
20 verification process is working in a company, they
21 have got to consider those issues. They have got to
22 consider the shaft and its dimensional stability.

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1 One of the things that is measured today
2 is pressure causing the shaft to burst. So as you
3 start to peel away thousandths of an inch, you know,
4 off of the balloon catheter, at some point there isn't
5 enough plastic left to pass those tests.

6 The verification and validation steps in
7 design controls require the manufacturer look at all
8 the possible risks associated with that change or that
9 modification and that they do appropriate testing to
10 ensure that the changes they have made do not
11 introduce new risks or cause the device to fail with
12 respect to those elements.

13 So I feel like that, with regard to the
14 tip, with regard to the shaft dimensions, etcetera,
15 that if they have design controls in place, they have
16 got to consider those. And I don't see the
17 manufacturers, at least today, putting out a balloon
18 catheter that would not undergo those verification
19 steps.

20 So, I mean, I don't know particularly what
21 elements you might be thinking of that wouldn't be
22 covered in a design verification or validation process.

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1 DR. KRUCOFF: Well, I mentioned a couple,
2 but I think -- Cases, you have certainly been involved
3 in designing these instruments from the ground up.

4 DR. PINKERTON: Right.

5 DR. KRUCOFF: Are you really comfortable
6 that these guidance documents tell us everything we
7 would need to know about a new influx of balloons at
8 the Class II level?

9 DR. PINKERTON: Yes. I think, really, as
10 I went over all the guidance descriptions and so
11 forth, that pretty much everything is covered. I
12 mean, the only unfortunate thing about doing a balloon
13 procedure is the person doing the procedure. I mean,
14 reading all the documents, we have to -- I think that
15 it is covered in the documents.

16 I think that, really, the complications of
17 most -- most of the complications, at least in the
18 past eight years, have not really been related to the
19 device. I think that the classification is fairly
20 well described.

21 DR. KRUCOFF: Okay. My last comment or
22 question is with regard to risks, unaccounted risks

1 and new risks. One of the things that worries me the
2 most about changing classification would be actually
3 more at the level of unaccounted risks, the duration
4 of the procedure, additional contrast.

5 If a balloon doesn't reach across or
6 dilate, we may well still have guide wire access. We
7 may well get the balloon out of there ultimately. We
8 may well get another balloon, get the patient off the
9 table without a major complication; but then they get
10 30 percent more die. They may spend more time on the
11 table.

12 I mean, these are unaccounted risks that,
13 in my estimation, the potential to open the door to
14 platforms that meet guidance definitions but that
15 might not actually perform in the complexities of
16 individual applications well, would not be well
17 captured.

18 That is what I consider unaccounted risks.
19 Any thoughts?

20 DR. FEARNOT: Well, I would like to just
21 say that I am not sure that those are all captured
22 today.

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1 DR. KRUCOFF: That's my point.

2 DR. FEARNOT: Yes. But I'm not sure that
3 reclassifying it would exacerbate the problem. I
4 think that the manufacturers, if they are following
5 what they are supposed to be following in terms of
6 validation procedures, they are supposed to be going
7 out and ensuring that that type of a situation occurs
8 less than it did five years ago when the validation
9 procedures were not in place.

10 Does that make sense? In other words,
11 that the manufacture is, by design control, pushed to
12 go out and evaluate their product all the way to the
13 end user. So does that address all the unexpected
14 risks? I don't think it can. I don't think today it
15 does. I don't think, with reclassification, it will
16 either.

17 The hope there is that the interventional
18 cardiologists are astute enough to understand and be
19 aware of that process.

20 DR. KRUCOFF: Well, we may be saying the
21 same thing, just from two different perspectives. To
22 me, it's the unmeasurable and unaccounted for elements

1 in our current process that would make me most worried
2 about doing this in human beings with devices that
3 come through a more liberal or easier process.

4 Let me just make one other comment about
5 risks and the comments that you have made a couple of
6 times, that we don't anticipate new risks because we
7 haven't seen any new risks.

