

1 In summary, my concerns and questions  
2 really are directed toward ensuring the good  
3 continued consistent performance that they appear  
4 to be achieving in the Ascension device.

5 [Slide.]

6 Materials--to summarize the source of the  
7 acceptable property ranges I think we would like to  
8 see the answer to. I would like to know how and  
9 where the hardness was determined, how they  
10 determined consistency of coating, and the  
11 relationship of hardness to fracture and fatigue.

12 I would like to see comparisons, if  
13 possible, between the fracture and fatigue results  
14 of the original and Ascension devices and what the  
15 actual fatigue limits of these materials are, and  
16 how intraoperative fractures are explained given  
17 the high fracture stress requirements that they  
18 estimate.

19 How as the coating consistency determined,  
20 and what is the performance of the worst-case  
21 properties given that they give acceptable property  
22 ranges that are substantially large?

23 The wear test--seeing as how, clinically,  
24 they tried to compare against the silicone, it  
25 would have been beneficial to know the performance

1 of silicone devices in their wear test. Was there  
2 any debris during the test; the original MCP wear;  
3 clinical wear--explanation, really; and morphology  
4 of the clinical debris.

5 Thank you.

6 DR. SKINNER: Thank you, Dr. Li.

7 Dr. Naidu, please.

8 DR. NAIDU: I'll speak from here. Thank  
9 you, Dr. Skinner.

10 I was given this task for clinical review  
11 of the clinical results proposed for the new MCP  
12 joint proposed by the sponsor.

13 The sponsors propose a new MCP joint  
14 replacement which is a two-component implant made  
15 of graphite pyrocarbon that is designed to be  
16 semi-constrained without an actual link between the  
17 two components.

18 The sponsors are to be applauded for  
19 taking on the daunting task of trying to design a  
20 two-component system for the MCP replacement.

21 The sponsor's main contention initially  
22 states that silicone essentially is not a very good  
23 joint replacement in the year 2001 for MCP joints;  
24 and second, they emphasize the fact that we do need  
25 something for high-demand patients.

1 First of all, I feel that it is my  
2 responsibility to try to explain what the MCP  
3 arthroplasty is supposed to accomplish, at least to  
4 the panel members.

5 Reconstruction of the rheumatoid hand in  
6 the year 2001 is mostly a soft tissue operation,  
7 with the Swanson silicone spacers merely providing  
8 the framework--it is an internal splint--for  
9 creating a new soft tissue sleeve and the so-called  
10 fibrous encapsulation process which was  
11 well-publicized by Dr. Swanson.

12 In the MCP joint reconstruction arena,  
13 Swanson implants have withstood the test of  
14 time--well over 40 years. The sponsors state the  
15 silicone synovitis is a big issue in the Swanson  
16 MCP joint. I agree with the sponsors in that of  
17 late, the Swanson implants have come under fire for  
18 the so-called silicone synovitis. One must,  
19 however, be clear that silicone synovitis is not a  
20 significant event in the MCP joint replacement.

21 What is silicone synovitis? Silicone  
22 synovitis is recurrence of pain, swelling, and  
23 recurrence of symptoms at an original site of  
24 arthroplasty where a successful implant was placed.

25 Silicone synovitis is an issue in the hand

1 literature in the carpal scaphoid, the basal joint,  
2 the carpal lunate, and the ulnar head implant.

3           Fortunately, we as hand surgeons in  
4 general are well aware of this phenomenon in  
5 silicone implants that are highly-loaded in axial  
6 fashion; but unfortunately, to date, there really  
7 isn't much data on silicone synovitis with regard  
8 to MCP joint.

9           There has been speculation that abrasion  
10 of the MCP implants in the endosteal canal  
11 generates silicone particulate debris, but this is  
12 really not very well-established in the clinical  
13 literature for the MCP implant.

14           Materially, the silicone rubber spacer is  
15 a safe and reasonable design and a safe and  
16 reasonable material for MCP arthroplasty for the  
17 rheumatoid population with very few early  
18 postoperative complications and reasonably good to  
19 excellent long-term clinical results.

20           Secondly, these rheumatoid populations in  
21 general are low-demand populations.

22           The other point that the sponsor tries to  
23 drive home is the concept that the MCP silicone  
24 device has high fracture rates. What is the  
25 consequence of high fracture rates in MCP implants?

1 Dr. Beckenbaugh in his presentation stated that he  
2 sees as much as 30 percent of these implants break.  
3 Dr. Andy Palmer confirms this. But both of them  
4 concur with the fact that none of these is really  
5 associated with decrease in function. In some of  
6 the longest follow-ups that we have to date, the  
7 fracture rate is 10 to 15 percent. There are other  
8 numbers that the sponsor has alluded to in the  
9 reports.

10 The reason the silicone implants fracture  
11 in the MCP joint is basically because of improper  
12 soft tissue balancing and inadequate soft tissue  
13 release, which is they key to successful silicone  
14 MCP arthroplasty. It is the very technically  
15 demanding part of the operation.

16 I must remind the panel that silicone  
17 rubber does not fracture because of the inferiority  
18 of the material itself. The silicone rubber does  
19 not deteriorate in the MCP joint. It is a  
20 crosslinked rubber. It has outstanding  
21 viscoelastic properties. Its rheologic properties  
22 remain stable throughout implantation.

23 What is the significance of fracture? The  
24 significance of fracture is that recurrent  
25 deformity will be the outcome if the fracture

1 occurs early.

2           What is the significance of late  
3 fracture? As Dr. Beckenbaugh and Dr. Andy Palmer  
4 stated, as many as 30 percent may be found to be  
5 fractured, yet very few clinically relevant  
6 findings are seen.

7           The maintenance of alignment of this  
8 so-called ulnar drift in silicone MCP arthroplasty  
9 in greater than 10-year follow-up studies further  
10 demonstrates that fracture is probably not a  
11 significant clinical problem in long-term follow-up  
12 in low-demand rheumatoid arthritis patients.

13           In short, the silicone MCP one-piece  
14 spacer concept is surgeon-friendly. I do not have  
15 stock in this implant; I don't own any shares of  
16 it. I am just saying that as a practicing surgeon,  
17 it allows the surgeon to concentrate more on the  
18 important aspects of the operation such as soft  
19 tissue balancing. Last but not least, it has good  
20 long-term follow-up in MCP implants. We should not  
21 beat it.

22           Now, when we go on to the Ascension  
23 device, it proposes a more anatomic reconstruction  
24 for the MCP joint. The sponsor states that we need  
25 something for the high-demand patients. They

1 present us with 147 implants; 138 of these implants  
2 are in low-demand rheumatoid arthritis and SLE  
3 patients. Only 9 implants are in the  
4 osteoarthritic or the post-traumatic patients,  
5 which I would consider as a high-demand group.

6 So the object of trying to design  
7 something for a high-demand population in my  
8 opinion is not very well-demonstrated in the  
9 clinical data that is provided.

10 In addition, it is a more anatomic  
11 reconstruction for the MCP joint; its focus is on  
12 the geometry, bony fit, restoration of the anatomy.

13 With all due respect to the larger joint  
14 surgeons like Dr. Skinner, it is really a soft  
15 tissue operation in the rheumatoid MCP joint. It  
16 may be true for low-grade synovitis, osteoarthritic  
17 MCP joint, or a post-traumatic arthritic patient  
18 with MCP joint, but not erosive or certainly not  
19 true for the rheumatoid hand, but soft tissue  
20 balancing is a significant component of joint  
21 replacement.

22 The Ascension device is semi-constrained  
23 by definition. The components must be matched. As  
24 a surgeon, the bony cuts become critical.  
25 Insertion of such rigid components into thin

1 rheumatoid bones can become a technical challenge.

2           The sponsors report 13 percent  
3 intraoperative fracture rate. Soft tissue  
4 balancing, again, is more of a challenge because  
5 this is a semi-constrained design; it is a  
6 two-component design. It is not a single-component  
7 like the Swanson.

8           In addition, the sponsors claim that their  
9 implant survival is about the same as the present  
10 MCP design. I went through the case histories in  
11 detail and outlined the first 25. I will give you  
12 an outline of the first 25 cases that I thought  
13 were significant. I will go through list by list.

14           The first case, page 415, the ring finger  
15 subluxed 2 days postop.

16           On page 421, the next patient, the ring  
17 finger subluxed less than 2 days postop.

18           On page 423, the small finger curls up one  
19 year postop.

20           The next case, the long, ring, and small  
21 fingers all needed soft tissue revisions 2 years  
22 postop.

23           On page 432, index finger failed because  
24 of malalignment in less than 3 months.

25           On page 435, index finger had to be

1 manipulated one month postop.

2           On page 441, in this patient, the index,  
3 long, ring, and small fingers were revised for MCP  
4 contraction 2 years postop.

5           On page 442, one month postoperatively,  
6 the index and long fingers were revised to Swanson  
7 implants.

8           On page 447, the index finger dislocated  
9 one month postoperatively.

10           On page 452, 6 days postoperatively, the  
11 index finger demonstrated malalignment.

12           On page 458, the index, long, ring, and  
13 small fingers, all at 4 months postop, had  
14 remarkable recurrence of ulnar drift--this is at 4  
15 months.

16           On page 472, the index, long, ring, and  
17 small fingers, in less than one year, had  
18 recurrence of ulnar drift.

19           On page 475, the index, long, ring, and  
20 small fingers had recurrent ulnar drift at one year  
21 follow-up.

22           On page 479, at 3 months postop, the fifth  
23 digit deviates ulnarly in a significant way.

24           On page 482, at one year postoperative  
25 follow-up, the fifth digit recurrent ulnar drive

1 was apparent at one year; the index, long, and ring  
2 dislocated at 2-year follow-up.

3 I could go on, but these are 16 out of 25  
4 patients. If you count the early complication  
5 rate, it is about 60 percent.

6 Therefore, at least by my definition as a  
7 surgeon, my definition would be an early success  
8 rate of 40 percent. Interestingly, the long-term  
9 success as defined by the sponsors is 37 percent at  
10 an average of 7-year follow-up.

11 Again, the sponsors also note that at  
12 long-term follow-up, only 61 of the 138 implants  
13 were reduced in the rheumatoid population. That  
14 means more than half of the implants were either  
15 subluxed or dislocated at 7-year follow-up.

16 One must keep in mind that the above  
17 complications are early, not late, and these are  
18 for Dr. Beckenbaugh and Dr. Linscheid, who are very  
19 eminent figures in the world of hand surgery.

20 With regard to the osteoarthritic  
21 patients, I think the sponsor has something great,  
22 they have something wonderful, but they have only  
23 provided us with 8 patients and 9 implants.

24 Both the case histories reported and the  
25 results reported are encouraging at 80 percent

1 success rate. Again, the patient number is small.  
2 Nevertheless, I think the sponsor has done a great  
3 job in trying to venture into a new field as far as  
4 designing a new implant for high-demand patients,  
5 but the study focuses on low-demand patients. I  
6 would encourage the sponsor to continue the study  
7 in the line of testing these devices in  
8 post-traumatic and osteoarthritic, where we truly  
9 need these joints.

10 Again I would like to thank the sponsor  
11 for providing me this information and the FDA for  
12 allowing me to review this interesting clinical  
13 study.

14 Thank you.

15 DR. SKINNER: Thank you.

16 We'll move on to Dr. Larntz.

17 DR. LARNTZ: Thank you.

18 First, I'd like to say that the  
19 presentations both by the company and by FDA were  
20 just superb. I compliment both of them. I thought  
21 they did an excellent job, and all parties, and I  
22 appreciate that. We mostly get excellent  
23 presentations, but sometimes we don't say that we  
24 do.

25 The ideal in the statistics world is to

1 take a treatment versus a control in a prospective  
2 randomized study. That is the ideal. It is not  
3 always done, and maybe it shouldn't always be done.  
4 It certainly wasn't done here. I guess I would  
5 take the point of view that it isn't always  
6 necessary.

7           Sometimes the indications for devices  
8 change. Sometimes, if I heard right--and I think I  
9 just heard the clinical reviewer indicate that this  
10 indication will be a broader indication than the  
11 silicone spacer, for instance--that is what I  
12 understand. Would it be proper to randomize  
13 patients and early populations to a silicone  
14 spacer? Well, we can talk about that later.

15           How do you get 10-year follow-up in a  
16 prospective randomized trial? That is just for  
17 instance. I guess if you are the Framingham study  
18 and you study heart disease for people's lifetimes,  
19 you can do things like that, but that is typically  
20 not going to be the case in the typical device  
21 study--no one would be in business if we required  
22 that, would they?

23           So what we have, then, is initially a  
24 comparison of the literature. What is the  
25 literature worth? Well, literature is always

1 problematic. I have done lots of literature  
2 studies--I do lots of literature studies, lots of  
3 literature controls. It is very hard. It is very  
4 difficult. The quality of the literature is--well,  
5 variable. How's that for a statistical term?

