

# TRANSCRIPT OF PROCEEDINGS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

CIRCULATORY DEVICES PANEL MEETING

Volume I

Pages 1 thru 213

Gaithersburg, Maryland  
April 23, 1998

MILLER REPORTING COMPANY, INC.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

CIRCULATORY DEVICES PANEL MEETING

VOLUME I

Thursday, April 23, 1998

8:00 a.m.

Ballroom  
Holiday Inn  
Gaithersburg, Maryland

MILLER REPORTING COMPANY, INC.  
507 C Street, N.E.  
Washington, D.C. 20002  
(202) 546-6666

## PARTICIPANTS

Anne B. Curtis, M.D., Chairperson  
John E. Stuhlmuller, M.D., Executive Secretary

## MEMBERS:

Tony W. Simmons, M.D.

## CONSULTANTS:

Lawrence Agodoa, M.D.  
Lance B. Becker, M.D.  
Julie A. Freischlag, M.D.  
Anne R. Roberts, M.D.  
George W. Vetovec, M.D.  
Leonard L. Vertuno, M.D.

## EXPERT:

John H. Fielder, Ph.D.

## INDUSTRY REPRESENTATIVE:

Mr. Gary Jarvis

## CONSUMER REPRESENTATIVE:

Donald Altman, D.D.S.

## FOOD AND DRUG ADMINISTRATION STAFF:

Lillian Yin, Ph.D.  
John W. Karanian, Ph.D.  
Carroll G. O'Neill, R.N., B.S.N., M.P.H.  
Daniel Spyker, Ph.D., M.D.  
Paul L. Chandeysson, M.D.  
Patricia Dubill, B.S., M.S.  
Ramiah Subramanian, M.D.

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

2                                    Call to Order

3            DR. CURTIS: I would like to call the meeting of the  
4    Circulatory System Devices Panel to order. The first order  
5    of business will be the conflict of interest statement, to  
6    be read by Dr. Stuhlmuller.

7                                    Conflict of Interest Statement

8            DR. STUHLMULLER: The following announcement addresses  
9    conflict of interest issues associated with this meeting,  
10   and is made part of the record to preclude even the  
11   appearance of an impropriety. The conflict of interest  
12   statutes prohibit special government employees from  
13   participating in matters that could affect their or their  
14   employers' financial interests.

15            To determine if any conflicts existed, the agency  
16   reviewed the submitted agenda and all financial interests  
17   reported by the committee participants. The agency has no  
18   conflicts to report.

19            In the event that the discussions involve any other  
20   products or firms not already on the agenda for which an FDA  
21   participant has a financial interest, the participant should  
22   exclude him or herself from such involvement and the  
23   exclusion will be noted for the record. With respect to all  
24   other participants, we ask in the interest of fairness that  
25   all persons making statements or presentations disclose any

1 current or previous financial involvement with any firm  
2 whose products they may wish to comment upon.

3 DR. CURTIS: I would like to go around and have  
4 everybody introduce themselves as we get started this  
5 morning. I am Anne Curtis. I am a cardiac  
6 electrophysiologist at the University of Florida, in  
7 Gainesville.

8 DR. VERTUNO: Leonard Vertuno, I am Professor of  
9 Medicine at Loyola University School of Medicine, in  
10 Maywood, Illinois, and I am a nephrologist of 25 years  
11 duration.

12 DR. SIMMONS: Tony Simmons. I am a cardiologist,  
13 electrophysiologist, Lake Forest University.

14 DR. FREISCHLAG: I am Julie Freischlag. I am Chief of  
15 Vascular Surgery and a vascular surgeon at UCLA Clinical  
16 Center.

17 DR. AGODOA: I am Dr. Agodoa, nephrologist at the  
18 National Institutes of Health.

19 DR. ALTMAN: Donald Altman, Director for the Arizona  
20 Department of Health, and I am the consumer rep.

21 DR. YIN: Lillian Yin. I am Acting Division Director  
22 for the Division of Cardiovascular, Anesthesiology and  
23 Neurology Division, FDA.

24 MR. JARVIS: Gary Jarvis, the industry representative.  
25

**New Business**

1  
2 DR. CURTIS: Thank you. We will get into our new  
3 business today. As a result of the Food and Drug  
4 Administration Modernization Act, which was signed into law  
5 in November, 1997, the generally one-hour open public  
6 session will be conducted in two segments, approximately 30  
7 minutes at the beginning of the panel meeting for general or  
8 specific issues, and 30 minutes at the end of the panel  
9 deliberations, prior to the vote, for interested persons to  
10 address issues specific to the submission before the panel.

11

12 No one has requested time to speak at the open public  
13 hearing, so I need to ask if anyone here, in the audience,  
14 wants to make any comments before we get started with the  
15 company presentation today. I see no one asking to speak so  
16 let's move directly on to the premarket notification  
17 application K972988, Possis Medical, Inc., the Perma-Seal  
18 graft. We are going to start with the company presentation.

19

**Overview of Clinical Studies**

20

**Jim Gustafson**

21

MR. GUSTAFSON: Thank you, Dr. Curtis.

22

23 DR. CURTIS: If each person representing the company  
24 could identify him or herself and what financial interest  
you have in the product.

25

MR. GUSTAFSON: We can do that now or as the presenters

1 stand up to speak.

2 DR. CURTIS: As each one stands up.

3 MR. GUSTAFSON: We will do that. Good morning.

4 [Slide]

5 My name is Jim Gustafson. I am an employee, an officer  
6 of Possis Medical, and my role there is as vice president of  
7 regulatory and clinical affairs. This morning I will  
8 present to the panel, for your review, the Possis Perma-Seal  
9 Dialysis Access Graft.

10 [Slide]

11 This is the schedule that we will follow for our  
12 portion of the meeting. I will present an overview of the  
13 clinical studies involving Perma-Seal. Dr. Jill Lindberg, a  
14 nephrologist from Ochsner Clinic, in New Orleans and a  
15 Perma-Seal investigator, will show you her perspectives on  
16 the graft. Dr. Marc Glickman, a vascular surgeon from  
17 Sentara-Norfolk Hospital and the principal investigator for  
18 the Perma-Seal study, will share his insights on Perma-Seal  
19 graft use, and will then be available, after FDA's  
20 presentation, to answer questions from the panel. ]

21 There are some additional personnel Possis Medical who  
22 are available to address questions, and I will ask them to  
23 raise their hands when I give their names: Dr. Rich Holton,  
24 consultant statistician; Mark Stenoien, our director of  
25 graft product development; Carolyn Modlin, our manager of

1 graft clinical studies; Mark Jensen, our manager of graft  
2 research; and Tim Anderson, our manager of graft quality  
3 engineering. So, the whole graft team is here to observe  
4 and participate if there are questions that they can help  
5 with. We will try to direct any questions from the panel to  
6 the person who is best able to answer the question.

7 [Slide]

8 Possis Medical is a Minneapolis-based developer and  
9 manufacturer of medical devices. We make both grafts and  
10 thrombectomy catheter systems.

11 Right now, we will pass out a couple of samples of our  
12 Perma-Seal dialysis access graft, along with some  
13 conventional ePTFE graft samples, and also some dialysis  
14 needles. You can play with the samples as we go through  
15 these presentations.

16 [Slide]

17 The graft has these conventional design  
18 characteristics, but it also has some unique ones. The  
19 product is made with solid windings of electrostatically  
20 spun silicone elastomer, and this provides self-sealing  
21 characteristics that you can test yourself by trying those  
22 needles on both the Perma-Seal samples and the ePTFE  
23 samples.

24 It has a porous outer surface to aid in tissue  
25 anchoring and a non-permeable blood contact layer to avoid

1 the need to pre-clot.

2 [Slide]

3 In this photograph, you can see the needle sealing  
4 characteristics differences between the Perma-Seal graft and  
5 ePTFE conventional grafts. In the ePTFE graft, which is  
6 shown above, the hole is still quite visible after needle  
7 withdrawal, but the hole has disappeared with the Perma-Seal  
8 graft.

9 [Slide]

10 This diagram shows the typical surgical layout with the  
11 Perma-Seal. This is similar to the layout for other ePTFE  
12 grafts.

13 [Slide]

14 The clinical study of the Perma-Seal graft was  
15 conducted under an IDE. It had a total of 250 patients  
16 enrolled at 6 study sites around the U.S., from 1993 to  
17 1997. The trial randomized patients to either Perma-Seal or  
18 to conventional ePTFE graft controls.

19 [Slide]

20 The objectives of the trial were to demonstrate that  
21 Perma-Seal graft supports high-efficiency dialysis; has  
22 patency and complication rates similar to the control;  
23 supports immediate access; and has rapid hemostasis after  
24 dialysis needle withdrawal.

25 [Slide]

1 The patient selection criteria are shown on this slide.  
2 They are unremarkable.

3 [Slide]

4 The clinical experience reported to date comprises 250  
5 patients, reporting a total of 270 follow-up years, and  
6 these are both divided roughly equally between the two  
7 treatment groups.

8 [Slide]

9 The first objective of the study was to show that the  
10 Perma-Seal graft could support high-efficiency dialysis.  
11 These results show that dialysis flow rates, line pressures  
12 and run times were equal in the two treatment groups.

13 [Slide]

14 The next objective was to compare patency. This figure  
15 displays Kaplan-Meier actuarial curves for freedom from  
16 patency salvage intervention for the two treatment groups.  
17 The Perma-Seal seal did not perform as well as the control  
18 in this measure.

19 [Slide]

20 Total patency is also called secondary patency or total  
21 useful graft life. By this measure also, the Perma-Seal did  
22 not perform as well as the control.

23 [Slide]

24 In the study, we defined a major complication to be any  
25 complication which required intervention or any aneurism or

1 pseudoaneurism. These plots show that Perma-Seal did not  
2 perform as well as the control in this category.

3 [Slide]

4 The study recorded the number of minutes required to  
5 achieve hemostasis after each dialysis session. All  
6 patients began with a 10-minute compression time, and the  
7 next session's time was increased or decreased by 1 minute,  
8 depending on whether 10 minutes was enough the first time  
9 around. Subsequent dialysis sessions were similarly  
10 titrated, and after about 2 months time all patients had  
11 achieved a stable hemostasis time. This figure shows the  
12 cumulative distribution of hemostasis times for the 2  
13 grafts.

14 To take an example off the graph, 80% of the Perma-Seal  
15 patients had a hemostasis time of less than 5 minutes, while  
16 only 20% of the control patients had that short a hemostasis  
17 time. This represents a true-time savings for the patient  
18 and the dialysis clinic.

19 [Slide]

20 Early first access or first stick for hemodialysis was  
21 not allowed by the protocol until about half the patients  
22 had been enrolled. Once it was allowed, most Perma-Seal  
23 took advantage of the option. This figure charts the  
24 cumulative distribution of first access times. More than  
25 40% of Perma-Seal patients had first access before day 10,

1 and only 1 control patient did, and that was at day 9. Many  
2 patients had first stick in the first 24-48 hours after  
3 implantation of the Perma-Seal graft. This experience shows  
4 that the Perma-Seal graft does support chronic dialysis  
5 immediately after implant.

6 [Slide]

7 We wanted to be sure that early access did not degrade  
8 Perma-Seal performance. This plot shows no difference in  
9 actuarial freedom from patency salvage intervention between  
10 Perma-Seal grafts with first access earlier than 10 days  
11 compared to first access later than 10 days.

12 [Slide]

13 Using the same dividing line of 10 days post-implant,  
14 this plot shows no difference in total useful graft life  
15 between early and standard access Perma-Seal.

16 [Slide]

17 In major complications also there was no difference  
18 seen between early and standard access Perma-Seal graft  
19 patients.

20 [Slide]

21 This graph shows the cumulative distribution sealing  
22 times for early and standard Perma-Seal. The early access  
23 Perma-Seal patients actually showed a small trend toward  
24 shorter sealing times, but this was not statistically  
25 significant.

1 [Slide]

2 From these results we concluded the following: First,  
3 the Perma-Seal graft supports high-efficiency dialysis.  
4 Secondly, the Perma-Seal has shorter patency, and more  
5 frequent complications but the same type of complications as  
6 the control graft; and, the Perma-Seal has shorter times to  
7 hemostasis and provides immediate access to support  
8 dialysis.

9 These are mixed results. The Perma-Seal performs worse  
10 on some endpoints and better on others. These results  
11 suggest that Perma-Seal would be best suited for patients  
12 who especially need the immediate access advantage which  
13 Perma-Seal provides.

14 Because this study was aimed at all patients, it was  
15 not able to well quantify this group. So, we understood  
16 some additional activities to better understand the value of  
17 early access and the kind of patients who would best benefit  
18 from it by looking at the use of temporary venous access  
19 catheters in conjunction with dialysis access grafts.

20 [Slide]

21 Conventional ePTFE grafts require about 2 weeks to  
22 mature before they can first be accessed for dialysis.  
23 Patients who require immediate dialysis typically have a  
24 temporary venous access, a TVA catheter, implanted through  
25 the neck or another region of the upper body to support

1 their need until the ePTFE graft is ready for us.

2       TVA catheters require a separate surgery. They add  
3 complications, patient discomfort and cost, and they have  
4 lower flow rates, which makes for longer and less efficient  
5 dialysis sessions.

6       [Slide]

7       This shows a typical jugular vein placement of a TVA  
8 catheter. From it, you can appreciate the kinds of problems  
9 that they could cause. Patients who need immediate access  
10 would benefit from a dialysis access graft which could be  
11 used immediately upon implant, and so avoid the use of these  
12 kinds of catheters.

13       [Slide]

14       To better characterize these patients and their needs,  
15 we sponsored an analysis of the national HCFA database for  
16 end-stage renal disease patients to compare graft  
17 performance with and without concomitant TVA catheter use.

18       The study was conducted by Dr. Alan Collins of  
19 Minneapolis. He reviewed the Medicare A and B claims  
20 database for 1994, which is the last full year available,  
21 comprising over 15,000 patients.

22       [Slide]

23       This slide is a bit busy so I will walk you through it.  
24 The analysis performed by Dr. Collins showed that 23% of all  
25 patients receiving a dialysis access graft implant also

1 received a TVA catheter within 2 weeks after. That figure  
2 is derived by 77% or almost 78% of the patients in this data  
3 set who did not receive a catheter within 2 weeks of  
4 implant, and the rest of these categories added together  
5 comprised over 23%.

6 Also, patients with both a graft and a TVA catheter  
7 exhibit significantly higher risk of both the first event  
8 and of multiple events, and that is seen in the next 3 rows.  
9 This is the relative risk of the first event, with a 95%  
10 confidence interval, the reference group being patients who  
11 received grafts only. You see that the relative risk is  
12 higher in all 3 of these subcategories of patients who  
13 received a temporary catheter of some kind or other after  
14 graft implant. The relative risk of multiple events is also  
15 higher. The relative risk of a final event is unchanged  
16 over the reference sample.

17 These patients also have a 10% higher monthly cost  
18 because of the TVA catheter implant and the additional  
19 events that are involved, about \$500 a month on average, and  
20 you can see that in these figures, here.

21 [Slide]

22 This analysis supports these conclusions: Many  
23 patients use TVA catheters in conjunction with dialysis  
24 graft implantation to provide temporary dialysis access  
25 while the graft matures. These patients experience

1 significantly higher complications and cost of care than  
2 patients receiving AV grafts only, in addition to the extra  
3 surgery needed to place the catheter itself.

4 [Slide]

5 Combining the findings of these two studies, we  
6 conclude the following: The Perma-Seal supports high-  
7 efficiency dialysis. The Perma-Seal patency and  
8 complication performance is lower than ePTFE graft controls.  
9 Perma-Seal has shorter hemostasis times, and Perma-Seal  
10 supports immediate dialysis access.

11 [Slide]

12 Continuing, a significant number of patients could  
13 benefit from use of a dialysis access graft which avoids the  
14 need for TVA catheters. The Perma-Seal is a viable AV  
15 access graft choice for such patients.

16 [Slide]

17 With these conclusions in mind, we will go back to the  
18 indications for use for the Perma-Seal graft. In the  
19 clinical study any patient who needed a graft to support  
20 chronic dialysis was eligible for enrollment, but this is  
21 too broad. The results show that the risk/benefit ratio for  
22 all such patients is not favorable.

23 But if use of the Perma-Seal graft is focused on  
24 patients who need immediate access for dialysis, but in whom  
25 TVA catheters can be expected to cause additional problems,

1 the Perma-Seal risk/benefit ratio is substantially  
2 equivalent to that for the combination conventional ePTFE  
3 grafts and TVA catheters used together. We, therefore,  
4 propose this modified indication for use to market the  
5 Perma-Seal graft.

6 Thank you for your attention. Now Dr. Lindberg will  
7 address the clinical and patient selection issues from a  
8 nephrologist's point of view, and after that Dr. Glickman  
9 will address similar issues from the surgeon's point of  
10 view. Dr. Lindberg?

11 **Nephrologist's Perspective**

12 **Jill S. Lindberg, M.D., F.A.C.P.**

13 DR. LINDBERG: I am Jill Lindberg. I am a nephrologist  
14 of 12 years, and I was in the Army first, and now in the  
15 Ochsner Clinic. It is a multi-specialty clinic in New  
16 Orleans, an urban population and a population in the bayou.  
17 I take care of about 300 dialysis patients and I do  
18 participate in some clinical research. I participated in  
19 this study, and my financial interests are the support of  
20 this study for myself, Dr. Money and Dr. Sternberg, vascular  
21 surgeons, for the conduction of the study in 28 patients,  
22 and my expenses to come here.

23 [Slide]

24 With that, I will get started. Those of us in the  
25 dialysis community know that this dialysis access is a

1 patient's lifeline, a patient's lifeline to keep them going  
2 on dialysis. With that, this becomes a very difficult area  
3 for the patient. They become very frightened when their  
4 access clots, when they have to go for line replacement, and  
5 declotting. It is a frustrating area for all of us.

6 In addition, we depend on the access because now, in  
7 the nephrology community, we are concerned with the dialysis  
8 outcome qualitative initiative, which was a very aggressive  
9 undertaking by the NKF and a pharmaceutical company where we  
10 developed some standards for adequate dialysis.

11 KT/V 1.3 prescribed what is recommended. There are  
12 nice epidemiologic studies in our community that show that  
13 this is associated with improved morbidity and mortality in  
14 our patients. So, now we have actually guidelines to help  
15 us dialyze these patients in a much more efficient,  
16 organized and a bit more scientific way. K is the numerator  
17 with time, and V is distribution of urea. So, we need good  
18 blood flow and, unfortunately, we now need longer times to  
19 obtain adequate dialysis.

20 [Slide]

21 Adequate blood flow is necessary for adequate dialysis.  
22 I showed you the equation. Adequate dialysis clearly  
23 decreases morbidity and mortality in our patients. They eat  
24 better, they feel better, they stay out of the hospital.  
25 But some of the most important months are those first few

1 months when they first start dialysis. They are very sick.  
2 They have been uremic, and they are malnourished and,  
3 unfortunately, many haven't sought care until the last  
4 minute.

5 [Slide]

6 At this point, access becomes our Achilles' heel. It  
7 is very difficult.

8 [Slide]

9 If you look at the DOQI standards, they looked at 3,460  
10 entries in the literature to look at vascular access, and  
11 they found that it is the most frequent cause of  
12 hospitalization in the dialysis population. Dr. Collins'  
13 '94 data review supports that.

14 [Slide]

15 What does it cost? It costs a lot. In 1994, \$11  
16 billion; \$14 billion in '95. Further statistics in vascular  
17 access is \$1 billion in '94 and \$2 billion in '95.

18 [Slide]

19 Why is that? Well, this is part of Dr. Levey's data  
20 from NKF meetings a few weeks back. He presented this from  
21 USRDS. In 1995, there were 70,000 new ESRD patients  
22 compared to 35,000 in 1990. We have over 270,000 patients  
23 now with end-stage renal disease. It is a big population.

24 [Slide]

25 That partially contributes to the cost but, in

1 addition, our population is changing. There are more  
2 elderly. They are sicker. They have more complications.  
3 We have a larger black population, genetically predisposed  
4 to hypertension diabetes and its renal complications. Lower  
5 socioeconomic classes cannot obtain health care often until  
6 they are very ill, and that has contributed to the  
7 complications. And, we have many obese patients, as we do  
8 in our industrialized country.

9 [Slide]

10 Our population is increasing in the diabetic. They  
11 live longer with the excellent care they get from all of our  
12 specialties in medicine and surgery. They have more  
13 atherosclerotic peripheral vascular disease and, yet, they  
14 are living longer on dialysis, which is great. Our KT/V  
15 modeling, has helped that. Therefore, we will see patients  
16 on dialysis 22-25 years and we have used up all of their  
17 access sites, and that is a tough area.