8 I think I have two problems with that.
9 One is, when we list every possible risk that can
10 occur because with these gadgets we can harm people in
11 so many ways that over the past 25 years we have
12 managed to do that. So our list already incorporates
13 basically everything you can do to hurt somebody.

14 The fact that we don't generate new risks
15 is not necessarily reassuring. We may generate the
16 same risks or more of them in new ways. One instance,
17 as Cases was mentioning: When you have a balloon that
18 ruptures at four atmospheres, the likelihood of
19 perforating a coronary -- about the only way you could
20 do that is by so grossly oversizing the balloon in a
21 soft segment of the artery that you tear it open.

22 DR. FEARNOT: Right.

1 DR. KRUCOFF: But when you have balloon
2 materials that can generate 30 atmospheres and they
3 burst, that may be the list and a check-list of the same
4 risk, but that is a risk that is precisely dependent
5 on the evolution of newer and different configurations
6 of materials in a balloon catheter. I think that
7 really has to be respected.

8 I am not sure I got from the flavor of
9 your comments that -- We have new ways of generating
10 the same old risks, because every risk possible is
11 already on the list, but I think we definitely in a
12 moving platform of delivery have new ways of
13 delivering those risks.

14 DR. FEARNOT: Yes. Do you feel like that
15 the pressure testing that these catheters undergo does
16 not adequately capture the burst pressures and the
17 testing that is conducted not only looks at the
18 pressure but the style of the burst, because it was
19 obviously recognized early that if it bursts in a
20 circumferential type manner that removing the catheter
21 is difficult.

22 So today's balloons are all designed to,

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1 if they do burst, burst in a longitudinal manner so
2 that they are still removable. But do you feel like
3 that that -- somehow in reclassifying that the present
4 standard for measuring the high pressure
5 characteristics would change, would be any worse?

6 DR. KRUCOFF: I think I am saying it the
7 other way around. I think burst pressures, for
8 instance, show us that current balloon platforms can
9 reach higher pressures than older balloon platforms,
10 and that with that an old risk, perforating a
11 coronary, becomes achievable in a new fashion.

12 My only point is that, to me, it is not
13 reassuring to say that we are not seeing any new
14 risks, because everything we can do to harm a person
15 is already on that list, and it is also a little
16 misleading to me to think that we don't have new ways
17 of generating those old risks in a platform of
18 technology that is essentially still in motion.

19 DR. FEARNOT: Have we really seen higher
20 rupture rates, though, with the higher pressure
21 balloons, higher rupture rates in terms of vessels?
22 I don't think we have.

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1 DR. KRUCOFF: Oh, I think you could
2 generally say that there are -- if nothing else, there
3 are more reports of coronary perforation in the past
4 eight years than in the eight years before that.

5 ACTING CHAIRPERSON TRACY: Dr. Domanski?

6 MR. DILLARD: Dr. Tracy, excuse me, just
7 before Dr. Domanski gets started, I just thought,
8 based on one of the things that Dr. Krucoff mentioned,
9 I thought, was worth a little clarification, that
10 being many of the accessory kinds of products,
11 including guide wires, are already Class II devices
12 and already are cleared through the 510(K) process.

13 So I don't know that there after PTCA
14 would be a next step into accessories or other kinds
15 of products, just for clarification.

16 DR. DOMANSKI: I guess it's not how I
17 would normally start this kind of discussion, but I
18 think in terms of coronary perforations, there may be
19 more coronary perforations, but some of the coronary
20 perforations relate to the newer guide wires that go
21 through stenoses more easily but, of course, also go
22 through vessel walls more easily.

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1 It's not all balloons, and of course, the
2 numbers of procedures have dramatically increased, but
3 I think our ability -- the diffusion of knowledge
4 actually in how to use a balloon and size it properly
5 is perhaps the key there. I don't know that that
6 interacts much with manufacturing stuff. But anyhow--

7 I have a few observations, and I'm not
8 sure I have a lot of questions, Cindy. So I'm not
9 sure exactly what format we should use. This is a
10 little different than the panel meeting that I'm used
11 to, but I want to make a few.

