

UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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MEDICAL DEVICES ADVISORY COMMITTEE
ORTHOPEDIC AND REHABILITATION DEVICES PANEL

+ + + + +

MEETING

+ + + + +

TUESDAY, APRIL 24, 2007

+ + + + +

The meeting came to order at 8:00 p.m. in the Grand Ballroom of the Hilton Washington DC North, 206 Perry Parkway, Gaithersburg, MD, Dr. John S. Kirkpatrick, M.D., Acting Chairman, presiding.

PRESENT:

JOHN S. KIRKPATRICK, M.D., Acting Chairperson
STUART B. GOODMAN, M.D., Ph.D. Voting Member
KATHLEEN J. PROPERT, Sc.D., Voting Member
MICHAEL B. MAYOR, M.D., Deputized Voting
Member
GLENN B. PFEFFER, M.D., Deputized Voting
Member
HARRY B. SKINNER, M.D., Ph.D., Deputized
Voting Member
DOUGLAS G. WRIGHT, M.D., Deputized
Voting Member
CONNIE WHITTINGTON, MSN, R.N., ONC, Consumer
Representative
PAMELA W. ADAMS, M.S., RAC, CQM, Industry
Representative
RONALD P. JEAN, Ph.D., Executive Secretary
MARK N. MELKERSON, M.S., DGRND Director

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C-O-N-T-E-N-T-S

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Adjournment

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

2 8:10 a.m.

3 CHAIR KIRKPATRICK: Good morning.
4 I'd like to call this Advisory Panel meeting
5 to order please. And this is the Orthopedic
6 and Rehabilitation Devices Panel. I'm John
7 Kirkpatrick, the Acting Chairperson for today.

8 At this meeting -- oh, let me first
9 introduce our Panel members, if that's okay.
10 As I mentioned, I'm John Kirkpatrick. I'm at
11 the University of Florida, Jacksonville, and
12 I'm predominantly a spine surgeon but also do
13 general orthopedics.

14 If we could just start over here
15 with Ms. Adams and we'll go around the table.

16 MS. ADAMS: I'm Pamela Adams. I'm
17 with Etex Corporation. I'm the Industry Rep
18 to the Panel. And I have over 20 years of
19 experience in medical devices.

20 MS. WHITTINGTON: My name is Connie
21 Whittington. I'm the Director of Nursing
22 Systems at Piedmont Hospital in Atlanta. I

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1 have over 35 years experience in orthopedics.

2 And I'm the Consumer Representative on the
3 Panel.

4 DR. WRIGHT: Douglas Wright, Bel
5 Air, Maryland. I'm an orthopedic surgeon. I
6 do foot and ankle and orthopedic trauma.

7 DR. JEAN: My name is Ronald Jean.
8 I'm the Executive Secretary of this Panel and
9 also a scientific reviewer in the Division of
10 General Restorative and Neurological Devices.

11 DR. SKINNER: My name is Harry
12 Skinner. And I'm an orthopedic surgeon. And
13 I do mostly hip and knee surgery. I'm from
14 the University of California, Irvine.

15 DR. PROPERT: I'm Kathleen Propert.
16 I'm a biostatistician from the University of
17 Pennsylvania, specializing in clinical trials.

18 DR. PFEFFER: Glenn Pfeffer,
19 orthopedic surgeon, Cedars-Sinai Medical
20 Center, Los Angeles. And I only do foot and
21 ankle work.

22 DR. MAYOR: Michael Mayor from

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1 Dartmouth, Professor of Orthopedic Surgery and
2 Adjunct Professor of the Thayer Engineering
3 School where John Collier and I run a
4 retrieval laboratory.

5 MR. MELKERSON: I'm Mark Melkerson.

6 I'm the Division Director for the Division of
7 General Restorative and Neurological Devices.

8 CHAIR KIRKPATRICK: Thank you one
9 and all.

10 At this meeting, the Panel will be
11 making a recommendation to the Food and Drug
12 Administration on the premarket approval
13 application, P050050 for the Link STAR Ankle
14 Prosthesis. This device is intended for use
15 as a non-cemented implant to replace a painful
16 arthritic and/or severely-deformed due to
17 rheumatoid arthritis, primary arthrosis, or
18 post-traumatic arthrosis.

19 If you haven't already done so,
20 please sign the attendance sheets that are on
21 the tables by the doors just outside. If you
22 wish to address the Panel during one of the

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1 open sessions, please provide your name to Ms.
2 Ann Marie Williams at the registration table.

3 If you are presenting in any of the
4 open public sessions today and have not
5 previously provided an electronic copy of your
6 presentation to the FDA, please arrange to do
7 so with Ms. Williams.

8 I note for the record that the
9 voting members present constitute a quorum as
10 required by 21 CFR Part 14. I would also like
11 to add that the Panel participating in the
12 meeting today has received training in FDA
13 device law and regulations.

14 Dr. Jean, the Executive Secretary
15 of this Panel will now make some introductory
16 remarks.

17 DR. JEAN: Good morning. I'd first
18 like to remind everyone present to please
19 silence your cell phones if you have not
20 already done so.

21 I will now read into the record two
22 Agency statements prepared for this meeting,

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1 the Appointment of Temporary Voting Members
2 Statement and the Conflict of Interest
3 Statement.

4 Appointment to Temporary Voting
5 Status, pursuant to the authority granted
6 under the Medical Devices Advisory Committee
7 Charter, dated October 27th, 1990 and amended
8 April 20th, 1995, I appoint the following as
9 voting members of the Orthopedic and
10 Rehabilitation Devices Panel for the duration
11 of this meeting on April 24th, 2007, Michael
12 B. Mayor, M.D., Glenn B. Pfeffer, M.D., Harry
13 B. Skinner, M.D., Ph.D., Douglas G. Wright,
14 M.D.

15 For the record, these people are
16 special government employees and are
17 consultants to this Panel or another Panel
18 under the Medical Devices Advisory Committee.

19 They have undergone the customary conflict of
20 interest review. And have reviewed the
21 materials to be considered at this meeting.

22 I also appoint John S. Kirkpatrick,

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1 M.D., as the Acting Panel Chair for the
2 duration of this meeting.

3 Signed by Daniel G. Schultz, M.D.,
4 Director, Center for Devices and Radiological
5 Health, on March 19th, 2007.

6 Now I'll read the Conflict of
7 Interest Statement.

8 The Food and Drug Administration is
9 convening today's meeting of the Orthopedic
10 and Rehabilitation Devices Panel of the
11 Medical Devices Advisory Committee under the
12 authority of the Federal Advisory Committee
13 Act of 1972. With the exception of the
14 industry representative, all members and
15 consultants of the Panel are special
16 government employees or regular federal
17 employees from other agencies and are subject
18 to federal conflict of interest laws and
19 regulations.

20 The following information on the
21 status of this Panel's compliance with federal
22 ethics and conflict of interest laws covered

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1 by but not limited to those found at 18 USC
2 Section 208 are being provided to participants
3 in today's meeting and to the public.

4 FDA has determined that members and
5 consultants of this Panel are in compliance
6 with federal ethics and conflict of interest
7 laws. Under 18 USC Section 208, Congress has
8 authorized FDA to grant waivers to special
9 government employees who have financial
10 conflicts when it is determined that the
11 Agency's need for a particular individual's
12 service outweighs his or her potential
13 financial conflict of interest.

14 Members and consultants of this
15 Panel who are special government employees
16 have been screened for potential financial
17 conflicts interests of their own as well as
18 those imputed to them, including those of
19 their employer, spouse, or minor child related
20 to the discussions of today's meeting. These
21 interests may include investments, consulting,
22 expert witness testimony, contracts, grants,

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1 CRADAs, teaching, speaking, writing, patents
2 and royalties, and primary employment.

3 Today's agenda involves the review
4 of a premarket approval application for the
5 Scandinavian Total Ankle Replacement System
6 sponsored by Link America. This system is
7 intended for use as a non-cemented implant to
8 replace a painful arthritic and/or severely-
9 deformed ankle due to rheumatoid arthritis,
10 primary arthrosis, or post-traumatic
11 arthrosis.

12 This is a particular matters
13 meeting during which specific matters related
14 to the PMA will be discussed. Based on the
15 agenda for today's meeting and all financial
16 interests reported by the Panel members and
17 consultants, no conflict of interest waivers
18 have been issued in connection with this
19 meeting.

20 Pamela Adams is serving as the
21 Industry Representative, acting on behalf of
22 all related industry and is employed by Etex

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1 Corporation.

2 We would like to remind members and
3 consultants that if the discussions involve
4 any other products or firms not already on the
5 agenda for which an FDA participant has a
6 personal or imputed financial interest, the
7 participants need to exclude themselves from
8 such involvement and their exclusion will be
9 noted for the record.

10 FDA encourages all of the
11 participants to advise the Panel of any
12 financial relationships that they may have
13 with any firm at issue.

14 Thank you.

15 I'll now turn the meeting back over
16 to our Acting Chairperson, Dr. Kirkpatrick.

17 CHAIR KIRKPATRICK: Thank you, Dr.
18 Jean.

19 There will be a brief presentation
20 before the main agenda topic. Dr. Jonette Foy
21 will give us an orthopedic update since the
22 last meeting -- or excuse me, since the

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1 September 19th, 2006 meeting.

2 DR. FOY: Good morning. This is
3 just going to be a brief update since we did
4 have a Panel meeting approximately two months
5 ago.

6 Here are the tentative Panel dates
7 that we have listed for the Orthopedic and
8 Rehabilitation Devices Panel. Please be on
9 the lookout for any FR notices which will
10 confirm when we have our next Panel meeting.

11 Just to give you a brief update,
12 there are three items listed here: the
13 reclassification of intervertebral body fusion
14 devices, it's currently under it's final
15 review. So be on the lookout for the Notice
16 of Availability.

17 We also have the comment period for
18 the reclassification petition for non-invasive
19 bone growth stimulator for established non-
20 union 1-2 level lumbar fusion which the
21 recommendation to deny that reclassification
22 petition comment period officially ended on

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1 April 17th.

2 And then lastly we have the metal-
3 on-metal hip joint prosthesis reclassification
4 petition which is currently under active
5 review.