6           And the survival curve that we saw which  
7 was presented--and I think it was a very nice  
8 presentation--do we really believe that there is no  
9 implant failure in 2 years? Do I believe that? I  
10 don't know. It looks pretty spectacular, the one  
11 that we did the comparison to. So I am not sure  
12 that I believe that curve, particularly with the  
13 amount of censoring that I understand is in that  
14 data--the amount censoring between the two series  
15 is drastically different--that has been pointed out  
16 several times--drastically different censoring. It  
17 is very hard to compare those survival curves,  
18 although you can always compute P value. Isn't  
19 that nice? That's the wonderful things about  
20 statistics. We can always give you a P  
21 value--whether it means anything is another  
22 question, okay?

23           So we cannot--and I think it was  
24 summarized very well--with statistical surety make  
25 a case for the usual criteria of equivalence. We

1 can't. That was said before, and I think that is  
2 absolutely true.

3 But what do we have here? We have a  
4 retrospective case study--case series. We have  
5 excellent data completeness and follow-up. I think  
6 this is incredible. I have looked at a lot of case  
7 series in my lifetime, and this is incredible. But  
8 how many Mayo Clinics are there, after all? Some  
9 of us who visited the Mayo Clinic once upon a time  
10 and looked at their data records know it is  
11 incredible how they manage and take care of that.  
12 Maybe that's a little bit too personal-interest to  
13 comment on, but I'll say it anyway, okay? They  
14 know the value of their information. In fact, they  
15 understood very early on that they had incredibly  
16 valuable information and wanted to preserve it, and  
17 they do a superb job.

18 So I applaud the effort with the case  
19 series. I think it is a spectacular data effort.  
20 It is incredibly complete. I don't know how you  
21 get that degree of information.

22 But we have to remember that that was the  
23 Mayo Clinic. It is one center. This was done by  
24 physicians at one center. So that's always  
25 something we have to keep in mind. It has

1 limitations. Will my orthopedist down the street  
2 be able to do this? Well, that's a question that  
3 clinicians will have to answer.

4           So where do we wind up? We have two  
5 indications, an RA and an OA indication. I don't  
6 know--I guess I would describe statistically--I am  
7 now being nonstatistical, subjective in my  
8 statistical talk--I would describe my statistical  
9 results for the RA group as good to fair, although  
10 I'm not sure that that's not a difficult  
11 population--good to fair--although "fair" was not  
12 one of their categories; I put it in there anyway,  
13 okay, because I think going all the way to failure  
14 with some of those longer-term results is not  
15 always appropriate. This was substantial "N". I  
16 think there are a substantial number of cases  
17 there.

18           What do we have in the OA? We have--and I  
19 think it was reiterated--what I consider excellent  
20 results with small "N"--with small "N"--we have to  
21 emphasize. I mean, 8 patients is not very many.  
22 But that's what we've got.

23           So where do I put this? I don't think it  
24 is a statistical issue per se, but let me put  
25 something statistical to you. Would you as a

1 clinician use a device that has 80 to 90 percent  
2 10-year survival--80 to 90 percent--I forgot the  
3 exact number, 84 percent or something like  
4 that--but 80 to 90 percent. That's what the  
5 confidence limits are about. Would you use a  
6 device that has 80 to 90 percent 10-year survival  
7 with the adverse event profile that we just heard  
8 about, particularly for early events, and quite  
9 likely it looks like an expanded indication--use  
10 earlier in a different group of patients. Should  
11 that be available? And that is your question, but  
12 that is me as a statistician putting that to the  
13 clinicians.

14 I'll stop there.

15 **Panel Discussion**

16 DR. SKINNER: Thank you.

17 Haney has changed the rules on us. We  
18 were going to go to lunch, but apparently our  
19 reviewers got through too quickly, so we will go on  
20 with some panel discussion at this time.

21 We have to answer the FDA questions, so  
22 let's put those up on the screen and go at those.  
23 We'll start off with some questions and go from  
24 there.

25 To get started, I'll ask Dr. Aboulafia to

1 make some general comments about what he thinks and  
2 maybe raise some questions with the Ascension  
3 presenters.

4 DR. ABOULAFIA: I'll keep my comments  
5 relatively brief.

6 I think some of the things that come to  
7 mind have already been discussed. There are some  
8 concerns about the fact that it is a retrospective  
9 study done at a single institutions; whether these  
10 results can be reproduced at another institution is  
11 in question.

12 The main issue is that I think inherently,  
13 we all have some reservations about looking at a  
14 retrospective, nonblinded, uncontrolled study. It  
15 does introduce bias. My concerns about that,  
16 though, are addressed appropriately by sponsor, who  
17 went to an independent review. Having some  
18 understanding of how that particular institution  
19 works with respect to the acquisition of clinical  
20 information, I think the integrity of the data is  
21 solid.

22 So while the study design is not how we  
23 would do it necessarily if we were designing a  
24 study prospective and had well-defined endpoints, I  
25 think the sponsor has addressed those concerns. To

1 me, that was probably the most compelling point of  
2 the data submitted.

3 DR. SKINNER: Thank you very much.

4 Dr. Peimer, would you like to make some  
5 comments?

6 DR. PEIMER: Yes, and may I also ask some  
7 questions?

8 DR. SKINNER: Yes.

9 DR. PEIMER: Thanks--in which case, I will  
10 not keep my comments brief--or my questions.

11 Let me start by reiterating my compliments  
12 to the submitters and their absolutely thorough and  
13 outstanding work and commitment to getting at the  
14 data and presenting it clearly, as well as to Mr.  
15 Goode of the FDA, who asked some very important  
16 follow-up questions that really should have been  
17 asked, and for a guy who is a non-doc, you got to  
18 the heart of a lot of matters that are of concern,  
19 and I certainly thank you.

20 The material was easy to understand both  
21 in the presentation and in the comeback.

22 With all respect to my hand surgery  
23 colleague on the panel and the presenters, I think  
24 that there are some other choices besides this and  
25 silicone implants and nothing, and if you do not do

1 hand surgery, but do surgery in the upper  
2 extremities in rheumatoids, one needs to understand  
3 that there are other choices. There are acceptable  
4 times and methods and successes with soft tissue  
5 reconstruction and rebalancing, synovectomies, and  
6 osseus realignment when joint surfaces are  
7 reasonably preserved but ligaments are not. So one  
8 can do osteotomies and soft tissue realignments,  
9 synovectomies, and expect patients potentially to  
10 do well until and unless. But for myself, I would  
11 say that the characterization that the company has  
12 made that silicone implants are withheld until the  
13 later time is correct and should be considered  
14 correct.

15           However, having said that, silicone  
16 implants, despite their limitations, have an  
17 advantage over this implant in that they incite a  
18 foreign body reaction. They are not cytotoxic, but  
19 that benign foreign body reaction of encapsulation  
20 is what protects the patient; the scarring that we  
21 call the "pseudo joint" protects the patient in the  
22 long-term postoperatively so that if you have a  
23 cracked implant in 30 percent--and actually, we are  
24 finishing a 10-year review of our implants, and I  
25 think that at 3 to 5 years, the implant fracture

1 rate in silicone implants in our series is going to  
2 be close to 100 percent, but the patients continue  
3 to do reasonably well, dependent on their other  
4 disease. So medical management is a major issue.

5 I want to get to the subset of patients  
6 who are rheumatoids and ask some specific questions  
7 of the company and the physicians.

8 However, the other part that--I'm  
9 sorry--to finish the thought, this implant does not  
10 incite the same reaction. If you put silicone in a  
11 heart valve, we know about those tragedies and  
12 where the FDA had to intervene. If you put carbon  
13 in a heart valve, we know about those successes.  
14 Unfortunately, there is no foreign body reaction  
15 here, and in a rheumatoid with suboptimal ligaments  
16 and limited reconstructive potential for a  
17 ligament, this implant is at a relative  
18 disadvantage for the later rheumatoid  
19 reconstruction unless perhaps you do some other  
20 things, invent some other things or take some other  
21 approaches, and I want to ask about that because it  
22 did not reveal itself in the data.

23 The other side of it is because we know  
24 about the heart valve experience, this implant, if  
25 approved in osteoarthritic patients, in

1 post-traumatic patients, will be a blessing. We  
2 have nothing. This would be in my opinion an  
3 outstanding addition to the surgical armamentarium.  
4 The majority of patients are not osteoarthritics,  
5 they are not post-traumatics, however, but it will  
6 change the landscape in reconstructive options.

7           So I want to ask some things specifically  
8 with respect to the troubling population--and I  
9 won't direct the questions at anyone in particular.  
10 I guess the first one is an engineering question  
11 and a clinical implications question.

12           The metacarpophalangeal head was  
13 redesigned for ease of insertion; it is now a  
14 straight cut. I wonder if any consideration was  
15 ever given to putting a slight radial inclination  
16 on the collar so as to overcompensate slightly for  
17 the tendency to go into ulnar deviation early and  
18 late?

19           DR. KLAWITTER: If I understood your  
20 question, let me just answer the question about the  
21 inclination on the collar. Regardless of how you  
22 put the collar, if you do have a spherical bearing,  
23 it won't make any difference. Now, the positioning  
24 off-center may, off the center line; if you care to  
25 move it from one side to the other so that it is

1 now positioned on the ulnar side of the center line  
2 so that the extensor and flexor tendons are now  
3 basically staying where they are but the center  
4 rotation is moved over, you might get a torque  
5 toward the radial side, and you may be able to do  
6 this.

7           These are thoughts that we have given, but  
8 really, for the approach we have taken now, we have  
9 taken a simple center, down-the-line approach,  
10 trying to gain experience, trying to follow where  
11 we have experience, rather than changing something  
12 and ending up not being able to leverage the  
13 experience that we have had at the Mayo Clinic.

14           I think there are possibilities to extend  
15 and improve these types of devices, and one of the  
16 things that we ask you is to give the hand surgeons  
17 the opportunity to try and bring these devices to  
18 the marketplace if you think that they are safe and  
19 effective.

20           DR. PEIMER: Okay. I'd like to ask Dr.  
21 Beckenbaugh or someone who did the data  
22 analysis--there were a lot of datapoints on the  
23 wrist pre- and postoperatively--was any comparison  
24 made in patients who might or might not have had  
25 wrist realignment procedures specifically, because

1 we know that wrist rotation may influence the  
2 incidence of recurrent ulnar deviation. So was a  
3 wrist realignment procedure routinely done or never  
4 done, and was there any outcome tracking made  
5 between wrist and recurrence of ulnar deviation or  
6 other deformity that you know of?

7 DR. BECKENBAUGH: As you know, it is our  
8 common practice to always try to correct the wrist  
9 before we correct the MCP joint because of the fact  
10 that wrist deformity will lead to recurrent MCP  
11 joint deformity. I don't think this concept was  
12 quite as popular in the early eighties as it is  
13 now. We do not have the specific information on  
14 whether or not the wrist was corrected.

15 I can tell you that one of the things that  
16 maybe would relate to what Dr. Naidu said earlier  
17 about technique and soft tissue rebalancing is that  
18 when we did this, we originally put them on the  
19 Swanson protocol, and we moved these patients at 3  
20 or 4 days, and unlike a Swanson device which might,  
21 with extensive therapy, reach 60 or 70 degrees in 2  
22 or 3 months, we could get 90 degrees in 4 weeks.  
23 As a result of this and the results of our  
24 postoperative program, we found that we were  
25 getting some subluxations, and then we had to do

1 soft tissue revisions to try to correct these.

2 Our subsequent recommendation at this time  
3 in our protocol that we describe are close to that  
4 suggested by Simmons, which is a 3- to 4-week  
5 period of immobilization postoperatively and  
6 extension.

7 We will be able to recommend, as I always  
8 do at this time, that wrist reconstructive  
9 procedures always be done first; if we have a  
10 carpal deformity, we would recommend that this  
11 always be corrected prior to the MCP prosthesis  
12 surgery. In this way, I think we will be able to  
13 use this in more and more rheumatoids.

14 Specifically, what we are looking at here  
15 is a little bit earlier use in rheumatoid surgery  
16 when that subluxation, pain, and synovitis are just  
17 beginning to develop, and in most of those  
18 patients, of course, the wrist is a little bit  
19 better, but we were taking some pretty severe  
20 deformities; we were taking all comers in this  
21 study, and I'm sure some of those patients had  
22 wrist disease.

23 DR. PEIMER: Bob, the surgical techniques,  
24 at least the only ones that I read, were in  
25 Amendment 3 on page 138, which would be 6.13, which

1 doesn't emphasize in surgical technique, at least  
2 as I read it--and I may not have understood it--but  
3 it did not emphasize in terms of postoperative care  
4 technique that a period of more prolonged  
5 immobilization is going to be needed. And it would  
6 be something I would say later in a panel  
7 discussion that I think that if the panel thinks  
8 this can be used in rheumatoids, I would suggest  
9 that immobilization for a period of time be a  
10 requirement. And I'll go two steps further--the  
11 company has made the statement that there ought to  
12 be something--and I'm not going to quote the  
13 words--but there ought to be something sort of like  
14 a ligament on the radial side or about the capsule.  
15 I would like your response to the boldness of my  
16 suggestion that one of the caveats in this I think  
17 ought to be a native, intact, repairable or  
18 reconstructible radial-collateral ligament complex,  
19 or you are not allowed to use this prosthesis since  
20 subluxation and recurrence is a problem.

21 DR. BECKENBAUGH: We certainly would agree  
22 with that. The soft tissue envelope must be able  
23 to be reconstructed.