12 First of all, not that it's important
13 necessarily to this proceeding, but I do think there
14 is substantial advantage to reducing the regulatory
15 burden where that doesn't impact negatively on public
16 health. I mean, the good thing about the regulatory
17 burden that we accept is that I think that we do
18 protect the public, but I think one can impose
19 unnecessary burdens, and I think, as time goes by,
20 burdens that are useful cease to be useful.

21 That's, of course, why this legislation
22 was in place. It frees up not only FDA time, I

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1 suppose, but it also frees up resources in the
2 companies to develop new products and so forth, and
3 reduces needless expenditure of funds and effort and
4 so forth. So I think the process is well thought out.

5 The concerns I have -- and some of these
6 could be addressed by the FDA. I think I understand
7 fully that, with the special guidelines that are
8 proposed for this particular device, that in fact a
9 new manufacturer coming into the field would
10 nonetheless have to provide the same sort of bench
11 testing that the established manufacturers are
12 currently doing. Is that correct?

13 MR. DILLARD: Jim Dillard. Let me maybe
14 take a couple of minutes here and expand upon that,
15 because your next question will probably be then do
16 they have to provide similar clinical information
17 also. Let me see if I can't kill two birds with one
18 stone.

19 The guidance document as it currently
20 outlines certainly has a discussion of bench type of
21 studies, animal type of studies, as well as clinical
22 information that, if it is necessary, gives some

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1 guidance about the type and what you need to actually
2 provide to FDA to satisfy a particular clinical,
3 preclinical or animal requirement.

4 So, actually, the way the guidance
5 currently is envisions all of those scenarios. I
6 think the way we approach a product that could be
7 subject to such a broad guidance document would be an
8 issues based approach, which is, if looking at the
9 design of the particular product we could answer those
10 issues with preclinical information alone, there is a
11 good chance that preclinical testing by itself would
12 be enough to demonstrate that the product could
13 function as safely and as effectively as other
14 products on the market, which would be the standard
15 for a Class II product.

16 If the preclinical or bench testing alone
17 didn't answer that issue, then animal and/or clinical
18 study information might be necessary in order to
19 answer that particular question.

20 So I think the guidance already envisions
21 enough flexibility, although I think there's been a
22 lot of good comments about ways it could be improved.

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1 But I think that particular scenario already exists.

2 I don't know. I hope that helped.

3 DR. DOMANSKI: Yes. I think the thing
4 that I am wanting people to say sort of on the record
5 is that somebody can't come along who is a less
6 experienced manufacturer with a much lesser product
7 and slide in, because, you know, we suddenly have some
8 sort of rigidity about what we can require them to do.
9 I don't see that being the case, and I hear you saying
10 that it's not.

11 MR. DILLARD: Without answering that
12 completely directly to allow a little flexibility,
13 maybe partially because I'm the government but
14 partially because it's appropriate, the fact is that
15 the standard would be that a manufacturer would need
16 to demonstrate that the product would function as
17 safely and as effectively as a currently marketed
18 product or that which was reclassified.

19 So I think in the current scenario where
20 we have many Class II products, the majority of them
21 have to have some fairly comprehensive bench studies
22 at the minimum in order to demonstrate equivalence.

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1 I would say that's the preponderance of our 510(K)s.
2 Very few come in with just a specification comparison
3 without any testing whatsoever.

4 I think then more the exception probably
5 than the rule would be animal and/or clinical
6 information. It is predominantly a decision making
7 process based on bench comparisons of data between
8 various products.

9 I think, if you look at our history,
10 that's really where the program sits as a Class II
11 program.

12 DR. DOMANSKI: So I think the next step in
13 proceeding, because I would express some enthusiasm
14 for this kind of a downclassification, but I think
15 that it should be restricted to precisely what we want
16 to restrict it to, and that's a particular type of
17 device.

18 I do have some thoughts about the
19 definition of a PTCA catheter. Is this an appropriate
20 time to discuss that?

21 ACTING CHAIRPERSON TRACY: Yes.

22 DR. DOMANSKI: It goes to question 1 that

1 the FDA asked, and I have several things, and I would
2 like to kind of open a little bit of a thing on that.