6 Just wanted to give you a brief
7 update about the orthopedic guidance
8 documents. All of the five guidance documents
9 that are listed there for orthopedics, I have
10 completed their review from our perspective.
11 They are currently under GGP review. So be
12 checking our website. Those were the ones
13 that were listed on our prioritized list for
14 2007.

15 I also listed here two general
16 guidance documents that are currently out for
17 comment period. These have been posted as
18 draft guidance documents. One of them is
19 related to devices subject to the PMA and the
20 PMA supplement decision-making process, which
21 I thought may be of interest.

22 And there is another guidance

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1 document that is currently out for comment
2 period which is related to conflict of
3 interest and eligibility for participation in
4 FDA advisory committees.

5 One of the things that we do at
6 this opportunity is to provide you an update
7 with regards to staffing. This time we have
8 actually added some additional folks. We have
9 Ms. Stephanie Bechtold, who is currently
10 serving in the Spine Branch on a detail. Dr.
11 John Lyons has recently joined us as an ORISE
12 contractor on a part-time basis for both
13 orthopedic branches but primarily in Joints.
14 And Ms. Tara Shepard has recently joined the
15 Agency in the Joint Branch.

16 The Agency has also -- as part of
17 our postmarket transformation, is working more
18 collaboratively with our other offices. And
19 we do have 50-50 shared people who are the ODE
20 and OSB collaborative reviewer program. We
21 have eight in all with DGRND and two that are
22 specifically from orthopedics, Mr. Christopher

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1 Hack and Jonathan Peck.

2 MDUFMA II last week you probably
3 noticed that the Agency did release an FR
4 notice as well as a news update with regards
5 to the qualitative and quantitative goals that
6 are associated with MDUFMA II. Just wanted to
7 draw your attention to that. And the fact
8 that there is a public meeting that is being
9 held on the FDA campus the end of this week.

10 And then lastly, our petition to
11 the folks that are in the audience and our
12 continuing support that we have from our
13 members who serve on our Advisory Panels like
14 those of you who are here today, if you are
15 interested in getting involved further, please
16 see the contact information that is provided
17 above for both of the Advisory Panels and/or
18 part-time or full-time employment at the
19 Agency.

20 Thank you.

21 CHAIR KIRKPATRICK: Thank you, Dr.
22 Foy.

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1 Before we move on to the open
2 public hearing, I would just like to recognize
3 the fact that we do have an excellent Panel
4 that is assembled here essentially taking time
5 out of their otherwise busy lives. And
6 appreciate their efforts.

7 I would also like to recognize the
8 dedication of our public servants in the FDA
9 with all the hard work that they do.

10 And I'd also like to recognize the
11 fact that there are other members of our
12 population that are dedicated to serving and
13 defending our liberties. And I wanted to
14 express my appreciation to them that are both
15 overseas and domestically protecting our
16 nation.

17 With that, I would like to proceed
18 on to the open public hearing portion of our
19 meeting. Prior to the meeting, two had
20 requested at the last moments to speak to the
21 open public hearing. Are those ready to speak
22 at this point? Or are they waiting to the

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1 afternoon?

2 The Chair recognizes Dr. Lowell
3 Gill as the first speaker. Would you like to
4 come forward please?

5 We have a few housekeeping matters
6 with regard to your presentation. We ask that
7 you please speak clearly into the microphone
8 to allow the transcriptionist to provide an
9 accurate record of your comments. Please
10 state your name and any financial interests
11 that you may have in this or another device
12 company.

13 Dr. Jean will now read the open
14 public hearing statement.

15 DR. JEAN: Both the Food and Drug
16 Administration and the public believe in a
17 transparent process for information gathering
18 and decision making. To ensure such
19 transparency at the open public hearing
20 session of the Advisory Committee meeting, FDA
21 believes that it is important to understand
22 the context of any individual's presentation.

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1 For this reason, FDA encourages
2 you, the open public hearing or industry
3 speaker, at the beginning of your written or
4 oral statement, to advise the Committee of any
5 financial relationship that you may have with
6 a sponsor, its product, and, if known, its
7 direct competitors.

8 For example, this financial
9 information may include the sponsor's payment
10 of your travel, lodging, or other expenses in
11 connection with your attendance at this
12 meeting. Likewise, FDA encourages you at the
13 beginning of your statement to advise the
14 Committee if you do not have any such
15 financial relationships.

16 If you choose not to address this
17 issue of financial relationships at the
18 beginning of your statement, it will not
19 preclude you from speaking.

20 CHAIR KIRKPATRICK: Dr. Gill, you
21 have approximately five minutes. Thank you.

22 DR. GILL: I'm Lowell Gill. I

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1 practice orthopedic surgery in Charlotte,
2 North Carolina, surgery of the lower
3 extremity. I do have royalty agreements with
4 the KMI Integra Company, KMI, which was bought
5 out by Integra for a design of a total ankle
6 arthroplasty named the Eclipse. That is a
7 sort of reverse conflict in the sense that I
8 stand to lose royalties if this product
9 becomes popular.

10 I also have a consulting agreement
11 with the Stelkast Company on outcomes work for
12 the total knee. And I have a royalty
13 agreement with the Zimmer Company for design
14 work on total knees.

15 I also -- my travel here and
16 probably some additional expenses will be paid
17 for by the Link Company.

18 I would like to start out by
19 recognizing -- pointing out the quality of the
20 team that has worked on this STAR ankle
21 project for the last eight or nine years. I
22 know them all. I know them all well. I

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1 trained under one of them. I trained with one
2 of them. I practiced with one of them for
3 many years in the arthrodesis group. And I
4 know them all through the Foot and Ankle
5 Society.

6 And you couldn't get a better team,
7 a more scientifically valid team. These
8 members, every single one of them, are leaders
9 in the field of foot and ankle surgery.

10 My own interest in total ankles is
11 natural because I am a total joint surgeon. I
12 do surgery, total hips and total knees of the
13 lower extremity. Approximately half my
14 practice is foot and ankle so I am naturally
15 interested in foot and ankle arthroplasty.

16 Because of that, I visited eight or
17 nine years ago one of the leaders in this
18 field and watched and participated with him in
19 doing nine total ankles in a week. It was an
20 extremely worthwhile experience because this
21 individual is a superb surgeon.

22 But at that time, eight or nine

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1 years ago, I had major concerns about the
2 designs of the prosthesis. And I made a
3 conscious decision that despite the fact that
4 I am an arthroplasty surgeon and a foot and
5 ankle surgeon, that I would not use that
6 prosthesis. And I still have those same
7 concerns.

8 And so for the last eight or nine
9 years, I have deliberately held back from
10 doing total ankle arthroplasty until I felt
11 that there was a design that would satisfy the
12 principles of joint arthroplasty that I was
13 familiar with hip and knee arthroplasty. And
14 so I have elected not to do total ankle
15 arthroplasty with the exception of a few
16 customs that I have done with the development
17 of the KMI Integra ankle which I have been
18 involved with in the last four or five years.

19 I did visit Peter Wood in England
20 who has about the most extensive experience as
21 any orthopedic surgeon in foot and ankle
22 arthroplasty and scrubbed in with him on six

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1 ankles.

2 I visit Dallas and scrubbed in with
3 Dr. Hakon Kofoed who designed the prosthesis
4 that is being discussed today.

5 I have visited other medical
6 centers and scrubbed in on doing total ankles
7 and have read everything I can get my hands on
8 and published on this subject because of my
9 interest in it, despite the fact that I've
10 held off on doing ankle arthroplasties until
11 the time that I felt that we had a design that
12 I felt confident using with my patients.

13 I will end by showing a few slides.
14 This unique design for a knee arthroplasty
15 was popular many years ago when I was in
16 training. It was a design that was ahead of
17 its time because it allowed triaxial motion.
18 And when you allow motion in more than one
19 plane, then the sheer stresses to the bone-
20 cement interface are reduced, which is one of
21 the things I wanted to see happen in ankle
22 arthroplasty.

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1 Unfortunately, this design did fail
2 because of the large amount of bone resection
3 required. And so there is an example of the
4 failure.

5 Witz in Denmark has shown with
6 studies that the bone strength at the ankle
7 gets progressively dynamically and markedly
8 weaker the farther away from the joint that
9 you get which is the same thing that we find
10 with the hip and knee. And although the talus
11 is 40 percent stronger, the distal tibia is
12 important in stress. And it is extremely
13 important to save as much of that bone as
14 possible.

15 In this 19-year-old athlete, you
16 can see the good quality of the bone. It is
17 all next to the joint. But most of our
18 patients are like the ones on the right where
19 there is compromised bone. And so it is even
20 more critically important that we save bone,
21 particularly in the distal tibia but really on
22 both sides. Bone cuts must be conservative

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1 because the vast majority of failures in total
2 ankles are due to loss of support because of
3 this inherent problem.

4 And yet this was the amount of bone
5 cut that is required in the ankle that I
6 scrubbed in on with nine cases almost ten
7 years ago. And I did not feel comfortable
8 with that. And I still don't feel comfortable
9 with it.

10 Forces are measured also in surface
11 area. In fact, surface area is part of a
12 fundamental definition of force. And a bone
13 sees force spread at its interface, which can
14 be markedly reduced by expanding the surface
15 area as you see in this much larger wing of a
16 megaton 747 compared to a Piper Cub. That
17 wing is there on purpose to reduce the force
18 per unit area or to provide the lift that is
19 necessary to lift that massive machine.

20 And yet this was the design that
21 was being used at the time when I looked at
22 ankle arthroplasties that did not take

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1 advantage of the entire surface area. And now
2 that has been improved. And I might add that
3 the developers of this prosthesis and many of
4 the leaders who are using it are superb
5 surgeons and their results speak for
6 themselves. They are quite good.

7 But I, as mentioned, did not feel
8 comfortable in using a design that didn't take
9 advantage of the surface area.

10 Also, bone is strong in an
11 eccentric pattern and the forces are often
12 eccentric. And just like that spherocentric
13 knee, it is important to provide motion in
14 another plane to reduce the transfer of sheer
15 stress to the bone-cement interface which is
16 where failure normally occurs in a total ankle
17 arthroplasty.