24 One of the things also that in the time we  
25 had allotted, we didn't go through in detail was

1 the surgical technique. The interesting thing  
2 about Ascension Orthopedics is that they have  
3 developed incredibly wonderful surgical  
4 instruments, and the precision insertion of this  
5 device associated with certain angle cuts and so  
6 forth is far superior to what I could do  
7 previously, so to speak, by hand.

8           You mentioned the accuracy and the ability  
9 to reconstruct the soft tissues in rheumatoid  
10 disease; it is certainly as critical here or more  
11 critical. We can put this prosthesis in straighter  
12 with the instrumentation we have now than we can  
13 with silicone. The surgical technique is extremely  
14 precise, and we have had a chance to demonstrate  
15 this.

16           DR. SKINNER: Dr. Beckenbaugh, correct me  
17 if I am wrong, but I think what you have said, both  
18 in terms of your postoperative management and your  
19 surgical technique, is that there is a learning  
20 curve on this, and perhaps your early results, even  
21 though they were pretty good, might have been  
22 better had the learning curve not been in effect.

23           DR. BECKENBAUGH: I don't think there is  
24 any question, and with the new device, we have  
25 developed a very extensive brochure that talks

1 about the necessary for this, and we would not  
2 expect that anyone would do this operation without  
3 specific onsite training with one of us.

4 We have an excellent brochure. It is very  
5 precise. It makes a huge difference. Hand therapy  
6 is extremely important postoperatively.

7 DR. SKINNER: But not only for any  
8 individual who would attempt this now, but your  
9 data was skewed by this.

10 DR. BECKENBAUGH: Yes.

11 DR. PEIMER: And I actually made the  
12 point. I would say that I think that if we are  
13 going to release this for rheumatoids, we need to  
14 give consideration to some clear instruction and  
15 reconstructive technique for ligaments where viable  
16 native or retained ligament tissue is not available  
17 and for training.

18 DR. BECKENBAUGH: That's correct. One of  
19 the things we can do with this is you can separate  
20 the soft tissue envelope because of the fact that  
21 it is a solid material, and by separating it or, so  
22 to speak, "jacking out" the soft tissues, many  
23 times that soft tissue envelope with an attenuated  
24 collateral ligament will become snug again, so you  
25 can make up for some problems there. If we don't

1 have a collateral ligament, we either don't do  
2 it--that is listed as a contraindication in our  
3 brochure--or we have to reconstruct it.

4 DR. PEIMER: Okay. Thank you.

5 DR. SKINNER: Further comments, Dr.  
6 Peimer?

7 DR. PEIMER: I'm just looking to see if I  
8 have covered my list. Other than being a voice  
9 crying out in the wilderness and nothing that the  
10 word "cosmesis" does not exist in a dictionary of  
11 the English language, and that most people in the  
12 United States do not wear their pants over their  
13 vests, which is a phrase used in the reconstructive  
14 booklet, my Boston origins are satisfied.

15 DR. SKINNER: Thank you.

16 DR. PEIMER: Thank you.

17 DR. SKINNER: We'll skip over Dr. Li and  
18 Dr. Naidu and give Dr. Finnegan a chance to make  
19 comments and/or ask questions.

20 DR. FINNEGAN: I have comments and  
21 questions in two areas. The first relates to  
22 carbon. I'm sure you are aware of the past history  
23 of bulk carbon in the musculoskeletal system. This  
24 has been in otherwise healthy, usually young  
25 people, and there have been two scenarios. One is

1 the late seventies, early eighties, with McKibbon's  
2 fixation plate used mainly on the tibia; and the  
3 other were the ACL reconstruction grafts made of  
4 carbon. Both of these were carbon fiber. And I  
5 will say up front that I am not sure I understand  
6 the difference between pyrocarbon and carbon fiber.  
7 However, leaching of the carbon was a significant  
8 problem, and I have two questions related to that.

9 In the baboon study, did you in fact look  
10 in the lymph nodes to see if in fact you could  
11 track particulate intra-abdominally or in the chest  
12 cavity, the carbon. And the second question has to  
13 do with the fact that a huge proportion of your  
14 patients are not only rheumatoids, but they have  
15 been rheumatoids for a long time, which means they  
16 are probably significantly immunosuppressed, and  
17 therefore you probably would not expect to see a  
18 reaction; and did you track their medications, or  
19 do you have any idea of the degree of  
20 immunosuppression for these patients?

21 I don't know who wants to deal with those.

22 DR. KLAWITTER: I am certainly aware of  
23 the use or perhaps misuse of carbon fiber early on  
24 in two applications, one to reinforce polyethylene  
2X5 components of the total knee, and the second was

1 to, in a braided form, act as a scaffolding to  
2 replace a ligamentous tissue, anterior cruciate, or  
3 other types of knee tissues.

4           These were carbon fiber. This carbon  
5 fiber is a carbonaceous graphite material that is  
6 highly aligned. It is a fine thread, so it is  
7 indeed a fiber; it is a yarn type of material. It  
8 is the basis for many of the carbon fiber composite  
9 materials that we see throughout our life now in  
10 sporting goods, all sorts of things.

11           The uses, then, in both of those  
12 applications--now it is easy retrospectively to say  
13 they seem now to be somewhat misguided. I am sure  
14 that at the time, there was a little more direction  
15 involved. The use of these materials with  
16 polyethylene would now be a considered a rather  
17 poor use because polyethylene would not be a good  
18 matrix material to reinforce high-modulous fiber  
19 flows. As the metal components wore across the  
20 tibial components, the little fibers would stand  
21 proud and get snapped off, so it was producing a  
22 tremendous amount of particulate debris in a manner  
23 that now, I think all of us would consider to be  
24 unacceptable.

25           Likewise, the use of braided carbon fiber

1 to reconstruct ligaments in the knee, I believe the  
2 intention at that time was to provide an inert  
3 scaffolding onto which we could develop a  
4 biologically functional ligament again. The  
5 unfortunate part was that there was a hole drilled  
6 into the bone. The carbon fiber, which is a  
7 brittle type of material, was threaded through, and  
8 through each one of the knee motions, the carbon  
9 fiber would work against that sharp edge of the  
10 bone, and before it even had a chance to develop  
11 this pseudo-composite ligament, it was damaged to  
12 such an extent that it also flooded the joint space  
13 with carbon particles.

14           There is also a serious question if you  
15 read the literature. These carbon fibers are  
16 intended for use in composite materials, usually  
17 with epoxies or other types of polymer materials,  
18 to transfer load to the high-strength fibers, and  
19 oftentimes they have sizing materials or bonding  
20 agents to the fibers when they are actually  
21 produced to help bond them to the composite  
22 materials.

23           There are some references in the  
24 literature as to whether these were actively  
25 removed in addition during this, perhaps because

1 not of a recognition of it.

2 I think at the end of the day what we see  
3 is a misuse of carbon fiber that some people may  
4 generalize to deal with carbon across the board.  
5 Certainly we have not seen this in heart valve  
6 reconstruction, and there have been millions of  
7 these devices.

8 The pyrolytic carbons are continuous  
9 monolithic coatings. They are not made of a fiber  
10 type of material. They have a structure which is  
11 somewhere between graphite and diamond. Carbon can  
12 exist in those two forms, the cubic form and the  
13 three-dimensional form in diamond. The sheet  
14 structure is graphite.

15 This manmade material which does not occur  
16 naturally has cross-bonding so that it has kind of  
17 those properties. So we really have to put aside  
18 what was done in the past with respect to the use  
19 with the fiber, because I believe it was really the  
20 fiber orientation, the inclination to use fiber,  
21 that caused that type of problem.

22 DR. FINNEGAN: But the black staining that  
23 you see now is similar to what was seen with the  
24 knees?

25 DR. KLAWITTER: I don't believe it was.

1 What was seen with the knee was mechanical damage  
2 to the actual fibers where one could look in and  
3 see fibers within the joint space as resulting from  
4 function.

5           What we have seen here--and I think it is  
6 almost exclusive if not exclusive--is some carbon  
7 debris that was generated by using highspeed burrs  
8 to use these at time of insertion when they had to  
9 be removed. I will testify that if you take a  
10 highspeed burr and put it through a piece of  
11 graphite like that, it produces something which is  
12 not dissimilar to India ink, and you have to flush  
13 that wound, and some of it is left there. I think  
14 that that is the staining that occurred. It was  
15 not during function, it was during perhaps the  
16 learning how to use these on the front end. And  
17 when we went back and looked at the histopathology,  
18 these particles did reside within the tissues, and  
19 we did not identify any foreign body reaction to  
20 them.

21           I think Dr. Beckenbaugh might be able to  
22 address the second half of your question.

23           DR. LI: Dr. Skinner, could I follow up on  
24 that for just a second?

25           DR. SKINNER: Yes, go ahead, Dr. Li.

1 DR. LI: Thank you.

2 Could you clarify for me in those cases  
3 that had synovitis, was there evidence of any kind  
4 of particulate debris in those cases?

5 DR. KLAWITTER: There were--I can't  
6 remember the exact cases--but obviously, synovitis  
7 is part of the disease process associated with the  
8 rheumatoid, so the fact that there is a recurrence  
9 of it happens with or without perhaps the influence  
10 of particles, be they silicone particles or be they  
11 whatever.

12 DR. LI: Right.

13 DR. KLAWITTER: So there were cases where  
14 there were no carbon particles seen at time of  
15 surgery, none observed histologically where there  
16 was active synovitis. There were cases where we  
17 saw active synovitis, but it did not seem to be  
18 related to foreign body reaction to fine particles  
19 that were seen within the tissue which I believe  
20 the majority if not all of which came from removal.

21 So I see no evidence, and the  
22 histopathology reports give no evidence that there  
23 is a reaction to these carbon particles. Likewise  
24 in the extended use in heart valves and in the  
25 animal studies that we have done and other people

1 have done, I see no evidence reported anywhere by  
2 anyone that there has been a reaction to these  
3 particles. That doesn't mean that we should drop  
4 our guard and not be looking at it. I'm saying  
5 that at the moment, I see nothing to raise that to  
6 a very high level of concern.

7 DR. FINNEGAN: Did your baboon study track  
8 the carbon at all?

9 DR. KLAWITTER: No, it did not.

10 DR. LI: So the answer is yes--I  
11 understand that there was no histological  
12 response--

13 DR. KLAWITTER: Yes.

14 DR. LI: --but the answer is in some cases  
15 there were signs, though, of particulate debris?

16 DR. KLAWITTER: Oh, there were some signs  
17 of particulate debris within the histo sections.  
18 There was nothing that indicated a foreign body,  
19 giant cell reaction, or any type of reaction to the  
20 particles themselves.

21 DR. LI: I understand.

22 DR. KLAWITTER: As one sees in the  
23 literature, when you look at what happened even  
24 with the carbon fiber, where I think there was a  
25 mechanical irritation, or where there might be some

1 chemical irritation due to the high service area.

2 DR. LI: How would you rationalize the  
3 presence--although they are apparently  
4 histologically benign--of wear debris clinically,  
5 but no wear in the test?

6 DR. KLAWITTER: First, I don't believe it  
7 is wear debris. I believe that those particles are  
8 generated at the time of removal of devices which  
9 fractured interoperatively when highspeed burrs  
10 were used to have to machine them out. That  
11 highspeed burr produces, I would say, millions and  
12 millions of particles, and although they are  
13 irrigated, some are left residing in the tissue.  
14 We saw no evidence that I can attest to wear debris  
15 that came from the actual joint articulation.

16 Dr. Beckenbaugh might be able to comment  
17 more about this, because not only did he reoperate  
18 on joints where he had to remove them, he  
19 reoperated on joints where they were doing soft  
20 tissue reconstruction where they would open the  
21 joint and close it again, and saw many joints at  
22 that stage when he can make a comment as to what  
23 did the joint space look like; was there any  
24 indication visually, or are we talking about  
25 something you have to look at with a microscope at

1 1,000x to find. I think he can give you a general  
2 sense of that.

3 DR. BECKENBAUGH: In the baboon study we  
4 found, as you know, different types of devices.  
5 They were small; the smallest device had to be used  
6 in the long metacarpal. We salvaged the  
7 metacarpals after 9 months to 12 months and found  
8 excellent bony appositional growth.

9 There were no studies done on those  
10 patients with regard to lymphadenopathy or other  
11 systemic findings. However, the co-investigator,  
12 Dr. Cook, who is here with us and can comment on it  
13 further if you would like, has done animal studies,  
14 dog studies, with hip replacements using pyrocarbon  
15 and has examined lymph nodes and other tissues and  
16 found no evidence of it.

17 In multiple opportunities, more than I  
18 would like to have had, in reoperation and  
19 exploring these for both soft tissue defects and  
20 some late defects, I have never observed any  
21 evidence of black tissue staining in any patient  
22 who has not had an implant either fractured during  
23 removal or insertion.

24 So it gets a little bit confusing. When  
25 we used this word "black tissue staining," we were

1 talking about when we go in there, and we drill  
2 that device to get it out, or we find that we  
3 perhaps cracked the tip of it pounding it in too  
4 hard, and then we had to drill it because we  
5 thought it should come out, and we would end up  
6 with some black soot, so to speak, in and around  
7 the joint. But these patients were examined after  
8 this soot was in the joint, and they didn't have  
9 the reaction that was synovitis. They sometimes  
10 would have a little swelling for a while, but it  
11 wasn't anything detrimental, and when we had those  
12 cases where we got tissue examples, they found that  
13 the particles were not within the cells, the  
14 histiocytes, and that they were not causing any  
15 reaction.