18 [Slide]

19 This is also from the 1997 USRDS data, also from Dr.  
20 Levey, and in our patients, 41% are diabetic and 31% are  
21 hypertensive. The other three categories are not associated  
22 with as much vascular disease and difficulty with vascular  
23 access as those top two categories.

24 [Slide]

25 Temporary venous access catheters are a big part of our

1 practice. They are important to us in the middle of the  
2 night. They can be used for immediate dialysis if the  
3 patient is hyperkalemic. We can put them in the IJ,  
4 subclavian or femoral sites. But there are problems with  
5 them, and there are trade-offs with them, like everything we  
6 do in medicine.

7 [Slide]

8 First of all, we are seeing an increased use because we  
9 are, unfortunately, seeing late referrals. There is another  
10 large initiative in our organization to try to stop that  
11 late referral but we haven't gotten there yet.

12 We see higher clotting in the PTFE graft due,  
13 primarily, to the characteristics of our patient population  
14 -- the severe vascular disease we see; the late emergency  
15 placement because of late referral; and we are also seeing  
16 the emergence of a hypercoagulable state in our patient  
17 population.

18 [Slide]

19 There are complications with temporary venous access.  
20 The rate of insertion-related complications is approximately  
21 5%, and in the thorax especially there are problems with  
22 pneumothorax, aeroembolism and hemothorax.

23 [Slide]

24 The subclavian location has become a difficult location  
25 for us in our practice. We use it primarily because,

1 obviously, it is set in the patient's chest rather than up  
2 in their neck. However, when we started to put the access  
3 in their arms, if they had any stenosis since stenosis is a  
4 fairly high frequency, 40%, if we use the subclavian  
5 location, especially using it repeatedly, what will happen  
6 is that the access in the arm does not work because of the  
7 back pressure from the stenosis of that vein.

8 The femoral site is an alternative, but not a great  
9 one. We immobilize patients when we put a big, long  
10 catheter in that femoral vein. It is stiff. You can  
11 rupture other vessels in that area, and it is obviously an  
12 area that is not very clean in terms of providing adequate  
13 sterile technique.

14 [Slide]

15 The temporary venous catheter has a finite use. As a  
16 nephrologist, my biggest problem with it is blood flow. The  
17 blood flow that I need to get adequate KT/V, in those  
18 earlier days especially, I can't get when the patient is  
19 standing on their head and twisting their neck in order to  
20 obtain blood flow. So, it decreases my K, my numerator, and  
21 I have decreased dialysis adequacy. We often have to use  
22 urokinase to improve flow and sometimes that does work for  
23 us.

24 [Slide]

25 This is also from DOQI standards. Again, they reviewed

1 the literature, and these are just direct quotes: The  
2 infection rate for central venous catheter placement is 7-  
3 10%. Bacteremia in dialysis patients is fairly frequent,  
4 0.1 to 1.4 episodes per 100 patient months. This is all  
5 literature review.

6       Metastatic complications -- what is that? That is  
7 metastatic to the heart valves causing endocarditis. It is  
8 metastatic to subcutaneous areas. The incidence is 25% per  
9 100 patient months. Of course, not surprisingly, most of  
10 the infections are skin organisms, gram positives.

11       [Slide]

12       It is a frustrating area for patients and staff. It is  
13 decreased quality of life for the patient and, certainly, in  
14 the hospitalization, in and out, changing the catheter.  
15 Those of you in the dialysis care-giving community know what  
16 happens frequently when these don't work and they get  
17 infected. I often have to use 4 to 5 hours, usually 5 hours  
18 on dialysis for these catheters to obtain adequate dialysis  
19 because of their poor blood flow. It is a long time, three  
20 times a week.

21       [Slide]

22       Most importantly, and I don't have any slides on these  
23 patients; they weren't in the study -- I didn't feel that  
24 their situation was safe enough to allow them randomization,  
25 and I obtained, about two years ago, compassionate protocol

1 use. One patient is a 59-year old male who is on our school  
2 board, very bright, but he couldn't accept the fact that he  
3 was starting dialysis. He has an AKA above the knee  
4 amputation on the left. He had 49 Quinton catheters in a  
5 year's time. We used up the left side completely. We had  
6 the right femoral left. Dr. Money and I felt that we really  
7 were up against the wall with this situation. We had lost  
8 all our sites. He had multiple abdominal procedures and, we  
9 did use the Perma-Seal graft off protocol for compassionate  
10 use in the right femoral area, and we were able to stick it  
11 the next day.

12 The second patient is from a different walk of life.  
13 She is not on the school board; she is a drug addict, and  
14 she has used up all of her vessels for recreational  
15 purposes, and we had nowhere to go again, but her left  
16 femoral. We used up what we could to dialyze her. She was  
17 not a candidate for PTFE because she is often homeless and  
18 often on the streets. Again, we obtained compassionate use  
19 in the femoral area. They are still in my unit and they  
20 still have their access and they are alive.

21 [Slide]

22 Everything we do in medicine often is choices,  
23 decision-making, trade-offs, and this is a trade-off. Mr.  
24 Gustafson just presented to you the parts about this access  
25 that are not the best outcomes. But, clearly, when you are

1 up against the wall and there are no other places to go it  
2 has been a very positive choice for me in my practice.  
3 Thank you very much.

4 **Surgeon's Perspective**

5 \  
6 Marc H. Glickman, M.D., F.A.C.S.

7 DR. GLICKMAN: Good morning. I am Marc Glickman, a  
8 vascular surgeon, board certified, from Norfolk, Virginia.  
9 I have been a participant in this study since its inception  
10 in 1993. I do not have any financial interest in the Possis  
11 Company. Our group has received a stipend for the research  
12 to participate in this study. I am on the medical advisory  
13 board of Possis Medical and do receive a nominal fee for  
14 participation on that board.

15 Today, I would like to speak to you about our clinical  
16 experience with the Perma-Seal graft, and what we see as  
17 both a team and nephrologists and surgeons of how this graft  
18 can be used in our practices.

19 [Slide]

20 We feel that the data over the course of four years has  
21 demonstrated that this graft can be utilized for early  
22 access. In fact, we have utilized this graft within the  
23 first 24 hours of implantation. We have found in many of  
24 our patients who have had previous failed accesses that this  
25 graft performed well and was an excellent alternative for  
the patients.

1           We felt that in those patients who had multiple  
2 catheter placements, with resulting concomitant  
3 complications as described by Dr. Lindberg, that this graft  
4 was a suitable alternative for these patients.

5           [Slide]

6           What are the trends of utilizations of temporary venous  
7 catheters in our medical practices today?

8           [Slide].

9           Well, as Dr. Lindberg suggested and demonstrated, a  
10 study in 1990 demonstrated that 90% of patients who had the  
11 subclavian route of placement of these temporary venous  
12 catheters ended up with significant concomitant  
13 complications, and this included either stenosis or  
14 occlusion of the subclavian vein. Once these were  
15 identified, and these were often silent until an access was  
16 placed and the patient had a swollen extremity, care of the  
17 chronic occlusion or stenosis was not met with excellent  
18 outcomes, as demonstrated by this slide.

19          [Slide]

20          A study at Wake Forest, in 1996, looked at a small  
21 patient population for what was the utilization of temporary  
22 venous catheters in this patient population. This  
23 demonstrates that there are 2.5 catheters used per year in  
24 this patient population, and 93 of these catheters were  
25 placed a week after the implantation of a hemodialysis

1 graft.

2 [Slide]

3 In fact, in this study, today, over 79% of the patients  
4 had placement of a temporary venous catheter for dialysis.

5 Well, what is the trend of utilization of prosthetic  
6 graft in the United States today? In 1986-87, by the  
7 Medicare standards, 51% of patients had a prosthetic AV  
8 graft placement. In 1990, this increased to 65.2%. In  
9 1990, who was increasing the utilization of prosthetic graft  
10 placement? It was in the female patient population, a  
11 diabetic patient population and the obese patient  
12 population. This utilization of prosthetic access was  
13 increasing within this subgroup of patients. Also as  
14 expected, as we see in our practices, the Medicaid  
15 population, the poorer people, were getting placement of  
16 prosthetic grafts. This trend is increasing. The 1995-96  
17 data also substantiates what I have demonstrated today.

18 [Slide]

19 A decision matrix between the nephrologists and  
20 vascular surgeons is very important in the utilization of  
21 the Perma-Seal graft. I would like to take you through our  
22 thought processes of how we see the Perma-Seal graft playing  
23 within our practices today.

24 [Slide]

25 First, the markedly obese patient population. As I

1 have said before, this group is increasing and does have  
2 significant problems for both the nephrologists and the  
3 vascular surgeons. Often the adipose subcutaneous tissue is  
4 very thick, and sometimes it is difficult to access these  
5 grafts. The Perma-Seal graft, as you noted, at the outer  
6 diameter is a little larger. So, it is a little easier to  
7 access this graft. Because of the components of the  
8 silicone, there is less edema in the surrounding tissues  
9 with this graft. So, it is easier to stick this graft than  
10 the present PTFE graft. Because of the early access ability  
11 of this graft, we do not need to use temporary venous  
12 catheters, which are often fraught with complications in  
13 this patient population.

14 [Slide]

15 An example of a patient from this study is D.E. These  
16 are real patients. She is a morbidly obese patient. She is  
17 4 ft. 2 in. She weighs 485 lbs. She requires hemodialysis.  
18 We were unable to place a catheter due to this enormous body  
19 habitus. She had placement in her right upper arm of a  
20 Perma-Seal graft. She was luckily randomized to this, and  
21 she had early access with this graft within 24 hours, and  
22 this graft functioned well for 6 months without any  
23 complications.

24 [Slide]

25 Absent central vein -- this is a very significant and

1 increasing problem for the vascular surgeon and  
2 nephrologist. As was stated before, this is secondary to  
3 complications from central vein usage. Once the subclavian  
4 and internal jugular vein is occluded, this really does  
5 prevent use of that ipsolateral extremity.

6 [Slide]

7 Another example from the patient population is C.G., a  
8 25-year old black male with a history of multiple failed  
9 accesses in both upper extremities. His central veins were  
10 occluded bilaterally due to previous temporary venous  
11 catheters. His status was right leg deep venous thrombosis  
12 from a previous temporary venous catheter. He needs a new  
13 left leg access. Left femoral vein is the only vein that  
14 was available, and he was luckily randomized to the Perma-  
15 Seal graft, placement of the Perma-Seal graft, with early  
16 access of the graft. The graft is doing well and so is the  
17 patient.

18 [Slide]

19 Socioeconomic factors are also extremely important in  
20 the decision matrix. As I have talked about before, the  
21 patient population is increasing, as seen by the 1990 data.  
22 The incidence of diabetes and end-stage renal disease  
23 population is also increasing. Peripheral vascular disease  
24 patients are increasing, and the Medicaid patient population  
25 is also increasing.

1 [Slide]

2 An example from this list of patients is D.P., a 29-  
3 year old white male with a history of multiple previous  
4 access grafts, in both of his legs, left arm, and he has had  
5 two previous failed kidney transplants. Left subclavian  
6 vein and left internal jugular vein were occluded. He  
7 needed a new access and urgent dialysis. We removed him  
8 from the study in order to place a Perma-Seal graft -- he  
9 did get a Perma-Seal graft in his upper right extremity. It  
10 worked well immediately. He returned to work within three  
11 days after placement of the graft as his job was very  
12 important to him. He did not have a temporary venous  
13 catheter, and was able to function without problems.

14 [Slide]

15 Chronic Coumadin anticoagulation, another increasing  
16 problem facing both the nephrologist and the vascular  
17 surgeon. These patients are growing. They are on Coumadin  
18 for multiple medical conditions, including having previous  
19 prosthetic valve replacement, history of deep venous  
20 thrombosis, history of the hypercoagulable states. These  
21 are real conditions that we are seeing within our practices.  
22 Chronic treatment anticoagulation can raise a significant  
23 problem to the nephrologists in the dialysis unit, as well  
24 as to the vascular surgeons.

25 [Slide]

1           Here is a patient example who was in this study. M.O.  
2 is 73-year old white male who was on Coumadin for prosthetic  
3 mitral valve replacement. He was hospitalized three times  
4 for temporary venous catheter placement and Coumadin  
5 reversal and heparin therapy. An PTFE graft was placed  
6 within this patient. The patient bled excessively following  
7 each hemodialysis decannulation with resultant hematoma  
8 formation. The patient had to be rehospitalized because of  
9 bleeding and, again, placement of temporary venous  
10 catheters, and this occurred frequently.

11           As we have seen in the data, patients who are on  
12 Coumadin following decannulation with the Perma-Seal graft  
13 do not have bleeding problems with utilization of this  
14 graft.

15           [Slide]

16           The elderly -- the elderly, as Dr. Lindberg said, is a  
17 rising group of patients, often requiring urgent and  
18 immediate dialysis. Because of the delay in making the  
19 decision, family decision or medical decision whether or not  
20 this patient should go on hemodialysis, a graft that can be  
21 accessed early or immediately would prevent the  
22 complications in patients often seen with temporary venous  
23 catheters.

24           [Slide]

25           Here is an example of a patient from our practice.

1 J.M. is an 86-year old white female who had placement of a  
2 temporary venous catheter. Poor flows were obtained via the  
3 catheter due to thrombosis of one of the lumens. Patient  
4 underwent lytic therapy through the catheter with,  
5 unfortunately, a complication resulting in excessive  
6 bleeding into her right shoulder, a significant fall in  
7 hematocrit. The patient developed myocardial infarction,  
8 pulmonary edema and needed urgent dialysis. Another  
9 catheter was placed. A cascade of unfortunate problems  
10 occurred, pneumothorax and a poor outcome.

11 A Perma-Seal graft that could have been accessed early  
12 would have perhaps helped this patient, preventing the  
13 problems associated with temporary venous catheter  
14 placement.

15 [Slide]

16 Lastly, quality of life issues are also very important.

17

18 [Slide]

19 The things that we have demonstrated is its quick  
20 sealing time. Unfortunately, in this study patients are in  
21 the same dialysis units, and patients would come to me and  
22 say, "I want what Johnny Doe has, next door to me. He  
23 leaves three minutes after decannulation and I have to wait  
24 for 20 minutes after decannulation." This has an impact on  
25 the quality of life of these patients.

1 [Slide]

2 This is another example from this study. D.S. is a 32-  
3 year old white male, who is on hemodialysis from 7:00 a.m.  
4 to 11:00 a.m., and he taught a class at 1:00 p.m. because he  
5 left within minutes after decannulation.

6 [Slide]

7 As Dr. Lindberg has said, there are trade-offs, and we  
8 realize that there are some trade-offs but we do need a  
9 graft that can be accessed immediately, where we can be part  
10 of a decision-making process in order to implant this graft  
11 into a group of patients that become more difficult to  
12 handle, more difficult to manage. Thank you very much for  
13 your time.

14 DR. CURTIS: We will move on now to the FDA  
15 presentation by John Karanian.

16 **FDA Application Summary**

17 John Karanian

18 MR. KARANIAN: Good morning, Dr. Curtis and panel  
19 members. I am John Karanian, and I am the lead reviewer in  
20 the Division for Cardiovascular and Respiratory Devices. I  
21 would like to introduce my colleagues who are involved in  
22 this review, Dr. Dan Spyker, who is the primary person who  
23 did the preparation of the panel pack; Dr. Chandeysson, who  
24 is the medical officer who did the principal clinical  
25 review; Gary Kamer, a statistician; and last but not least,

1 Dorothy Able, who has been involved from the beginning, the  
2 initiation of this clinical trial.

3 DR. CURTIS: Excuse me, why don't we have the people  
4 from the company step back now?

5 MR. KARANIAN: My presentation is about as long as the  
6 introduction, so I think we can get right to the point.

7 [Slide]

8 A clinical trial was designed, conducted and compared  
9 Perma-Seal to two marketed PTFE grafts which were randomly  
10 chosen by the clinical investigators, a Gore-Tex or an Impra  
11 marketed graft.

12 The results indicated, as you heard already, that the  
13 Perma-Seal graft had a lower patency rate and a higher  
14 complication rate compared to the control graft. The  
15 subject device had a shorter time to hemostasis compared to  
16 the control graft, and there was not a statistical  
17 difference between patency or complication rate of the  
18 subject graft cannulated before 10 days as compared to that  
19 cannulated after 10 days.

20 [Slide]

21 Given that analysis, we proceeded to request panel  
22 review. It is proposed, based upon these data, that the  
23 Perma-Seal graft is intended to provide early and chronic  
24 vascular access for hemodialysis in patients in whom venous  
25 catheters are deemed undesirable.

1 [Slide]

2 Given these data, the panel is requested to answer the  
3 following questions since the clinical data indicate the  
4 Perma-Seal graft is different from other grafts, with lower  
5 patency and higher major complications, but may contain  
6 benefits for a potential subpopulation needing immediate  
7 access and sealing time, the questions are: Are there  
8 patients for whom the lower patency rate and higher  
9 complication rate would be acceptable, given that the device  
10 may be accessed before the typical two-week healing time?

11 Who are these patients? And, does the indication for  
12 use statement adequately define this patient population?

13 **Panel Discussion**

14 DR. CURTIS: Thank you. We will move on to the panel  
15 discussion now. Dr. Vertuno?

16 DR. VERTUNO: Just as a bit of background, as Dr.  
17 Lindberg so cogently pointed out, vascular access is really  
18 the linchpin and lifeline for these patients, and over the  
19 last 30 years the options available to both the patient and  
20 practicing nephrologist has been limited only by the  
21 ingenuity of the vascular surgeon community and those  
22 individuals who have been interested in this problem, and  
23 the biomedical engineering community.

24 If we take a look at the data presented today, first of  
25 all, we are talking probably about 20% of the patients who

1 need dialysis who would be candidates for this particular  
2 device. Second is that there are, as has been quite  
3 adequately demonstrated, many, many problems with temporary  
4 venous access catheters.

5 This is a personal view because I haven't done great  
6 research for this, but most of these are due to the  
7 inappropriate use of the catheter, temporary catheters for  
8 long-term dialysis. If every temporary venous access  
9 catheter was used for two weeks for the maturation of  
10 probably the tetrafluorine catheter we would have a lot less  
11 problems. But the infection rate, and particularly the  
12 stenosis and loss of access site is due to duration which  
13 is, in my personal experience and I think generally accepted  
14 throughout the country, far, far too long.

15 Third, as again has been demonstrated, there are  
16 people, perhaps a very small number but there are people who  
17 would benefit from this even though the catheter duration is  
18 shorter than the standard catheter. If somebody is 4 ft.  
19 tall and weighs 400 lbs. he is not a good candidate for a  
20 subclavian catheter insertion. People who have heart valves  
21 and are on Coumadin are at great risk for a cannulated  
22 central vein. So, I think there is an absolutely definable  
23 population where this would be a benefit.

24 A couple of other comments, the efficacy of the device  
25 in terms of providing adequate dialysis is proven. As a

1 practical matter, I am not so concerned about the  
2 inefficiency of the venous catheters if they are used for a  
3 couple of weeks. If they are used for six months, it is a  
4 bit problem. If they are used for two weeks it is really  
5 not an issue.

6 The area which I think needs to be defined, and is not  
7 defined in the present study, is if you take a look at  
8 people who have a dialysis experience of ten years, you  
9 would probably use up dialysis access sites faster with this  
10 device than you would with two weeks of a temporary venous  
11 catheter and a standard PTFE catheter.

12 I think the investigators have demonstrated what they  
13 started out to demonstrate. I think that it has at least a  
14 role as niche device, and I think its use in the general  
15 population of dialysis patients is yet to be defined.

16 DR. AGODOA: I have a couple of questions that I would  
17 like to pose to the sponsors of this. It is not very clear  
18 to me what the frequency rate of revision is compared with  
19 the regular PTFE grafts. What is the frequency rate of  
20 revision? As Dr. Lindberg pointed out, the vascular access  
21 can constitute a very expensive portion of the budget for  
22 this treatment, and much of that is due to access revision.  
23 Do you have any data? That is my first question.

24 My second question, based on the presentations, it  
25 seems like we are comparing the Perma-Seal with PTFE,

1 obviously, when this gets to the market we know it is going  
2 to be used as a permanent access, basically. So, why are  
3 all the data being compared with PTFE?