18 I also was concerned about the
19 contact stresses on a design when there may be
20 eccentric forces or point contact loading
21 which could cause early polyethylene failure.

22 As opposed to that, this design

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1 which is being considered today has greatly
2 improved the surface area for bone support
3 which should help prevent or decrease the
4 likeliness of failure at the bone-cement
5 interface which is where the vast majority of
6 failure occur.

7 And it allows motion in another
8 plane, in a different plane, which is on the
9 top of this polyethylene insert right here.
10 And that reduces the shear stresses which tend
11 to be transferred to the bone-cement
12 interface.

13 And so for that reason, I've waited
14 a long time for the development or approval in
15 our country of a Class III device that allows
16 motion in more than one plane. This device
17 has been used extensively in Europe with
18 excellent success which can be seen in the
19 literature. And I feel that our patients and
20 our public would benefit by having what I
21 would consider an improved design.

22 And so the reason I was really

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1 willing to come and give this speech which
2 could adversely effect my own potential future
3 royalties is that I feel that this is in the
4 best interest of patient care. And that is
5 fundamentally what we are all about.

6 Thank you.

7 CHAIR KIRKPATRICK: Thank you, Dr.
8 Gill.

9 We've had the arrival of Dr.
10 Goodman to our Panel. And so I would like him
11 to please introduce himself.

12 MEMBER GOODMAN: My name is Dr.
13 Stuart Goodman and I'm a Professor of
14 Orthopedic Surgery at Stanford University.

15 CHAIR KIRKPATRICK: Thank you, Dr.
16 Goodman.

17 Is there anyone else in the room
18 who would like to address the Panel?

19 (No response.)

20 CHAIR KIRKPATRICK: Seeing none at
21 this time, we appreciate the comments from the
22 open public session.

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1 Please note there will be a second
2 open public session in the afternoon. If
3 anyone else would like to address the Panel
4 about today's agenda topic, you may speak in
5 the afternoon.

6 With the sponsor's permission, we
7 are a little bit ahead of schedule. And if
8 the sponsor is prepared, we would like to
9 proceed to the sponsor presentation. Is the
10 sponsor prepared? Thank you.

11 We will now proceed to the sponsor
12 presentation for the Link STAR ankle. Before
13 Link's presentation, I would like to remind
14 the public observers at this meeting that
15 while this meeting is open for public
16 observation, public attendees may not
17 participate except at the specific request of
18 the Panel.

19 The sponsor will introduce their
20 own speakers. The first Link presenter, I
21 believe, will be Mr. Greenberg.

22 Thank you.

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1 Oh, I'm sorry, you have
2 approximately 75 minutes for your
3 presentation.

4 MR. GREENBERG: I can speak very
5 fast. Hi, I'm Andy Greenberg. I am the
6 President of Link Orthopaedics. We are the
7 sponsor of the PMA, designers of the device.

8 I have with me today presenting
9 members Dr. Roger Mann, Dr. Charles Saltzman,
10 Dr. Mike Coughlin. We also have advising us
11 Dr. Tom Clanton, Dr. Jeanette Ahrens, and Paul
12 Postak. Dr. Mann, Dr. Coughlin, and Dr.
13 Clanton are all former Presidents of AOFAS,
14 the American Orthopaedic Foot and Ankle
15 Society. Dr. Saltzman is former Secretary and
16 current Chair of Orthopedics, University of
17 Utah. Dr. Ahrens is the President of Pivotal
18 Research, our CRO, and Paul Postak runs the
19 test lab at Orthopedic Research in Cleveland,
20 Ohio.

21 Link Orthopaedics is the sister
22 company of Waldemar Link in Hamburg, Germany.

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1 We've been manufacturing total joints since
2 the mid-`60s. We designed and manufactured
3 devices dedicated to care of orthopedic
4 patients. We do hips, we do knees. I'm proud
5 to say that our hip is the leading one in the
6 Swedish Registry as is our Uni Knee.

7 All the devices, including the one
8 we are here to discuss today, are designed,
9 engineered, tested, and manufactured using the
10 same materials, processes, and sterilization
11 procedure.

12 Today we're going to discuss the
13 STAR ankle. It is a three-part device. It is
14 the most widely used total ankle replacement
15 outside of the U.S. It has been marketed
16 outside since 1990 and, obviously, it has the
17 CE mark.

18 Interestingly, in the United
19 States, people are confined to two-part
20 ankles. Internationally, while two-part
21 ankles were widely available, they have
22 essentially been abandoned. Three-part ankles

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1 have been used almost exclusively outside of
2 the U.S. for the last 15 years.

3 Two-part ankles are cleared through
4 the 510(k) process not requiring clinical
5 data. They are cleared for cemented use
6 although interestingly they, as far as I know,
7 are all used off label, non-cemented in the
8 U.S.

9 The three-part ankle requires a PMA
10 and an IDE, obviously extensive data and
11 resources. The Link Company has decided to
12 pursue this. We also think it is in the best
13 interest of the patients.

14 I'd like to introduce Dr. Roger
15 Mann to really begin the presentation for you.

16 DR. MANN: Good morning, ladies and
17 gentlemen. I'm Roger Mann. I'm an orthopedic
18 surgeon from Oakland, California. I am a
19 consultant to Link Orthopaedics. For this I
20 am paid for my time and expenses both to
21 attend meetings and to educate people. I also
22 have no royalties. I have no equity. And I

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1 have received no grants.

2 Arthroplasty history goes back a
3 long way. It was introduced in the `70s. Our
4 early complications eliminated it as a
5 standard procedure internationally. This is
6 mainly because it was large, two-part implants
7 with major bone resection. It was cemented
8 and constrained. This is what caused it to
9 fail.

10 Historically, it was difficult to
11 revise due to the amount of bone that had been
12 resected. Success in other joint replacements
13 have led to the pursuit of a refined total
14 ankle arthroplasty.

15 The limitations of the two-part
16 ankle design used now in the United States, it
17 has high interface stresses. As the result of
18 this, you get bone implant interfaces. We get
19 incongruent metal/polyethylene articulation.
20 And it doesn't dissipate the transverse
21 rotation.

22 You have difficulty balancing the

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1 ligaments. It is labeled for cement fixation
2 but is commonly used cementless. It is
3 specific to most commonly used for the need
4 for large bone resection. And requires an
5 external fixator for insertion.

6 The three-part ankle design used
7 internationally for over ten years is
8 presented here. You can see the multiple
9 designs that are used in Europe. None of
10 these are allowed in this country because of
11 lack of approval.

12 The use of the European three-part
13 ankle in the United States is very
14 interesting. Basically what you saw a second
15 ago was this device right here called the
16 Salto. And this is a three-part design in
17 Europe. In order to enter the U.S. market,
18 they attach their polyethylene to the tibial
19 component, making it into a two-part ankle
20 which has now been approved for U.S. market.

21 There are no studies regarding this
22 prosthesis in the United States. The

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1 prosthesis has never been used in this manner.

2 Yet it has been allowed to come into our
3 country.

4 The description of the device, the
5 Scandinavian Total Ankle Replacement System,
6 the advantage is minimal bone resection. You
7 only need to resect 10 to 12 millimeters of
8 bone in order to insert this prosthesis. It
9 is unconstrained. It is non-cemented. And we
10 have porous ingrowth interface.

11 There are three functional
12 components: a standard cobalt
13 chromium/aluminum tibial component, an ultra-
14 high molecular weight polyethylene mobile
15 bearing, and we have a standard
16 cobalt/chromium alloy talar component.

17 The mobile design permits multiple
18 planes of motion, dorsiflexion and plantar
19 flexion, and most importantly, transverse
20 plane rotation. This reduces the shear and
21 torque forces that can lead to loosening at
22 the bone-metal interface.

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1 The implant congruency is designed
2 to decrease polyethylene wear and you are able
3 to obtain near normal ankle motion. This
4 demonstrates motion in both the dorsiflexion
5 and plantar flexion. And you can see the
6 transverse motion that can occur which
7 dissipates the transverse rotation in the
8 lower extremity.

9 The STAR bone stock preservation is
10 very important. As I said, only 10 to 12
11 millimeters of bone is resected, leaving
12 sufficient bone stock to revise the ankle
13 arthroplasty or to perform an arthrodesis.

14 What we have shown you here in the
15 yellow where it says STAR, that demonstrates
16 the amount of bone that is resected, carrying
17 out the STAR prosthesis. What we see in blue
18 is the prostheses currently used in this
19 country. And you can see the amount of bone
20 that is resected. And as a result of this,
21 you get into the soft bone instead of the hard
22 cortical bone that we see in the subchondral

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1 areas.

2 The indications for use is to
3 replace a painful arthritic ankle due to post-
4 traumatic arthritis, rheumatoid arthritis, and
5 primary arthritis. It is designed as an
6 alternative to ankle arthrodesis. This allows
7 our patients to regain or retain ankle
8 mobility and function.

9 Dr. Charles Saltzman, Chairman of
10 the Department at University of Utah, will now
11 discuss the preclinical testing.

12 Thank you.

13 DR. SALTZMAN: Thank you, Roger.

14 I think he said the components are
15 cobalt, chrome, aluminum. They are cobalt,
16 chrome, molybdenum.

17 Conflicts, I am paid as a
18 consultant to prepare and for this meeting and
19 the expenses. When I was at the University of
20 Iowa, probably around 1999, our laboratory
21 received a small grant from Link to do some FE
22 work that will be shown here. No royalties,

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1 no stock options, or any other conflicts.

2 So I'm going to talk about a couple
3 of things. I've been asked to talk about
4 preclinical testing and to then move into sort
5 of the study design area. So you'll see --
6 it's a few different areas that we are going
7 to try and cover.

8 The in vitro testing of the STAR
9 ankle involved mechanical testing to evaluate
10 the device, intrinsic stability, mechanical
11 testing of contact stresses, finite element
12 analysis of the stresses on surface and within
13 the poly mobile bearing. We're testing under
14 simulated functional use conditions and
15 explant analysis.