3 First of all, incorporating some of the
4 suggestions, I would suggest that this definition
5 begin with the sentence that "PTCA catheters comprise
6 angioplasty systems that operate on the principle of
7 hydraulic pressurization applied through an inflatable
8 balloon attached to the distal end." Period.

9 Then the next sentence begins with: "This
10 typically features a balloon constructed from a high
11 density polymer."

12 You notice what I am doing is eliminating
13 certain words that restrict it, like "minimally
14 compliant." I don't know what "minimally" means in
15 that definition. Okay? You know, I think it's
16 unnecessary verbiage.

17 Then it says the balloon is designed to
18 uniformly expand to a specified diameter. I would
19 eliminate the word "uniformly," because it may be that
20 somebody wants to design a balloon that isn't exactly
21 uniformly expanded. I don't know if they all are, and
22 maybe I should even ask that question. What do you

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1 think of that kind of change?

2 DR. FEARNOT: I think the vast majority
3 today are inflated to a uniform diameter.

4 DR. DOMANSKI: No, no, not to a uniform
5 diameter. I mean uniformly expanded. Maybe the
6 problem is I don't understand what you mean exactly by
7 uniformly expressed then.

8 DR. FEARNOT: I believe that the word
9 uniform refers or relates to the guidance which
10 requires a manufacturer measure the diameter of the
11 balloon at a certain pressure along its length to
12 ensure that it doesn't bulge in the middle or --

13 DR. DOMANSKI: Then I miss it?

14 DR. FEARNOT: I believe that is what FDA
15 was looking at.

16 DR. DOMANSKI: Okay. Then fine. Then
17 I'll leave it uniformly expands. Everybody but me
18 probably understood that. "Uniformly expand to a
19 specified diameter and length at a specific pressure
20 as labeled, with" -- and then the word "acceptable" I
21 don't like, and we can talk about it. But I would
22 just say "with rates of inflation/deflation that are

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1 known."

2 You know, of course, it is acceptable. I
3 think it is implied, but I'm not sure -- you know,
4 again I'm not sure what the word acceptable means. So
5 it needs a definition if it is going to stay.

6 "The device generally features" -- I think
7 a radiographic marker -- I don't know what "a type of"
8 means -- to facilitate fluoroscopic visualization of
9 the balloon during use.

10 I'm wordsmithing this definition, and
11 that's how I would wordsmith it, but I think that that
12 carefully captures pretty much everything, and under
13 those circumstances it seems to me that it gives the
14 FDA a very clear definition. I mean, the definition
15 is pretty good the way it's written. I am just trying
16 to wordsmith a little bit. So that's a second thing.

17 The other is under number 2 and the health
18 risks. Again, this constitutes wordsmithing, because
19 I do favor downclassifying these things. But
20 "identified health risks" -- A balloon rupture, and
21 this really is wordsmithing, but a balloon rupture and
22 guide wire fracture or entrapment cause certain types

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1 of problems.

2 By themselves they are not health risks,
3 but they produce health risks. And I guess I wonder
4 whether saying identified health risks makes sense to
5 talk about how the thing produces it underneath this
6 heading.

7 So I probably would have eliminated those
8 two things, since balloon rupture and guide wire
9 fracture or entrapment pretty much are subsumed under
10 the identified health risks, except I suppose that the
11 fracture, one might say, retained fragment or
12 something. But I think, if we are going to put it
13 out, it ought to look pristine in terms of how the
14 list is thought out.

15 Then finally, with regard to the guidance
16 documents, clearly, some of the guidance documents are
17 in the process of being updated and need to be. Is
18 there -- and as new documents come out or new
19 guidances are generated in the out-years, those
20 guidances presumably would replace earlier versions.
21 Is that a fair statement?

22 MR. DILLARD; Jim Dillard. Generally, we

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1 will make modifications to guidance documents as
2 necessary. We will go through the normal good
3 guidance or GGP practices. So it would be very
4 common, any guidance that would be appropriate for a
5 particular product, for us to update it on a fairly
6 regular basis.