16           So I felt extremely comfortable with the  
17 material and never observed what I would consider  
18 to be a breakdown or wear. When you removed the  
19 device, the device looked like it did when you put  
20 it in.

21           DR. FINNEGAN: Okay. And actually, I have  
22 one other question on your data, and there is a  
23 subset to it.

24           First, looking at your case histories--I  
25 couldn't find this otherwise--of the 53 case

1 histories, 24 of those patients were not examined  
2 by the operating surgeons longer than 5 years out,  
3 which really means that your 10-year follow-up is  
4 pretty close to the 50 percent mark, and I did not  
5 include the people who died or--there were a couple  
6 of other patients who had extenuating  
7 circumstances--which would bring you to less than  
8 50 percent who actually had more than a 5-year  
9 follow-up.

10           Then, if you look at the 9 trauma  
11 patients, 5 of them are over the age of 60--that  
12 includes the one woman--leaving 3 who are under 50.  
13 In the 50-year-old, it appears to be in his  
14 dominant hand, although it is not documented, and  
15 it loosened within a little over a year. A  
16 37-year-old had it in his left hand--and again, I  
17 don't know about dominance; and then, the  
18 22-year-old's follow-up was only 6 weeks, and then  
19 follow-up was by phone but no examination.

20           So I am wondering how comfortable with the  
21 "N" that you are looking at.

22           DR. BECKENBAUGH: I am pretty comfortable.  
23 The 22-year-old I called on the telephone after  
24 trying to find him for about 3 years, and we  
25 finally found an address in Minneapolis actually

1 just a couple of months ago. I talked to him, and  
2 he was happen with his hand. He said it didn't  
3 move very much. He started out with tendon damage  
4 and a totally destroyed arthrides [phonetic] joint.  
5 We were happy to know--he was working in  
6 construction--that he didn't have any pain in his  
7 joint, and the hand was functioning.

8           So I felt very comfortable with that. We  
9 offered to pay for x-rays, we offered to have him  
10 come down--I even offered to go out and see  
11 him--and he wasn't interested in any of that; he  
12 just had too much work to do. But we really tried  
13 hard to get him, but I felt comfortable that he was  
14 doing all right.

15           The patient who had all the problems, the  
16 only one we know of--the other one had ALS and died  
17 too early--the patient who had all the problems in  
18 the osteoarthritis was not a terribly cooperative  
19 patient--he wasn't a bad patient--but he had  
20 traumatic arthritis, and he went back to very, very  
21 heavy work. And when he did that work, he caused  
22 loosening of the prosthesis, one of the only ones  
23 we had seen. And it seemed logical because it was  
24 loose and because we were using cement in other  
25 areas to perhaps use cement to try to keep it from

1 loosening, because he was using hammers, and he was  
2 doing very heavy work. And also some of the others  
3 did that, his did loosen; he was the only one. And  
4 he had pain, and he would keep going back to using  
5 it; after we cemented it, it worked well for a  
6 while, but eventually, the cement complex loosened,  
7 and we had to take it out and go back to silicone,  
8 and his result was semi-successful after that.

9           So I am very, very confident. I haven't  
10 seen a patient who had had a bad-looking joint.  
11 You know, we go back in on elbows and wrists and  
12 everything else, and we see metallosis and all  
13 sorts of staining or polyethylene effects, and I  
14 have never seen anything like that with this  
15 pyrocarbon material.

16           DR. SKINNER: Is that it, Dr. Finnegan?

17           DR. FINNEGAN: Yes, thank you.

18           DR. SKINNER: Dr. Lyons, feel free to make  
19 any comments, or if you don't have any comments,  
20 feel free to say that, too.

21           DR. LYONS: Okay. I had one question,  
22 just one question, and you have already grazed it,  
23 and I don't know which sponsor would prefer to  
24 answer it for me.

25           I really don't have any problems with the

1 articular surface. My question is on these parts,  
2 because I know Bob and how he would put them  
3 in--they would be lock-solid. But there will be  
4 patients who may not have good bone stock, or the  
5 surgeons may not get it locked in as well. My  
6 question was about the endosteal abrasive wear and  
7 if that has been looked at closely to see that that  
8 is not going to be a source of concern for  
9 particulate debris, because I don't think I know  
10 enough about the bonding on this particular device,  
11 and I didn't see the shear testing--Dr. Li, I'm not  
12 sure if you felt it was comfortable enough. But my  
13 interest is on the testing that may have been done  
14 for the material on the endosteal surface in those  
15 cases where the components may be under load but  
16 also loose. That's the only thing I wanted to know  
17 more about.

18 DR. COOK: Steve Cook. I am at Tulane  
19 University, and I have done the majority of the  
20 animal studies over the last two decades.

21 DR. SKINNER: Your financial interest?

22 DR. COOK: I am an equity owner in  
23 Ascension Orthopedics.

24 DR. SKINNER: Thank you.

25 DR. COOK: I implanted the baboons with

1 Dr. Beckenbaugh as well as dogs, hips,  
2 transcortical implants characterizing the  
3 apposition to the implant.

4 In placing the implants with interference  
5 fits, we would point them in place; there is really  
6 no carbon abrasion. We have actually done abrasion  
7 tests with the carbon material in an undersized  
8 hold using cortical bone, the transcortical model,  
9 where you undersize them 50 microns, which is a  
10 very tight fit in cortical bone, very similar to  
11 what we have done with porous materials looking for  
12 bead shedding.

13 You don't see the carbon coming off in  
14 removal and pushing out of the carbon materials,  
15 they get a very strong osteo-integration to the  
16 point of in a push-out test, you can actually leave  
17 some of the carbon material attached to the bone,  
18 they are so firmly attached--very similar to what  
19 you see in the hydroxylapatite-coated [phonetic]  
20 implants when we do testing, where you will leave a  
21 portion of the material behind. In that case, it  
22 is more likely a biochemical bonding in the carbon  
23 that is truly an apposition to the inert surface.

24 The short answer is it is very  
25 abrasion-resistant. We have placed it through

1 cortical bone, specifically in the abrasion tests  
2 that were similar to what is done for porous  
3 materials as well as HA-coated metal materials.

4 DR. LYONS: Thank you.

5 DR. SKINNER: Dr. Wright?

6 DR. WRIGHT: I'll be brief. Are you still  
7 doing these implants, other than the series that  
8 you presented?

9 DR. KLAWITTER: The device currently has a  
10 CE/Merck [phonetic] approval. It received CE/Merck  
11 approval in 1999. The device is commercially  
12 available in Europe; several hundred have been  
13 used. We are beginning to establish a distribution  
14 system for these devices, although we have been  
15 moving carefully, looking at training and gaining  
16 further experience.

17 DR. WRIGHT: You mentioned that you have  
18 an extractor. I was amazed that someone actually  
19 broke these. But you mentioned that you have an  
20 extractor and that it is some type of blunt  
21 osteotome?

22 DR. KLAWITTER: Yes. At the moment, our  
23 concern was that if one is interested in extracting  
24 it, and you are at the surgery, you are likely to  
25 take a chisel or some sharp object, put it through

1 there, and start tapping on it. That's probably  
2 what I would do. So what we have done initially,  
3 at least, with an extraction system is to provide  
4 something which is soft but of the same design so  
5 that someone can get a little purchase and begin to  
6 tap it out.

7 It does take an effort, and there was a  
8 comment made about breaking and putting these in,  
9 and how could you do it. Those are substantial  
10 hammers that you find in surgery, and the impacts  
11 are quite large, and if you start banging on those,  
12 the forces are substantial. And I believe that,  
13 yes, when you angulate these over a small  
14 angulation, you can generate 32,000 psi, and there  
15 is no question in my mind because they have been  
16 broken.

17 So that yes, that is possible, but it is  
18 our intention to try to have available to the  
19 individual using these instruments, which we will  
20 continue to develop, which minimize the chance for  
21 damage.

22 DR. WRIGHT: Thank you.

23 DR. SKINNER: Was that all, Dr. Wright?

24 DR. WRIGHT: Yes, that's it. Thanks.

25 DR. SKINNER: Dr. Klawitter, as long as

1 you are standing up, could I ask you to address the  
2 fatigue endurance limit of pyrolytic carbon?

3 DR. KLAWITTER: Yes, I will do that. This  
4 actually is an issue that concerned us, of course,  
5 which is why we were doing fatigue testing. It has  
6 been an issue probably for the last 15 years in  
7 mechanical heart valve design, and there has been a  
8 tremendous amount of work, because here we are  
9 talking about a device which undergoes 40 million  
10 cycles per year and 600 to 1 billion cycles in its  
11 lifetime. So there are both the type of testing we  
12 do, which is survival testing, and then there is  
13 actually some science being done as well to try to  
14 find out what are the mechanisms, is there a  
15 fatigue generation mechanism, how do these  
16 materials function under cyclic loading.

17 The most recent articles published by  
18 George Sines [phonetic] out on the West Coast have  
19 demonstrated what I think most people believe and  
20 what the experience with the heart valves would  
21 indicate, and that is that these materials do not  
22 undergo a fatigue failure similar to metals--there  
23 is no crack generation mechanism--and you can cycle  
24 them at increasing loads up to the single-cycle  
25 failure for extended periods of time up to tens of

1 millions of cycles and not see failure.

2           The strength of these materials because  
3 they are brittle has a distribution. So in doing  
4 these tests it is difficult to creep up to this  
5 unknown area because there is a distribution, and  
6 in the data we presented, we present this strength  
7 as a wibel [phonetic] distribution, which is  
8 probably the best way of doing it because we are  
9 looking at failure probabilities. The testing that  
10 has been done by George Sines has really found a  
11 means of trying to see does indeed pyrolytic carbon  
12 not have an inherent crack generation/fatigue  
13 mechanism, and I believe the evidence is there now  
14 that that is true, and it is backed up by the  
15 millions and billions of cycles of heart valve  
16 experience.

17           What we have done is I think a simpler  
18 experience where we have taken a worst case,  
19 applied what we think is a demanding load, that is,  
20 8 to 80 pounds, do it 10 million times, go ahead  
21 and look at devices. We have subsequently broken  
22 those devices afterward, gone back and looked at  
23 those data to see whether they fit back into the  
24 failure probability that we would expect; they  
25 indeed do, and they are not weakened, so that

1 provides additional evidence to us that if handled  
2 properly, these are extremely resistant to cyclic  
3 loading and the types of failures that concern all  
4 of us.

5 DR. SKINNER: Thank you.

6 Dr. Cheng?

7 DR. CHENG: With all due respect to the  
8 expertise and stature of the surgeons and the  
9 scientists who developed this, I'd like you to take  
10 my comments in light of the view that it is my  
11 charge to evaluate this critically and provide  
12 advice to the FDA.

13 In so doing, I couldn't help thinking when  
14 I initially reviewed this that this was a  
15 relatively weak PMA, and the reason I felt that was  
16 because we were asked to provide advice and  
17 approval on a product which was not the actual  
18 device that was studied, with the exception of some  
19 preclinical testing, and the former device or the  
20 original device that we have information on was not  
21 studied in any prospective matter yet in a  
22 retrospective manner, with subsequent selection  
23 bias. And there is no statistical validation, as  
24 we have just heard from the statisticians, and it  
25 is case series data only.

1           Nonetheless, as I went through looking at  
2 this a little further and hearing some of the  
3 discussions today, I think it is probably more  
4 meritorious than I initially thought, and I had  
5 some issues that I wanted to address so that I  
6 could provide the FDA with an opinion on what I  
7 think and not maybe on what I know, because I'm not  
8 sure that we know the answers to these questions.

9           Looking at some of the statistical issues,  
10 however, and some of the discussion, it appears to  
11 me--and I am not a hand surgeon, so I don't pretend  
12 to be an expert in the techniques of this--but the  
13 soft tissue balancing of this semi-constrained is  
14 what makes it perhaps a little bit more difficult  
15 to perform than the constrained Swanson device.  
16 This is what I am hearing from the hand surgeons.

17           So reoperation--most of the data was  
18 presented in terms of implant survival, but  
19 reoperation for any reason would seem to me to  
20 perhaps be a more valid look at the success or  
21 failure of this device, because maybe it isn't as  
22 constrained.

23           So I am wondering if a survival curve with  
24 the endpoint that is reoperation might be a more  
25 valid way of comparing this. Now, the problem is

1 that you have nothing to compare it to, because in  
2 the historical literature, the data is not all that  
3 well-presented, either, so we can't compare it and  
4 make a good equivalence statement, yet it will give  
5 us some insight as to the success of the device.

6 I am wondering if anyone could comment on  
7 that.

8 DR. KLAWITTER: Could you maybe compress  
9 the question--

10 DR. CHENG: So the question would be what  
11 is the success of the device with the endpoint  
12 being reoperation for any reason.