16 The mechanical testing, the STAR
17 ankle exhibited minimal constraint in
18 rotational AP and medial-lateral displacement
19 modes, which we think with low chair with
20 adjacent soft tissues and reduced stresses at
21 the bone implant interface.

22 The context stress testing was

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1 first done with Fuji Film. As you can see
2 over here, we put little Fuji Film on both
3 sides. And then stressed the implant and then
4 developed an FE model, which is -- this is
5 just one of the many pictures from the FE
6 model. This picture would show that the
7 highest stresses on this side view of the poly
8 actually occurs right at the thinnest point,
9 which is not surprising.

10 That an internal stress von Mises
11 on the FE picture. The internal stresses were
12 within tolerable limits as were the context
13 stresses. The internal stresses and context
14 stresses are raised with a thinner poly.

15 And if the poly was unsupported by
16 the metal above, which we call overhang, and
17 I'll give you a picture of that in a second,
18 this would be overhang where the poly is not
19 supported by the tibial metal above.

20 I just wanted to mention the
21 background on this. The FDA approved this IDE
22 without requiring wear testing at all. This

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1 was initiated by Link as part of their due
2 diligence. It was actually never requested by
3 the FDA.

4 The testing protocol was developed
5 by the Orthopaedic Research Laboratory
6 affiliated with Cleveland Clinic that set pre-
7 mode directs. And Paul Postak is here to
8 advise us if there are any specific questions
9 on that testing.

10 The testing conditions were sort of
11 stacked against the implant, if you will. We
12 used the smallest implant, the thinnest poly,
13 the overhang condition, continuous loading,
14 and fairly high loads. The one thing to know
15 about the smallest implant is we used the
16 extra, extra small talar component and the
17 extra small tibia component. And very, very
18 few of these were ever put in. And we used
19 the six millimeter poly, which is the smallest
20 poly. So if you want to use an extra, extra
21 small, you have to look for a dwarf or
22 something to fit it into the patient.

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1 And the idea was to simulate
2 gradual loss of materials from a high number
3 of normal gait motions. And we expected
4 device failure most to be wear through and
5 cold flow. Continuous loading was done for
6 ten million cycles, which is approximately ten
7 years of use.

8 This is a classic graph that if you
9 are in the ankle world you will have seen many
10 times. This was done by Ed Chao and Stauffer
11 at the Mayo Clinic in the mid-`70s. And this
12 was when they were putting in Mayo implants.

13 But what this graph shows during
14 the stance phase, the amount of percent of
15 body weight that is thought to go through the
16 ankle using inverse kinematics. And this
17 would be a normal patient getting all the way
18 up to four-and-a-half times body weight. But
19 a patient with arthritis or with replacement
20 rarely reaches three times body weight. And
21 only for a brief moment in the full stance
22 phase.

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1 And so because of that, 3,000
2 Newtons, which is approximately four times
3 body weight of a 75-kilogram man who was used
4 in this testing -- and again, overhang,
5 smallest implant to simulate the worst case
6 scenario, was done.

7 In the testing, there were no
8 samples of demonstrated functional failure
9 including wear through, breakage, that is, or
10 cold flow. But it wasn't designed to test the
11 circumstance of ligament imbalance, deformity,
12 or transient high forces due to a traumatic
13 event. So this was designed to test sort of
14 continuous wear and degradation of the poly.

15 There was an explant analysis. It
16 was not requested by the FDA during the IE
17 process and the investigational plan did not
18 contain a formal explant protocol. So when
19 devices were explanted, they were shipped and
20 stored in a reasonably uncontrolled manner.
21 And then the FDA requested this after the PMA
22 submission. So then we went and tried to put

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1 this together.

2 There were 35 mobile bearings
3 available for analysis. This is from three --
4 and I'll describe this for you later -- but
5 through the three parts of the study, there is
6 a pivotal, bilateral, and a continued access
7 part. And all told, we're looking at over 60
8 patients.

9 And the assessments included rating
10 of burnishing, abrasion, pitting, surface
11 deformation, delamination, scratching, debris
12 capture, and fracture. The most common
13 findings were burnishing, scratching, pitting,
14 and abrasion. I can tell you having removed a
15 couple of these mobile bearings during the
16 course of my -- I was a clinical investigator
17 -- I didn't really know that there was a
18 protocol and there wasn't one.

19 So I would always stick the Coker
20 in, grab it from side to side, and this
21 immobile bearing, try to pull it out. And a
22 few times I scratched it pretty well on the

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1 sides. And then finally got the bearing out.
2 So I think some of the uncontrolled nature
3 could lead to some of the findings that we see
4 here.

5 There were four mobile bearings
6 that actually fractured. Now this is an
7 important point because the size was not a six
8 millimeter. The four that we had were seven,
9 nine, nine, and ten millimeters. There were
10 no fractures in the six millimeters. They
11 were all associated with joint imbalance,
12 deformity, and trauma. And fractures are not
13 associated with wear. So that is four out of,
14 again, about 600 patients.

15 There was loss of polyethylene on
16 the edge of the component in nine of 35 of the
17 retrievables or 26 percent associated with
18 contact with heterotopic bone to support
19 perhaps the use of the Coker, as I did.

20 Conclusions from the preclinical
21 testing or that we thought the preclinical
22 testing and expert analysis demonstrated

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1 suitability of the STAR ankle for
2 implementation and function as long-lasting
3 prosthetic ankle replacement design. Testing
4 conditions were appropriate to evaluate the
5 mechanical stability of the device. And this
6 confirmed the clinical experience from Europe.

7 Next I'm going to move to discuss
8 clinical protocol overview. There were three
9 phases or parts of the study: the pivotal
10 study, the bilateral study, and the continued
11 access study.

12 The pivotal study and the continued
13 access study have evaluations for safety and
14 efficacy. The bilateral study, safety only
15 because the efficacy is confounded by the
16 interpretation of pain on one side versus the
17 other foot.

18 The object was to evaluate the
19 safety and efficacy of the STAR ankle versus
20 ankle arthrodesis to treat patients with
21 moderate or severe ankle pain, loss of
22 mobility, and loss of function due to

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1 arthritis. This was a multi-centered clinical
2 trial.

3 It was designed as a concurrent,
4 nonrandomized, controlled trial with ten STAR
5 ankle sites and five arthrodesis study sites.

6 A two-to-one ratio of STAR ankle to
7 arthrodesis was designed. We also have had
8 historical arthrodesis controls. This was
9 obtained from a meta-analysis and provided
10 further comparative safety data and overall
11 data on the use of fusion.

12 The current arthrodesis was our
13 control. We used a concurrent control group.

14 And it considered at the time in 1999 when
15 this was designed the current surgical
16 standard of care for patients with arthritic
17 ankles. And it involves, as you all know,
18 obliteration of the ankle joint, with
19 placement of screws to maintain alignment so
20 bone bridging occurs.

21 In the concurrent control group, we
22 did not have patients with external fixators

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1 because we thought that would confound. We
2 also had a historical control group and this
3 was done by meta-analysis based on numerous
4 articles in the scholarly literature, captured
5 the clinical experience surrounding the
6 procedure, and augmented our safety analysis
7 for arthrodesis control group.

8 This was originally suggested by
9 the FDA as the sole control group. They did
10 not suggest that we run a concurrent control
11 group. We did anyway. But their point is
12 probably well taken that the meta-analysis
13 gives you a really good understanding of
14 arthrodesis since it is a procedure that has
15 been done for a long time.

16 The endpoints included the primary
17 -- the primary efficacy endpoint was the mean
18 total Buechel-Pappas score. I'm going to
19 describe what that scale is in a few minutes.

20 The composite safety endpoint was not
21 specified as a primary in the protocol but
22 involved the composite of no major

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1 complications, no device failures, revisions,
2 or removal, and some radiographic criteria.

3 For the STAR ankle group, that
4 criteria was no radiographic evidence for
5 device loosening or migration. And for the
6 control group, it was different. It was no
7 radiographic evidence for non-union, delayed
8 union, or malunion. As I will point out
9 later, the delayed unions we sort of -- we
10 think we under report but that is the way it
11 is.

12 Sample size was calculated based on
13 a non-inferiority study. Ten point efficacy
14 delta on the mean BP scale was used. And a 15
15 percent safety delta.

16 Sample size estimates based on this
17 for efficacy we would need 24 STAR ankle
18 patients and 12 arthrodesis patients. But for
19 safety, we would need 134 STAR ankle patients
20 and 67 arthrodesis patients. The study was
21 powered based on the safety endpoint because
22 of the larger group needed. The patients

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1 enrolled ultimately were 158 STAR ankle and 66
2 arthrodesis patients.

3 The major inclusion criteria,
4 primary ankle arthritis, post-traumatic
5 arthritis, or rheumatoid arthritis, moderate
6 or severe pain, which is a less than 20 on a
7 40-point scale, loss of mobility and function
8 of the ankle, failed trial of a foot and ankle
9 arthrosis, and/or analgesic medicine for three
10 months, and a minimum of six months of
11 conservative treatment prior to inclusion into
12 this study.

13 The major inclusion criteria
14 included hindfoot malpositioning greater than
15 35 degrees, forefoot malalignment which would
16 preclude a plantigrade foot, AVM of the talus
17 or tibia, severe osteopenia or inadequate bone
18 stock, insufficient ligament support, active
19 or prior deep infection in the ankle or
20 adjacent bones, and neuromuscular impairment.

21 The post-op protocol is pretty
22 straightforward for arthrodesis. For the

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1 first six weeks, they wear a non-weight-
2 bearing cast. And then after that, they are
3 put in a partial weight-bearing cast until
4 they fully weight bear, which, in general,
5 means three to four months of being in a cast.

6 The STAR ankle patients were in a
7 splint, immobilized, non-weight-bearing for
8 two weeks, then put in a below-knee cast,
9 allowed to put some weight on it, 50 percent
10 for two weeks, and then full weight on it in
11 the cast until the six-week mark at which
12 time, in general, the cast was removed and the
13 patients were moved along and taken out of
14 immobilization.

15 The follow up visits are listed
16 here. And x-rays were taken at six months, 12
17 months, and 24 months and interpreted.