4 DR. CURTIS: Please come back up to the microphone.

5 MR. GUSTAFSON: Dr. Agodoa, we did analyze that. We  
6 have linear rates calculated for patency salvage  
7 intervention, as well as the actuarial rates, and in your  
8 panel pack, actually page 4-5, there is a listing of the  
9 patency salvage interventions -- section 4, page 5. Also,  
10 in FDA's summary, tab 4, page 5. The number of patency  
11 salvage interventions for Perma-Seal within 30 days was 20  
12 and for the ePTFE control was 14. The number of patency  
13 salvage interventions beyond 30 days for Perma-Seal was 339,  
14 for ePTFE it was 152.

15 DR. AGODOA: Thank you.

16 MR. GUSTAFSON: Your second question was?

17 DR. AGODOA: Well, I was impressed that a lot of the  
18 comparative data was on temporary venous access and, yet,  
19 this is really going to market as permanent access, not  
20 really temporary access.

21 DR. LINDBERG: I think there are a couple of answers to  
22 that question. Number one is that the point is that TVAs,  
23 when you have to keep putting them in and taking them out,  
24 you use up sites, where there is a greater risk of higher  
25 clotting, infection incidence and the risk of placing TVAs

1 in and out, in and out in these very complicated patients.  
2 that we are describing. That is pretty much why it was  
3 compared to TVAs.

4 DR. VERTUNO: The question I have is, and this is for  
5 my vascular surgeon colleagues where I work -- you have two  
6 choices, to place a permanent access or to place a temporary  
7 venous access. But I think if we place the permanent access  
8 at the same time we place a temporary venous access, we can  
9 pull the temporary venous access in a couple of weeks and we  
10 would have the long-lasting PTFE graft in place. We don't  
11 do that at our place, to my perpetual dismay, but I think  
12 that would solve part of the problem.

13 I was comfortable with your data comparing your graft  
14 to the standard PTFE graft. I think it clearly showed that  
15 it works earlier and doesn't last as long. I think if we  
16 had data comparing the use of this graft with optimal use of  
17 central venous access with appropriate placement of the  
18 standard PTFE graft, we could get data, an area under the  
19 curve, so to speak, in six or eight years and find out who  
20 really has had the longer successful access and less  
21 complication rate. But that is a study that is yet to be  
22 done and will come from experience.

23 This question occurred to me, why do you think the  
24 patency rates -- is this the thrombogenicity of the  
25 material? I would assume it clots faster when you take

1 somebody off dialysis for the same reason that the graft  
2 doesn't last as long. If anybody has any insight into that,  
3 I would appreciate it.

4 DR. GLICKMAN: I think there are several answers to  
5 that. I don't know the real answer. Schematically, one  
6 would think that this graft would have a little higher  
7 patency rate because silicone has been shown to decrease the  
8 incidence of minor intimal hyperplasia in the venous system.  
9 We did not see that. But I think the size of the vein --  
10 vein size has a significant impact on the patency rates of  
11 this graft. I think the larger the vein in the upper  
12 extremities and the legs, the performance that we have  
13 looked at within our practice, is comparable. So the size  
14 of the vein is very important. And, I think the high flow  
15 that this graft achieves may be increasing a lot of  
16 turbulent blood flow, therefore, increasing the incidence of  
17 intimal hyperplasia at the venous link.

18 DR. AGODOA: So, is the failure really at the distal  
19 anastomosis?

20 DR. GLICKMAN: Yes, the majority of the time it is at  
21 the venous link.

22 DR. STENOIEN: I am Mark Stenoien, with Possis Medical.  
23 I am the director of vascular graft product development. We  
24 did look at the clinical data to determine whether --

25 DR. CURTIS: Would you state your financial interests?

1 DR. STENOIEN: I am an employee of Possis Medical.

2 DR. CURTIS: Thank you.

3 DR. STENOIEN: We did look at the clinical data to  
4 determine whether there was a correlation between graft  
5 patency and flow rate. It was a non-statistically  
6 significant trend, but it did appear, as Dr. Glickman has  
7 indicated, that there was a trend towards roughly equal  
8 patency in the patients who had larger venous outflow. It  
9 was not reported, however, in our submission because it was  
10 not significant.

11 DR. CURTIS: Do you have any other questions or  
12 comments?

13 DR. AGODOA: No.

14 DR. CURTIS: Okay. Dr. Freischlag?

15 DR. FREISCHLAG: Certainly, in our vascular surgery  
16 discussion over the last two years, we feel that the best  
17 graft is not one of prosthetic nature at all for the  
18 dialysis patients, and I think we all agree that the best  
19 graft actually is autologous. There has been a big move in  
20 the country now to help us do that for some of the same  
21 reasons that he suggested, having earlier referral, as Dr.  
22 Lindberg pointed out, and to create an autologous fistula  
23 which would require some sort of temporary access for the  
24 maturation time, which is sometimes four to six weeks.

25 One of my concerns with the Perma-Seal graft is that it

1 is an easy fix in the sense that unless we watch who it is  
2 going to be placed in, you could place it in a patient and  
3 it could be used tomorrow, and that sounds pretty easy for  
4 everybody, however, it does have some limitations because of  
5 its complications. Therefore, I think specific patients,  
6 which you all have mentioned, such as those on Coumadin or  
7 those with proven central venous occlusions could be  
8 candidates for this graft. However, there is a real doubt  
9 in my mind that people may just pay attention to only that  
10 because of the quick fix thought, sort of the microwave  
11 generation -- if you can get it done in ten seconds, it is  
12 great. It is certainly easier than waiting for six weeks.

13 I have quite a few questions --

14 DR. GLICKMAN: Could I just answer one thing? One  
15 thing with this study, it took us four years to enroll  
16 patients, and that is because within our appropriate  
17 institutions autogenous access is the route that we all  
18 attempt to achieve. And, people say, "what took you so  
19 long, enrolling patients, trying to do best for the  
20 patients?" Access prosthetic graft in either type of  
21 situation is not our first-line course, our first-line  
22 course is autogenous graft. So, that is why it took a long  
23 time, since 1993, to conclude this study, because autogenous  
24 access in all of our practices is the first-line of choice.

25

1 DR. FREISCHLAG: I just felt that I needed to state  
2 that in our discussion --

3 DR. GLICKMAN: And, I needed to tell you that we just  
4 didn't put prosthetic grafts in anyone who walked in.

5 [Laughter]

6 DR. FREISCHLAG: I have quite a few questions. The  
7 first one, I want to go back to this intervention. I did  
8 read your 4-5, but I don't understand it. In intervention  
9 less than 30 days and greater than 30 days, I want to know  
10 did the graft clot. Were you doing intervention because  
11 there was a stenosis and you noted decreased flow rates, or  
12 were they thrombosing and you intervened? Certainly, we all  
13 know that can have an impact on what happens to the graft.  
14 So, even though you do tell us what interventions were done  
15 in each of the grafts and in what time frame, I don't know  
16 what the interventions were for. So, I am very interested  
17 in that -- maybe it is because I am a vascular surgeon -- to  
18 know if there were differences between stenosis versus  
19 thrombosis in the patients.

20 I too am a little concerned about the comparison to the  
21 temporary venous catheter. I think the group of patients  
22 that you are reporting to us from the study that was done on  
23 the HCFA patients tells about a group of patients that have  
24 a lot of problems anyway. They had temporary venous  
25 catheters, it seems to me, because they were dialysis

1 problem patients and, therefore, the fact that they had  
2 trouble with their graft, I am not sure, is due to the  
3 temporary venous catheter or if it just happened to occur in  
4 those patients. Therefore, I guess I wanted an explanation  
5 from you why you thought that having a temporary venous  
6 catheter in you causes your access site to have problems  
7 when we know subclavian stenosis is not present in all those  
8 patients. I have a feeling patients are just high risk  
9 patients and they do bad no matter what you do to them.  
10 Therefore, I guess I would like you to tell me a little bit  
11 more about that group of patients because I have a feeling  
12 we may just be describing a population that has a bad time  
13 anyway.

14 I wanted to ask the vascular surgeon how is the graft  
15 sewn? It seems very stiff, and if you have to go to an  
16 intervention, is it easier than ePTFE or more difficult to  
17 cut down upon it and to operate upon it? Did you have  
18 problems reclosing it, and were there issues with the  
19 reclosure suture lines, or was it easier? I wanted to know  
20 a little bit about its handling.

21 Then, my last comment was about the complications. I  
22 was real concerned that there were a lot of infections in  
23 the Perma-Seal graft, and that 37 of them had to be  
24 explanted versus 15 in the PTFE group. Explantation is  
25 something I don't do that often with these kind of grafts,

1 and it is usually because of infection. When I reviewed all  
2 of those descriptions of each patient, it seemed that 80% or  
3 90% of them were explanted for infections. And, once you do  
4 that, you do lose a site for dialysis, and that makes me  
5 very concerned that there is such a high explantation rate.

6 I also didn't understand the differences between  
7 aneurism and pseudoaneurism in your complication list, and  
8 why sometimes infection and aneurism was a major  
9 complication and sometimes it was a minor complication. If  
10 you could maybe explain to me how you have minor infection  
11 or minor aneurism or minor pseudoaneurism, that would be  
12 helpful to me.

13 So, I guess maybe you could answer my questions and  
14 then I will save my final comments until after I hear what  
15 you have to say.

16 MR. GUSTAFSON: You had a series of questions. I will  
17 see if I can traffic direct here and get the right people to  
18 address them. Let's start with the last question first, and  
19 that had to do with the definition of minor complications  
20 and major complications, and how we drew that distinction.  
21 Carolyn Modlin, our manager of graft clinical research will  
22 address that.

23 MS. MODLIN: Carolyn, Modlin. I am employed by Possis  
24 as manager of graft clinical products.

25 Our major complication was defined as any complication

1 that was an aneurism, pseudoaneurism or required  
2 intervention. A minor complication did not require  
3 intervention, surgical intervention and, therefore, an  
4 infection that may have been treated with antibiotics was a  
5 minor complication, and infections that required surgical  
6 intervention was a major complication. Any aneurism or  
7 pseudoaneurism was considered a major complication by our  
8 definition, and those were determined by the site as to how  
9 they determined aneurism or pseudoaneurism. Possibly Dr.  
10 Glickman can address a little better how that would be  
11 determined at the site.

12 MR. GUSTAFSON: Dr. Glickman, could you talk briefly  
13 about that?

14 DR. GLICKMAN: I am going to try to answer all of your  
15 questions, if I can. Explant -- why did we explant as many?  
16 I guess, as I think about this, we probably treated this  
17 graft differently than we treated ePTFE grafts. This was an  
18 unknown graft material. This wasn't a blinded study. I  
19 mean, we knew if we had ePTFE; we knew if we had Perma-Seal.  
20 So, I think that we treated this in what we would consider a  
21 conservative route by removal of the graft, explanting the  
22 graft when it became infected. So, I think we were a little  
23 bit more aggressive surgically because we did not have any  
24 clinical experience of what was going to go on, and we  
25 wanted to follow a fairly conservative route in dealing with

1 this problem. That is number one.

2 Handling -- it sews very easily. It is a little  
3 stiffer than ePTFE. There is a learning curve in how to  
4 deal with this graft, finding the vein; going into deep  
5 corners high in the axilla, smaller veins -- it is a little  
6 bit more difficult. In sewing you use fewer sutures because  
7 it doesn't bleed. Anastomosis on one side would probably  
8 take about six sutures on either side. There is no bleeding  
9 through any of the holes. Thrombectomy -- the core comes  
10 out with one pass of the embolectomy catheters. It is  
11 easier to thrombectomize than with conventional PTFE. There  
12 is no adherent pseudo intima for the Perma-Seal graft, as  
13 opposed to what we sometimes see with PTFE grafts.

14 Aneurism formation -- it was defined by center. If  
15 they saw some swelling and it was not significant -- I found  
16 some of that data a little bit confusing in how it was  
17 stated. Pseudoaneurism is a pseudoaneurism, is a  
18 pseudoaneurism. So I don't think that that is defined as  
19 well.

20 Infection rate was increased, and I think, looking at  
21 some of the data in a little different detail, because of  
22 the incidence of increasing our interventions, i.e.,  
23 thrombectomy or for steal, etc., when we did have an  
24 intervention it increased the risk of infection. In fact,  
25 we looked at this subset of patients and per incidence of

1 intervention the PTFE and Perma-Seal incidence was the same  
2 per intervention, but because interventions were more often  
3 for the Perma-Seal, that is why the infection rate was a  
4 little higher in that group of patients.

5 DR. FREISCHLAG: I guess I still want somebody to  
6 comment a bit about the HCFA data and talk to me a bit about  
7 my question about how you are correlating those two things  
8 together.

9 DR. LINDBERG: Well, first of all, one of the first or  
10 second questions you asked about was why these sick, sick  
11 patients -- why we are looking at them in terms of why this  
12 graft was a choice for them. The two I presented didn't  
13 have any other options. I don't have any other options in  
14 my practice. This was an option. It is a trade-off option,  
15 as you so well described and the whole group has, but there  
16 are trade-offs in a lot of things we do when we make choices  
17 for patients I think in all of our areas. It has a trade-  
18 off, but it was an option for these patients and it worked.  
19 But I think it are very clearly areas that it works better  
20 in, and I think Dr. Glickman has referred to that in terms  
21 of the vessel size, etc.

22 DR. CURTIS: Dr. Roberts? Maybe you want to introduce  
23 yourself since you were a little bit late.

24 DR. ROBERTS: Yes, I apologize for coming in at the  
25 last minute, and I also apologize if I ask questions that

1 were covered. It is simply that I missed the presentations.  
2 I am Dr. Anne Roberts. I am an interventional radiologist  
3 at UC San Diego.

4 I share I think maybe some of the other panel members'  
5 concerns. One I am very concerned about is this infection.  
6 In this group of patients, I think 33% was the number that I  
7 saw for these patients, which is way higher than the other  
8 group. Now, I agree, in looking at the patient descriptions  
9 of the events that went on and the complications, when you  
10 read those descriptions it does seem to be that it is due to  
11 the increased need to do some kind of intervention on these  
12 grafts. But I think that that just points out the fact --  
13 and excuse me if I misunderstood the graphs that you showed,  
14 but my understanding from looking at the graphs is that the  
15 major complications are above and beyond the thromboses. In  
16 other words, thromboses are one group, and they show that  
17 this graft does not work very well in terms of thromboses.  
18 But the major complications, which are also significantly  
19 higher in this graft, are above and beyond thromboses. So,  
20 it does, I think, raise some real concerns about using this  
21 graft in terms of the thromboses and the increase in  
22 infections.

23 One of the other things that I am pretty concerned  
24 about, and I think this probably goes along with Dr.  
25 Freischlag's concerns, is that I understand why you might

1 view the use of temporary venous access as a bad thing, and  
2 it certainly is, and I think that anything that we can do to  
3 avoid the use of these temporary catheters is all to the  
4 good. On the other hand, if you are trading a temporary  
5 catheter with a PTFE graft that is going to stay and give  
6 you better patency, what is the cost -- and you are looking  
7 at a lot of this in terms of cost of putting in these  
8 temporary catheters, you know, and that it is a little more  
9 expensive to do that -- well, can somebody give me the  
10 numbers of what it costs to put in -- you know, basically it  
11 looks like half of these grafts fail in, you know, less than  
12 nine months. What is the cost of having to replace those  
13 grafts every time? Has anybody looked at what that cost  
14 might be?

15 MR. GUSTAFSON: The study did measure costs. Perhaps  
16 Dr. Glickman can talk briefly about what it takes to revise  
17 Perma-Seal graft, and for how long the graft is out of  
18 service when a revision takes place.

19 DR. GLICKMAN: I guess it would be the operating room  
20 cost and the cost of thrombolytics and angioplasty, the same  
21 costs that would pertain to a PTFE graft -- operating time,  
22 in and out surgery, utilization of the graft immediately  
23 after that.

24 Complication rates -- I think we know that the  
25 infection rate is increased, but this is probably secondary

1 to the number of interventions, interventions being  
2 thrombosis probably because of a small vein that was  
3 utilized, or the steal phenomenon that occurs requiring  
4 intervention as well. I think there was some data there  
5 with interventions causing thrombosis. But the cost would  
6 be the same as the cost of revising a standard PTFE.

7 DR. ROBERTS: Yes, but what I am saying is that it  
8 looks like it is, you know, double or triple the number of  
9 times that you would revise, or that you would have patency  
10 in terms of the PTFE.

11 DR. GLICKMAN: Well, again, we didn't collect the data  
12 on the economics of this and the comparison of the temporary  
13 venous catheter to this. It isn't really what I would  
14 consider part of a decision-making process at this time.  
15 But it is two times -- it is not three times, it is two  
16 times the incidence of requiring an intervention.

17 DR. ROBERTS: Well, the reason I bring this up is that  
18 I think that when we start looking at the indications for  
19 which patients should get this, I mean, one of the proposed  
20 indications is in patients where you want to avoid, you  
21 know, temporary venous access. Well, that is 100% of the  
22 patients. You don't want to put a temporary venous access  
23 in anybody.

24 But what I am saying is that I think we are going to  
25 have, you know, some stricter indications in terms of

1 patients because I agree with Dr. Freischlag that one of the  
2 concerns that I have is that, you know, people are going to  
3 start wanting to use this because of your patient who says,  
4 "hey, doc, I'd like to have that graft because I don't have  
5 to sit here for another ten minutes," are you going to  
6 explain to them, yes, that is right but they are going to be  
7 in three times as often to get your graft declotted than the  
8 guy who is waiting ten more minutes, and give them the  
9 trade-off? You know, do you want to be in, having  
10 thrombolysis and angioplasty or having a thrombectomy? You  
11 know, is ten minutes worth it? That is where I have my  
12 concerns. I agree, I think the patients who are on  
13 Coumadin, who are going to have trouble with bleeding, that  
14 may be a very good patient population for these grafts, but  
15 I have my concerns about -- now, the marketplace may also  
16 speak to that.

17 DR. GLICKMAN: I would say two things. I feel that the  
18 marketplace is going to make a statement, number one.  
19 Number two, I don't feel that this should be designed for  
20 every patient, or be safe for every patient who needs a  
21 prosthetic AV graft. I tried to say that in my talk. There  
22 is a decision matrix for a very complex group of patients  
23 that often need something like this. But I don't think for  
24 Mary Jane, who is going to have a temporary venous catheter  
25 for two weeks -- PTFE is probably the right way to go with

1 that patient. So, I think what you are saying is correct,  
2 that just because it is more convenient in the dialysis unit  
3 is not necessarily what we want to look for all the time.  
4 But I think it does have a place in the decision matrix that  
5 goes on.

6 DR. ROBERTS: Let me just ask you what would be your  
7 indication for putting this graft in?

8 DR. GLICKMAN: Well, I showed that with my decision  
9 matrix. The morbidly obese patient is certainly a patient  
10 population that we think it has excellent value because  
11 these patients are very difficult patients to manage from a  
12 prosthetic graft placement and from a temporary venous  
13 catheter placement. Number one.

14 Number two, the chronic Coumadin, the patients who are  
15 on warfarin because of various medical conditions, either a  
16 hypercoagulable state, DVT, mitral valve replacement. That  
17 is number two.

18 Number three, the patients who are elderly, who need  
19 urgent dialysis and who need high flows. Those patients we  
20 would consider to be utilizing this.

21 All the patients in that decision matrix that we  
22 discussed would be patients that I would be concerned about.  
23 Patients who have absent central veins, who have one vein  
24 left, femoral vein. What are we to do? Because if we put a  
25 temporary venous catheter, I will tell you that the

1 incidence of infection is going to be increased in those  
2 patients.

3 DR. ROBERTS: So, basically what I am hearing is that  
4 the morbidly obese, patients on chronic anticoagulation, and  
5 patients where there is only --

6 DR. GLICKMAN: Absent central vein.

7 DR. ROBERTS: Okay, absent central vein.

8 DR. SIMMONS: First of all, I guess not having to deal  
9 with, you know, constantly finding venous access for chronic  
10 use like this, I guess I approach looking at this a little  
11 differently. Somehow, it seemed to me if I had one site  
12 left to get this patient's lifeline, this would not be the  
13 device I would choose. If I had one site left in the sort  
14 of patient which you have been describing throughout this, I  
15 want a device that was going to last longer, or have the  
16 highest chance of lasting the longest. You know, you keep  
17 bringing up this patient with one vein left. Well, if that  
18 guy has one vein left, wouldn't you really want to use a  
19 device that is going to last the longest, not the least?

20 DR. LINDBERG: What are you going to use until the PTFE  
21 is ready to stick for two weeks?

22 DR. SIMMONS: Like I said, I don't do this, but I guess  
23 you are saying that this is a critical patient, and if this  
24 is the only access that you are ever going to have, wouldn't  
25 it be better to go with something temporary until you can

1 get --

2 DR. LINDBERG: When you have one site left, you may  
3 have ended up sticking it already with a temporary venous  
4 catheter because you have no other way to dialyze that  
5 patient. You have one point left and this could be stuck  
6 the next day.