13 DR. BECKENBAUGH: I would like to ask one  
14 of our statisticians to come up, because they are  
15 more familiar with the intricate data. I can tell  
16 you that one of the reasons, as we discussed  
17 earlier, for the reoperations is because of our  
18 early mobilization program, we had some subluxation  
19 and recurrent ulnar deviation. And sometimes we  
20 would go in there and say this is going to be tough  
21 to correct. I can specifically recall one patient  
22 in whom, when we went in, the flexor tendon as seen  
23 through the dorsal incision was well-displaced to  
24 the ulnar side. And I said there is no way I am  
25 ever going to be able to correct that in this

1 patient in whom I had put this prosthesis. Many of  
2 them are converted to silicone.

3 In others, I was able to feel like I could  
4 repair the radial hood, which is the thing that  
5 stabilizes the central tendon and/or advance the  
6 central tendon, or in some of Dr. Linscheid's  
7 cases, perform intrinsic transfers to try to  
8 correct this. And these, as a rule, I would say my  
9 gut feeling would be that they weren't terribly  
10 successful. If they did have this early failure,  
11 we could make them better with the surgery, but it  
12 did not result in our best results.

13 Does one of you have further comments?

14 DR. COOK: We looked at the survival curve  
15 in a variety of what we consider best case and  
16 worst case, best case being removal of the  
17 implant--the implant had to come out--and that is  
18 the survival curve that you see where it is in the  
19 mid 80 percent.

20 We also looked at a worst case. There  
21 were several patients who were dislocated, but due  
22 to the progression of their disease, removing them  
23 in additional surgery really wasn't warranted. We  
24 counted those as failures. Also, there was a  
25 patient with implants that wouldn't move, again due

1 to the disease progression; they were located, but  
2 there was no movement. We considered those as  
3 failures.

4           Some of this data is in the original paper  
5 that we published in Journal of Bone and Joint  
6 Surgery. But if you look at a worst case,  
7 considering patients that aren't moving,  
8 dislocated, for any reason not discounting that  
9 they had other medical problems, the survival curve  
10 I believe was 68 percent or on that order, 68 to 70  
11 percent, at 14 years, that we published in the  
12 journal.

13           DR. CHENG: How many patients had  
14 bilateral hand procedures done, and did any  
15 patients decline having the operation done on the  
16 contralateral hand?

17           DR. KLAWITTER: To answer some of these  
18 questions, I think we are probably going to have to  
19 go back to the data that we have submitted and dig  
20 a little bit of it out. If we could get those  
21 summarized, perhaps over the lunch break, we could  
22 take the time to do that. It's going to take a  
23 little bit of an effort. There are approximately  
24 4,000 pages of documentation sitting over here--

25           DR. CHENG: Maybe I should just read the

1 questions, then; would that be easier?

2 DR. KLAWITTER: I'm saying I think I can't  
3 answer that question without finding the data--

4 DR. CHENG: I understand.

5 DR. KLAWITTER: --and I don't think I can  
6 find it immediately; so a little bit of a break,  
7 even 5 minutes, and you can go on to another  
8 question while we look--Peter has done better than  
9 I thought.

10 MR. STRZEPA: In direct answer to the  
11 question, 7 patients had bilateral surgeries done.

12 DR. CHENG: And did anyone decline to have  
13 the procedure done in the opposite hand--in other  
14 words, indicating a dissatisfaction or suggesting  
15 or inferring a dissatisfaction with the procedure.

16 MR. STRZEPA: I can't answer that. Bob,  
17 do you--they were Dr. Beckenbaugh's patients.

18 DR. BECKENBAUGH: I do not recall any  
19 patient in that situation. The only scenario we do  
20 have is several patients who had both silicone on  
21 one side and pyrocarbon in the other, including one  
22 with inflammatory arthritis at very long-term  
23 follow-up, and there is a tremendous different in  
24 the result, the pyrocarbons being nonreactive and  
25 the silicone being associated with painful

1 synovitis fracture.

2 DR. CHENG: So do you have some sense as to  
3 the patients' satisfaction with one versus the  
4 other device--the silicone as opposed to the--

5 DR. BECKENBAUGH: We don't really have  
6 enough people on both sides that I can say anything  
7 other than the two that I can specifically recall  
8 that were dramatically in favor. We had a dentist  
9 who was able to continue to work for many years  
10 with the pyrocarbon side and was unable to use his  
11 left side. But most of those are quite anecdotal,  
12 because we didn't have a lot of those.

13 DR. CHENG: Looking at the follow-up of  
14 the patients, I am assuming these are mostly  
15 physician assessments; is that correct--they were  
16 not patient assessments or questionnaires.

17 DR. BECKENBAUGH: Well, some of them were  
18 questionnaires, and some were telephone calls, but  
19 the majority of these patients when they come back  
20 to the clinic are seen by a resident, and then they  
21 fill out a complex form, a total joint form, and  
22 then they are seen by us for clinical discussions.

23 DR. CHENG: So to perhaps address the  
24 issue of selection bias, from your data, it looks  
25 like some patients have received silicone

1 prostheses during the same time period as well as  
2 the proposed device. How would you make that  
3 selection between the two?

4 DR. BECKENBAUGH: I'm sorry. Could you  
5 repeat that?

6 DR. CHENG: It appears that some patients  
7 have gotten silicone devices as well as some  
8 received the device that we are talking about  
9 today. So how would you decide between the  
10 Ascension device or the silicone device?

11 DR. BECKENBAUGH: The decision might be  
12 made actually at the time of surgery. If we felt  
13 that we could not stabilize somebody, we would do  
14 that. We would tell the patient that we have a new  
15 device, we think it might be better for them, we  
16 would like to make a decision at the time of  
17 surgery based upon their soft tissue. And we did  
18 some rather severe patients, but there were also  
19 others who were even more severe--for example, with  
20 90 degrees of extension lag--that we would get in  
21 there, and even we could tell then that these  
22 patients wouldn't work. We subsequently found out  
23 that the real severe ones, or the real loose  
24 rheumatoids, wouldn't do as well, either. So the  
25 doc needs to make a decision at the time, and

1 that's what we were doing, and I think we have a  
2 pretty good idea now that these will work in early  
3 rheumatoid arthritis. It is very logical. We can  
4 reconstruct the soft tissue envelope, but if we  
5 can't do a reconstruction of the soft tissue  
6 envelope, we wouldn't suggest that it be used. In  
7 fact, it would be contraindicated, and that is what  
8 our indications will reflect.

9 DR. CHENG: So am I correct in  
10 interpreting this to mean that there may be some  
11 bias toward using this in the less severe  
12 rheumatoid patients, and in the more severe  
13 rheumatoid patients without good soft tissue  
14 stability, the more constrained device was used?

15 DR. BECKENBAUGH: That's exactly what we  
16 believe.

17 DR. CHENG: I see.

18 DR. BECKENBAUGH: We believe this is  
19 indicated in earlier rheumatoid arthritis, and  
20 silicones will be used more as a salvage procedure.

21 DR. CHENG: So we just need to interpret  
22 the data in light of that, apparently.

23 The last question I have is actually for  
24 Dr. Palmer.

25 Dr. Witten, was this device available

1 during the 1990's to be implanted, or was  
2 distribution not allowed in the United States  
3 during that time period?

4 DR. WITTEN: It wasn't commercially  
5 available at that time.

6 DR. CHENG: I see.

7 Well, Dr. Palmer, I was going to ask you  
8 if you had had any experience personally with these  
9 yourself.

10 DR. PALMER: None.

11 DR. CHENG: Okay.

12 DR. SKINNER: Is that it, Dr. Cheng?

13 DR. CHENG: Yes. Thank you.

14 DR. SKINNER: We still have two more panel  
15 members who have to have a chance before we go back  
16 to the original general panel reviewers. So I  
17 think this is a good time to break for lunch, and  
18 in the interest of making sure that we stay close  
19 to on time, let's make it in 45 minutes and one  
20 second.

21 [Whereupon, at 12:55 p.m., the proceedings  
22 were recessed, to reconvene at 1:46 p.m.]

## 1 AFTERNOON SESSION

2 DR. SKINNER: We are in the situation  
3 where we have had discussion from many of our panel  
4 members. We still have to finish up with questions  
5 from a couple of the panel members and then go back  
6 to our primary reviewers.

7 We'll start off with Mr. Dacey. Would you  
8 like to make some comments about this application?

9 MR. DACEY: My issues are really in the  
10 patient labeling, and I guess when we get to that  
11 question is when I can discuss it a little bit  
12 better.

13 DR. SKINNER: Okay. That leaves Ms.  
14 Maher, Esquire.

15 MS. MAHER: Thank you.

16 Actually, I only have a comment, no  
17 questions. I think the panel should keep in mind  
18 as they are asking their questions later in  
19 reviewing this that what we are making a  
20 determination on is that the device has been shown  
21 to be reasonably safe and effective for its  
22 intended use and not safer than another device that  
23 is already on the market or more effective than. I  
24 think we need to keep that in mind as we are  
25 looking at the clinical data that is before us.

1 Thank you.

2 DR. SKINNER: You're saying that it should  
3 be evaluated on its own merits rather than in  
4 comparison to another device.

5 MS. MAHER: That's correct.

6 DR. SKINNER: Okay. That leaves us with  
7 the three primary reviewers, and we'll start with  
8 Dr. Li.

9 Dr. Li, you don't have to say anything.

10 DR. LI: I understand. I asked a bunch of  
11 questions in my presentation, and I'd like to get  
12 an answer on a couple of them if I could.

13 DR. SKINNER: Sure; and then, let's get  
14 some comments from some of the Ascension people.

15 DR. LI: Yes. One question I had was on  
16 where the range of acceptable properties was for  
17 the On-X coating. You gave a column of nominal  
18 properties which looked like to be the averages of  
19 properties, and then you gave a range of acceptable  
20 properties.

21 So my question is how did you determine  
22 that that was the range of acceptable properties.

23 DR. KLAWITTER: What we have is control on  
24 manufacturing processes where this product is  
25 produced for us by Medical Carbon Research

1 Institute. They use the same manufacturing process  
2 they use for this to create a PMA-approved heart  
3 valve in the United States.

4 We follow very carefully the types of  
5 quality control that they have instilled in their  
6 product and has been associated with this for some  
7 30 years. Out of that, we have then taken devices  
8 produced in this material and conducted mechanical  
9 testing where we can see both the strength and  
10 distribution of strengths. From that, we have  
11 found that the distribution of mechanical  
12 properties and strength and what we have seen in  
13 wear resistance meets our needs.

14 So staying with the assessment of  
15 properties that we get from them and looking at the  
16 distribution of strengths that we get in the final  
17 product, we feel satisfied with those.

18 In addition, of course, we have a quality  
19 system which ensures that we do maintain a quality  
20 manufacturing. This has been inspected and  
21 validated under 9001 as well as a QRS inspection.  
22 Many of us come from the value business, and we  
23 take quality seriously and believe that we do  
24 produce a quality and highly reliable product.

25 DR. LI: I guess my more specific question

1 was, for instance, the fracture toughness value  
2 you provided could range from 1.0 to 2.6, a factor  
3 of 2.6, obviously. So on the devices that you  
4 would typically envision selling, you would then  
5 expect the same factorial performance, or excellent  
6 performance, actually, of your device even if the  
7 fracture toughness value was at the one end rather  
8 than at the 2.6 end?

9 DR. KLAWITTER: That has been our  
10 experience. With the number of mechanical  
11 specimens we have looked at, which have been  
12 several hundred, we have seen nothing that falls  
13 outside of that. There is no way we can determine  
14 what the fracture toughness is on an individual  
15 specimen based on the difficulties in actually  
16 doing fracture toughness measurements.

17 We rely on the fact that the experience  
18 gained over the years has given us various means of  
19 inspecting the quality of each product. These are  
20 batch-produced. Each time we produce a batch, we  
21 sacrifice one part. That part is then used for  
22 determining hardness at various what we call  
23 critical locations. It is also used for an  
24 inspection of thickness and uniformity. In  
25 addition, it is used on metalgraphic specimens to

1 look for any irregularities which might give  
2 indications of anysotropy or any other kinds of  
3 process variations.

4 Here again, we do rely to a great extent  
5 upon the experience gained over a period of years  
6 of manufacturing.

7 DR. LI: Thank you.

8 DR. SKINNER: Dr. Naidu, would you like to  
9 proceed with some questions or comments?

10 DR. NAIDU: Yes, I do have several  
11 questions that I would like to pose to the  
12 Ascension panel.

13 From what I am understanding at this point  
14 from what all the presentations have suggested, it  
15 appears as if we are trying to make this device for  
16 early rheumatoid arthritis. Am I correct in  
17 understanding that?

18 DR. KLAWITTER: Let me make a few opening  
19 comments, and then I will ask Dr. Beckenbaugh to  
20 comment, because I think it is a question where  
21 there is strong clinical relevance.

22 Our intention is to produce a total joint  
23 replacement for the metacarpophalangeal joint of  
24 the hand. As I look at the need myself as an  
25 engineer--I have been working in this field for

1 several years--I recognize the importance place  
2 that silicone rubber has played and will continue  
3 to play. Let there be no misunderstanding. We are  
4 not saying that this is going to replace all need  
5 for silicone rubber joints. And in fact, these are  
6 quite complementary.