18 The success endpoints we are going
19 to discuss. The efficacy success endpoint was
20 greater than a 40-point improvement in the
21 100-point BP score. The safety success
22 required no radiographic failure, no device

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1 failure, revisions, or removal, and no major
2 complications.

3 And then the overall patient
4 success was a patient who had both efficacy
5 success and safety success.

6 Secondary efficacy endpoints
7 included a pain, visual analog scale, 100-
8 millimeter scale, well validated. The patient
9 satisfaction rating system, the quality of
10 life scale, the SF-36 we used for that, and
11 medication usage.

12 Now the BP scale, the Buechel-
13 Pappas scale is one that has been used in
14 total ankle replacement. It was selected for
15 this. It involves 40 points for pain. It
16 involves 40 points for functions and these are
17 the functions. And then gives 20 points for
18 examination, which is 15 for range of motion
19 and five for deformity. I'm going to bring
20 this up again as well as the pain part again
21 as we move along here.

22 There were multiple ankle scales

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1 considered in 1999, none validated in ankle
2 replacement patients. The BP scale was
3 previously used to evaluate total ankle
4 arthroplasty patients with both clinical and
5 functional measures.

6 The BP subscale that we described
7 has a few considerations. There is bias in
8 the scale that potentially favors the STAR
9 outcome due to range of motion, okay, so range
10 of motion would bias the scale and that is 15
11 points.

12 Bias potentially favors arthrodesis
13 patients who are known to have very good pain
14 relief after surgery. But with the pain
15 subscale, and that's 40 points.

16 But we think that all these
17 subscales are important in evaluating patient
18 success. Pain is very important. Function is
19 important. And motion is important.

20 We define major complications as
21 any patient who had a surgical intervention
22 for infection, wound problem, fracture, or

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1 bone changes such as cysts, osteolysis, AVM,
2 or heterotopic bone formation. You will see
3 as you go through the pack that major
4 complications, and then you will see somewhere
5 else surgical interventions. And it is a
6 little confusing perhaps because the surgical
7 interventions that are not removal and
8 revision surgeries that are considered serious
9 are in this group, major complications.

10 The radiographic review was done a
11 little differently for the arthrodesis than
12 the STAR ankle group. The arthrodesis group
13 had the investigator, him or herself evaluate
14 the fusion status and there was no independent
15 confirmation of fusion status. Whereas the
16 STAR ankle group had radiographs evaluated for
17 all time periods using a zonal analysis
18 developed prior to the study.

19 All the radiographs were evaluated
20 by one central reviewer who was I. And I did
21 it as part of an Orthopedic Research Education
22 Foundation career grant that was asking

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1 questions about the initial position after
2 total ankle replacement and ultimate outcomes.

3 So I felt very fortunate to be able to look
4 at all these radiographs, which came on the
5 heels of looking at thousands of radiographs
6 in the Agility studies.

7 The arthrodesis fusion status was
8 defined the following way: union was greater
9 than 50 percent boney bridging at less than
10 four months, delayed union, greater than 50
11 percent boney bridging between four and six
12 months, and nonunion, less than 50 percent
13 boney bridging. It should say greater than
14 six months.

15 So if you go out to six months and
16 you don't have boney bridging and you have
17 pain, you probably have a nonunion.

18 The STAR ankle radiographic review,
19 its goal was to identify radiographic signs
20 that predict eventual failure, clinically
21 significant loosening or migration. That was
22 the criteria in the original study packet

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1 agreed on by the FDA.

2 It is important to understand that
3 pre-study, there really was no information
4 available to guide the development of a
5 radiographic analysis plan for uncemented
6 ankle replacements, especially this one. And
7 the initial PMA radiographic analysis, which
8 was performed by statisticians here based on
9 the findings on the x-rays, was inconsistent
10 with the goal.

11 We feel it was inconsistent with
12 the goal and protocol, we being the clinical
13 investigators. We revised the radiographic
14 analysis in a way that we think is more
15 accurate and consistent with the original
16 intent of the protocol for an uncemented ankle
17 based on our experience and further
18 understanding of what is clinically
19 significant or not.

20 Now we're going to go through two
21 small groups of patients that we actually
22 reclassified after the statisticians in the

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1 company had made their original report to the
2 FDA. First, we thought there was
3 inappropriate carrying forward of radiographic
4 information. In the initial PMA analysis, the
5 STAR ankle subject who were not radiographic
6 successes at six or 12 months were considered
7 failures at 24 months, regardless of the 24-
8 month results.

9 And seven of these subjects met
10 radiographic success by 24 months. And we
11 believe should be considered radiographic
12 successes.

13 Second, inappropriate
14 interpretation of early radiographic findings
15 as predictive of long-term clinical failure,
16 early settling of an implant that subsequently
17 stabilizes was not found predictive of 24-
18 month -- or a 48-month actually clinical
19 outcome.

20 We had five subjects who were
21 initially classified as safety failures. They
22 were classified -- three at six months and

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1 two at 12 months -- but they had no further
2 change in radiographs and had satisfactory
3 clinical results at 48 months. And we believe
4 should be considered radiographic successes at
5 24 months.

6 There is a bilateral study arm.
7 This is the bilateral study. It involved a
8 single-arm, multi-center study of bilateral
9 treatment of 21 patients. These patients were
10 initially enrolled in the pivotal or continued
11 access studies within developed bilateral
12 disease or were presenting initially with
13 bilateral disease.

14 As I mentioned, only safety
15 analysis were performed for these. Patients,
16 their efficacy data was utilized up until the
17 point of the contralateral ankle treatment and
18 then censored.

19 Between 2002 and 2004, LINK
20 received FDA approval for a multi-center
21 registry continued access study. This allowed
22 them to have their investigators increase the

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1 number of patients with three phases of 150
2 patients each, total of 450. Same sites that
3 participated in the pivotal study also
4 participated in the continued access study.

5 The co-investigators at some sites
6 were able to perform STAR ankle procedures.
7 And this begins to give us some insight into
8 the learning curve as we will discuss later.

9 The STAR ankle requires an anterior
10 surgical approach. I'm going to mention a few
11 things about lessons learned here and one of
12 the lessons -- some of the lessons are related
13 to the approach -- at the study outset,
14 anterior approach was less familiar to us than
15 the lateral approach, which is very familiar
16 to most foot and ankle surgeons.

17 This approach is used for all ankle
18 arthroplasties. Experience and awareness
19 increased nationally during the course of the
20 study with this approach as more use of other
21 ankle replacements emerged. And increasingly
22 this approach has been taught in our residency

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1 and fellowship programs. So it would be more
2 familiar now.

3 The approach is susceptible to
4 wound problems because there is thinner skin,
5 less subQ fat, and the incisions runs right
6 down the center of an angiosome so that the
7 blood supply is not perfect. It is
8 susceptible to transient or permanent sensory
9 loss in the medial dorsal aspect of the foot.

10 And there is usually a small branch
11 either here or even up higher and the patients
12 will lose some sensation. About one out of
13 five patients loose that from stretch or
14 transection of fine terminal branch from the
15 medial branch of the superficial peritoneal
16 nerve, very similar to the infrapatellar
17 branches when you do a total knee of no
18 clinical significance -- I guarantee that.

19 Some of the lessons we learned was
20 how to deal with that incision. And I'll
21 describe that. And we refined the
22 instrumentation and technique in these

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1 patients with better patient selection and
2 more rigorous post-op education.

3 We lengthened the incision as we
4 went into the later part of the pivotal study,
5 as you will see. It became recognized that we
6 were putting too much tension on the incision.

7 Eliminating self-retaining retractors
8 eliminates skin staples. I believe this will
9 reduce the rate of major complications related
10 to the wound.

11 Interoperatively we try protect the
12 medial malleolus with a couple K-wires when we
13 do our cuts. And we, in general, try to
14 insert thicker poly and downside the talar
15 components so it doesn't hit up against the
16 sides and cause other postoperative problems.

17 We also have better instruments.
18 We have better capturing of the saw blade with
19 decreased bony problems and I'm going to show
20 you that on the next slide. Towards the end
21 of the pivotal period, the manufacturer got us
22 this device that allows us to make our cuts

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1 medial/laterally much more accurately than we
2 able to make. And so we have had less
3 instance of interoperative and postoperative
4 problems related to bone cuts against the
5 malleoli.

6 This is an important -- a small
7 addition but very important. We added talar
8 trials and a talar fin to help assess accuracy
9 of bone preparation and improve device
10 placement. These came in right at the end of
11 the pivotal group and right before the
12 continued access. So mostly they were
13 available to us during the continued access
14 only.

15 This is pretty straightforward.
16 This is a guide to tell you whether you made
17 your cuts in your talus okay. Now it seems
18 pretty easy but when you are looking at it
19 from in front, you can't see the back and you
20 can't see the sides perfectly. You don't know
21 if you've got it right.

22 When you put one of these devices

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1 on, if you cut a little too much bone, what
2 tends to happen is the device will just sink.

3 And it will sink pretty quickly in the first
4 six months or so. And then sometimes it just
5 stops.

6 And that relates to the five
7 patients that we think should be reclassified
8 for early sinkage, if you will.

9 Finally, our patient selection
10 criteria is changing a little with increased
11 awareness with difficulties with coronal plan
12 deformity and ligament instability.

13 This kind of deformity is more
14 likely to lead to problems. So we are less
15 enthusiastic about a large coronal plane
16 deformity. We are excluding patients with
17 peripheral neuropathy. We've improved our
18 patient instruction post op manual.

19 So to sort of sum up what I've just
20 said in the last 20 minutes or so, I've
21 reviewed the preclinical testing, I've
22 reviewed of the radiographic issues and the

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1 issues related to our review and analysis.
2 And I have tried to discuss some of the
3 lessons that we have learned in preparation
4 for Dr. Coughlin's talk.

5 The preclinical testing, I think,
6 was adequate and improved our understanding of
7 the mechanics of the joint. The radiographic
8 review showed us that our initial analysis
9 approach needed to be revised to more
10 clinically appropriate.

11 And this is related to the fact
12 that we did not have any prior art to work
13 with to make the appropriate decisions about
14 what is important and what is not in
15 uncemented ankle replacements.