7 DR. SIMMONS: That has to be a rare patient where you  
8 can't get some venous access.

9 DR. LINDBERG: I can tell you in my population, this  
10 past year, we took care of nine patients in that situation.  
11 Of those nine patients, five of them had been on dialysis  
12 longer than twenty years, and they exist.

13 DR. CURTIS: As a follow-up to that, then a year from  
14 now when this thing doesn't work any more, what do you do?  
15 Do you put another one in?

16 DR. LINDBERG: You would put another one in if you can  
17 stick it right away. It is a very difficult patient.  
18 Usually these patients die, and they usually don't have  
19 options. You keep them in the hospital and you stick  
20 femoral Quintons in them every third day, and you keep them  
21 at bed rest. You can only do that so long. They aren't the  
22 most common patient. I agree with you.

23 DR. SIMMONS: I mean, using your logic, the same logic  
24 that you were just bringing up, that is, you know, that  
25 patient has that one venous access and this device is least

1 likely to last longer, but it is also more likely to have to  
2 be removed because of infection, and you are going to lose  
3 that access completely forever.

4 DR. LINDBERG: In terms of the issues with infection --  
5 I am not a surgeon, but Dr. Glickman's opinion is that more  
6 intervention, certainly, puts the patient at risk for more  
7 infection, which we all know to be true. I think the larger  
8 vessels work better for this graft. The two patients I had  
9 that had compassionate use still have their grafts. They  
10 are in the femoral area.

11 DR. SIMMONS: I guess, if I can read 4-12, it has Table  
12 2, summary of clinical trial results, and in the control  
13 group there is a 50% risk of some major complications in 30  
14 days. To me, looking at that number, it seems a very large  
15 number. Like I said, I am a cardiologist; I don't deal with  
16 this, but 50% major complication rates in 30 days, is that  
17 common? Is that standard?

18 DR. ROBERTS: It is under Tab 3, page 12. Actually,  
19 while we are on that table, I couldn't quite figure it out  
20 from the way that the data was laid out, it looked like the  
21 time to the first hemodialysis access in both of these  
22 groups was almost 30 days. I am assuming, although I am not  
23 sure, that these numbers included the patients before you  
24 were allowed to do the early. What were the numbers if you  
25 were to take that set of patients out? I am not sure if I

1 knew where that was. Sorry, I didn't mean to interrupt you.

2

3 DR. SIMMONS: Oh, it is okay.

4 MR. GUSTAFSON: The table that is in Tab 3, labeled  
5 summary page 4 and stamped page 12, is from the original  
6 summary of substantial equivalence from the 510(k), in  
7 August. The data that was presented here this morning is  
8 updated through a couple of months ago. So, the data, Dr.  
9 Roberts, that you are referring to is out of date. What we  
10 presented this morning is the most current. We do have a  
11 slide, Dr. Roberts, that perhaps you missed. I am trying to  
12 find it, that would address your question.

13 In your slide set that you got at your table this  
14 morning, the first set of the three sets, page 9, the first  
15 of those two slides shows the cumulative frequency  
16 distribution of when the first stick occurred. About half  
17 way through the enrollment period the Perma-Seal patients  
18 received the option of getting first stick as early as same  
19 day of surgery. Once that became available, a majority of  
20 Perma-Seal patients took that option, either because they  
21 needed it or wanted it. But, of course, because of the  
22 randomization and the patient selection criteria, not all  
23 did need it. This study did not limit itself to those  
24 patients who only needed urgent dialysis access, but here  
25 you see that there were a significant number of patients

1 from the cohort overall that received first access quite  
2 early.

3 DR. AGODOA: A follow-up question, Dr. Glickman, from  
4 your report and your answers to some of these questions, I  
5 think, if I understand you correctly, the increased rate of  
6 thrombosis and the increased rate of infections in the  
7 Perma-Seal -- you attribute these to small vein size and,  
8 therefore, I guess what I gather from your presentation is  
9 that this particular device is ideal for or suitable for  
10 patients who have relatively large vessels. Yet, some of  
11 the patients in whom you think this is indicated are  
12 patients who typically have small veins, or not really large  
13 veins. It makes it a little bit difficult to marry these  
14 two.

15 DR. GLICKMAN: Well, I think because you are morbidly  
16 obese, it doesn't mean you are going to have small veins.  
17 The morbidly obese can have large veins in the axillary  
18 region, femoral region, etc. So, you may have large veins  
19 in any of these patients.

20 DR. AGODOA: But there are a lot of diabetic patients.

21 DR. GLICKMAN: Their arteries may be small but the  
22 veins may be normal. Diabetics can have normal veins, as  
23 non-diabetics.

24 DR. AGODOA: Well, typically, the individuals in whom  
25 we put these grafts are individuals who don't have very

1 large veins.

2 DR. GLICKMAN: Large superficial veins.

3 DR. AGODOA: Right.

4 DR. GLICKMAN: But they may have a basilic vein or an  
5 axillary vein that is satisfactory.

6 DR. AGODOA: So, as a surgeon, once you go in, if you  
7 have a choice and you go in to put an access in -- if I  
8 refer a patient to you how do you gauge the size of the vein  
9 and, therefore, would prefer PTFE?

10 DR. GLICKMAN: By measuring the size of the vein,  
11 looking at the vein, seeing its adequacy, and clinical  
12 experience in measuring size; 3 mm veins are probably too  
13 small; 4 mm, 5 mm are adequate.

14 DR. AGODOA: So, that would be your advice to surgeons  
15 who have a choice.

16 DR. GLICKMAN: The size of the outflow vein.

17 DR. AGODOA: Thank you.

18 DR. SIMMONS: I have a couple of quick ones. I guess I  
19 agree, I suspect that the transvenous access complication  
20 rate must be overestimated. I know putting in permanent  
21 pacemakers in, and putting in two, three and four or five  
22 wires in some of these subclavian veins that have been there  
23 for years and years -- we go back in and pull those things  
24 out. I mean, it is anecdotal, but you have certainly  
25 presented a lot of anecdotal data here as well. I don't see

1 70% venous occlusions.

2 DR. GLICKMAN: Can I answer that?

3 DR. SIMMONS: Sure.

4 DR. GLICKMAN: The difference between what you are  
5 dealing with and what we are dealing with is the turbulent  
6 flow that develops during dialysis. If you look, what  
7 happens is that turbulent flow, that eddy current, occurs  
8 within the vein. That catheter is flopping back and forth,  
9 causing neo-intimal damage to the vein, as opposed to a  
10 guide wire that is in place for a pacemaker. There is not  
11 much movement there except with the cardiac cycle. But with  
12 the high turbulent flow that occurs during hemodialysis,  
13 that is probably what is causing the constant irritation of  
14 that. Number one.

15 Number two, a large bore intraclavicularly, that angle  
16 and that compression from the clavicle with a larger bore  
17 diameter material does also accelerate problems, which you  
18 don't see with pacemaker wire.

19 DR. ROBERTS: I would agree. These venous accesses are  
20 very, very destructive to the vein, you know, when they are  
21 left in for a long period of time. If they are left in for  
22 a short period of time, particularly if they are put through  
23 a right jugular approach, I don't think it is as much of a  
24 problem. But when they are put in through a subclavian  
25 approach and when they are left in for long periods of time,

1 they really do cause major problems.

2 DR. SIMMONS: But do you think it is 70% when they are  
3 left in for two weeks?

4 DR. ROBERTS: No, I don't think it is 70%, but  
5 oftentimes what happens is they get multiple ones.  
6 Unfortunately, I think there has been a trend towards -- at  
7 least I can only speak for our place, and there is a trend  
8 towards leaving these in for longer and, quite honestly, it  
9 is because the surgeons are busy and aren't able to get the  
10 grafts put in for a while. So, sometimes it is just left in  
11 because of that.

12 DR. SIMMONS: One last comment, I would actually  
13 suggest that patients who have mitral valves, aortic valves,  
14 who have anticoagulation for other cardiac reasons may not  
15 be good candidates for this device because of your very high  
16 risk of infection. I mean, I agree from your standpoint  
17 that getting venous access is important, but from a  
18 cardiologist's standpoint, having 50%, 33%, whatever it is,  
19 occurrence rate of infections and bacteremia on a prosthetic  
20 valve is not thought to be a good thing either. Maybe those  
21 patients should be excluded as potential candidates.

22 DR. CURTIS: Mr. Jarvis, any comments?

23 MR. JARVIS: No.

24 DR. CURTIS: Dr. Altman?

25 DR. ALTMAN: In the manual, under Tab 2, labeling page

1 5, it says "patient manual," but there is nothing there.  
2 Has information been provided to the patients? If so, what  
3 is that information?

4 DR. LINDBERG: The information provided to the patients  
5 in terms of the study was the consent form. In addition, in  
6 our institution, we do a fifth grade level description of  
7 the study that is IRB approved, that they keep with them.  
8 That is the study.

9 In terms of the access itself, it varies between  
10 institutions. In our institution we have an actual task  
11 force for patient education and we give them an entire book,  
12 and we show them a video, again at fifth grade level in  
13 Spanish and English, which is appropriate for where I live,  
14 to describe how to take care of the access. It tells you if  
15 your access is red, or infected, or tender, or clotted,  
16 etc., what to do. That is pretty standard to give the  
17 patient information like that in either the dialysis unit or  
18 from the vascular surgeon. I think it depends on the  
19 institution.

20 DR. ALTMAN: But now that we have done some trials and  
21 we have seen some patients, are these patients informed of  
22 the contraindications? Do they know that there has been an  
23 increased rate of infection in this study?

24 DR. LINDBERG: They know what happens to their grafts  
25 if they are one of the patients. We don't use the grafts

1 right now. The study is closed.

2 DR. ROBERTS: I understand that, but while they were in  
3 the study?

4 DR. LINDBERG: Well, during the study -- it was  
5 randomized and I was one of the last centers to use the  
6 graft. You know, I was not giving the patient that  
7 information, except there are some benefits in the consent  
8 form which really describe this, and that as an IRB-approved  
9 consent form.

10 MR. GUSTAFSON: The interest in a patient manual, once  
11 a product is brought to the market, is a recent one that was  
12 suggested by FDA, and we are prepared to do that, depending  
13 the outcome of this meeting, to work on an appropriate  
14 patient manual which would be included in the package  
15 labeling.

16 DR. VERTUNO: You know, it is really interesting.  
17 Language is very important. We are talking a lot about  
18 temporary venous access, but I don't think it is any  
19 accident that the trade-in for what we use is called Perm-  
20 Cath, and I think that is what gets us into trouble. If you  
21 were to work at the institution where I work, where our  
22 radiologist is conscientious, interested and helping us with  
23 the patient population, and our vascular access surgeon is  
24 not, we have an inappropriately high use of temporary venous  
25 access for long term.

1 I think what is clear is that this device has an  
2 advantage. It is for a relatively select, small population.  
3 The data that I would really like to see is to take two  
4 groups of patients who needed immediate dialysis, one group  
5 that had this in and another group that had temporary venous  
6 access and a standard PTFE catheter put in at the same time  
7 or within a few days, and used in its appropriate time  
8 frame, two or three weeks, and look at the data three years  
9 down the road. The problem with the temporary venous  
10 catheters is their long-term use, not if they are used for  
11 ten days or two weeks. I think that would help us better  
12 define the population that would benefit from this type of  
13 device.

14 DR. FREISCHLAG: I have another question regarding your  
15 interventions. When you went back to intervene on the  
16 Perma-Seal grafts, you said because you did that, that led  
17 to increased infection. If it is because of increased  
18 thrombosis or increased stenosis at the venous end, and most  
19 of us believe intimal hyperplasia may be due to non-  
20 compliance, and because this is so stiff you may have more  
21 non-compliance on vibration, were you ever tempted to put  
22 PTFE at the venous end next to this, and would that be  
23 something to think about? This would be great to stick and,  
24 actually, what is nice sometimes is if you fix a  
25 pseudoaneurism you sort of circle it for the dialysis unit

1 and they go stick the other part that you didn't touch the  
2 next day, and they can still dialyze through it. Did you do  
3 that? Did you think about that? Is that something that may  
4 be the best thing, a combo?

5 DR. GLICKMAN: Yes, but we are not allowed to do that.  
6 This is where you get into a little bit of a problem with  
7 FDA. I think there is a role for that, personally. I am  
8 speaking for Marc Glickman. But within our study the  
9 definition was well defined in 1993, with some minor  
10 changes, but I do think that the compliance mismatch is  
11 important although, as you note, the literature goes up and  
12 down on how important compliance mismatch is to formation of  
13 neo-intimal hyperplasia. But I do think what you are saying  
14 is suspect to a lot of good ideas.

15 DR. CURTIS: Not being a nephrologist or a vascular  
16 surgeon myself, I would like to get a point of information  
17 to understand this better. Why is it that earlier access is  
18 possible with this graft compared to the PTFE? What makes  
19 you have to wait with those other ones to mature, and why is  
20 this different? Was that something that you suspected from  
21 the design of this in the first place, that it was going to  
22 be something that you could stick earlier?

23 DR. GLICKMAN: There are several ways that I can answer  
24 that. One is that the design intrigued me when they first  
25 brought it to my office, in 1993. The silicone elastomer, I

1 thought, had the potential of being able to be accessed  
2 early without bleeding. It is kind of self-sealing.

3 The PTFE is not approved by FDA for early access, and  
4 the reason for that is the perigraft hematoma formation  
5 which can develop because ingrowth has not occurred. The  
6 graft is not sealed after decannulation of the material and,  
7 therefore, one can have either bleeding to the surface or  
8 bleeding perigraft in the tunnel. But the FDA has not  
9 approved that.

10 So, we had to monitor a little bit what is approved  
11 presently on the market to what the situation is. Number  
12 one. Number two, again, self-sealing by the silicone  
13 elastomer --

14 DR. CURTIS: You thought it would be less likely to  
15 cause hematoma formation early on.

16 DR. GLICKMAN: And our sealing time demonstrated that.  
17 As the study evolved, we saw that the sealing times were  
18 real, and so we did that study for about a year and a half  
19 and then saw that sealing times were occurring, and then we  
20 sent an addendum to the FDA to attempt early access.

21 MR. STENOIEN: I just wanted to follow-up on that  
22 question.

23 DR. CURTIS: Go ahead.

24 MR. STENOIEN: Yes, this graft was designed for early  
25 access, both by the selection of the material, which is an

1 elastomeric material, and also in the structure of the wall  
2 which prevents serum leakage in the early post-implant  
3 period and allows rapid sealing. That has been well  
4 characterized in bench studies, long before we entered the  
5 clinical trial.

6 DR. CURTIS: Thank you. In Tab 5, under "clinical  
7 summary," page 16, there is a list of all the major  
8 complications of the Perma-Seal graft versus the control.  
9 There are several that jump out and that have been mentioned  
10 all along -- the difference in the rate of aneurism,  
11 infection, pseudoaneurism, thrombosis. I was just  
12 wondering, are there any thoughts as to why there might be  
13 some of these differences, particularly with the infections?  
14 In terms of thrombosis, I think I can understand that with  
15 the fact that it seals easier and that there is less  
16 bleeding than with the other ones. But do you have any  
17 clues as to why there are some of those differences? Might  
18 it be anything in the study patients themselves as a clue to  
19 why there would be a difference in the infection rate, for  
20 example?

21 DR. GLICKMAN: I think, again, a thrombotic event  
22 increased the incidence of infection within the graft. We  
23 have data that should have been part of this but we just  
24 recently looked at it. But 90 days or 120 days out from an  
25 episode the infection rates were similar between the PTFE

1 and the Perma-Seal, but within 90 days after an intervention  
2 our infection rate increased with this graft. My feeling is  
3 that thrombosis occurred, intervention occurred and then we  
4 saw the introduction of infection and that complication  
5 occurred afterwards.

6 Other than that, I think that pseudoaneurism -- I think  
7 all those things are comparable between the control and the  
8 Perma-Seal graft. Steal was a little bit higher with the  
9 Perma-Seal graft. I think it is because of a little bit of  
10 the stiffness of the graft compared to the PTFE.

11 DR. VERTUNO: Could you comment on the problem with  
12 skin erosion compared to the PTFE?

13 DR. GLICKMAN: Yes, again, I think because of the  
14 larger size graft, until we got an adequate tunneling device  
15 that we use now, skin erosion was a problem but with the new  
16 tunneling device that came in later in the study, that  
17 decreased our incidence of skin erosion.

18 DR. ROBERTS: Excuse me, could I ask why you think this  
19 graft causes steal? Or, at least there seems to be an  
20 association? I mean, there is a higher incidence of steal,  
21 which is not a terribly common problem in the first place.

22 DR. GLICKMAN: As you see on that same page, page 16,  
23 there were 7 in the control and 12. So, it is a little  
24 higher. I don't know if it is statistically different, but  
25 because the graft is a little bit less flexible, a little

1 bit more non-compliant, perhaps the higher flows cause more  
2 blood to want to go through the graft as opposed to going  
3 down in the arm.

4 DR. ROBERTS: Because it is less compliant?

5 DR. GLICKMAN: Yes, it is firmer. Blood would go to an  
6 area that would have perhaps less resistance, if you think  
7 of what causes steal.

8 DR. ROBERTS: Steal is usually because there is less  
9 resistance --

10 DR. GLICKMAN: And higher flow through the graft.

11 DR. ROBERTS: -- less resistance in the graft than  
12 there is in the distal vessels. I don't know, maybe it is  
13 because there were more diabetics, or something or other.

14 DR. GLICKMAN: We are showing that there are a little  
15 higher flow rates through this graft as opposed to PTFE.  
16 So, your higher flow rates through the graft could possibly  
17 increase the incidence of steal.

18 DR. FREISCHLAG: Were you also making your venous  
19 anastomoses a bit larger?

20 DR. GLICKMAN: No.

21 DR. FREISCHLAG: They were the same?

22 DR. GLICKMAN: Yes, that is a problem. That is one of  
23 the things that we looked at. They were the same -- perhaps  
24 a little larger than our PTFE. Because of the way the graft  
25 angles you are able to get a little smaller vein anastomosis

1 with PTFE than with your Perma-Seal.

2 DR. CURTIS: There is a table in the tab after 5, and  
3 the page is labeled, "HCFA database analysis, page 2 of 6."  
4 I have seen this table. I think you showed it on a slide.  
5 I wasn't quite following it. I just want to make sure I  
6 understood. From the table, events by catheter use, there  
7 has been graft only versus all the other ones. Temporary  
8 catheter to me means the temporary venous catheter that you  
9 have been talking. What is graft and what is Perm-Cath?

10 DR. LINDBERG: This is the description from Dr.  
11 Collins. Perm-Cath is a catheter that is tunneled under the  
12 skin and put directly into the vessels of the upper thorax.  
13 It depends which vessel, depending on what is available. It  
14 is a temporary but more permanent catheter. It is softer.  
15 A temporary catheter, as Dr. Collins described, is harder --  
16 usually the brand name is Quinton -- under the subclavian or  
17 in the IJ. It is a harder catheter. You sew it in by a  
18 little butterfly device on the side of it. That is what he  
19 described as temporary.

20 Often you will see a patient who will have an AV  
21 fistula placed to mature. The vascular surgeon will put a  
22 Perm-Cath in because it might take up to two months to  
23 mature. Sometimes they will have an AV fistula in, the  
24 Perm-Cath that quits working, and they end up with a  
25 temporary catheter because this becomes clotted. That is

1 what he is describing. I did ask him myself. That is why I  
2 am able to answer your question.

3 DR. CURTIS: So, the graft itself refers to either an  
4 AV fistula or a PTFE?

5 DR. LINDBERG: Either. It doesn't differentiate in his  
6 work between autologous or prosthetic.

7 DR. CURTIS: And this Perm-Cath is another form of a  
8 temporary catheter? He just called it that?

9 DR. LINDBERG: He called it a Perm-Cath because we call  
10 them permanent. They are permanent temporary catheters in a  
11 sense.

12 DR. CURTIS: But there is an external --

13 DR. LINDBERG: Yes, it looks like a Hickman. It really  
14 looks like a Hickman.

15 DR. CURTIS: All right.

16 MR. STENOIEN: I would like to make a couple of  
17 clarifying comments. The data that Dr. Collins worked with  
18 is from the HCFA national billing data. He was going by  
19 CPT-4 codes. The CPT codes differentiate between permanent  
20 catheter and temporary catheter. Typically, the permanent  
21 catheters are cut and are tunneled so that they do not exit  
22 directly from the venous site. But the actual definition in  
23 this study is did the attending physicians code them as a  
24 permanent catheter, or did they code them as a temporary  
25 catheter.