7 Our idea is to produce a total joint which  
8 can be used when appropriate by the hand surgeon to  
9 provide a greater range of treatment to the public  
10 and in this way, to advance the state of total  
11 joint reconstruction in the hand and to try to  
12 bring a high degree of science and quality to that  
13 effort. That is our intention. It is certainly  
14 not to say that there is no place for silicone  
15 rubber joints. I believe there is, and I believe  
16 that likewise there are some areas where there are  
17 shortcomings, and we intend to provide a product  
18 where there can be an informed choice made by the  
19 surgeon based upon his decision on how to treat an  
20 individual.

21 DR. BECKENBAUGH: I certainly would  
22 reiterate what Dr. Klawitter has suggested.

23 I think that our thought process here is  
24 that we have a very good joint for osteoarthritis  
25 that is very easily recognizable and for traumatic

1 arthritis; but we also have a joint that can be  
2 very effective in rheumatoid arthritis. Under no  
3 circumstance would I want to see silicone implants  
4 removed from this market, because I use them, but I  
5 have used them in relatively late-stage disease.

6           When I see a patient with synovitis and  
7 pain and early subluxation of their  
8 metacarpophalangeal joints, I would like to be able  
9 to do a synovectomy on them, and if I can, and  
10 their joint surfaces are all right, I do that. If  
11 the same patient has articular erosions as  
12 articular thinning and damage to the bone joints  
13 themselves, I will not generally do a silicone  
14 implant on that person because their disease  
15 deformity is not bad enough to warrant doing the, I  
16 would say, limited-expectation surgery that we see  
17 with silicone. But I think the expectations are  
18 higher with this type of device, and I think the  
19 durability is potentially higher in this type of  
20 device.

21           So in that type of patient, the patient  
22 with early destructive joint disease, but not  
23 severe enough deformity to warrant a salvage  
24 procedure such as a silicone arthroplasty, and in  
25 that same patient who might be in his 30s or 40s or

1 younger than the usual patient that we would talk  
2 to about arthroplasty, I am much more confident in  
3 this material than I am in silicone. I know we  
4 have had our differences in thoughts about  
5 silicone. I believe that Dr. Stern's work is  
6 showing us that there are significant problems with  
7 silicone. I do not want it taken away, but I want  
8 to have the option to use a joint that I can use on  
9 these types of patients, and I think I can offer  
10 them a better option.

11 DR. NAIDU: Thank you.

12 DR. SKINNER: No more comments?

13 DR. NAIDU: Actually, I do have a few more  
14 comments.

15 Would you be modifying your postoperative  
16 regimen? Would you be following the new Simmons  
17 protocol as far as immobilization, rather than  
18 being aggressive with early--

19 DR. BECKENBAUGH: Yes, we have. We have a  
20 protocol that is basically suggesting 3 weeks of  
21 immobilization in a cast. Simmons, of course,  
22 suggested 4 weeks. At 3 weeks, we apply dynamic  
23 splint, but we do so with a new type of flexion  
24 block which allows flexion only to 45 degrees.

25 So our goal in the first 6 weeks is to

1 achieve only 45 degrees of flexion and then only 60  
2 degrees of flexion as the max at 3 months.

3 So our therapy protocol, which with the  
4 splinting is extremely important, is guided exactly  
5 in that way.

6 DR. NAIDU: Just a few more questions, Dr.  
7 Beckenbaugh, please. Would you perform anything to  
8 quantitate the bone stock for these patients  
9 preoperatively before inserting these--

10 DR. BECKENBAUGH: We haven't done that.  
11 We generally feel that we can assess the bone  
12 quality pretty well from the x-rays, but as you  
13 know, it is not obvious. If we were to go in and  
14 find that we had a mushy, fatty marrow, there would  
15 be very little likelihood that we would use this  
16 prosthesis. We would generally use silicone as  
17 perhaps a safer device--although the possibility of  
18 doing other things to improve bone quality might be  
19 there. That would be a type of patient whom I  
20 would think would be a poorer candidate for this  
21 type of procedure as we have described it right  
22 now.

23 DR. NAIDU: Dr. Beckenbaugh, as I read  
24 through the case histories that were provided to  
25 me, I did not one fact, that it appears as if the

1 ring and the small fingers tend to get into more  
2 trouble than the index and the long in general.

3           Would you use a combination of these  
4 devices in any patient, or would you go for--

5           DR. BECKENBAUGH: Yes, we did. In fact,  
6 in some of these patients, we did find that there  
7 was more instability at the ring and the small, and  
8 we would do two implants of the index and long and  
9 do silicone at the ring and the small because we  
10 were concerned about instability.

11           Having said that, I think this joint can  
12 be used in all joints, but again, we have to make  
13 the same clinical judgments about our capability of  
14 stabilizing them, and I think it can be a little  
15 bit more difficult with the ring and the small  
16 fingers.

17           DR. NAIDU: Thank you.

18           DR. SKINNER: Dr. Larntz, would you like  
19 to--

20           DR. LARNTZ: Nothing further.

21           DR. SKINNER: Thank you.

22           We are around the panel one more time. Is  
23 there anybody on the panel who would like to make  
24 any more comments, questions, et cetera, before we  
25 start with the questions?

1 [No response.]

2 DR. SKINNER: Hearing nothing, I think we  
3 should start with our panel questions.

4 Mr. Goode, can we have the first panel  
5 question?

6 **Discussion of Panel Questions**

7 MR. GOODE: The first panel question has  
8 to do with safety.

9 "Based on the retrospective clinical data  
10 in the sponsor's case series which included 53  
11 patients and 147 primary uncemented pyrocarbon  
12 implants, do the data demonstrate there is  
13 reasonable assurance that the probable benefits to  
14 health from the use of the Ascension MCP for its  
15 intended use and conditions of use, when  
16 accompanied by adequate labeling, outweigh any  
17 probably risks?"

18 "Specifically, what is the impact of the  
19 following complications and adverse events as they  
20 relate to safety and effectiveness of this product:  
21 device removals and post-implantation soft tissue  
22 reconstruction; intraoperative fractures; and black  
23 tissue staining an synovitis."

24 You all should have copies of the  
25 handouts, so we you can refer to both of these

1 questions at the same time.

2 DR. SKINNER: We've got three main issues  
3 to deal with, and I think we should deal with those  
4 first.

5 I thought that the black tissue staining  
6 and synovitis had been adequately addressed with  
7 Dr. Finnegan's question. Is there any comment on  
8 that?

9 [No response.]

10 DR. SKINNER: I think we are okay on that  
11 one.

12 We don't feel that black staining and  
13 synovitis are necessarily a problem; is that the  
14 consensus of the panel? Okay.

15 Why don't we talk about the device  
16 removals and post-implantation soft tissue  
17 reconstructions? I think probably the person who  
18 is most up on that would be Dr. Naidu.

19 Do you have any comments about how you  
20 feel that impinges on safety, Dr. Naidu?

21 DR. NAIDU: Yes, I do. Specifically from  
22 what Dr. Beckenbaugh stated, at this point, it may  
23 be that this device would be more useful for  
24 early-stage rheumatoid arthritis conditions.

25 Dr. Beckenbaugh also stated clearly that

1 the results that were presented were based on  
2 protocols which mobilized these patients early, and  
3 therefore, there was a significant amount of  
4 reoperation.

5           What is concerning is that 16 of the 22  
6 joints were reoperated within one year  
7 post-implantation for soft tissue matters. A total  
8 of about 14 percent of the implants were removed; 3  
9 were removed for loosening, 18 were removed for  
10 soft tissue deformity. And at long-term follow-up,  
11 it appears as if only 61 of the implants remain  
12 reduced.

13           There appears to be quite a bit of  
14 postoperative complications based on at least the  
15 data that were provided, but the indications now  
16 appear to have evolved as the discussions have gone  
17 on. It appears as if it may be a device that is  
18 more suitable for early rheumatoid disease. It may  
19 be a device that is more suitable for people who do  
20 not have as much soft tissue deformity as the ones  
21 that were presented in the data.

22           Therefore, it is very difficult to make  
23 this judgment based on the data that is provided at  
24 this point. Dr. Beckenbaugh's clinical impression  
25 is that these will do well in rheumatoid arthritis

1 which is early in nature. It is very hard for me  
2 to make that judgment at this point.

3 With regard to that, I would defer more  
4 comments to my colleague Dr. Clay Peimer, if he  
5 could address that issue.

6 DR. SKINNER: Let me address that first.

7 Dr. Beckenbaugh, would you be kind enough  
8 to describe what you consider early-stage  
9 rheumatoid arthritis/SLE?

10 DR. BECKENBAUGH: We can go through the  
11 two extremes, the first one being that of just  
12 joint synovitis without any joint damage or  
13 subluxation, to the extreme salvage procedure where  
14 the patient has 90 degrees of extension lag.

15 Our experience in taking all comers would  
16 suggest that those who had severe 90-degree  
17 extension lag would not do well with this device,  
18 although we didn't have an opportunity to do that  
19 in patients with long-term immobilization which is  
20 now more popular in the orthopedic world.

21 Specifically, we have estimated our  
22 guidelines to be that we would have patients  
23 described with early arthritis as those who do not  
24 have severe subluxation, less than one centimeter;  
25 those who do not have greater than 30 degrees of

1 ulnar deviation; and those who do not have 45  
2 degrees of extension lag or greater.

3           Those are the general guidelines that we  
4 have been using. In the final run, though, it is  
5 going to be a clinician's decision, because some  
6 people can have those deformities and have very  
7 poor soft tissues, and other people can have more  
8 severe deformities but have better soft tissues.

9           So in the final end, it has to be the  
10 surgeon's judgment. The principle that we would  
11 like to teach surgeons who will use this is that  
12 this would be used very early on, but they still  
13 have to use their judgment; and we would anticipate  
14 that considerable training and explanation would be  
15 necessary for the surgeons to help them achieve  
16 this--but I think it is possible to do.

17           DR. SKINNER: Thank you.

18           Dr. Peimer, would you like to comment on  
19 that also?

20           DR. PEIMER: Dr. Beckenbaugh has said it  
21 as well or better than I can. I think that my  
22 concerns have been addressed and answered. I want  
23 to make some comments about labeling for  
24 physicians' use and implantation guidelines and  
25 restrictions relative to training, but I am

1 comfortable with this device within the parameters  
2 that are being described, with the revised postop  
3 protocol.

4 DR. SKINNER: Regarding Question 1, then,  
5 regarding device removals and post-implantation  
6 soft tissue reconstruction, you would feel that the  
7 description that Dr. Beckenbaugh just laid  
8 out--basically, moderate subluxation, less than 30  
9 degrees of ulnar deviation, and 45 degrees of  
10 extension lag would be the range of soft tissue  
11 destruction that you would have to deal with as an  
12 indication, or something on that order?

13 DR. PEIMER: Yes, and I was thinking as he  
14 was saying it, and then he voiced the caveat--with  
15 reconstructible soft tissues.

16 DR. SKINNER: Yes.

17 DR. PEIMER: And he is very careful to  
18 include that, and that is critical.

19 So those would be the guidelines, yes,  
20 absolutely.

21 DR. SKINNER: He felt earlier that the  
22 radial-collateral ligament would be key or  
23 reconstructible.

24 DR. PEIMER: Right.

25 DR. SKINNER: And of course, that would

1 fall into that category.

2 DR. PEIMER: Yes, sir.

3 DR. SKINNER: Are there any other comments  
4 on the issue of device removals and  
5 post-implantation soft tissue reconstruction from  
6 any of the rest of the panel?

7 Dr. Naidu, have you pondered that one  
8 also? I was going to go to intraoperative  
9 fractures unless you had some more comments on that  
10 particular part of Question 1.

11 DR. NAIDU: Well, as I stated before, the  
12 retrospective data does not support that; at this  
13 point, at least, the soft tissue  
14 reconstructions--actually, quite a few, based on  
15 the data alone that was submitted--is that the  
16 question that you are asking me--

17 DR. SKINNER: We have to deal with  
18 Question 1 here and specifically, what is the  
19 impact of device removals and post-implantation  
20 soft tissue reconstruction on the safety and  
21 efficacy of this product.

22 DR. NAIDU: Based on the parameters that  
23 Dr. Beckenbaugh has described, it may be okay for  
24 the early rheumatoid arthritis and SLE group, but  
25 not based on the data that was presented.

1 DR. SKINNER: Okay. Dr. Finnegan?

2 DR. FINNEGAN: Actually, I would like to  
3 reinforce that, and I think that goes back also to  
4 the black tissue staining. I do think it was  
5 explained fairly well, but I would like to  
6 reinforce the concept that there is not enough data  
7 here for me to feel comfortable making a decision,  
8 and I will preface that by saying I think this is a  
9 wonderful implant; I think the engineering has been  
10 very nicely done--but there are not enough numbers  
11 here for us to be able to make any kind of  
12 decision. I think the data is really missing.

13 DR. SKINNER: Any other comments?

14 [No response.]

15 DR. SKINNER: I'd like to address the  
16 issue of intraoperative fractures. My feeling was  
17 that Dr. Beckenbaugh addressed this somewhat in  
18 that there was new equipment for insertion of his  
19 prosthesis, and he felt that that problem had been  
20 largely solved.