16 And the lessons learned have
17 resulted in improved safety as evidence by the
18 improved safety in the continued access group
19 as you can see in your Panel pack.

20 Well, thank you very much for your
21 attention.

22 Our next speaker is Dr. Michael

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1 Coughlin who is a Clinical Professor of
2 Orthopedic Surgery at Oregon Hill Sciences,
3 Director of the Idaho Foot and Ankle
4 Fellowship, Past President of the American
5 Orthopaedic Foot and Ankle society, and Past
6 President of the International Federation of
7 Foot and Ankle Societies.

8 Thank you.

9 CHAIR KIRKPATRICK: Just as a point
10 of information, you have approximately 40
11 minutes remaining. Thanks.

12 DR. COUGHLIN: I'm Mike Coughlin.
13 I'm from Boise, Idaho. I'm a clinical
14 investigator, a consultant to Link. I've
15 received no royalties, grants, and have no
16 equity in this company.

17 In 2000, we came before you and
18 obtained the IDE for this study. Now seven
19 years later, we return with our results both
20 from the pivotal and continuing access study.

21 One-fourth of my orthopedic career has been
22 involved in the design and execution of this

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1 study.

2 Dr. Mann and I want you to know
3 that while we did not perform total ankles in
4 the 1970s, we witnessed the debacle of the
5 two-part cemented total ankle and we were not
6 about to risk our hard-earned reputations or
7 the safety of our patients on this or any
8 other ankle without firm data.

9 Thus you will see we collected an
10 enormous amount of information and dwelled
11 sometimes on minor or inconsequential adverse
12 events in an attempt to cover every aspect of
13 the prosthesis and surgical technique.

14 Please understand we often bias
15 both the clinical and the radiographic
16 assessments against the STAR when compared to
17 ankle arthrodesis. But we wanted to know
18 everything about the STAR. And we ask you to
19 take this into consideration when you review
20 this information.

21 We sought out excellent
22 investigators from renowned institutions for

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1 the study. We enlisted surgeons for the
2 pivotal STAR group who believed in total ankle
3 replacement and wanted to perform them.

4 For the arthrodesis group, we
5 wanted to enlist those who believed in
6 arthrodesis and would use a similar operative
7 technique and had long-term experience. For
8 example, if someone used an Elizeroff or an
9 external fixator, the infection rate might
10 have been higher and bias the data against the
11 arthrodesis group.

12 We did not want people who were
13 committed to the Agility ankle. They might
14 cherry pick and do just the difficult
15 arthrodesis cases and bias the study against
16 that group.

17 We wanted them to use a similar
18 technique that we could then use to compare
19 with the meta-analysis in the literature. And
20 they needed good support staff. And they
21 needed to be good recordkeepers. And they
22 needed to be reliable and competent

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1 investigators.

2 The end result we had two equally
3 talented and experienced groups. However, the
4 arthrodesis group was doing what they did
5 often and did well and had done for a long,
6 long time.

7 There was no learning curve for
8 them. From an experience viewpoint, they
9 start the 1,600 meter race at the 800 meter
10 mark. The STAR group started at the starting
11 line.

12 It wasn't difficult to enroll the
13 candidates for ankle replacement but we
14 predicted that the desire for motion and
15 reservations about functional difficulties
16 following an arthrodesis would make enrollment
17 in the control slower and more difficult. We
18 only needed 24 and 12 patients to prove
19 efficacy in this study, the primary endpoint.

20 At 12 and 24 months, our follow up
21 was excellent for the STAR group. Motivation
22 for the arthrodesis group was more difficult.

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1 They had no vested interest, received a
2 standard operation treatment, and were helping
3 another group.

4 Likewise, the extensive follow-up
5 requirements for the control, who were only
6 receiving standard treatment, led to a loss of
7 follow up in the control with the passage of
8 time. And this made for a small sample size,
9 which eventually made our safety delta,
10 although close, much more difficult to attain.

11 Now I realize you understand this
12 but the three groups were intent to treat,
13 those at the starting line, completers, those
14 who reached the finish line, and per protocol,
15 those with no deviations that would disqualify
16 them from the study.

17 This slide justifies the ITT
18 completers and per protocol patient
19 populations. And I refer you to the
20 submission document regarding that.

21 There were no significant
22 differences in gender or race in the STAR and

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1 control groups. The STAR patients were
2 significantly older and increasing age
3 probably biases data against the STAR group as
4 function is lower. But I suppose you can make
5 the argument that expectations are lower here
6 as well. The implications are obviously
7 important in these areas.

8 In the STAR group, the incidence of
9 rheumatoid patients was two-fold greater. And
10 this does portend multiple joint involvement,
11 increased pain, higher complication rates,
12 decreased function, and biases against the
13 STAR.

14 Now let's look at the Buechel-
15 Pappas numbers, the scoring method that we all
16 agreed to use to evaluate both groups. It was
17 designed for total ankles in 1978. And in
18 your packet on page 50 of the protocol, it
19 awards 40 points for pain, 40 for function, 15
20 for range of motion, and five points for
21 deformity.

22 The score was administered prior to

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1 and following surgery. And we needed this
2 control, the control group for this
3 comparison. You want points. You want a high
4 score. So if you look at the pain score, the
5 STAR has a lower score. They hurt more than
6 the control group. No pain would give you 40
7 points here.

8 Likewise, the function, where 40
9 points would be normal, the STAR group has a
10 lower function level. At baseline, range of
11 motion was slightly better in the STAR and
12 deformity was the same for the two groups.

13 In summary, the two populations
14 were similar for gender, weight, and height.
15 But the STAR group was more debilitated
16 because of a higher number of rheumatoids,
17 older age, higher pain, and lower function.

18 At the time of surgery, despite
19 this being a relatively unfamiliar surgical
20 approach, coupled with implanting a new and
21 unfamiliar prosthesis, variables of operative
22 time, estimated blood loss, and hospital

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1 lengths of stay were similar.

2 At 12 and 24 months, the STAR had
3 significant improvements in the total BP score
4 when compared with the control group. The FDA
5 requested us to delete the 15 point range of
6 motion component on the BP scoring system to
7 see what happened.

8 Now this has never been reported in
9 the literature or done to my knowledge. But,
10 you know, it was a reasonable question. Is
11 this all about motion? That's what I think
12 patients believe.

13 You will see, as we proceed, it is
14 much more than this. But even without giving
15 credit for the motion, the STAR group did
16 greater than the control group.

17 This is in regards to deformity.
18 Here you want points as well. Let's look at
19 improvement components of the BP scoring
20 system. These are interesting and shows why
21 the STAR did better. Deformity, only given
22 five points, is composed of alignment, leg

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1 length inequality, and having the foot plant
2 at grade on the ground.

3 Those with an arthrodesis and
4 slight equinus will back knee. Those in
5 slight varus will roll out. Those with a
6 short leg, and many with a fusion do have a
7 short leg, will complain. And they did. And
8 the STAR showed significant improvement here.

9 Regarding functional improvement,
10 again a significant improvement in this area.

11 A total of 40 points are available with eight
12 points each for limp, standing, walking, stair
13 climbing, the use of a cane, crutch, or
14 walker. We will dissect this further in a
15 moment.

16 The pain score, you want points
17 here in all of these subgroups. A total of 40
18 points are available. And these numbers apply
19 to improvement over baseline.

20 Now this was a surprise to us. We
21 would have expected greater pain relief in the
22 arthrodesis group. They hurt less due to

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1 rigid internal fixation. But at 12 and 24
2 months, the pain score improvement in the STAR
3 was greater. And we believe the answer is
4 just like with a fused hip, the spine takes a
5 beating. A total hip replacement spares
6 adjacent joints. So, too, with the STAR. It
7 spares the hindfoot.

8 Range of motion improvement, this
9 is critically important to the quality of
10 life. It is the reason these people offer a
11 total ankle replacement. It allows my
12 patients to cross country ski, to hike in the
13 hills, to walk up an incline, to stand with
14 ease, and to wade in a river. And, of course,
15 the mobile ankle was superior.

16 Patients preoperatively gave a
17 score for motion. And they had a lower score
18 after arthrodesis, hence the negative value.

19 Improvement in the BP score was
20 almost two-fold over the control. We set a
21 40-point improvement as a goal. And that was
22 the mean score, a highly significant

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1 difference. And without motion -- the reason
2 for doing the total ankle replacement was for
3 motion. Let's be clear about that.

4 But when we were asked to eliminate
5 motion and check the scores, the scores, you
6 can see, were still greater. They were
7 substantially different. And that is
8 impressive to me.

9 But let's look more closely at
10 function. This is where flexibility is so
11 critical. There are eight points available
12 for each of these subgroups. Realize these
13 are improvement scores, not total scores:

14 Stair climbing, significantly
15 better; standing, significantly better;
16 support with walking, better; walking -- this,
17 interestingly, was on level ground -- it was
18 better but I wish it had been suggested a
19 slope for the test and it would have
20 differentiated these two groups more
21 specifically; limp, significantly better due
22 to leg length inequality, lack of flexibility.

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1 In all but one of these subsections, the STAR
2 scored better.

3 Now realize there has never in the
4 history of orthopedics been a prospective
5 arthrodesis study or a total ankle replacement
6 study of this magnitude and depth. Now we set
7 the bar high -- at 40 points for improvement
8 in the BP score. Why? Well, we wanted to
9 prove a difference.

10 The STAR group was significantly
11 better at 12 and 24 months with motion and
12 with motion removed, it was still superior.

13 In our protocol safety success
14 required the criteria in the left-hand column.

15 While no specific hypothesis was attached to
16 the safety endpoint, the observed difference
17 in the safety endpoint was less than the 15
18 percent delta for all populations when the
19 non-inferiority delta was not met.

20 This information is original data,
21 not adjusted for porous ingrowth and delayed
22 stabilization of the components. We will

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1 discuss in depth later. But for our
2 radiographs, at the beginning of the study we
3 had no prior studies for us to set the bar.
4 We had hip and knee studies but our criteria
5 was more inclined towards cemented total ankle
6 replacement.

7 We wanted to pick up any migration
8 or periprosthetic lucencies. In submitted
9 ankles, these signs routinely and regularly
10 herald failure. This is not necessarily true
11 for components with biologic fixation as has
12 been shown, especially in total knee
13 replacement.