1           Also, the data we reported was for only synthetic  
2 vascular grafts. We did several cuts of the data. We  
3 looked at natural autogenous and the results really were not  
4 a lot different. We also looked at catheters placed before  
5 the graft placement and, again, the results were very  
6 similar. So, we used a subsection that we felt was the most  
7 conservative, in other words, patients who came to dialysis  
8 without a temporary catheter. They needed immediate  
9 dialysis and, therefore, a catheter was placed in order to  
10 obtain that dialysis.

11           DR. CURTIS: Thank you. I think this would be a good  
12 time to take a break. We will reconvene in 15 minutes.  
13 Thank you.

14           [Brief recess]

15           DR. CURTIS: Well, I am not sure anybody else has any  
16 more issues to bring up. Does anybody else on the panel  
17 have anything else they want to comment on or discuss?

18           DR. ROBERTS: Could I add one more request? I think I  
19 asked this before but I will ask it again. In looking at  
20 this HCFA data, my sense is that what you are trying to tell  
21 us is that by putting in this graft it is going to save the  
22 government money, which is an admirable thing, and that,  
23 hopefully, it is going to save the patient some adverse  
24 events, which is wonderful.

25           I would like you to show me, given the data that you

1 have presented in terms of the increased thrombosis rate and  
2 the requirement for surgery, either thrombectomy and  
3 revision or a new graft, what the aggregate cost of that is  
4 for a patient over a year.

5 DR. CURTIS: If I could make a comment on that first,  
6 for the FDA panel, we are charged with looking at issues of  
7 safety and effectiveness and we can't use cost issues to  
8 base our recommendations on.

9 DR. ROBERTS: No, but I think it would be an important  
10 thing to see in terms of adverse events, so that even if you  
11 don't give us the cost data, at least in terms of the  
12 adverse events in terms of you, you know, you were to say  
13 per patient per month -- I mean, you have a relative risk of  
14 events. Isn't that correct, in this chart? I mean, I think  
15 it would just be important for people to sort of see that in  
16 terms of this graft because we are talking about the  
17 collection of data that is grafts that are PTFE grafts. So,  
18 in other words, what we are seeing in this data is what the  
19 standard is, and then the standard graft plus the catheters  
20 and those kinds of things. I really think it would be  
21 important just to see what the adverse events are with this  
22 graft, you know, over a year or whatever it would be. I  
23 think that would be just important to sort of get a feeling  
24 for what we are talking about here.

25 MR. GUSTAFSON: Sure. In your panel pack at Tab 5,

1 summary page 12, Table 11 on that page has the total count  
2 of the number of patency salvage events, and then the rate  
3 per year calculated for both the Perma-Seal cohort and the  
4 PTFE cohort. Then again on page 15, the same table appears,  
5 this time tabulating the number of major complication  
6 events. So, if you just add those up you can come up with  
7 the total aggregate number of events per year for Perma-Seal  
8 and the number of events per year for PTFE. Then from there  
9 you can make some assumptions about how much those events  
10 cost. And then from those assumptions you can compare to  
11 the increased events that are suggested by the HCFA data set  
12 in the second tab.

13 DR. ROBERTS: Just extrapolating and doing this very  
14 quickly, it would mean, for example, that the relative risk  
15 of multiple events, if we looked at the HCFA database, under  
16 graft only it would be 1.2; grant and perma-cath would be  
17 1.7; graft and temporary catheter would be 1.4; graft,  
18 permanent and temporary catheter would be 2.15; and the  
19 Perma-Seal would be 2.8. Would that be fair?

20 MR. GUSTAFSON: Is that a fair way to do it? Those  
21 aren't comparable numbers.

22 DR. ROBERTS: Could you tell me what the comparable  
23 numbers are then?

24 MR. GUSTAFSON: No, we can't. That wasn't an analysis  
25 that was available to us. The HCFA data set shows relative

1 risk ratios, which is not the same as actually counting the  
2 number of events occurring in a year.

3 DR. ROBERTS: Oh, I see.

4 MR. GUSTAFSON: Whereas, in our data set we do that.  
5 So, the most we could do is give you a feel.

6 DR. CURTIS: Any other comments from any of the members  
7 of the panel? If not, we need to resume the open public  
8 hearing, which means that anyone who is not on the panel,  
9 who is in the room here who would like to make any comments  
10 about the issues that have been brought to the panel today  
11 can comment. Is there anybody who would like to speak?

12 I don't see anyone so, at this time, for the panel I  
13 would like to go through the questions that have been posed  
14 to us, and you can find that at the beginning of the panel  
15 pack, under Tab 1. These are the specific things that we  
16 have been asked to address and give recommendations to the  
17 FDA.

18 The first question we are being asked is, is there a  
19 population of patients in whom the risk/benefit of the  
20 Perma-Seal, in other words earlier access versus a lower  
21 patency rate and higher complication rate, may be  
22 considered?

23 Some of these things we were discussing this morning,  
24 including issues like the very obese patient, the patient  
25 who has very limited access, and the patient who is on

1 chronic anticoagulation therapy with Coumadin. Those are  
2 the sorts of patients who sound like they might be good  
3 candidates for this. Anybody have any comments they would  
4 like to make on this?

5 DR. AGODOA: Actually, one of the comments I made  
6 earlier about chronic anticoagulation in individuals who  
7 have heart valves, and they have an increased rate of  
8 infection here, would you still think that this is a group  
9 that should be subjected to this device? I don't.

10 DR. VERTUNO: That is a complex question. You need to  
11 know the cumulative incidence of infection between a  
12 combination of this device versus the standard PTFE plus the  
13 temporary venous access, which has a high rate of infection  
14 as well. So, I don't think I can get to that question from  
15 the data.

16 DR. AGODOA: Well, we don't have data from this  
17 database about the infection rate between the combined  
18 limited use of temporary access and PTFE versus Perma-Seal.  
19 So, if infection is a concern we don't have enough  
20 information so that I can say that this group of individuals  
21 should be targeted for this device.

22 DR. SIMMONS: I think I agree given that it is an  
23 unknown quantity, and I think it behooves the company to  
24 prove that it is safe to use in those patients, not that it  
25 is okay simply because that is a group of patients that are

1 at a higher risk. So, I would say patients with heart  
2 valves ought to be excluded unless there is some other  
3 overwhelming reason, or patients at high risk for  
4 endocarditis -- prosthetic devices should be excluded unless  
5 there is some overwhelming reason, or the company wants to  
6 provide some other reason why this should be used.

7 DR. CURTIS: I think one of the issues that comes up is  
8 that in many of these cases we may be talking about the  
9 temporary venous catheter versus the Perma-Seal, both of  
10 which have some sort of infection risk if you are talking  
11 about the need for early access. If you are talking about  
12 long-term, the PTFE appears to have the advantage of lower  
13 infection rates. You are right. But, depending on the  
14 individual patient, the actual comparison that you would  
15 want to make may not be between the Perma-Seal and PTFE, but  
16 it may be between the Perma-Seal and use of a temporary  
17 venous catheter.

18 DR. AGODOA: But they are combined. The combined use  
19 of PTFE and temporary access, I think that is what, to me,  
20 would be a comparable comparison, between that and Perma-  
21 Seal.

22 DR. CURTIS: That is true. And, another issue is that  
23 anticoagulation can be done for many reasons, one of which  
24 is prosthetic heart valves. So, patients who are on  
25 anticoagulation for other reasons might have some reasons to

1 benefit from this. But I think the point is very well about  
2 patients with heart valves. Infection is a problem,  
3 especially blood stream infections.

4 All right, so you would have a concern then about the  
5 patient with a prosthetic heart valve. We mentioned  
6 anticoagulation for other reasons. The very obese patient  
7 where central access is a difficult problem, I think that  
8 probably sounds reasonable. Does anybody on the panel have  
9 other comments about particular kinds of patients who seem  
10 to be appropriate for this device?

11 Let's go ahead and try to have each panel member  
12 comment on these issues. Any other comments? Patients that  
13 you think would be particularly appropriate?

14 DR. VERTUNO: I think that the currently proposed  
15 indications for use are too vague, and I think the instances  
16 where temporary central venous access are undesirable or  
17 unwarranted need to be defined. Anticoagulation is one;  
18 body habitus is another, and I would have to think about  
19 what might be some others.

20 DR. FREISCHLAG: I think that anticoagulation is  
21 important, especially if you have had a PTFE graft where you  
22 are having trouble with hemorrhage after dialysis. I think  
23 that patient could be a candidate if the anticoagulation is  
24 not for heart valve. The obesity issue, I agree that that  
25 would be an indication. Then, as far as the central venous

1 thing, I think those patients that don't have any central  
2 veins left, that it is documented that the subclavian and  
3 superior vena cava are thrombosed or not available, I think  
4 those patients would be the undesirable venous patients. I  
5 think just the fact that you don't want to put a catheter in  
6 and they have patent central veins, I don't think should be  
7 an indication. Just those with documented lack of central  
8 veins, I think would be the patients that you would need to  
9 put an access in and use because you can't use a temporary  
10 one and wait for one to mature. So, you would need to have  
11 a quick access, and you can't use a central access catheter.

12

13 DR. CURTIS: Dr. Agodoa, any other comments?

14 DR. AGODOA: Dr. Glickman gave the decision matrix  
15 where we have all these individuals, economic factors,  
16 Coumadin anticoagulation -- and we have discussed some of  
17 those. I am not particularly impressed by the socioeconomic  
18 factor as an indication for this particular device, but  
19 other than that, I don't have any other comments.

20 DR. CURTIS: Dr. Roberts?

21 DR. ROBERTS: No, I don't think so. The only comment  
22 that I would have is that I would disagree with the  
23 indication for usage being in patients in whom venous  
24 catheters are deemed undesirable because that would  
25 basically be all dialysis patients.

1 DR. CURTIS: Good point. So, there are some patients  
2 for whom this sounds to be appropriate. We made some  
3 comments about that. Any other comments on the first  
4 question?

5 DR. SIMMONS: I guess I am hoping that somehow the FDA  
6 will phrase the indications maybe in a little different way  
7 than they normally do for other devices. It really seems to  
8 me like this is a device where the indications have to be  
9 phrased that this is only indicated in certain things. I  
10 don't know exactly what I am trying to say for sure, but,  
11 you know, this is a difficult issue and I think that this  
12 device actually went through a clinical trial to try and  
13 prove that it was good for one thing, and it failed that and  
14 now we are trying to find a niche for it. I think the  
15 indications should reflect that, that this is a very  
16 specific -- that this is excluded from use as a regular  
17 device. I can just see this device being used -- it has a  
18 significant abuse potential in being a replacement for a  
19 temporary catheter. Obviously, I am not the guy that is on  
20 the front line, trying to buy venous access, and I hope I am  
21 not being overly critical here, but I would like to see the  
22 indications be much more rigid than they usually are as far  
23 as devices.

24 DR. CURTIS: I think too the issue about, "hey, how  
25 come he got up and got out of here in three minutes and I

1 have to wait?" I mean, that is a very real issue --

2 DR. SIMMONS: And that really bothers me. That should  
3 be out of there. That sort of implies that this was a good  
4 thing for that guy and that is wrong. This is not a good  
5 device for that professor.

6 DR. CURTIS: Actually, in a way what you are discussing  
7 is question number two. I think in number one we have some  
8 ideas about where the niche might be for these patients, and  
9 I think you have opened up the discussion for number two:  
10 Do the following indications for usage adequately define the  
11 patient population? The way it is currently written, it  
12 says the Perma-Seal graft is intended to provide early, and  
13 then in brackets, and chronic vascular access for  
14 hemodialysis in patients in whom venous catheters are deemed  
15 undesirable. It sounds like what you are saying is that it  
16 is a little too broad and you would like it reworded. How  
17 could that be done? What would you suggest?

18 DR. SIMMONS: I am a cardiologist. I should defer to  
19 the renal experts to rephrase that.

20 DR. VERTUNO: I think we pretty much discussed that the  
21 first go around, that we need to define the patient  
22 population specifically. I don't have anything to add to  
23 the comments that we have already made about this.

24 DR. CURTIS: Maybe some of the other ones here can make  
25 a comment. As a nephrologist, if you were to say, all

1 right, of all my patients that I take care of, who would I  
2 say this thing was indicated for? What would you say?

3 DR. VERTUNO: I would say it was indicated for somebody  
4 who needed immediate dialysis and I was fearful that  
5 cannulation of central vein would be hazardous.

6 DR. CURTIS: Okay.

7 DR. FREISCHLAG: I think I would be even a little  
8 stronger than that, that it would only be to provide  
9 dialysis for patients acutely whose venous access is not  
10 available. It is not there; not that we are fearful but  
11 that it is physically impossible.

12 I don't know how to word anticoagulation because we  
13 have patients who have PTFE grafts and who are on  
14 anticoagulation who do okay. So, you almost want them to  
15 prove that they can't have a PTFE graft before you put this  
16 in because there are patients that can do that. And, I  
17 don't know how to word the anticoagulation part. The venous  
18 part, you can image central venous access and you can prove  
19 that it is not available. But, as far as anticoagulation,  
20 it is a rare patient who hemorrhages out of the PTFE graft  
21 that is two or three weeks old. So, it would be almost an  
22 exclusion that you had a PTFE graft and you failed it.  
23 Again, for an anticoagulation patient the best graft is  
24 autologous. You know that is the graft they should have,  
25 with a temporary catheter, and then they won't have any of

1 these problems. So, I guess I don't want it to say if you  
2 are anticoagulated you get this graft, and I don't know how  
3 to phrase that.

4 DR. CURTIS: So, then the ideal would be an autologous  
5 fistula with temporary venous catheter until the fistula  
6 matures.

7 DR. FREISCHLAG: That is one woman's opinion.

8 DR. CURTIS: Well, that is what we are looking for.  
9 And, the PTFE graft is an alternative to that. So, then the  
10 Perma-Seal comes up and the patient in whom that is not  
11 possible or desirable, for whatever reason. So, that is  
12 where this thing is going to fit in. That would be your  
13 indication for usage.

14 DR. FREISCHLAG: I actually think in my practice the  
15 central vein issue would be the more common one, that you  
16 would have these young patients, the 20-year patients on  
17 dialysis in whom all the central veins go. That would be  
18 the patient that I would address this in the most. As she  
19 mentioned, she had nine patients out of her 300. So, it is  
20 not a huge number of those, but those would be my majority  
21 and not really the anticoagulated ones. I don't see that as  
22 nine; I see that as even fewer.

23 DR. CURTIS: Okay. Dr. Agodoa?

24 DR. AGODOA: I don't have any more comments on that.

25 DR. CURTIS: Dr. Roberts?

1 DR. ROBERTS: No comments.

2 DR. CURTIS: All right. So, the concern here would be  
3 the patient in whom you cannot get central venous access, or  
4 you think it would be undesirable to do that for whatever  
5 reason, that would be a patient you would be looking for.  
6 So, possibly rewording those indications for usage well, it  
7 says in whom venous catheters are deemed undesirable; maybe  
8 rewording that a little bit stronger and more explicitly.

9 DR. SIMMONS: How about saying something about  
10 demonstration of central venous access problems by duplex or  
11 other methods -- something on that order?

12 DR. CURTIS: Or patients in whom you already know that  
13 you have used up the access.

14 DR. SIMMONS: Yes, a physical demonstration of central  
15 venous access issues, rather than just "desirable."

16 DR. FREISCHLAG: The word I am thinking of is  
17 "available," something physical rather than emotional.

18 DR. CURTIS: Exactly. I think the comment that  
19 temporary venous catheters are undesirable all the time is  
20 true. But it is what we use, and it needs to be used.

21 Going along with those indications for usage, number  
22 three, should the bracketed phase be included in the  
23 indications for usage, where it says "and chronic vascular  
24 access." I would think the answer to that would be yes. I  
25 think that is a fairly straightforward thing, that it is not

1 just for early use but that you can use it longer term.

2 DR. ROBERTS: I guess the concern I have a little bit  
3 about that is that I think that, just by looking at the  
4 indications, we have said that this is something in someone  
5 where you need acute dialysis management. In that patient,  
6 obviously, you are not just going to put it in and put in  
7 something else at the same time, like you would if you were  
8 using it like a catheter where you would put in the catheter  
9 and put in a PTFE. On the other hand, the thing that I am a  
10 little bit concerned about from this data is that as you  
11 look at it, I mean, once this thing starts to fail, you  
12 know, maybe what you ought to do is do a thrombectomy and  
13 immediately put in a PTFE some place else because this thing  
14 is going to fail again pretty quick. So, the idea of not  
15 putting in the chronic is that it sort of does suggest to  
16 people that, you know, maybe this is not something you ought  
17 to put in as your first-line of dialysis access, except in  
18 these cases where there is a pretty good indication that you  
19 need something that is going to go in very acutely and that  
20 you can use right away.

21 DR. AGODOA: I would like to echo that a little bit.  
22 If we have that word "chronic" in there, we are not going to  
23 say it in parentheses. If it is chronic, it is chronic.  
24 They are going to put it in and they are going to use it as  
25 chronic. We know it is not as good a chronic access, so I

1 am a little bit concerned about that.

2 DR. FREISCHLAG: I guess I would like to connect them,  
3 so it would provide early with subsequent chronic, that it  
4 is not either/or because if you do "and" chronic -- if you  
5 don't read it carefully you could say, well, I used it for  
6 chronic. So, I would say early with subsequent chronic  
7 according to our indications because you don't want it to  
8 ever be used just a tad. It gets into the definition of  
9 early and chronic too. I don't know when it becomes  
10 chronic; I guess after a week. But early with subsequent  
11 chronic use -- I would feel comfortable with that.

12 DR. CURTIS: Any other comments on that issue? All  
13 right, number four, are there any contraindications for the  
14 use of this device? There are always issue in labeling  
15 about contraindications versus precautions and warnings, and  
16 there are all these fine-tuned definitions to all these  
17 different things. Is there anybody in whom it would be  
18 absolutely contraindicated to put this thing in?

19 DR. ROBERTS: The only one that I can think of is if we  
20 really believe -- and I don't know if there is any data from  
21 the company in terms of patients who were anticoagulated for  
22 heart valves. I didn't see in here under major  
23 complications anything about there being infected heart  
24 valves, but if we really believe that those patients are at  
25 high risk for that, I mean, maybe we need to think about

1 that as being a possible contraindication if we think that  
2 infection is a possibility. Maybe it should be a precaution  
3 rather than a contraindication.

4 DR. AGODOA: Because patients who have heart valves  
5 still get PTFE, and PTFE is not without an infection rate.  
6 So, I don't think it is an absolute contraindication.

7 DR. SIMMONS: I guess I have forgotten, is there a  
8 distinction there between an absolute contraindication, a  
9 relative contraindication and a precaution? Because a  
10 precaution sounds kind of wishy-washy, and I would say this  
11 device should not be used in patients with mechanical or  
12 prosthetic heart valves unless there is no other device  
13 available.

14 DR. CURTIS: Okay. Well, that gives us a perfect  
15 opportunity to clarify the issue. Could someone from the  
16 FDA clarify for us the difference between a  
17 contraindication, a warning and a precaution?

18 DR. SPYKER: Well, we have recently merged warnings and  
19 precautions. So, we recognize that there is no important  
20 distinction. What we used to teach to medical students was  
21 that a warning was something that would hurt the patient and  
22 a precaution was something that would compromise the  
23 effectiveness or maybe hurt the device. So, we don't see it  
24 as an important distinction.

25 Contraindication, what I teach the folks is that it is

1 something that you would be willing to sort of drop your  
2 day-to-day work and go testify against any doctor who does  
3 this. So, it is something we very carefully guard against  
4 putting into contraindications that would compromise a  
5 clinical decision. In other words, we are very careful  
6 about that. So, it has to be something that would never be  
7 appropriate. For example, we don't put contraindications --  
8 don't put this device in someone who might be allergic to  
9 it, unless there is evidence there really has been a  
10 problem. So, we are very careful about contraindications.

11 DR. CURTIS: All right. So, given that, what you were  
12 just describing sounds like a warning or a precaution. I am  
13 not sure I could think of an absolute contraindication to  
14 the use of it.

15 DR. SIMMONS: Unless you wanted to put in there that,  
16 you know, any patient would be acceptable for an autologous  
17 --

18 DR. CURTIS: But that is not an absolute  
19 contraindication. I think you could say it is not wise; it  
20 is not good medical practice; it is not the best decision.  
21 But it is not contraindicated. There is a difference.