7 DR. DOMANSKI: Yes. So you don't wed
8 yourself to -- If a petition like this is approved,
9 you don't wed yourself to those guidances on that
10 date, but rather to the ongoing -- or to others that
11 come along as time goes by.

12 MR. DILLARD: Correct.

13 DR. DOMANSKI: Well, you know, under those
14 circumstances I think this is a pretty carefully
15 worked up document, and with some modification, small
16 modification, I would be enormously in support of
17 moving along with this and approving it.

18 ACTING CHAIRPERSON TRACY: Dr. Laskey?

19 DR. LASKEY: Well, I would certainly
20 second that sentiment. However, I do think that these
21 are all living, breathing things, and they need to
22 reflect the times we live in. So I would like to just

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1 go after the stent era issue a little bit more.

2 We do live in the stent era, and balloons
3 are rarely being advertised, sold or distributed to
4 open arteries at seven atmospheres. I mean, the
5 prevailing sentiment now is that it has something to
6 do with a stent, and we are not talking about primary
7 deployment here, but we are talking about using
8 balloons that are coming down the pike or may come
9 down the pike in people that have had stents placed
10 that are all mangled and stenosed or possibly
11 maldeployed and so on and so forth, to follow up on
12 Mitch's point, that there are things that we probably
13 have not listed here that do expand on this list.

14 We have not seen everything. We have seen
15 an awful lot, but I don't think we are quite done. I
16 would like to ask how you would propose failsafing
17 additional balloons in this climate of reclassifying
18 them that address the modern era or the times we live
19 in.

20 DR. FEARNOT: That is a good question.
21 Let's segment the answer into a couple of different
22 areas.

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1 I think when balloons are used
2 adjunctively with a new therapy where there is an
3 interaction between that new therapy and the balloon
4 such that something could occur, in that combination
5 I think that this reclassification process and using
6 the 510(K) should not apply; because I think the
7 combination of a balloon catheter with another device
8 can present totally new scenarios.

9 So that whole combination of a device
10 would end up through PMA process. That's reasonable.

11 I think another general scenario would be
12 in the situation where balloons are used to dilate
13 vessels that have been treated with a device before,
14 be it a stent which is a permanent device or some
15 other atherectomy device where the device has actually
16 been removed but there is a disease process or
17 reaction ongoing.

18 I think at that point we have to ask
19 ourselves is the dilatation of that resultant
20 hyperplasia or response any different than dilatation
21 of the original lesion? I think in many cases we find
22 today that there is not a difference in the dynamics

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1 of opening a stenosed area, be it because of a
2 previous angioplasty, when you contrast it with the
3 original lesion.

4 Obviously, the mechanism of -- the
5 biological mechanism leading to the stenosis is
6 different, but the dilatation process is not
7 different, and the balloons have not been different.
8 There have not been different balloons used to open
9 those stenoses compared with the original.

10 So the dynamics, if you will, of using a
11 balloon to open a stenosis, independent of its origin,
12 has been dealt with, I think, generally as a single --
13 from a single point.

14 I think you raise an interesting category
15 which I would put in a separate group from dilating a
16 stenosis, let's say, in a properly placed stent. In
17 six months the patient comes back. There is a
18 stenosis inside some stent. There is endothelium over
19 the whole inner layer of the stent, inner lumen of the
20 stent, as well as the typical smooth muscle cell
21 proliferation and fibrotic material. That's one
22 situation.

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1 The other situation you raise, though,
2 which I think is a good one and worth some discussion,
3 is using a balloon to correct some misplaced stent.
4 I think that is a risky procedure in any regard. If
5 some medical device has been used in intervention and,
6 for some reason or other, it's either fractured, it's
7 been maldeployed, it's caused vessel damage, it's
8 become entrapped, those are special situations.

9 I am not sure that in a general sense from
10 a manufacturing approval process that those are best
11 dealt with. I think those are rare. I think they are
12 special situations, and I think at that point you look
13 at the patient's safety and make the best choices.