14 And in the originally PMA
15 application, the initial radiographic analysis
16 was performed by the company in consultation
17 with its data analysts and statisticians
18 without any input from the clinicians. They
19 incorrectly assumed that if a patient did not
20 meet the radiographic success criteria at six
21 or 12 months, that they were a failure and,
22 therefore, carried forward as failures.

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1 They didn't take into account bony
2 ingrowth implants with a dynamic interface.
3 This situation was only realized by us
4 clinicians earlier this year during our
5 extensive review of the data in PMA. This is
6 what has prompted the revised and clinically
7 appropriate re-analysis of the radiographs.

8 There were two different areas of
9 concern in the original analysis. The first
10 concern was the inappropriate carrying forward
11 of early radiographic failures.

12 Seven patients had early
13 radiographs that either demonstrated a lucency
14 or were suggestive of component migration.
15 These findings were not present at 24 months.

16 In that 24 months, these patients
17 unequivocally met the radiograph success
18 criteria. There is no debate about their
19 success.

20 The second concern was the
21 inappropriate interpretation of early
22 radiographic findings as predictive of long-

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1 term clinical failure. A cemented prosthesis
2 that subsides should not improve and will
3 likely fail. An ingrowth prosthesis may
4 stabilize with further ingrowth and succeed.

5 And we have several of these that
6 settled initially and were stable at 12
7 months. These patients continued to do well
8 clinically and functionally through the 48-
9 month follow up.

10 The impact of an appropriate
11 evaluation of the pivotal STAR patients found
12 these additional 12 subjects who were
13 considered radiographic successes at 24
14 months, who had met all other safety criteria.

15 The criteria remained unchanged. We changed
16 our analysis. And we firmly believe that this
17 is not only fair but it is appropriate.

18 In the analysis of safety
19 endpoints, the initial difference of 12
20 percent rate gets closer with appropriate
21 radiographic analysis. We believe the success
22 of the control group is overestimated and the

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1 delta is affected, of course, by the small
2 number of control subjects.

3 No specific hypothesis was attached
4 to the safety endpoint. Observed differences
5 in safety success rate was less than the 15
6 percent delta for all populations. The non-
7 inferiority delta was not met. The difference
8 between the two groups is largely related to
9 major complications and surgical
10 interventions.

11 So on this side we see revised
12 numbers based on the seven patients carried
13 forward and the five patients who initially
14 settled and then stabilized. Initially the
15 difference was 12 percent but with these two
16 adjustments, we see a comparable safety
17 success of 76.1 and then 79.6 percent.

18 The delta is met with the 12
19 patients, but if just the seven carried
20 forward patients are included, this is only a
21 six percent difference but the lower bound of
22 the confidence interval at 17 percent is

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1 affected, again, by the small number of
2 patients in the control.

3 The safety endpoint is met for the
4 STAR group in the pivotal study with the
5 appropriate radiographic analysis. And we
6 strongly suggest that the success of the
7 control is overestimated because of under-
8 reporting of fusion failures by using
9 investigator classifications. And most likely
10 the 86.5 percent fusion rate could not be used
11 because these patients were not fully weight-
12 bearing at four months, 13 percent of them
13 were not fully weight bearing at four months
14 and were still casted after the fourth-month
15 visit.

16 And with the more appropriate
17 radiographic analysis for both the control and
18 STAR groups, we have a more comparable safety
19 success rate. Now the overall success, and
20 that would be safety and efficacy, was 45
21 percent versus 13.7 percent in the control.
22 If you will, it was 49.3 percent.

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1 Patient success rates by
2 investigational site were not statistically
3 significant and I think the p-value tells the
4 whole story. And again, without using motion,
5 the STAR still does well or is superior to the
6 control group.

7 When looking at pain, you want a
8 low score here. Zero equals no pain. When
9 looking at pain score improvement, the STAR
10 group hurt more before and had a larger
11 reduction in pain scores as evidenced by a
12 higher improvement score. This is notable
13 achievement for a mobile-bearing ankle joint
14 compared to an arthrodesed joint or fused
15 joint.

16 Using our subjective questionnaire,
17 both groups were happy. Both were improved
18 over their subjective preoperative condition.

19 The satisfaction of the arthrodesis
20 group, however, made it difficult to keep them
21 coming back. Once their issue was solved,
22 there truly was little motivation to keep them

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1 coming back as time passed.

2 And as we now address adverse
3 events, they were more common in the STAR
4 group. Some are due to the criteria we used.

5 And some are only seen with the anterior
6 approach.

7 And some are not really reported in
8 the control group like fracture of the
9 malleoli. This is due to the need to resect
10 bone from the distal tibial region. It is
11 well described in our prior literature -- a
12 risk of the procedure. But our quest was to
13 reduce this once we observed the incidence in
14 the pivotal study.

15 Pain and swelling, a short-term
16 event, it is expected with a moving joint and
17 is of little consequence long term.

18 Nerve injury, this is a risk of the
19 exposure as well. We truly thought we might
20 see posterior tibial nerve or greater
21 saphenous nerve injuries from our group. But
22 these reports refer to the small sensory

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1 branch shown by Dr. Saltzman.

2 The increased range of motion was
3 probably a function of patient expectations.
4 And wound problems, this isn't just the STAR.

5 It is any total ankle that uses an anterior
6 approach.

7 Regarding fractures, we succeeded
8 in reducing this in the continued access with
9 our change in technique and instrumentation
10 that was elaborate. These fractures were of
11 little consequence long term but remember, we
12 again under report the arthrodesis group. One
13 hundred percent of the fibula and many of the
14 medial malleoli in that group were
15 intentionally cut or fractures.

16 We see here adverse events. And
17 this is at 24 months. Here we do give proper
18 credit to delayed union by history in the
19 lower right-hand corner, at up to 13.5
20 percent, for those that still are not weight
21 bearing at four months or still in a cast at
22 16 weeks.

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1 I again call attention to that tiny
2 superficial branch of the peroneal nerve that
3 can be stretched or severed, leaving a small
4 area of numbness analogous to following a
5 total knee, numbness from severing the
6 infrapatellar branch of the saphenous nerve.

7 No patients in our study had a
8 major nerve injury of any long-term
9 consequence during the pivotal study. Even
10 though AEs were more common in the pivotal
11 STAR group, many of them did not have
12 significant clinical consequences or long-term
13 sequella. Many are not captured in the
14 control group.

15 There was marked decrease in major
16 complications in the continued access. Pain
17 was comparable in both groups. Nerve injury,
18 the superficial branch of the peroneal nerve
19 that I mentioned is clinically insignificant
20 and comparable to total knees.

21 Bone fracture, rarely significant,
22 intrinsic to arthrodesis, and reduced in the

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1 continued access arm.

2 Soft tissue edema, characteristic
3 of all arthroplasties, transient really, and
4 apparent with only early cast changes. It is
5 seen with early weight bearing. Decreased
6 range of motion is more intrinsic to
7 arthrodesis.

8 Wound problems, characteristic of
9 the anterior approach, improved in the
10 continued access study with our technique
11 changes. The infection rate was lower in the
12 STAR group and bony changes such as exostosis,
13 heterotopic bone, fracture, that is similar in
14 rate and incidence to the non and delayed
15 union rate in the control group.

16 And when we say major
17 complications, wounds and nerves and fractures
18 were rarely a major complication requiring
19 later surgery as we see in the right-hand
20 column.

21 At 24 months, the study endpoint,
22 revisions were more prevalent in the STAR

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1 group, a function of arthroplasty in
2 comparison to arthrodesis. Reoperations
3 included ORIF of malleoli, debridement
4 heterotopic bone, revision, and in two cases,
5 an arthrodesis. As per the literature, clean
6 outer salvage with revision or arthrodesis is
7 an inherent risk of a mobile joint.

8 Other interventions were more
9 prevalent in the STAR group, a function of the
10 debilitated state of the ankle at baseline.
11 Removals were more common in the control
12 group, a function of symptomatic hardware.

13 This slide enumerates component
14 revisions. Meniscal component removals are
15 standard practice when visualized for any
16 reason such as just with a total knee
17 replacement. But other components were only
18 removed for visible abnormalities at the bone
19 implant interface.

20 Please realize there were really
21 two purposes of this study. From a company
22 perspective, they wanted to gain approval.

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1 From Dr. Mann's and my perspective, we wanted
2 to define all the issues with total ankle
3 replacement, not necessarily fusion. Hence
4 you will see us collecting enormous amounts of
5 information on AEs and interventions.

6 These questions capture more issues
7 with total ankles. For example, we captured
8 heterotopic bone formation with the STAR. It
9 happens often with arthrodesis but we did not
10 capture it there. We also believe that the
11 control group results are probably superior to
12 any other published study and reflect the
13 expertise of the investigators in that arm of
14 the study.

15 Major complications up to 24 months
16 were captured to identify those events that
17 should indicate failure of an arthroplasty
18 subject. STAR ankle complications largely
19 reflect the anterior surgical approach and
20 articulating nature of the device.

21 We did not include delayed union or
22 malunion in the arthrodesis group, which is

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1 generally considered a major complication
2 following arthrodesis. Definition of major
3 complications focused largely on the
4 arthroplasty, wound problems associated with
5 the anterior approach, bone problems that were
6 a natural consequence of a motion-preserving
7 device.

8 So how did we react and learn? And
9 what differences did it make? For wound
10 problems and bone problems, you have heard
11 what we did to reduce the AEs. And we
12 succeeded. And please recall the published
13 literature does demonstrate for the STAR and
14 other total ankle replacements that revision
15 arthroplasty or arthrodesis is a realistic
16 option when failure occurs. It results in
17 high success rates.

18 Now I've detailed the anticipated
19 difficulty enrolling patients to the
20 arthrodesis control: permanent loss of ankle
21 mobility, degeneration of adjacent joints,
22 availability of an FDA-cleared ankle

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1 prosthesis, and reluctance of patients to
2 comply with extensive long-term protocol
3 requirements.