22 Let's get into number five, have you any other  
23 suggestions for labeling? If you have warned warnings and  
24 precautions, what do we call them now? Warnings or  
25 precautions?

1 DR. SPYKER: Warnings and precautions.

2 [Laughter]

3 DR. CURTIS: Okay. Let's discuss warnings and  
4 precautions. What should be in the labeling? Dr. Vertuno?

5 DR. VERTUNO: I was hoping that you wouldn't always  
6 start with me --

7 [Laughter]

8 DR. CURTIS: Well, you are to my left. I think the  
9 labeling should try to define the appropriate population as  
10 closely as possible. I think we have discussed most of  
11 those, but I think we need to get away from the emotional  
12 and putative benefits. This is not an acceptable  
13 replacement for either a PTFE, and certainly not for a  
14 native AV fistula, and it would be a big mistake if it went  
15 on the market and was used as a replacement for those. I  
16 think the labeling has to clearly state that. But there are  
17 clearly people who will probably do okay with this, but it  
18 is not the vast majority of the dialysis patients.

19 DR. CURTIS: I think there has to be a very explicit  
20 statement that the long-term patency rate of this graft is  
21 lower than for a PTFE graft. So that would be one thing;  
22 and that the complication rate is higher. Because people  
23 who didn't participate in the clinical study, they may hear  
24 about the graft, hear about the fact that you can hemostasis  
25 faster, and it could easily become something that looks

1 very, very attractive. So, having those problems, which are  
2 very well spelled out in this submission -- I think those  
3 need to be stated. The lower long-term patency and the  
4 higher complication rate need to be very explicit there.

5 DR. ROBERTS: I would suggest -- I don't know how often  
6 this is done for these submissions that are not a PMA, but I  
7 would suggest that some consideration be given to putting in  
8 the table and graph that show the patency rate and the  
9 complication rate. I think that that is something that  
10 helps people, if they were to look at the product insert, to  
11 see that that is there. You know, it is probably than words  
12 saying, well, the patency rate is lower and the complication  
13 rate is higher. I think it gives them a nice way of looking  
14 at it. You have the data there and it is nicely displayed  
15 in the panel pack.

16 DR. VERTUNO: I think that is an excellent suggestion.

17  
18 DR. CURTIS: Other comments about precautions and  
19 warnings? We have the one about the heart valves. Right?  
20 That, given the higher infection rate, it is unknown what  
21 the risk of endocarditis would be, and it is something that  
22 you would want to think through carefully before implanting  
23 one of these in a patient with a prosthetic heart valve.

24 DR. AGODOA: Is this something that could be looked at  
25 postmarket?

1 DR. CURTIS: Sure, yes. It is going to be a small  
2 population group. Can we have a clarification from the FDA  
3 about what you can and cannot do in terms of postmarketing  
4 studies?

5 DR. YIN: It is very difficult for the process that we  
6 are going through. If we are using the 510(k) process, that  
7 is not the easiest thing to do. You are aware that this is  
8 not a PMA. Right?

9 DR. CURTIS: So, it would be unusual with a 510(k) that  
10 there would be any kind of postmarketing studies?

11 DR. YIN: Yes, it would be difficult.

12 DR. ALPERT: Susan Alpert, Director of the Office of  
13 Device Evaluation. FDA MA, the Modernization Act, addressed  
14 the kinds of situations in which it is appropriate to ask  
15 for postmarket surveillance studies on devices going to  
16 market as class I or class II. The general gist, because I  
17 don't have it in front of me to give you the specific  
18 wording, is that there needs to be an issue that must --  
19 that really requires addressing for the safety and  
20 effectiveness of the product, not for its original marketing  
21 but a focused issue that raises the concern to a level where  
22 a study is needed for us to require, because it is  
23 requirement when we issue an order for postmarket  
24 surveillance on a 510(k) device.

25 They have directed us to be very focused in our

1 requests and not do this as a routine for 510(k) devices,  
2 which means if you have a specific concern, then it can be  
3 considered. The procedures and the criteria are, I believe,  
4 out for comment in terms of whether we have hit the right  
5 thresholds for limiting such studies. But we do have the  
6 authority to require them. We have just been asked that it  
7 be very focused and as specific as we can make it.

8 DR. CURTIS: Thank you. I think one of the problems  
9 here is that a comment was made earlier that it took a long  
10 time to get the study done because they weren't putting  
11 these things in every patient. Then if you are saying,  
12 well, you have to find a patient who has a Perma-Seal graft  
13 and who happens to have a prosthetic heart valve, you know,  
14 you are going to have one or two patients per center over  
15 many, many years to kind of figure this out. So, I think it  
16 would be hard to examine that issue.

17 DR. AGODOA: It may be hard, but then if you say  
18 individuals who are anticoagulated are suitable for this and  
19 they have heart valves, and we don't specify that, but we  
20 don't have the data to specify that, are we not putting  
21 these patients at risk, increased risk?

22 DR. CURTIS: I think one possible way that could be  
23 settled would be to say that there is no information on the  
24 patient with a prosthetic heart valve in terms of that issue  
25 about of a higher infection rate; here you have a patient

1 with a prosthetic valve -- we don't know what is going to  
2 happen. I think it could be said explicitly in the labeling  
3 that we don't know. There may be a potential for a higher  
4 infection rate, and then a separate issue about whether you  
5 would do a study.

6 DR. ROBERTS: I might also just suggest that in terms  
7 of what might be displayed in the labeling, it might be  
8 reasonable. I do think it is important because it wasn't  
9 clear to me when I was reading. I mean, I got the  
10 impression but it took me a while to pick it up, the fact  
11 that the major complications are above and beyond the  
12 thromboses; above and beyond the problems with the patency.  
13 I think maybe just a word to make that clear to people, and  
14 perhaps just a very small table with some of the major  
15 complications that sort of stand out from this clinical  
16 summary 16, Table 14, such as infections and skin erosion,  
17 hematoma, maybe the aneurisms, pseudoaneurisms, you know,  
18 just so that people have a sense of where the major  
19 complications break down. This business of there being no  
20 venous stenoses, somebody obviously made a mistake when they  
21 filled that line out.

22 DR. CURTIS: Okay, and to follow-up on the issue of the  
23 prosthetic heart valves, of course, that is not the only  
24 time when there is a risk of endocarditis. There are other  
25 cardiac conditions in which a patient has a high risk of

1 endocarditis. Probably if any statement is going to be  
2 made, it would have to include those other issues too.

3 Any other comments about precautions or warnings? All  
4 right, then we get to the follow-up questions, number six,  
5 what type of follow-up would be appropriate for the AV  
6 access graft-treated patients?

7 I think six and seven actually pretty much go together.  
8 Are there any other issues of safety or effectiveness not  
9 adequately covered in the labeling which need to be  
10 addressed in further investigations before or after device  
11 approval? We have just heard that you have to be very, very  
12 selective in what we would think would be important or  
13 necessary to do in another study. Any comments on that?

14 DR. FREISCHLAG: I just have one question. We are  
15 telling people that you can only use this for specific  
16 indications. What if Dr. Smith in some town started putting  
17 in a lot of these and didn't pay attention to that? Is that  
18 a follow-up that is necessary? That they were being placed  
19 in patients, all his vascular patients? Who would know?  
20 Who would care? How would we know that? Is that something  
21 that needs to be followed-up, that there isn't someone who  
22 decided that they liked the fact that it sealed faster and  
23 their patients could leave the dialysis unit faster? Would  
24 we know just by the fact of how many grafts got sold this  
25 year? I mean, if there are very few we know people are

1 paying attention, but if there are 100 being sold in a small  
2 town in Oregon next year, then I guess I would wonder who is  
3 getting them, and can you follow that? How do you do that?

4 DR. ROBERTS: My feeling is you probably can't do that.  
5 I mean, the FDA is not in the practice of legislating how  
6 people use devices that are out there. They say basically,  
7 you know, if you have a reason to use it, then go ahead and  
8 use it but, hopefully, you have some good scientific  
9 background to base that decision on.

10 I think, on the other hand, one of the things that is  
11 important -- anybody, correct me if you don't like the way I  
12 phrase that -- but I think what is important is that if we  
13 give people the information, the scientific information in  
14 the labeling that shows them that the infection rate is  
15 somewhat higher, quite a bit higher; that the thrombosis  
16 rate is a lot higher; and the patency rate is not as good,  
17 people can use that in terms of making their decisions, and  
18 if they feel that in their patient population not having to  
19 hold pressure on the graft is worth having a lot of  
20 thromboses -- I mean, I think they are going to have to  
21 defend that with whomever it is that they have to defend  
22 that with.

23 DR. CURTIS: I agree. I think once you get it out  
24 there it is going to be used. I think if the labeling is  
25 explicit, and if you look at the issues about patency and

1 complication rates, and if people are still going to use it,  
2 they are going to use it. I don't think there is anything  
3 that we can do, nor would any kind of a postmarketing study  
4 really solve issues like that. I mean, somebody who uses  
5 them a lot thinks he or she has great reasons for using them  
6 a lot. All somebody would need to say is, well, my patient  
7 needed earlier hemostasis and they have an indication for  
8 it. So, I don't think you can get around that issue.

9 I am not sure that I could think of any specific kind  
10 of investigation or study that would need to be done for  
11 this particular device. I would love to know too long-term  
12 infection issues but that is not something that I think is  
13 easy to do at all. Any comments about number six or number  
14 seven?

15 DR. AGODOA: Even though FDA may not require it,  
16 wouldn't it be scientifically justified to actually find out  
17 something from the company's point of view? I guess they  
18 may not want to know.

19 DR. CURTIS: That may be true. The problem always is  
20 funding things that, you know, may turn up bad news, I  
21 suppose.

22 DR. FREISCHLAG: I have a question for the company. I  
23 assume you are going to publish this. I hope you are going  
24 to publish this. I think it would be really important to  
25 put it in a journal that is read by a lot of people.

1 Unfortunately, I don't read nephrology journals and I don't  
2 think nephrologists read vascular surgery journals often  
3 either. So, I am not sure where the right place is or how  
4 to get it into both our literatures so that we both know it.  
5 Maybe that would make me feel better, if I know that it is  
6 going to be widely published and widely presented so that  
7 everybody hears about it.

8 DR. CURTIS: I think at least some of these tables of  
9 information should get into labeling, which has been done  
10 before, it would be very reasonable and at least you would  
11 have that. But I agree, it would be good to disseminate the  
12 information.

13 All right, I think we have addressed all the questions  
14 here. We will reconvene at one o'clock. For the people on  
15 the panel, there is an area that has been set aside in the  
16 restaurant for us to eat together today. We will adjourn  
17 for the time being. Thank you.

18 [Whereupon, at 11:00 a.m., the proceedings were  
19 recessed, to be resumed at 1:00 p.m.]

## 1 AFTERNOON SESSION

2 **Devices to be Used as Adjuncts to the Heimlich maneuver**

3 DR. CURTIS: This afternoon the topic of discussion is  
4 data requirements for evaluation of devices as adjuncts to  
5 the Heimlich maneuver.

6 Some of the members of the panel have left and we have  
7 them replaced with other people who weren't at the morning  
8 session. So, I would like to go ahead and have everyone  
9 introduce themselves again, starting over here.

10 DR. SIMMONS: Tony Simmons, cardiologist and  
11 electrophysiologist, Lake Forest University.

12 DR. FIELDER: John Fielder. I am a bioethicist at  
13 Villanova University.

14 DR. CURTIS: I am Anne Curtis. I am a cardiac  
15 electrophysiologist with the University of Florida.

16 DR. BECKER: I am Lance Becker. I am an emergency  
17 medicine physician at the University of Chicago.

18 DR. ROBERTS; Ann Roberts, interventional radiologist,  
19 from University of California, San Diego.

20 DR. FREISCHLAG: Julie Freischlag, vascular surgeon  
21 from UCLA Medical Center.

22 DR. ALTMAN: Don Altman, Director, Arizona Department  
23 of Health, consumer rep.

24 DR. YIN: Lillian Yin. I am the Acting Division  
25 Director for the Division of Cardiovascular, Anesthesiology

1 and Neurology Division.

2 DR. SPYKER: Dan Spyker, medical officer and I am  
3 Lillian's deputy.

4 MR. JARVIS: I am Gary Jarvis, the industry  
5 representative.

6 DR. CURTIS: Thank you. There will be an open public  
7 hearing at the end of the initial discussions from industry,  
8 the FDA and the panel. So, if anybody from the public has  
9 comments to make about what we are discussing, that can be  
10 done then.

11 We are going to start first with the industry  
12 presentations. The first presentation will be by the  
13 representatives from the Heimlich Helper. If each person  
14 would introduce him or herself and then tell us what  
15 financial interest you have in the product or the company.

16 **The Heimlich Helper**

17 **Introduction, Frank Fani**

18 MR. FANI: I am Frank Fani. This is my partner,  
19 Charles Funk. We own the company so far. I would like to  
20 tell you about the Heimlich Helper but, first, I am going to  
21 give you a little story about how it came about.

22 About three years ago, my mother was in a restaurant,  
23 and she is a rather large Italian woman, and she started to  
24 choke, and nobody could get around her to give her the  
25 Heimlich maneuver. Well, luckily, my son was there and he

1 has had enough martial arts that he went in front of her  
2 pressed on her diaphragm hard and through the air passage.  
3 Well, this worked. When they came home, they told me what  
4 happened and I realized that there had to be something else  
5 that could help people that were this big or in wheelchairs,  
6 or whatever. So, there had to be some kind of an extension.

7  
8 So, I put together a few little things and came up with  
9 this, and went to a paramedic friend of mine. He looked at  
10 the design. He liked it. A couple of friends of mine who  
11 worked on a ski patrol, they liked it. So, from there, I  
12 went and got a patent and then realized that this is not my  
13 forte. So I got a partner. He is more equipped to tell you  
14 more about it with the overheads. So, I would like to  
15 introduce you to Charles Funk.

16 **Presentation of Data, Charles Funk**

17 MR. FUNK: We were going to have some music but --

18 [Laughter]

19 [Slide]

20 First of all, really the basis for what we are trying  
21 to do here is compare what we call the maneuver against what  
22 we call the Heimlich Helper. Our position really is that it  
23 is the same thing in 90% of the time that it has been used.

24

25 For instance, the purpose of the maneuver is to cause

1 compression of the lungs through upper pressure on the  
2 abdomen and a point below the rib cage and above the navel,  
3 forcing air out through the windpipe induced by an upward  
4 thrust of the arm and clenched fist. The purpose of the  
5 Helper is to cause compression of the lungs through an upper  
6 pressure of the abdomen, at a point below the rib cage and  
7 above the navel, forcing air through the windpipe induced by  
8 an upward thrust of the Heimlich Helper device. Basically,  
9 our device and the Heimlich Helper perform the same act.

10 [Slide]

11 The maneuver is designed solely as an emergency method  
12 to treat persons whose airway is obstructed by a foreign  
13 body causing breathing to stop. The Heimlich Helper is  
14 designed as a tool to help perform the Heimlich maneuver.  
15 It is expressly limited for emergency use to treat persons  
16 whose airways are obstructed by a foreign body that causes  
17 breathing to stop. Again, basically what we are trying to  
18 do is the same thing.

19 [Slide]

20 The indicated use performed for the maneuver is  
21 performed by administering an abdomen thrust. The  
22 administrator stands behind the victim, wraps his arms  
23 around the victim, makes a fist, places the fist below the  
24 rib cage and above the navel and performs a quick, upward  
25 thrust. The Heimlich Helper is a tool which helps perform

1 the abdomen thrust of the Heimlich maneuver. The user  
2 stands behind the victim, places the Heimlich Helper around  
3 the front of the victim, administers an upward thrust below  
4 the rib cage and above the navel. Again, we are trying to  
5 do the same thing.

6 [Slide]

7 The manual technique of the maneuver relies on the  
8 anatomical design of the human arms and the fist to carry  
9 out the intended purpose, which means that you have to wrap  
10 your arms around somebody.

11 [Slide]

12 The ball in the maneuver is designed to represent the  
13 fist, and it is in the center of the Heimlich Helper, and it  
14 is to duplicate the size of the clenched fist which  
15 constitutes the pressure point of the abdominal thrust. The  
16 hand protruding outward from the center of the oval shaped  
17 ball replicates human arms which, like the Heimlich  
18 maneuver, provide the power source for the technique.

19 [Slide]

20 We did a little bit of testing. What we did, we found  
21 a representation of what Dr. Heimlich did -- actually, it is  
22 not a representation; it is a chart, on page 99 of your  
23 book. In the lab trials instrumentation was used to measure  
24 the airflow volume and pressure of the Heimlich maneuver.  
25 What Dr. Heimlich came up with is an increase in airflow

1 from 62 L/minute to 215 L/minute in the early stage of  
2 performing the Heimlich maneuver, on the first part of that  
3 chart. On the second part of the chart, which is the late  
4 stage of exhale, are the increases from 19 L/minute to 100  
5 L/minute.

6 [Slide]

7 Our test results with the Heimlich Helper showed the  
8 efficiency of the Heimlich Helper. The expulsion flow rates  
9 increased from 61.6 L/minute to 281 L/minute, which is a  
10 little bit better than what Dr. Heimlich was saying. In the  
11 late stages we are pretty much the same. It is 26.8  
12 L/minute to 235 L/minute. In essence, again, what we tried  
13 to see here was whether our device was doing the same thing  
14 as Dr. Heimlich's manual device was doing.

15 [Slide]

16 The target population -- the maneuver was designed to  
17 free the airway of a victim whose airway is obstructed by  
18 food or another foreign body. The target population is  
19 basically anybody that is choking. What our target  
20 population is, is a little broader. That is basically the  
21 Heimlich Helper can do the same thing the maneuver has been  
22 doing, except where we excel is in very large people,  
23 handicapped people in wheelchairs, those people that are not  
24 in optimum positions to have the maneuver performed.  
25 Basically, what that amounts to I will show you in a minute.

1 [Slide]

2 We took some photographs, and what we did was, on  
3 purpose, utilize two distinctly different size people. As  
4 far as we are concerned, if you have a large person and a  
5 small person is trying to perform the maneuver, the handles  
6 on the Helper actually can get better leverage to perform  
7 maneuver either in a standing or a sitting position, whereas  
8 it is a bit more difficult to try to get arms around  
9 somebody if they are at such different sizes.

10 [Slide]

11 This clearly states that if you have a very small  
12 person and a large person, as shown in Figure 1 and 2, you  
13 really can't get your arms around these people. Figures 3,  
14 4 and 5 demonstrate that with the Helper you can easily get  
15 the Helper around, and with the extensions of the arm you  
16 can utilize and perform the maneuver more easily than you  
17 could without it.

18 [Slide]

19 The last piece, if somebody is in a wheelchair, again a  
20 large person-small person, extremes, if they are sitting, if  
21 they are in a chair or if they are in a wheelchair, the  
22 Helper makes their job easier. And, that is kind of what it  
23 is all about. Thank you.

24 DR. CURTIS: All right. Now we have representatives  
25 from the QuickAir Choke Reliever.

1                                   **QuickAir Choke Reliever**

2                                   **Wayne Whitbeck**

3           MR. WHITBECK: You have copies in your pack of their  
4 slides and the FDA slides. On the first page it says  
5 "addenda," dated April 23. I passed them out first thing  
6 this morning. So, everyone on the panel should have a copy  
7 of that.

8           Thank you, Madam Chair, panel, representatives from the  
9 FDA, ladies and gentlemen. It is a privilege to be here  
10 with you this afternoon.

11           I just wanted to comment that this process with a non-  
12 predicate is difficult. I think we have all been saying  
13 that to one another, but I do want to say before we start  
14 that we at, Precious Life Saving Products, do appreciate the  
15 tremendous professionalism that was shown to us by your  
16 representatives, Carroll O'Neill and Dan Spyker. We really  
17 appreciate that. It has made our job a lot easier to have  
18 representatives like that. You do your organization proud.

19           At this time, I would like to introduce Steven Sham,  
20 who is the CEO of Precious Life Saving Products.

21           DR. CURTIS: Did you say who you were?

22           MR. WHITBECK: I am Wayne Whitbeck. I am sorry, I may  
23 not have said that.

24           DR. CURTIS: What is your financial interest in the  
25 company?

1 MR. WHITBECK: I am a consultant to Precious Life  
2 Saving Products, and I am also a part owner of the company.

3 [Slide]

4 This is Christy, and forgive me, I am going to give a  
5 few details of how we started as a company, which don't  
6 necessarily relate to the specific data testing that the FDA  
7 is asking us to present. But I felt it was important  
8 because what we found out about choking determined in every  
9 way what we did in designing the Choke Reliever, a video and  
10 the instructional booklet.