21 Does anybody have a comment that they  
22 would like to deal with on that particular issue?

23 DR. CHENG: May I have permission to  
24 speak?

25 DR. SKINNER: Yes.

1 DR. CHENG: Do you have a picture or a  
2 sample of the new instrumentation that is  
3 available?

4 DR. KLAWITTER: We can have an example of  
5 it here in 5 minutes, and we'll bring it to you.

6 DR. SKINNER: Let's go on, then, as we are  
7 waiting for that.

8 Dr. Witten, do you feel that the panel has  
9 adequately addressed the issues involved in  
10 Question 1?

11 DR. WITTEN: I would just like to put one  
12 general follow-on question in case anybody has  
13 anything additional to say. That is, your answers  
14 have focused on the three things we highlighted as  
15 particular concerns or issues of interest we wanted  
16 you to address, but in general for safety, are  
17 there any other aspects of safety of this product  
18 that anybody on the panel thinks are important for  
19 us to consider?

20 DR. SKINNER: Dr. Li?

21 DR. LI: Thank you.

22 Maybe just one follow-up question so I can  
23 stop thinking about the particle debris. For those  
24 few times that you have seen either tissue staining  
25 or particles with synovitis, can you tell me

1 anything about the size range of those particles,  
2 because if there are a few particles and they are  
3 also really charge, then I'm going to have  
4 virtually no concern at all, but if you tell me  
5 there are a bunch of them, and they are submicron,  
6 that would be a different level of concern.

7 DR. KLAWITTER: The particles that we have  
8 seen histologically and the nature of the surfaces  
9 after wear testing indicate that the particles are  
10 in the 2 to 5 micron size.

11 DR. SKINNER: In other words, you can see  
12 them under light microscopy.

13 DR. KLAWITTER: Yes, you can.

14 DR. LI: Thank you.

15 DR. SKINNER: That, Dr. Li, didn't really  
16 address the issue that Dr. Witten brought up, and  
17 that is safety. That is obviously why we are here,  
18 safety and efficacy, and safety is a very important  
19 thing.

20 Does anyone want to address the issue of  
21 safety anymore? Does anyone feel that this product  
22 is unsafe?

23 [No response.]

24 DR. SKINNER: Does anybody feel that the  
25 product is safe?

1 DR. CHENG: I might have one question for  
2 the manufacturer. You have indicated the wear is  
3 minimal, if at all, and that there is no  
4 osteolysis, but you have had them come loose. So I  
5 am wondering what would be the mechanism of  
6 loosening; is it dislodgement? Have you thought  
7 of--in the larger joints, obviously, you have  
8 thought of various surface modifications to try to  
9 avoid that.

10 DR. KLAWITTER: Right. And to some  
11 extent, it's speculation on my part, so you are  
12 going to have to give me a little leeway. My  
13 experience both with animal studies and in general,  
14 having done this for several years, where we are  
15 looking for an integration of a device into the  
16 skeletal system, we are not using a grouting agent,  
17 a cementing agent, or something like that, is that  
18 if you have a good, tight initial fit, you give  
19 time for the healing process to integrate these  
20 in--and it's like fracture healing. You want good,  
21 immobile, no micro movement, no movement between  
22 the device and the bone. In these cases, I think  
23 we can achieve the endpoint.

24 If it is a "wiggler," as I would say, if  
25 there is a motion all the time, I think you go to

1 the same endpoint as non-union; it's the same type  
2 of problem you see. In the cases that we have seen  
3 at the clinic, the 147 patients, I'm sure that some  
4 of those were probably the result of a less than  
5 adequate initial fit and something that may not  
6 have been discernible at the time.

7           Likewise is again the possibility due to  
8 high mechanical loading after surgery. I don't  
9 think that we have been able to identify anyone of  
10 those, but it is a combination of those, and that  
11 is why we have looked carefully at instrumentation,  
12 the ability to get a good press-fit, and I think  
13 those go with the common sense of trying to provide  
14 a device which is initially stable, which I think  
15 is necessary for final stability.

16           DR. CHENG: Is it an engineering issue as  
17 to why you cannot either plasma-spray this or put  
18 some kind of coating on there, a porous coating or  
19 something--the approach that one would take with  
20 other intramedullary stem devices.

21           DR. KLAWITTER: There is certainly the  
22 possibility of that, and we considered that. We  
23 considered several types of surfaces and surface  
24 treatments. We chose not to do it for several  
25 reasons. First of all, the experience that we had

1 was without it, and we wanted to stay as close to  
2 the center line as possible.

3           Second of all, I think that the issue of  
4 being able to remove these and do revisions and be  
5 able to get the parts out is an issue of some  
6 concern. In discussions with Dr. Beckenbaugh, he  
7 felt that from his point of view, he could obtain  
8 sufficient initial stability the way they were.

9           It was my initial idea to use some sort of  
10 surface activation such as an HA coating; you can  
11 put them on. I think that these parts will evolve  
12 into subclasses where we are looking at ways of  
13 enhancing as we gain experiences. Certainly it's  
14 possible. We chose not to.

15           DR. SKINNER: Regarding the safety issue,  
16 could I ask Dr. Palmer a question?

17           Dr. Palmer, if a patient with moderate or  
18 maybe slightly worse rheumatoid arthritis had one  
19 of these implants implanted, and it failed, and the  
20 patient subsequently went on to have a silastic  
21 implant, would that patient be permanently harmed  
22 by the initial implant from Ascension--in your  
23 opinion. Obviously, you have no personal  
24 experience.

25           DR. PALMER: Yes, I have none, because I

1 have never put this in. I think it would depend on  
2 how difficult or easy it was to remove the original  
3 implant. If we were able to get the implant out  
4 and then put the silastic in, I expect they would  
5 not be harmed at all. It would also depend on the  
6 changes that had taken place in the metacarpal or  
7 the phalanx as a result of the implant. Depending  
8 on that, you could reconstruct the bone.

9 So my thought is that most likely it would  
10 not be a problem.

11 DR. SKINNER: Dr. Finnegan, one more  
12 question.

13 DR. FINNEGAN: Just a question about  
14 whether they have any histology for the bone  
15 implant contact areas, either from the baboons or  
16 from autopsies.

17 DR. COOK: We did sections with the  
18 implants in place in both transcortical models in  
19 dogs as well as the baboons. In about 65 to 70  
20 percent of the baboons, we had direct bone  
21 apposition. In several of the implants, we had a  
22 fibrous encapsulation indicating they didn't  
23 achieve a direct bone apposition yet they were  
24 still functioning.

25 In the dog models where there is a good

1 initial fit, again remembering that in baboons as  
2 in the humans, in the initial human experiments,  
3 there was limited broaching, limited  
4 instrumentation. But in dog models where we can  
5 get a perfect apposition, you get high percentages  
6 of the surface, on the order of 90 to 95 percent,  
7 like we would see with an HA-coated surface.

8 DR. FINNEGAN: So it's more trabecular  
9 bone than it is cortical bone, or is it actually  
10 like a corticalization?

11 DR. COOK: It's more of a corticalization,  
12 and in fact, there is really a condensation of bone  
13 along the interface of these carbon materials that  
14 forms and is very easy to visualize because of the  
15 radiolucency of that half-millimeter coating. So  
16 you see a differentiation from the substrate to the  
17 bone, and you can actually see that consolidation,  
18 and you can really identify osteo-integration real  
19 well with these implants.

20 DR. SKINNER: Dr. Witten, have we  
21 addressed the safety issue adequate?

22 DR. WITTEN: Yes. Thank you.

23 DR. PEIMER: Sorry. I just have a point  
24 of information.

25 Dr. Witten, if this implant were approved,

1 and the manufacturer wanted to plasma-spray it or  
2 do something else, what happens? Do they just do  
3 it, and it appears in new form or a new flavor, or  
4 do they have to come back? What is the procedure?

5 DR. WITTEN: Well, in general, if someone  
6 is going to modify their device on the market, if  
7 it is a PMA device and it is a modification, they  
8 would need to come back for an approval of that.  
9 If it is a modification, it would be as a  
10 supplement. So it would likely be something we  
11 would do an assessment of; that's why the panel  
12 doesn't usually see those kinds of applications.

13 DR. PEIMER: Thank you.

14 DR. NAIDU: Could I just make a comment.

15 DR. SKINNER: Dr. Naidu, please.

16 DR. NAIDU: Thank you.

17 With regard to the issue of safety, Dr.  
18 Palmer stated that when the implants are extracted,  
19 as long as there are no intraoperative fractures,  
20 it is probably safe to use the device.

21 There were six fracture events that  
22 occurred in three patients during revision  
23 operations of 42 components. Six out of 42 leads  
24 to a 14 percent intraoperative fracture rate. I  
25 think the issue to answer is whether 14 percent is

1 a safe number based on all the comments that have  
2 been provided now. I have to leave that up to  
3 further discussion at this point.

4 DR. SKINNER: Would you like Dr.  
5 Beckenbaugh to respond?

6 DR. NAIDU: Please.

7 DR. BECKENBAUGH: Thank you.

8 There were 6 implants that were fractured  
9 during removal. However, this did not result in  
10 any adverse effects, and that's a very important  
11 differential to make. In other words, there was a  
12 technique in which the devices were drilled, they  
13 were removed, and there was some material that was  
14 necessarily in the soft tissues that could not be  
15 completely washed away. But these patients did not  
16 experience a post-removal reactive synovitis.

17 DR. NAIDU: Thank you.

18 DR. SKINNER: With that, I think we can  
19 move on to Question 2.

20 Mr. Goode?

21 MR. GOODE: The second question has to do  
22 with device effectiveness.

23 "Based on the retrospective clinical data  
24 in the sponsor's case series, which included 53  
25 patients and 147 primary uncemented pyrocarbon

1 implants and the sponsor's retrospectively-defined  
2 success/failure criteria and analysis, do the data  
3 demonstrate there is a reasonable assurance that in  
4 a significant portion of the target population, the  
5 use of the Ascension MCP for its intended use and  
6 conditions of use, when accompanied by appropriate  
7 labeling, will provide clinically significant  
8 results? Please consider whether the data support  
9 each of the proposed indications for use."

10 DR. SKINNER: Well, I think that we have  
11 to discuss the topic of efficacy and effectiveness,  
12 and I'd like to ask Dr. Peimer as a hand surgeon to  
13 start out on that, and then we'll give anybody else  
14 on the panel a chance after that.

15 DR. PEIMER: I think that the data  
16 presented are interpretable in a number of ways, as  
17 with the first question in that the effectiveness  
18 of the device is outstanding for osteoarthritis,  
19 which is one of the indications, and a work in  
20 progress for rheumatoid arthritis with evolved  
21 indications.

22 I think that it is going to be--my belief,  
23 based on the information and my own experience, is  
24 that it is going to be a very effective device  
25 within the limitations proscribed. I think it

1 should have labeling, and I will make some specific  
2 comments later. I think it should have some  
3 specific physician labeling restriction guidelines  
4 and training guidelines so that it does not become  
5 available to everyone in early days.

6 In addition regarding effectiveness, I am  
7 going to later make a recommendation about  
8 follow-up data, because I think that with the  
9 additional guidelines in rheumatoid patients, we  
10 can better judge effectiveness. But I would say  
11 that overall, looking at the "when accompanied by  
12 appropriate labeling will provide clinically  
13 significant results," my answer would be yes; yes,  
14 it will. That's my expectation.

15 DR. SKINNER: So you would conclude that  
16 it is efficacious?

17 DR. PEIMER: Yes. That's a big word for  
18 me, but yes.

19 DR. SKINNER: Any other comments from the  
20 panel?

21 Dr. Naidu?

22 DR. NAIDU: Based on the data that is  
23 provided, it is quite clear that the osteoarthritic  
24 population does pretty well. These are isolated  
25 osteoarthritic patients who do not have significant

1 soft tissue deformities. So I think the efficacy  
2 of this device in osteoarthritic conditions is  
3 definitely there. I mean, the device has great  
4 promise in this area.

5 On the other hand, based on the data that  
6 is provided with rheumatoids, it is very hard for  
7 me to make that judgment. Dr. Beckenbaugh has  
8 stated that this would be a good device for early  
9 rheumatoid arthritis, but the data do not support  
10 that at this point. I think it is probably a very  
11 good device for osteoarthritis and post-traumatic  
12 arthritis. It may be an okay device for early  
13 rheumatoid arthritis. That's pretty much all the  
14 conclusion that I can reach based on the data that  
15 is provided to me.

16 DR. SKINNER: Any other comments?

17 Dr. Finnegan?

18 DR. FINNEGAN: I'm going to sound like a  
19 broken record. From what I can see, only three to  
20 four of the osteoarthritis patients, which is an  
21 "N" that is too small to make any conclusions, are  
22 under the age of 60, which is going to be the  
23 target population, and of those, the one who is  
24 going to do what most of the patients do, which is  
25 misbehave with regard to the load that is put on

1 the joint, there was some loosening.

2 So again, while I think this is a  
3 wonderful product, I don't think we have the data  
4 to make any decisions.

5 DR. SKINNER: Are there any other comments  
6 from the panel?

7 [No response.]