4 But the meta-analysis helps us to
5 supplement the pivotal study safety data. How
6 did we pick these 12 articles? Trying to be
7 correct and fair, we chose articles with
8 similar operative technique. We also tried to
9 eliminate those with external fixators. We
10 chose papers that gave us an honest and true
11 picture of an arthrodesis experience.

12 When we look at the historical
13 controls, interventions are lower, delayed
14 union is under-reported depending upon the
15 definition, and the revision of device failure
16 is equivalent to the STAR procedure.

17 Control results are much better
18 than historical results for ankle
19 arthroplasty. Safety results observed in the
20 STAR group of the pivotal study are
21 representative of historical controls. And
22 the safety profile of the STAR was based upon

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1 a period when the technique was being refined.

2 Now in 2005, the FDA raised a
3 question regarding radiographic review for
4 continued access patients. The company
5 performed the analysis of the first group of
6 the patients in the continued access and all
7 24-month radiographs that were available were
8 reviewed. Five of the 85 patients had
9 incomplete radiographic data due to either the
10 quality of the radiographs or the position of
11 the ankle, to determine the status of success
12 or failure.

13 The independent radiographs were
14 reviewed by Medical Metrics, a highly regarded
15 independent orthopedic imaging core lab which
16 is involved in numerous IDE trials.

17 Now we see at 24 months all three
18 groups side by side. And using the
19 independent radiographic review for the
20 continued access group, all continued access
21 success rates are higher than the pivotal
22 study. The delta is met both for efficacy and

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1 for safety success. For overall success,
2 there was not a delta but the p-value is most
3 impressive.

4 In continued access, we were able
5 to substantially improve instrumentation and
6 technique, including some sequential ligament
7 release to balance the ankle joint during
8 surgery. We have learned lessons and have
9 implemented them, as you see in the results of
10 continued access.

11 Now as an orthropod, I'm venturing
12 on somewhat tenuous statistical grounds
13 talking about imputed results, however we
14 continue to assess this in both a careful and
15 conservative fashion. We see the STAR pivotal
16 results initially at 71 percent. Then with
17 the clinical-appropriate analysis, 79.6.

18 And for continued access, for those
19 without independent radiographic review, we
20 used the success rate for the pivotal study.
21 So thus you see a rate of 78.2 percent and
22 then 84.2 percent, which is combined with the

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1 radiographic review from Medical Metrics and
2 using for the rest of the patients the rate
3 from the pivotal study. And the delta is made
4 with both.

5 At 24 months, we see surgical
6 interventions occurring at one-half the
7 frequency in the continued access study. And
8 wound problems, resultant infection, and
9 osseous problems were markedly reduced in
10 continued access with over twice as many
11 patients with the same number of
12 complications.

13 The published European experience
14 and the two-part American total ankle
15 experience did not prepare us for these
16 problems. We had to experience in them, then
17 we had to solve and react. And we did.

18 So across the board, we see
19 surgical interventions and major
20 complications, all over the same time period
21 of 24 months. There was a substantial
22 decrease in the continued access arm in

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1 revision and removal and major complications
2 were comparable to the controls and to the
3 historical arthrodesis meta-analysis.

4 Furthermore, five of the 12 pivotal
5 revisions were poly exchanges. In continued
6 access, the 7.1 revision, removal, and major
7 complication combined is lower than the
8 control rate of 10.6 percent. And for all the
9 STARs done, 9.2 percent is lower than the
10 control rate as well.

11 It is very clear that the overall
12 results are superior for the STAR group. The
13 Buechel-Pappas scores, which we chose to use
14 as our yardstick were superior for the STAR
15 group at 12 and 24 months. And the BP
16 improvement scores were also better for the
17 STAR with or without range of motion. And
18 functional improvements were most impressive.

19 Superior efficacy results for the
20 mean BP score and the greater than or equal to
21 40-point improvement of BP scores were seen at
22 12 and 24 months. Superior and non-inferior

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1 efficacy results for the mean BP score, minus
2 range of motion subscore at 12 and 24 months
3 was seen as well.

4 For the continued access study, the
5 modifications to the surgical procedure and
6 new techniques result in lower adverse event
7 rates. Additionally, physician experience was
8 associated with improved safety, efficacy, and
9 overall outcomes.

10 We are dealing with an orphan
11 joint. And for those of us who treat foot and
12 ankle problems, our patients have waited a
13 long time for a solution to their problems.
14 It is an orphan joint and witness that none of
15 the major orthopedic companies of America are
16 here today presenting this PMA.

17 We have needed biologic ingrowth, a
18 non-cemented solution, and a three-part mobile
19 bearing to address the failures experienced in
20 the 1970s with cemented two-part ankles.

21 We have kept meticulous records and
22 reported minor and major adverse events. Many

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1 of them are important for us to know but of
2 limited long-term consequence. And we have
3 had to balance those risks and we ask you to
4 balance them against the functional impact for
5 patients.

6 And when you do, while the AEs were
7 higher in the pivotal study, many of these
8 were minor and resolved and have demonstrated
9 a definite reduction in the continued access
10 with our experience and changes that we have
11 had to figure out.

12 Both arthrodesis and arthroplasty
13 have comparable risks. But we thought we knew
14 in 2000 that we now know, ankle arthrosis
15 after an ankle arthrodesis, as Coster and
16 Saltzman showed, leads inevitably and
17 regularly to a hindfoot DJD.

18 And as Pyevich showed following the
19 Agility ankle, and Horton showed after the
20 STAR, ankle replacement protects the hindfoot
21 and reduces the rate of DJD in adjacent
22 joints. This doesn't get any credit with any

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1 score. But it is vitally important.

2 Now remember the options for
3 salvage with revision or arthrodesis have high
4 success rates as well. We don't expect later
5 surgery but alternatives for revision surgery
6 demonstrate relatively high success rates.

7 But what about other clinical
8 benefits that our patients tell us about when
9 they visit us in the office? For them to be
10 able to stand comfortably, to climb a slope in
11 the forest, on the farm, or on the golf
12 course, to be able to walk up a flight of
13 stairs, to wade and cast a fly in a river at a
14 rising fish, to maintain near-normal mobility,
15 we wanted to give patients with arthritic
16 ankles a safe, effective alternative to ankle
17 arthrodesis. And this truly is what our
18 seven-year journey was all about.

19 Thank you.

20 CHAIR KIRKPATRICK: I would caution
21 the sponsors to recognize you have seven
22 minutes remaining. Please try and stick to

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1 facts. Thank you.

2 MR. GREENBERG: I'm from New York.

3 It's no problem.

4 Okay, I'd like to talk a little bit
5 about our training program. We did a learning
6 curve analysis and what we did is we evaluated
7 the comparative rates of intraoperative
8 fractures, major complications, and surgical
9 interventions. The pivotal study against the
10 first 15 of the surgeries in the continued
11 access and then later 15.

12 And what we found is, as we have
13 said before, the rate of problems goes down
14 markedly from the pivotal study to the
15 continued access. But the evidence becomes
16 much less clear after those first 15 in
17 continued access. While it seems the
18 intraoperative fracture rate continues to go
19 down, other rates it is really unclear, and
20 major complications not clear at all.

21 One thing we had going for in the
22 continued access study is we did have some new

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1 investigators that were not in the pivotal
2 investigation. So these people we could see
3 if they were able to jump the learning curve
4 using the new techniques and instrumentation.

5 And you will see on the right, their results
6 were actually very, very good.

7 Intraoperative fracture rate, lower
8 than the pivotal investigators in the
9 continued access and, obviously, lower than in
10 the pivotal study.

11 Major complications, on 26
12 patients, they had zero. And surgical
13 interventions, they had one.

14 So with increased awareness and
15 training the anterior surgical approach in the
16 United States is also something that has
17 happened in the last seven years. So that has
18 given surgeons a chance to learn the anterior
19 approach.

20 So they have had training with
21 Agility in other two-part ankles and they have
22 also now had training provided in residency

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1 and fellowship programs on the anterior
2 approach.

3 So for new surgeons, improved
4 instrumentation and patient selection yield
5 results similar to those of our original
6 investigators who have had substantial
7 experience.

8 We plan to run a training course
9 requiring certification of all surgeons before
10 they are able to perform a procedure. The
11 training program consists of a day-and-a-half
12 of didactic and cadaveric labs. Each surgeon
13 will leave with a video, procedure manual,
14 implant and instrument manual, and contact
15 information obviously not only for the company
16 but for at least one of the instructors as
17 well.

18 There will a lecture in the
19 training covering the history of ankle
20 arthrodesis, the STAR device subscription
21 rationale, indications and contraindications,
22 warnings, precautions, and surgical pitfalls,

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1 adverse events, how to avoid and manage them,
2 and recent changes to the instrumentation and
3 technique.

4 We will review a STAR surgical
5 procedure video and we will have a STAR
6 surgical cadaveric lab, a final lecture
7 reviewing patient instructions and post-
8 surgery follow-up regimes, and revisions and
9 reoperation strategies when necessary.
10 Everyone will have to pass certification
11 testing.

12 We also plan a post-approval study.
13 We've suggested a two arm study basically,
14 one looking at long-term result and one
15 looking at the learning curve. The long-term
16 results looking for revision and removal rates
17 for the STAR, we will look at the continued
18 access patients, all of them, including those
19 that have previously failed.

20 The learning curve, we're looking
21 for new surgeons, five new sites with 125
22 newly-recruited patients. Important to note,

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1 it may be a while getting this information to
2 FDA because there are a lot of sites where the
3 volume is expected to be quite low.

4 The principle endpoints on the long
5 term will be revision or removal rate for the
6 STAR ankle at four years, confirmed at six
7 years, and eight years.

8 For the learning curve, major
9 complications within 12 months, revisions,
10 removals, wound problems, infections, and
11 perioperative fractures that require surgical
12 intervention and fixation.

13 We really don't see a need for a
14 study group. The principle endpoints of the
15 study: long-term revision or removal rate are
16 really a principle interest to the surgeons
17 and the patients. Arthrodesis have been well
18 known and well documented and well described
19 in the literature. And don't change greatly
20 after the 12-month point.

21 Length of study follow, as
22 mentioned, for the long-term arm, six weeks,

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