11 This is Christy. She choked on a hot dog. She is the  
12 daughter of a friend of ours. Her father knew the Heimlich  
13 maneuver, administered it immediately in their family home,  
14 was unsuccessful in removing the portion of the hot dog that  
15 Christy had eaten, and she died. We asked if we could put  
16 that in the video, and the reason we did that is because  
17 choking is extremely real; it is extremely tragic. We all  
18 feel the same about it, and we wanted our package to show  
19 that everyone -- everyone -- should know about choking.

20 [Slide]

21 The actual person who gave us the idea for the QuickAir  
22 Choke Reliever is a man by the name of Albert Marcucci, also  
23 Italian -- they are good inventors, those Italians! This is  
24 just a picture of Albert. This is shot from our training  
25 video of Albert thrusting a grapefruit into his abdomen, and

1 that is how he saved himself around 1992. It was a piece of  
2 chicken skin that was the offending foreign substance in  
3 that case.

4 [Slide]

5 So, our mission at Precious Life was to help save lives  
6 by use of the QuickAir Choke Reliever and other proven  
7 methods in the event of choking. We first started out by  
8 trying to define the problem for ourselves, and we did an  
9 extensive literature search. We wanted to design the right  
10 package that would address the problem, not symptoms that  
11 maybe we thought for the first couple of days were the  
12 problem.

13 [Slide]

14 I realize that from where you are sitting you can't  
15 read this. These are the death statistics reported by the  
16 National Safety Council. So, I will just point out a couple  
17 of things. This column, here, is the number of deaths per  
18 year, starting in 1974 and going down to 1996. This is in  
19 the U.S. It averages about 3000 a year, and it has not  
20 changed. As we know, the Heimlich maneuver was approved  
21 initially in 1975.

22 The other thing that is very significant from the chart  
23 is as the age, going up to 75. You can see that half of  
24 those that die of choking incidents are 70, 75. In fact,  
25 the 80% point, 80% of the people who die of choking,

1 according to the statistics collected by the National  
2 Research Council, are 47 years old or older; 20% of those  
3 that die due to choking are younger than that.

4 We felt that those statistics may be low because of the  
5 term pathway coronary coming up repeatedly in the  
6 literature, and that originally was written about by Hogan  
7 in 1963 where some autopsies happened to be done, and  
8 corrected the view of death away from a coronary to, of  
9 course, choking, and we all know that.

10 [Slide]

11 There are many other incidents in the literature that  
12 discuss it. This one is from 1974. The actual incidence is  
13 probably much higher, as indicated by a recent report of  
14 unsuspected food choking found at postmortem examinations of  
15 three patients thought to have died of myocardial infarction  
16 in one nursing home last year. Well, that was 1974. So,  
17 quite some time ago.

18 However, we believe from our discussions and other  
19 articles that we have read, and discussions with  
20 statisticians, and following the paper trail of the  
21 postmortems, that this incidence of 3000 per year may be  
22 still low.

23 I would like to discuss the public awareness aspect  
24 that we found while reading the literature. I just have  
25 three or four slides on that, and then we will get into the

1 technical issues of QuickAir Choke Reliever.

2 [Slide]

3 In 1976, Hughes compiled data on the maneuver on 550  
4 people, and we found that 70% of the rescuers were unskilled  
5 in cardiopulmonary resuscitation, and 50% listed magazines  
6 and newspapers as their source of information on the  
7 technique.

8 I believe Dan, you may be talking later this afternoon  
9 to us about some of the complications, the serious  
10 complications that have arisen from use of the Heimlich  
11 maneuver.

12 [Slide]

13 We found 17 and I think, Dan, you have another one.  
14 So, 18. Of those reports in the literature of serious  
15 complications, the awareness or the training level of the  
16 rescuer is known in 9 of them that were reported in the  
17 literature. Of the 9, 5 were untrained; 4 were trained. We  
18 don't know about the other 8 or 9.

19 [Slide]

20 In the 1992 emergency cardiac care given in the  
21 guidelines for cardiopulmonary resuscitation, there was this  
22 statement, which shows that it is still recognized as a very  
23 important aspect in choking, public awareness. That is the  
24 American Heart Association. The earlier the information is  
25 transmitted to the community, the stronger the impact on

1 mortality and morbidity. Therefore, efforts should be made  
2 to teach basic life support in the schools.

3 Precious Life Saving Products strongly agrees with this  
4 statement. From the previous slides, you can see why we are  
5 convinced that this is the right direction -- public  
6 education, public awareness.

7 [Slide]

8 I have a slide on training. I spoke with the national  
9 coordinators of Emergency Cardiac Care Training at both the  
10 American Heart and the American Red Cross who gave me last  
11 year's data for the number of people that were trained.  
12 This is that data.

13 You can see American Heart on the top, American Red  
14 Cross on the bottom, people who are taking the course for  
15 the first time; those that are being retrained, they had  
16 been in this category and now they are in this one; and the  
17 total. So, for the American Heart Association, in 1997, 5.2  
18 million CPR providers passed the course, and 900,000 were  
19 retrained, for a total of 6.1 million. You can see the  
20 numbers for the American Red Cross there. So, the totals  
21 for 1997 are 7.3 million new people that became CPR  
22 providers, trained CPR providers.

23 I asked what happened in the other years, what happened  
24 in the previous 10 years, how many did you train then? They  
25 said, well, we don't have that easily accessible; we can get

1 it. I said that is all right. It is something just less  
2 than that.

3 So, what we did, we looked at the 7.3 million and we  
4 said, okay, over the last 10 years there was probably an  
5 average of 6.5 million trained by these two major  
6 organizations. That means 65 million Americans within the  
7 last 10 years at least have been trained in CPR. Of course,  
8 basic life support training includes choking. So, that  
9 means that there are 25% or less of the population that have  
10 received training, and some of that 25%, their training is  
11 becoming fairly -- well, if their memory is like memory, it  
12 may be dulling a bit.

13 So, this again, led us to believe that awareness is an  
14 aspect that we should consider in our product when designing  
15 it. So, for that reason we put together the best training  
16 video that we could, as well as a very accurate booklet to  
17 describe choking, what causes it, the symptoms, how to avoid  
18 it, how to use the QuickAir Choke Reliever, and how to use  
19 the Heimlich maneuver if you don't have one immediately  
20 accessible.

21 [Slide]

22 As far as the use of the Heimlich maneuver, there are  
23 several papers, all of them written by Drs. Heimlich or  
24 Patrick, ranging from 1975 to 1995. I believe most are  
25 referred to in the panel pack. During those 20 years, the

1 statistics that we saw earlier, that we were already aware  
2 of is that 3000 people at least died during those same years  
3 per year, therefore, at least 60,000 people died during that  
4 20-year period, during which there were 10,000 choking  
5 victims who received the Heimlich maneuver that were  
6 reported. So, this again tended to reinforce in our mind  
7 awareness -- awareness -- awareness is a very big key to  
8 reducing the death statistics.

9 [Slide]

10 The serious complications, just a quick summary, there  
11 were 17 that we saw; 12 were male, 5 female. The average  
12 age, not surprisingly from the death statistics, was 64.  
13 The rescuers, as mentioned, there were 5 untrained, 4  
14 trained. We don't know about the others.

15 The outcomes -- stomach rupture along the smaller  
16 curvature or upper curvature of the stomach was the most  
17 prevalent, with 7; 2 aortic valve ruptures; 2 diaphragm  
18 ruptures; 2 thromboses of the abdominal aorta; and the other  
19 ruptures were esophageal, jejunal mesenteric and 1  
20 aspiration pneumonia.

21 Percentage-wise, of course, this isn't a large number.  
22 It is less than 0.2% of the 10,000 administrations of the  
23 Heimlich but no less tragic.

24 [Slide]

25 In assessing the effectiveness of the QuickAir Choke

1 Reliever, these are our own results and I think Dan has done  
2 a very good job on some statistical analysis of our results.  
3 To test the QuickAir Choke Reliever, we used the same  
4 parameters that were used to compare the effectiveness of  
5 the back slap in the early '70's, mid '70's to the Heimlich  
6 maneuver. That is, what is the peak pressure developed at  
7 the mouth with the administration with a blocked mouth, and  
8 what time duration is used?

9       So, we rented a very expensive computerized spirometer  
10 and made graphics which gave us the trace, and that is in  
11 the panel pack, the tracings of the pressure curves using  
12 the Heimlich maneuver without the device and with the  
13 device. On average, the QuickAir Choke Reliever provided  
14 approximately 32 mmHg pressure at the mouth, and with the  
15 Heimlich maneuver we got 17 mmHg on average. This seemed  
16 fairly consistent to us. That is the yellow peak there,  
17 which was 17 on average. This seemed fairly consistent to  
18 us with what was in the literature. So, we thought the  
19 amount of pressure that we are using to administer the  
20 Heimlich maneuver must be somewhere in the range similar to  
21 what other scientific investigators have used.

22       Dan, will you be giving more information on this later?

23       DR. SPYKER: Yes.

24       MR. WHITBECK: Thank you.

25       [Slide]

1 Another very important piece of information we felt was  
2 some information that was presented by Gordon, back in 1977.  
3 On 6 normal human subjects, he developed this data with 2  
4 positions, standing and supine for each of the 6. The lungs  
5 were at resting position for this data, this lower pressure  
6 of 10 and 11 for the 2 positions, standing and supine. At  
7 the end of inspiration, in other words with full lungs, the  
8 pressure developed at the mouth against the blocked mouth,  
9 the same conditions as we had in our test, were 15 and 13.  
10 So, the improvement in effective pressure to relieve a choke  
11 is shown by Gordon's data. It is about 30-35% depending at  
12 what point the person choked, if he or she had a full lung  
13 or half way.

14 The reason why we thought this was so important is that  
15 if there is a weak or ineffective thrust given to a victim  
16 valuable air in the lungs could escape past the obstruction,  
17 deflate the lungs, with less potential pressure from  
18 subsequent thrusts.

19 [Slide]

20 So, we concluded from Gordon's data that the first  
21 thrusts are the most important. A weak thrust may deflate  
22 the lungs, causing more and probably less effective thrusts,  
23 and also causing possibly the use of more force as the  
24 unknowledgeable, perhaps, rescuer is not sure how hard to  
25 pull back, not sure how hard to administer the Heimlich

1 maneuver, doesn't administer it hard enough, air leaks out  
2 of the lungs, but then panics as time is going by and the  
3 person may be falling unconscious or isn't able to breathe  
4 or cough, and therefore administers much more force but by  
5 this time the lungs are less full.

6 I am about half way through. I would just like to stop  
7 for a moment and ask if there are any questions or comments.

8

9 [No response]

10 Thank you. I would like to talk about the design of  
11 the device now. I was supposed to show you this earlier,  
12 the QuickAir Choke Reliever presents more energy for similar  
13 effort compared to the Heimlich maneuver. Therefore, as we  
14 mentioned, there should be less thrust, less chance of  
15 deflating the lungs ineffectively, and a lower final force  
16 exerted to achieve resuscitation.

17 [Slide]

18 Here are some of the technical design features of the  
19 QuickAir Choke Reliever. The first one I would like to  
20 mention to you is the deflection. The deflection is with 35  
21 lbs. pressure on each handle, totaling 70 lbs. So that 35  
22 and that 35 totaling 70 is represented there. So, I have  
23 just shown the 2.5 in. deflection. And, with 80 lbs.  
24 pressure, which would be 40 on each handle, there would be  
25 2.9 ins. in deflection. Then, at 90 lbs. we are in the

1 plastic range of the 200,000 psi steel reinforcing bar,  
2 which runs all the way through the handles and back in one  
3 continuous, seamless piece of steel. I think the FDA took  
4 it apart and did some testing on it, and there is going to  
5 be a report on that later this afternoon.

6 So, the purpose behind this was to make sure that if  
7 what we just saw on the previous slides was happening, where  
8 we had a panicking rescuer who was not resuscitating the  
9 victim, the handles would wrap around the abdomen and would  
10 limit the top level of force that could be exerted. I will  
11 talk a little bit more about that later.

12 [Slide]

13 Another safety feature which we feel is inherent in the  
14 product is that the victim, if he or she has read the  
15 booklet or viewed our video, will help position the device  
16 if it is in the wrong place because they will say, "hey, get  
17 off my xiphoid, will you?" as long as they are conscious  
18 when found by the rescuer. So, again, awareness of what  
19 these maneuvers are all about is key.

20 [Slide]

21 The use with children -- I have pictured here some of  
22 the topography of the abdomen of a 1-year old girls. The  
23 reason I wanted to use a girl here is because they are  
24 slightly smaller at this age than a boy. That is the only  
25 reason. So, here we have the rib cage, xiphoid, the

1 umbilicus is the yellow button in the middle and then the  
2 bi-cristal dimension there, which is the horizontal distance  
3 between the crest of the hip bones. So, that is the scale,  
4 the hip bone width and the distance between the umbilicus  
5 and the rib cage of a 1-year old, average 1-year old. What  
6 is in red is the area of the QuickAir Choke Reliever at this  
7 part right here, at the base. What is in green is a  
8 slightly smaller area, and that is the area of the impeller  
9 ball or hump, which is all we think a child of that age will  
10 need to receive. If they have 15 lbs. or so, or 20 lbs. or  
11 so of pressure, that is all the area that the abdomen will  
12 see.

13 [Slide]

14 I have done the same thing for a 2-year old and a 3-  
15 year old. Of course, we can see from the slide that my  
16 drawing isn't very accurate with the sharp edges of the  
17 impeller ball. They don't exist on the device, they do on  
18 the slides so it looks like you could, you know, maybe put  
19 something sharp into the rib cage which, of course, isn't  
20 the case.

21 Here is the 2-year old. Of course, the umbilicus is a  
22 little bit further away from the rib cage and the bi-cristal  
23 dimension is a little bigger. From a percentage point of  
24 view, the 3-year old, which I am about to show you, doesn't  
25 have as much change as from 1 to 2, but there is still some

1 increase in body trunk length.

2 I have some slides that we have captured out of our  
3 video that I would like to show you, the QuickAir Choke  
4 Reliever as it is actually used and as we are showing people  
5 it should be used. We also have slides for you that show  
6 the Heimlich maneuver, which we have put in the video as  
7 pairs, Choke Reliever and Heimlich.

8 [Slide]

9 First of all, before I go into this, has anyone seen  
10 the video? Carroll, has, Dan. Thank you. For those of you  
11 who haven't seen it, there is the landmarking with the  
12 rescuer holding the QuickAir Choke Reliever, on the left.

13 [Slide]

14 Then, zeroing in, the rescuer is bringing the QuickAir  
15 to the proper point on the abdomen.

16 [Slide]

17 There, he is pulling it back with the full force. We  
18 rehearsed this so that we used the same force that we used  
19 in our tests to be consistent and to try and show how much  
20 the device should bend. Not that we want anybody practicing  
21 with it because, if you have read our literature or seen our  
22 video, we emphasize and reemphasize over and over again that  
23 you do not practice using the device.

24 [Slide]

25 I would like to show the fact that the device is

1 actually on the victim's abdomen, all the way around. I  
2 would guess that is at around 35 lbs. pressure.

3 [Slide]

4 The video then goes through the same thing, landmarking  
5 for the Heimlich maneuver in the same way.

6 [Slide]

7 Administration of the Heimlich maneuver didn't show  
8 that but it is there. This is landmarking on yourself to  
9 use the QuickAir Choke Reliever from the video --

10 [Slide]

11 -- and then administration with the QuickAir.

12 [Slide]

13 Then finally, landmarking if you don't have the device,  
14 if it is not immediately available, then this is what you  
15 do.

16 [Slide]

17 And administration of the Heimlich maneuver to self.

18 The video also shows this same person using the other  
19 methods proposed by Emergency Cardiac Care Training. The  
20 back of the chair is shown on the video; the edge of the  
21 counter is also shown on the video to get leverage on  
22 yourself.

23 [Slide]

24 For the supine position, this is the way in which the  
25 video shows to do the landmarking. We chose to use the tip

1 of the hips landmarking method for that.

2 [Slide]

3 Of course, one thing we wanted to emphasize with our  
4 product is that it is not a toy or a gadget and will never  
5 be marketed as such, but it is a piece of emergency  
6 equipment, and needs to be on the side of the refrigerator  
7 or a wall in the kitchen, wherever food is eaten, in the  
8 proximity where diners could be consuming food.

9 [Slide]

10 Just to summarize the training aspects that are  
11 included in the existing basic life support, in the three  
12 positions, standing, seated and supine, basic life support  
13 now, of course, proposes the Heimlich maneuver and there is  
14 no discussion of the seated position, and in supine, of  
15 course, the Heimlich maneuver with the abdominal thrusts is  
16 used. In the Precious Life Saving Product training items  
17 that we have -- the video, and there is also a poster and a  
18 booklet -- we do both, as I have just shown you in the snaps  
19 of the video. We also, probably for the same reasons, do  
20 not cover a person in the seated position, how to use the  
21 device in the seated position because we don't really  
22 recommend it. In our video we show a seated man in a  
23 restaurant, choking, and the rescuer, the trained rescuer  
24 asks him to stand up. So, everything is administered  
25 standing up. Of course, we also show him falling

1 unconscious, and that is where you saw the landmarking. So,  
2 we show both the standing position and then supine, but we  
3 did not include the seated and we think people who put the  
4 Emergency Cardiac Care Training together were probably very  
5 wise with that. There are too many variables in the seated  
6 position.

7 I am not saying that this device or the Heimlich  
8 maneuver should never be used in the seated position. There  
9 may be cases, such as an airplane, with a large person at a  
10 window seat where you may have to come from the front.

11 The QuickAir Choke Reliever is not discussed for the  
12 supine position. We originally didn't think it was needed,  
13 but then we saw how much additional energy Dr. Patrick was  
14 finding with the device and we thought, okay, we can include  
15 it in the booklet later.

16 [Slide]

17 A key component to the QuickAir Choke Reliever and  
18 Precious Life Saving Product program has got to be outcome  
19 analysis. We discussed this with the FDA. I think we all  
20 agree that it is very difficult to do test dummies and  
21 expect that we will replicate the actual conditions of a  
22 choking situation. We don't think that we can do that very  
23 well. We think we have tested as many people and many  
24 different sizes as is appropriate.

25 [Slide]

1           So, what we are proposing here is to do a very good job  
2 using a third-party, very credible company to do the outcome  
3 analysis. I included their proposal, one company only -- we  
4 are not necessarily going with that company but it is the  
5 style and it is the type of credibility that we think a  
6 third party should have. So, that is included in the  
7 appendices of the panel pack.

8           [Slide]

9           What we would want them to do, rather than us, is to do  
10 the questionnaire development and pretests, the interviewer  
11 training and questionnaire implementation.

12          [Slide]

13          What we would be looking for, and there may be other  
14 things that you would be looking for but, certainly, what we  
15 are interested in at this point is victim demographics;  
16 location of the incident; anything on product safety that  
17 would come under an actual choking incident; any health  
18 outcomes; symptoms, whether they be at the onset, prior to  
19 or during; severity of any symptoms; risk factors, was the  
20 person eating food, laughing, having a great time, whatever.  
21 I hope they were but some of those things are not too  
22 healthy, as we have found out. Any prior health problems;  
23 victim preferences and perceptions, which have to do with  
24 the training. Anything that would help us get a better hold  
25 on why people die due to choking, and if there is any way we

1 can improve the product, that is what we want.

2       So that is the end of the slides. I would like to  
3 mention a couple of things about the Choke Reliever. With  
4 the design of the Choke Reliever this is what we were  
5 thinking initially -- the reason why the Choke Reliever is  
6 giving so much better data, and we were just playing around  
7 in the lab really with the spirometer, seeing what shape is  
8 best, and, of course, we came up with the diamond shape  
9 because it ergonomically fits the rib cage shape. That is  
10 why we chose that.

11       We chose the degree of slope and the rate of slope so  
12 that we would be slightly larger than the hand, more  
13 compressible, much more compressible than the wrist which in  
14 the Heimlich is not compressible. The material is  
15 polyurethane self-skinning foam, which is the material on  
16 the dashboards of all our cars so that it is tough, strong  
17 and won't crack, and is soft. Because of all the rib  
18 fractures because of the interference of the wrist when you  
19 do the Heimlich, there is steel on the edges and, yet, it  
20 will support and push the ribs in a bit but will not break  
21 them. The steel inside is 200,000 lbs. psi, a carbon steel  
22 which cannot break. It will actually deform. It is a  
23 continuous piece. It is only joined once at the end, and  
24 that can't break either because if the rescuer has his hand  
25 on there, even if it did come apart, the rescue operation

1 could proceed safely.