8 DR. SKINNER: Do I take the silence as  
9 meaning that in general--with one effective and one  
10 not effective or partially effective and one  
11 totally ineffective, where is the consensus of the  
12 panel on this?

13 DR. WRIGHT: I think the device is  
14 effective.

15 DR. SKINNER: Dr. Lyons, any comments?

16 DR. LYONS: I understand that the  
17 population is small, but the principles seem good;  
18 the thought process in it seems good; and I think  
19 the patients are going to be better off than having  
20 nothing or just a silastic. So I think it is  
21 efficacious, although the numbers, I agree with  
22 Maurean, are very small to base it solely on that  
23 experience.

24 DR. SKINNER: Do I take that to mean that  
25 you feel that it would probably be efficacious for

1 osteoarthritics and patients with early to  
2 not-so-early rheumatoid arthritis and less so for  
3 severe arthritis?

4 DR. LYONS: Yes.

5 DR. SKINNER: Dr. Cheng, any comments? We  
6 have got to get enough comments so that Dr. Witten  
7 will be happy with us.

8 DR. CHENG: My first comment is I  
9 think--although I don't know--I think it is likely  
10 to be effective. I think there are some  
11 limitations--there are some severe limitations to  
12 trying to interpret this data. I think the  
13 sponsors even acknowledged them. In  
14 osteoarthritis, the reality is either you release  
15 it or you don't. If you release it, it's going to  
16 be used. It sounds like for the osteoarthritis and  
17 the traumatic cases, there is no other alternative  
18 other than to take the finger off or fuse it, so  
19 those are going to be the options for the patients,  
20 I think--or an arthroplasty like this--and I think  
21 that can be addressed in discussions with the  
22 patients given the circumstance when they don't  
23 have other options.

24 My thought about the labeling in terms  
25 of--we have talked about the soft tissue stability

1 quite a bit--is that perhaps, instead of  
2 emphasizing the early arthritis, the real issue is  
3 whether or not you can reconstruct the soft tissue  
4 envelope with sufficient stability for a  
5 semi-constrained joint. So why not approve it for  
6 that indication instead of for a broader indication  
7 like it is? I know that's the next question, but I  
8 have to address it with this one. I would probably  
9 see that as part of the indications, as Dr.  
10 Beckenbaugh has even stated. That would be part of  
11 the indications instead of just a blanket, overall  
12 approval for any situation.

13 DR. SKINNER: Dr. Aboulafia?

14 DR. ABOULAFIA: I think the lack of  
15 comments from the panel members is that, at least  
16 for me, we see this moving in a certain direction  
17 that will be addressed sort of with a lot of  
18 labeling issues, and it is probably more  
19 appropriate to save some of our comments for  
20 labeling issues and guidance and training.

21 DR. SKINNER: Okay.

22 Are there any other comments before I ask  
23 Dr. Witten if we have discussed this enough and  
24 given her some guidance?

25 [No response.]

1 DR. SKINNER: Dr. Witten?

2 DR. WITTEN: Yes, thanks.

3 DR. SKINNER: Then, let's move on to  
4 Question 3.

5 I thought Dr. Cheng's comments were  
6 particularly cogent for a tumor doctor, dealing  
7 with a hand problem.

8 DR. PEIMER: He did mention amputation.

9 MR. GOODE: The third question has to do  
10 with patient labeling.

11 "Please identify what additional  
12 information, if any, the sponsor should provide in  
13 their patient labeling."

14 DR. SKINNER: It sounded like Dr. Cheng  
15 said that if the soft tissue envelope could be  
16 adequately reconstructed, that should be the  
17 labeling criterion. Does that sound--

18 DR. CHENG: Well, from the discussion of  
19 the hand surgeons here, it is more that indication  
20 rather than early arthritis. I think the inference  
21 is that that occurs in early arthritis; is that  
22 correct?

23 DR. PEIMER: I think that both Sanjiv and  
24 I have said it and Bob Beckenbaugh has said it.  
25 The verbiage in the labeling must indicate clearly

1 that the capsular structure, especially the  
2 radial-collateral ligament, is either intact,  
3 reconstitutable, or reconstructible. And I think  
4 that some guidelines with respect to preoperative  
5 position and instability are reasonable ones for a  
6 physician to keep in mind; but with that specific  
7 caveat being even if it is only "x" degrees, 10  
8 degrees, whatever it is, if you don't have a  
9 reconstructible ligament, this clearly isn't going  
10 to work. This is not the device.

11 So labeling for restriction to that  
12 patient group, however the FDA in its wisdom does  
13 that, is an essential to safe and efficacious  
14 application of this device.

15 And then, I may as well put in the others.  
16 I think that soft tissue rebalancing in the hand  
17 and wrist should be emphasized in the labeling,  
18 although hand surgeons should know that it should  
19 be emphasized, including release of the ulnar  
20 intrinsics, and I can explain to you later what  
21 that is. But that is something that would cause a  
22 recurrence or tend to also cause a recurring  
23 deformity.

24 Then, my final caveat would be specific  
25 training in the use of this device. I don't think

1 this should be released without a hands-on training  
2 session. I am an experienced hand surgeon, but I  
3 looked at the instruments, and I know that I would  
4 need some practice; I would need some instruction  
5 and practice, probably more than most, to use them  
6 properly.

7 DR. SKINNER: Happily, JAHCO [phonetic]  
8 would agree with you.

9 DR. WRIGHT: I might make an additional  
10 information on removal, with specific reference to  
11 implant fracture, that this has been addressed by  
12 the petition, we have beaten it like a dead horse,  
13 we know it happens occasionally, it happened early,  
14 they have modified the instruments, and we think  
15 that there is probably less of a problem now with  
16 implant fracture on removal, but I think it would  
17 probably be appropriate in the labeling to say that  
18 this does happen and what their recommendations for  
19 removal would be in the event that this does  
20 happen. It sounds like they recommend drilling  
21 this, drilling it out, because it sounds like it is  
22 probably going to need to come out, the stem is  
23 going to need to come out, if you are going to  
24 revise this to either silastic or to another  
25 implant. So I'd just make a reference, an

1 addition, on removal of a broken stem.

2 DR. SKINNER: You are saying that you  
3 think there should be a particular--

4 DR. WRIGHT: Product labeling.

5 DR. SKINNER: --product labeling and  
6 protocol for removal?

7 DR. WRIGHT: No, not a protocol, but I  
8 think that the manufacturer should address product  
9 labeling, that fractures do occur and make the  
10 surgeon aware how to remove this should this occur.

11 DR. SKINNER: Okay.

12 DR. LI: I have a follow-up on that, Dr.  
13 Skinner.

14 DR. SKINNER: Dr. Li.

15 DR. LI: A question to the hand surgeon.  
16 It seems to me that fracture of a device as you are  
17 removing it really isn't a--I actually don't  
18 understand the down side to that. But if you drill  
19 it, it sounds like you could create small  
20 particulate degree that you can't wash out.

21 DR. WRIGHT: The down side is where it  
22 breaks. I had trouble with this when I read it  
23 first, but what happens is this thing looks like a  
24 mushroom, and the head breaks off the implant, but  
25 the stem is still in the bone, so if you are

1 removing it to put in a new prosthesis, you can't  
2 put a new prosthesis in until you get that stem  
3 out. And if you don't have any experience with  
4 that, you're going to have a tremendous amount of  
5 bony destruction or whatever.

6 DR. LI: Thank you for that clarification.

7 My only concern would be that they seem to  
8 have gone to a lot of effort to make a joint that  
9 wears essentially zero in the laboratory, and by  
10 drilling it out, you are creating 10,000 times more  
11 debris than you would ever--

12 DR. WRIGHT: That's how they told us they  
13 get it out--

14 DR. LI: I understand that.

15 DR. WRIGHT: --and if they have a better  
16 way, I'd be happy to hear about it, too.

17 DR. LI: It's just a comment. I don't  
18 know how you'd get around that, but it seems like  
19 those are the choices.

20 DR. WRIGHT: Dr. Beckenbaugh, would you  
21 like to address that?

22 DR. BECKENBAUGH: Thank you.

23 There are some new instruments. You saw a  
24 little plastic device which is utilized to  
25 disimpact the device.

1           The other ones were probably harder to get  
2 out, and we didn't know what to do with them. We  
3 didn't want to particularly leave them in, so the  
4 only thing that seemed logical was to drill them,  
5 and in fact that did result in a capability of  
6 getting them out. I have used exactly the same  
7 technique on cemented polyethylene devices in the  
8 fingers when we were using those.

9           This would probably not be necessary. I  
10 think with two different techniques, that of using  
11 the plastic disimpactors, or now, as I would use as  
12 I do in revisions of elbows and wrists, you would  
13 be able to split the metacarpal and tap the stem  
14 out from the proximal side. The metacarpal then  
15 closes back up like a book. You can use  
16 nonabsorbable sutures, and it is a technique that  
17 we use in some upper extremity revisions  
18 particularly, for example, in the wrist when we do  
19 that. This is a satisfactory way to do it.

20           In any event, I think we can certainly  
21 include the precautions and have in our brochures  
22 that describe the fact that fracture is possible,  
23 and you need to take care and so forth.

24           DR. SKINNER: Dr. Witten?

25           DR. WITTEN: Can I just make a comment

1 about this questions? I appreciate all of these  
2 remarks, and actually, these are part of what we  
3 consider an answer to Question 2. So while we are  
4 on this subject, maybe I could ask--this is about  
5 the second part, which I guess there was more to  
6 say about than I realized--about the proposed  
7 indications for use.

8           So maybe instead of having John Goode  
9 flash it up again, you can just look at the  
10 proposed indications for use in your packet and see  
11 if you have any other comments. And then, after  
12 that, I should tell you what this question was  
13 actually meant to mean.

14           Let me just say on this question about  
15 patient labeling, we usually have a patient  
16 information sheet that would go with this kind of  
17 device, so this question really meant what do you  
18 consider to be important information that the  
19 sponsor should provide in this patient information  
20 sheet in addition to what they have. But since we  
21 are still on the previous question about the  
22 indications, which we would like to hear any  
23 additional discussion about, maybe I could just  
24 refer people back to that sheet on your handout.

25           DR. SKINNER: This is the

1 second-from-the-last page. The questions are on  
2 the last page. And in the bottom left-hand corner  
3 are the proposed indications.

4 Dr. Aboulafia?

5 DR. ABOULAFIA: I was looking for the  
6 proposed indications for use as well as in the  
7 CDROM looking at the indications and  
8 contraindications, and what sponsor submitted in  
9 writing versus what they have said here is a bit  
10 different. One is a little more broad.

11 Just to use some of the quotes that  
12 sponsor presented, one of the contraindications was  
13 "severe deformity and rheumatoid arthritis." I  
14 think it is worth putting that. Another one was  
15 "absence of a reconstructible radial-collateral  
16 ligament." I think go ahead and put it.

17 And everyone is nodding their heads yes,  
18 so I think we could probably get to it if we just  
19 listed them pretty quickly, and everyone would be  
20 okay with that.

21 Another one was "specific onsite training  
22 with one of us." Sponsor is agreeable to that, and  
23 I think we all want that.

24 I think the one that becomes a little bit  
25 touchy is how best to handle it from FDA's side

1 about indications. I recognize the fact that  
2 physicians use things off-label, so when you list  
3 indications, it doesn't mean that it couldn't be  
4 used outside of those indications. I thought other  
5 indications that were appropriate to include were a  
6 lag less than 45 degrees, ulnar deviation of 30  
7 degrees or less, or one centimeter of subluxation.  
8 And whether we include that as indications, it  
9 doesn't mean that a surgeon who has experience and  
10 judgment could not use the device outside of those  
11 indications. And I think it would address, at  
12 least for me, every concern I have.

13 DR. SKINNER: What does the panel feel  
14 about that?

15 Dr. Peimer?

16 DR. PEIMER: Yes, I agree.

17 DR. SKINNER: Basically, contraindications  
18 or relative contraindications, severe rheumatoid,  
19 unreconstructable radial ligaments--

20 DR. PEIMER: Well, inadequate bone stock  
21 on reconstructible collateral ligaments, active  
22 infection--

23 DR. ABOULAFIA: Those are already  
24 included. I deleted the ones that are already  
25 included.

1 DR. PEIMER: Okay.

2 DR. ABOULAFIA: And then, the only  
3 comment--and I was looking to see if I had written  
4 that--is that I would put some kind of cautionary  
5 word about the tendency for complications increased  
6 with ring and small digits and that those two  
7 joints should be looked at carefully prior to  
8 proceeding with reconstruction using this device.

9 DR. SKINNER: How does everybody else feel  
10 about that?

11 Dr. Naidu?

12 DR. NAIDU: Those are all reasonable  
13 suggestions. My impression was that we were to  
14 make a judgment and recommendations based on the  
15 clinical data that was provided to us. I think all  
16 the suggestions are reasonable. If I had to  
17 recommend this prosthesis to anybody based on the  
18 data that was provided, I would probably recommend  
19 it for the post-traumatic and osteoarthritic group.  
20 But based on the data that is provided, it is very  
21 hard to draw any conclusions, and we could put in  
22 all the labelings that we want, but if I were asked  
23 to judge based on the data that was provided, other  
24 than the osteoarthritics, I'm not so sure that I  
25 am convinced at this point with its use in