14 I'm not sure how that actually goes back
15 and affects device labeling for a balloon. Let me
16 just give you a particular situation.

17 Let's say we were to contraindicate for
18 all balloons use of balloons in a stent that is
19 deployed. I don't think that would be what a
20 clinician would look at if they felt at that point in
21 time that it was best for the patient and they thought
22 they could correct the situation.

1 So I think we have to put those anomalies,
2 if you will, in a separate category and deal with
3 them, looking at the whole clinical scenario for the
4 patient.

5 So I would say, coming back, that a
6 general PTCA balloon used to open a stenosis, whether
7 it is de novo, restenotic or restenotic with a stent
8 in it, has all been dealt with reasonably equivalent
9 results.

10 I think the areas where you are using a
11 balloon to deal with some anomaly or misplaced stent
12 or some major problem is a different category, and I
13 think there should be warnings associated with those.
14 But I don't think we can restrict clinicians from
15 using any tool they have to address those situations.

16 So I would basically say that in-stent
17 restenosis in a properly placed stent today is no
18 different in terms of the dynamics or the requirements
19 for a balloon.

20 DR. LASKEY: I don't wholeheartedly agree
21 with you, but I basically agree with you. Many times
22 you don't know what is going on by angiography, as you

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1 know. You need to look at these things from inside
2 out, and you do see funny things that are not apparent
3 on angiography and, worse yet, they don't behave as
4 you would expect them to behave when you are trying to
5 cross the device.

6 I just foresee in a world which is moving
7 towards 80-90 percent stenting that these issues will
8 not be anomalous or trivial or perhaps in single
9 digits. They may be more frequent. I just wonder out
10 loud what the implications of that will be for this
11 process down the road. It's as simple as that.

12 When these rules were written, they were
13 written in the mid-eighties to apply to opening a
14 narrowing in a native coronary artery or a vein graft.
15 No one imagined asking a balloon to do what it is
16 being asked to do currently within these reconstructed
17 arteries. So we might want to give some thought to
18 that in the special controls aspect of this.

19 Then I just have some small housekeeping
20 thoughts along the lines of Dr. Domanski's
21 suggestions, which is that unstable angina is really
22 not a risk of the PTCA.

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1 Infarction, of course, is, but unstable
2 angina is a clinical syndrome that's -- blah-blah.
3 It's very different from what goes on in a cath lab as
4 a consequence of the mishap. So you might want to
5 just delete that.

6 Reactions to contrast agents have nothing
7 to do with the balloon catheter itself. So you might
8 want to clean that up.

9 Of course, the coagulopathy issue is
10 peripheral to the catheter itself or the catheter
11 procedure. So that would just clean that up a bit and
12 modernize it a bit. But thank you for your exhaustive
13 presentation.

14 ACTING CHAIRPERSON TRACY: Dr. Hartz?

15 DR. HARTZ: Hartz, Tulane. I also
16 appreciate the review, and I don't think that the
17 panel will have any questions at all answering the
18 first question to us about has the device been
19 adequately described. Certainly for the patients
20 being treated to date, that's a good description.

21 I don't think we can go ahead and answer
22 the question concerning health risks without further

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1 clarification of the data. Jim, you may have to help
2 us do this.

3 Specifically, we have to go back to your
4 slide, number of PTCAs, on the bottom of page 8.
5 There are 3 million angioplasties talked about, and we
6 know in the late eighties there were 80,000, 100,000.
7 You say that maybe last year there were 400,000.
8 Probably there were more like three-quarters of a
9 million, something like that, and every year there's
10 300,000 coronary bypasses.

11 So we have a denominator, a minimum
12 denominator, of 3 million angioplasties over a 14-year
13 period. We have 7500 MDR/MAUDE events. Okay? There
14 were a percent and a half deaths and 19.3 percent
15 injuries in your quote that quotes they are
16 decreasing. Where do those numbers come from?

17 What is the database to which these cases
18 were reported? Is there an FDA database? We know we
19 can get Medicare data, but we can't get data from the
20 literature for patients under age 65.

21 So I think, since these are so similar in
22 number to the multivaried analysis you have here, I