2 We think that when you see this hanging up, if there is  
3 an emergency and someone has not read or viewed a video but  
4 they know it is for choking because somebody said in the  
5 restaurant that it is for choking, and then that person, who  
6 is rather ignorant about choking sees the device, we think  
7 that they will just look at it and they will kind of  
8 intuitively say, "okay, I think I can use that. Look at  
9 those handles, I must stand behind them and pull." We hope  
10 so, anyway. Thank you very much.

11 DR. CURTIS: Thank you. We will have the FDA  
12 presentation now. Carroll O'Neill is the lead reviewer.

13 **FDA Review**

14 **Introductory Comments, Carroll O'Neill**

15 [Slide]

16 MS. O'NEILL: Good afternoon. My name is Carroll  
17 O'Neill. I am a reviewer in the Circulatory Support and  
18 Prosthetic Devices Group in the Cardiovascular Division. I  
19 am the lead reviewer for this group of devices.

20 The devices that we are discussing today, and that I  
21 just passed around, the QuickAir Choke Reliever and the  
22 Heimlich Helper, are examples of the category of device. I  
23 want to remind you that they are examples of the category of  
24 device that we want you to look at and give us your advice  
25 on. We are not looking for approval or disapproval of these

1 devices at this time.

2 [Slide]

3 The QuickAir Choke Reliever was described very well by  
4 Wayne, and you have it right in your hands. So, I don't  
5 think I need to go into a detailed description of it. The  
6 Heimlich Helper is the red one. I think they can make it in  
7 different colors if they wish. The Self-Helper is a third  
8 one, and that was included in your panel packets, a picture  
9 of this device.

10 These devices came to our attention through various  
11 routes. One came by application. One came through a  
12 telephone call. They were asking for information, as did  
13 the third. The third came with a letter asking for  
14 information about how they could get these devices to  
15 market.

16 In response, we formed a review team to identify and  
17 discuss the issues that this type of device might present.  
18 The review team included an engineer, physiologist and  
19 emergency nurse, a statistician and three physicians. Our  
20 team identified issues regarding the safety and  
21 effectiveness of these devices. We did an extensive  
22 literature search to ensure that we had all the available  
23 data on complications, safety, effectiveness and  
24 controversies regarding the abdominal thrust maneuver.

25 In addition, we contacted an FDA panel member with

1 expertise in emergency medicine to advise us, as a homework  
2 assignment, concerning use of any device in this type of  
3 acute emergency.

4 Team members will discuss their particular focus in our  
5 efforts to address the issues with these devices. Following  
6 their presentations, I will return to list the questions we  
7 would like you to consider during the discussion.

8 I would like to introduce Dr. Paul Chandeysson, the  
9 medical officer in Circulatory Support and Prosthetic  
10 Devices Group, who will present the effectiveness of the  
11 abdominal thrust maneuver.

12 **Effectiveness of Abdominal Thrusts in Relieving Acute Airway**  
13 **Obstruction, Dr. Paul Chandeysson**

14 DR. CHANDEYSSON: Good afternoon.

15 [Slide]

16 To help assess the potential of these devices in  
17 assisting the relief of acute airway obstruction, a  
18 literature search was done to answer three questions:

19 [Slide]

20 What is the success rate of conventional abdominal  
21 thrusts in relieving acute airway obstruction? If the  
22 success rate is near 100%, there is no potential for  
23 improvement.

24 Two, is the improvement in pressure afforded by these  
25 devices in the right range of pressure to improve the

1 success of abdominal thrusts?

2 Three, are the airway pressure measurements that were  
3 reported by the manufacture of abdominal thrusts done  
4 without the device consistent with the pressure measurements  
5 reported in the medical literature?

6 [Slide]

7 An article by J.S. Redding, in Clinical Care Medicine,  
8 reference 8, provides information relevant to the first  
9 question. The article gives data on case reports of the  
10 American Heart Association. In 110 patients in which  
11 abdominal thrusts were used as the first attempt to relieve  
12 acute airway obstruction, there were 74 successful attempts  
13 and 36 failures, for a success rate of 67%. This indicates  
14 that there is a potential for improvement of the  
15 effectiveness of abdominal thrusts.

16 [Slide]

17 Of the 36 patients in whom abdominal thrusts were not  
18 initially successful, 30 were rescued by subsequent  
19 maneuvers. This suggests that other maneuvers may be  
20 effective after abdominal compression has failed.

21 [Slide]

22 The success rate of abdominal thrusts in relieving  
23 acute airway obstruction was 79% when the results of the  
24 first attempt and the subsequent attempts were combined.  
25 The success rates of other maneuvers is also shown.

1 [Slide]

2 An article by Rubin and McNaughton, in Practitioner,  
3 reference 7, gives some experimental data on the air  
4 pressure needed to dislodge food from the airway. The  
5 article describes an experiment with a cast of human lungs,  
6 made of silicone rubber, which was used to determine the air  
7 pressure needed to dislodge pieces of food, such as beef,  
8 mutton and orange segments. When the pieces of food were  
9 not completely wedged in the cast the pressures needed to  
10 dislodge them were 52 mmHg, 15 mmHg and 11 mmHg respectively  
11 for the beef, mutton and orange segments. When the pieces  
12 of food were firmly wedged in the cast, the beef and mutton  
13 could not be dislodged with the greatest air pressure that  
14 was available, which was 74 mmHg, and it required 26 mmHg to  
15 dislodge the orange segment.

16 These data suggest that the improvement in air pressure  
17 provided by the device, which averaged 30.7 mmHg with the  
18 device compared to 14.6 mmHg without it, is in the right  
19 range of pressure to improve the effectiveness of relieving  
20 acute airway obstruction. Other factors, such as the  
21 duration of pressure, may also be important in determining  
22 the success rate.

23 [Slide]

24 A book chapter by Gordon, Belton and Rudolof, entitled,  
25 "Emergency Management of Foreign Body Airway Obstruction,"

1 reference 6, describes measurement of airway pressure in 6  
2 unconscious apneic volunteers. The mean airway pressure for  
3 abdominal compression was reported as 15 mmHg in standing  
4 subjects with blocked airways. This agrees well with the  
5 mean airway pressure of 14.6 mmHg reported in the Canadian  
6 series of tests on 7 volunteer victims.

7 [Slide]

8 An article by Gilder, Williams and Subich, in the  
9 Journal of American College of Emergency Physicians,  
10 reference 5, reports the range of airway pressure generated  
11 by abdominal thrusts in 6 anesthetized adult male  
12 volunteers. It was 10-34 mmHg with the subject in the  
13 horizontal position and 10-29 mmHg with subjects in the  
14 sitting position. These results agree fairly well with the  
15 range of pressure in the Canadian series of tests.

16 The literature search confirmed that there was a  
17 potential for improving the success of conventional  
18 abdominal thrusts, and that the measured pressure  
19 improvement is in the right range for potentially providing  
20 that improvement. The agreement of the measured airway  
21 pressure developed by a conventional abdominal thrust with  
22 the results published in the literature lend some confidence  
23 to the measurement procedure.

24 Thank you for your attention. Now Dr. Spyer will  
25 discuss an approach to displaying the pressure and time

1 data.

2 **Pressure Data from Human Volunteer Studies,**

3 **Dr. Dan Spyker**

4 [Slide]

5 DR. SPYKER: Dan Spyker, medical officer in CDRH. One  
6 of the things that we struggled with the most when we  
7 gathered information is how to make sense of it, how to take  
8 it from being data into being something that is useful to  
9 tertiary reviewers, such as the panel members.

10 This is typically an intensely interactive project with  
11 the sponsors, and I thought since, clearly, one of the kinds  
12 of information that is going to be pertinent, or may be  
13 pertinent in your deliberations is the kind of pressure/  
14 time data that was just described, representing pressure  
15 over time, we took a sample of some of the data from your  
16 panel pack and went through the process up front. So, the  
17 folks that may be contributing data to us or to you who may  
18 be looking at data can help us in this process. So, I will  
19 take about five minutes and do that.

20 A typical study design, the kind we are hearing about  
21 today, is human volunteers and there is always a struggle  
22 between results versus reality. By that, I mean do you want  
23 to choose a population that you really know the outcome on  
24 or are convinced you can get some benefit on, or do you want  
25 to more reflect reality? Do you want a whole spectrum of

1 patients that are large and small, fat and skinny, and so  
2 forth? So, that is always a struggle as you design a study.  
3 Obviously, specifying the position is important. Are you  
4 going to not consider seated victims? And, we need the  
5 position of the victim and the rescuer, of course.

6 Typically, you are recording airway pressure over time,  
7 and the data that you see in your panel packs represents  
8 both what I will call a regularity assumption, that is, the  
9 first set of data you see reports peak pressure multiplied  
10 by duration. So, for that to be meaningful, you are  
11 assuming that it is regular -- triangular or rectangular,  
12 some regular shape versus area of the curve, the second set  
13 of data in your panel pack is from a planimeter, like  
14 cutting out the area of the curve and weighing it, if you  
15 will, measuring the area of the curve in a mathematical,  
16 more precise approach. So, that needs to be considered.

17 The usual design, or the ones that you see in your  
18 panel pack and probably the most statistically powerful  
19 design is what we call a crossover. So, each patient and  
20 each victim with and without the device. Okay?

21 The one thing that I want to emphasize is that it has  
22 been certainly a struggle for us as we have looked at the  
23 data that we have seen, and as is incumbent on us as we  
24 design studies for the future, how we do these simple  
25 crossover studies and minimize bias. How do we avoid the

1 appearance even that the reason that, say, the device looks  
2 better is because both the victim and the rescuer think what  
3 a great idea? You know, "I'll tense up a little more, or  
4 I'll pull harder." So, we must at least give some up-front  
5 consideration to how we design such studies to minimize  
6 bias.

7 [Slide]

8 The primary data display that I alluded to is really  
9 just a graphical and numerical data array. Those of you who  
10 have seen panel packs I think will get a little bit better  
11 at having a figure on top and the data array below, and have  
12 it sort of self-contained, and typically repeated throughout  
13 your panel pack several times. Once you get one figured  
14 out, or at least once we get one figured out, then there is  
15 some consistency across the presentation. So, that is what  
16 I mean by primary data display.

17 We would like, if possible, to see the raw data,  
18 perhaps both in graphical and numerical form, and what I am  
19 going to show you today has both. If we are really clever  
20 or work hard enough, we can usually get both descriptive and  
21 differential information from the graphic, and what I am  
22 going to show you does both those. It ought to be self-  
23 contained. By that, I mean it shouldn't have to refer out  
24 for methodology statements. So, footnotes are usually a  
25 part of these. And, one page is always -- I am told by some

1 of my friends that I am "one-page Dan."

2 [Slide]

3 So, we would like to list all the raw data. We would  
4 like to have a scatter plot. I am going to show you one for  
5 this. Conventional versus device assisted point estimates.  
6 That is the average, for those of you who aren't trained in  
7 statistics. And dispersion, and that is confidence  
8 intervals, my favorite kind of standard deviation type  
9 thing.

10 [Slide]

11 So, this is the raw data. This is from page 3-29, Tab  
12 3, in your panel packs. There were 9 trials for this. This  
13 was pressure duration. In other words, I just took the peak  
14 pressure, multiplied by the duration. So, we are assuming  
15 regular; we are assuming a triangular shape, if you will.  
16 This is millimeters of mercury times seconds for the  
17 conventional and the device assisted. This is the  
18 difference, subtracting these two. The ratio, of course, is  
19 simply the ratio of this number to this number. I have done  
20 that for each of the trials.

21 [Slide]

22 This is a scatter plot. I like scatter plots a lot  
23 because every data point is there. You immediately see the  
24 range of data, in this case ranging from 5-25 or 17 or so.  
25 So, this represents a particular patient who, on

1 conventional, generated about 12 mmHg seconds, and with the  
2 device about 30 mmHg. So, you are not hard-pressed to see  
3 some relationship. In general, when a greater pressure was  
4 generated for a patient, with the conventional method the  
5 same was generated. Note that the scales are different.  
6 This is 0-30 and 0-90. In the panel pack I have a  
7 correlation for these data with a coefficient of 0.96, and a  
8 slope and intercept for this particular regression curve.

9 [Slide]

10 We would like to see some simple statistics, in this  
11 case how many observations there were; what is the min/max  
12 for each of these terms; what is the average or the mean;  
13 standard deviation; SEM, which is just this divided by the  
14 square root of M; and the confidence interval. This is what  
15 I think is perhaps among the most valuable pieces of  
16 information, particularly if you look at the difference  
17 here. So, the average difference was 20 mmHg seconds, and  
18 the 95% confidence interval in that is 10-30, 10-31.

19 This is the same thing done with the ratios. The  
20 average ratio assisted to conventional is 2.3. Notice that  
21 the confidence interval here excludes zero. The confidence  
22 interval here excludes 1. Since this is a paired  
23 comparison, that means that there was a statistically  
24 significant difference in those numbers or the ratio of  
25 those numbers.

1 [Slide]

2 This picture shows exactly the same data in a graphic  
3 format. Here is the average and confidence interval for the  
4 conventional and for the device-assisted. More importantly  
5 from the inferential standpoint is the difference. So, here  
6 is the difference; the average; and the confidence interval.  
7 Notice that it excludes zero. So, that means we are 95%  
8 sure the difference is greater than zero. In fact, that is  
9 the range we think it is in.

10 [Slide]

11 So, this is what a typical primary data display would  
12 look like, one page with appropriate footnotes, and so  
13 forth.

14 [Slide]

15 So, our suggestion then or the things that we think are  
16 important to make a successful gathering of this kind of  
17 data is to specify the hypothesis, the endpoints and  
18 analysis plan as early as possible; develop a primary data  
19 display such as the process that we just went through here;  
20 and interact with the review team early and interact with  
21 the review team often. These are the things we think will  
22 help to make this procedure work.

23 I would like to welcome my colleague, Patricia Dubill  
24 to the podium. She is going to talk to us about some of the  
25 preclinical or what we call bench testing that we think

1 might be suggested for this kind of device.

2 **Suggested Bench Tests for Premarket Evaluation of**  
3 **Abdominal Thrust Devices, Patricia Dubill**

4 [Slide]

5 MS. DUBILL: I am going to be talking about some  
6 suggestions that we have for bench testing of these kinds of  
7 devices. By bench testing, I mean that there will be no  
8 direct assessment of the clinical effects of the device on  
9 humans or animal models. What I am talking about is tests  
10 that involve engineering or other in vitro type tests that  
11 are needed, in addition to preclinical and clinical testing,  
12 in order to ensure device safety and effectiveness.

13 [Slide]

14 What I have done here is list some of the types of  
15 tests that we think would be useful. This is just a summary  
16 of them. I will go into a little more detail later,  
17 including our rationale for why we think they are necessary.

18 Basically, the tests I have listed here are intended to  
19 cover a range of possible device designs, not one specific  
20 device and it would not be limited to the two that you saw  
21 earlier this afternoon. They are directed at devices that  
22 are used to assist in performing abdominal thrusts, not any  
23 kind of mechanical devices performing extrication or any  
24 other kind of treatment of choking.

25 The first three that you see listed here are used to

1 characterize the mechanical operation of a device and the  
2 durability of a device. The next one is addressing a safety  
3 concern with potential for organ rupture. The last one has  
4 to do with concerns about user error with use of the device.  
5 Then, the last one is a general "other" category which I  
6 will discuss a little bit later. So, I will go into these  
7 in a little more detail.

8 [Slide]

9 First, I listed static load testing. This is testing  
10 where the manufacturer should determine the amount of force  
11 and pressure that would be applied by the use of the device,  
12 both the expected average and range, and then characterize  
13 the mechanical performance of the device for that range.  
14 For example, measure the resulting deformation functionality  
15 of the device, and address any implications for safety and  
16 effectiveness.

17 This kind of testing is needed to understand the basic  
18 operation of the device and to characterize the fundamental  
19 mechanical performance during use.

20 [Slide]

21 The next test I have listed is mechanical shock  
22 testing. If there is a possibility that the device might  
23 fail as a result of being dropped during use, then it should  
24 be subjected to drop testing. We think that because these  
25 are devices that are small and light and are handled quite a

1 bit during use, they might easily be dropped and they should  
2 be able to withstand the resulting mechanical shock.

3 [Slide]

4 The next test is fatigue testing. This is cyclic type  
5 testing of the device that should be performed under loading  
6 conditions that simulate clinical use. The number of cycles  
7 tested should be reflective of the expected useful life of  
8 the device. Any surface deterioration, such as tearing,  
9 cracking or wear, or overall device failure such as  
10 excessive deformation or breakage should be reported.  
11 Another thing, if there is any labeling attached to the  
12 device, it is important that not become detached or  
13 illegible with repeated use.

14 These types of devices are going to be used repeatedly,  
15 possibly on one choking victim and also on multiple victims  
16 most likely, so we felt that it was important that  
17 manufacturers show that the device performance does not  
18 deteriorate with repeated use.

19 [Slide]

20 These are fairly simple types of devices and the tests  
21 I have listed so far are fairly simple. This next test gets  
22 into a little bit more complex issue, and that is a safety  
23 concern. We think some testing of the device on some kind  
24 of an in vitro model would be helpful to estimate the  
25 potential for abdominal injuries associated with use of the

1 device relative to use of conventional methods.

2       The need for this test, we think, is because gastric  
3 rupture and other types of injuries have resulted from the  
4 use of abdominal thrusts. Although rare, these problems can  
5 be fatal at times. Certainly the most urgent concern is  
6 relief of choking, but you also don't want to seriously  
7 injure the patient in the process of relieving choking.

8       Given that some of these devices seem to offer some  
9 mechanical advantage, such that greater pressures are  
10 produced, we are concerned that the relative risk of organ  
11 rupture or other injury from use of the device versus  
12 abdominal thrust needs to be estimated in order to  
13 facilitate risk/benefit determinations. If it is shown that  
14 maybe there is a little bit increased risk of gastric  
15 rupture, or something, but the device is more effective,  
16 then that certainly would probably outweigh any concerns  
17 about gastric rupture because ultimately choking has to be  
18 treated.

19       With respect to this issue, ideally it would be  
20 preferable to have some kind of clinical data, perhaps on  
21 intraabdominal pressure produced using the device versus  
22 abdominal thrust, but that kind of data would be rather  
23 difficult to obtain given the invasiveness of most of the  
24 available measurement methods. So, in lieu of that type of  
25 testing, we are suggesting that some kind of bench

1 simulation testing be performed, and we would appreciate the  
2 panel's thoughts on this.

3 [Slide]

4 Finally, I have labeling and human factors testing  
5 listed. We think the manufacturer should be required to  
6 demonstrate that lay people can understand and follow the  
7 device instructions, both with respect to device placement  
8 and applied force. The rescuer should cover a range of  
9 sizes and educational levels. Here, we could use models  
10 rather than testing on human subjects.

11 The need for this testing is because many of the  
12 abdominal thrusts that are performed are done so by lay  
13 people, and many of the associated complications are  
14 believed to be a result of improper technique. So, the  
15 adequacy of the supplied instructional information is really  
16 critical to safety and effectiveness of the devices.

17 [Slide]

18 Finally, I did have one category here that I designated  
19 as "other testing." We tried to anticipate possible designs  
20 of devices but we can't anticipate everything. So, this is  
21 something that covers whatever we might not have thought of.

22

23 Basically, the manufacturer should assess all of the  
24 potential failure modes for the device, and make sure that  
25 any additional testing that might be necessary to account

1 for failure modes not addressed in my discussion should be  
2 conducted.

3 So, that concludes my discussion of our suggestions for  
4 bench testing. Again, these are tests that would supplement  
5 any clinical testing that might be done in order to  
6 characterize the mechanical performance of the devices and  
7 address other safety concerns that we have.

8 The next speaker will be Dr. Subramanian. He is a  
9 pathologist in the Cardiovascular Division in ODE, and he  
10 will be discussing adverse events associated with abdominal  
11 thrust maneuvers.

12 **Adverse Events Associated with the Abdominal Thrust Maneuver**

13 **Dr. Ramiah Subramanian**

14 DR. SUBRAMANIAN: Nice to see you again. In case you  
15 are not overcome by Goddess Morpheus, the pathologist will  
16 do it for you now.

17 [Laughter]

18 [Slide]

19 Although I personally do not worry about choking on  
20 broccoli, being a vegetarian, the procedure is known to save  
21 lives and the FDA wanted to know what the adverse events are  
22 associated with this procedure. As we are wont to do, we  
23 are concerned with safety.

24 [Slide]

25 In order to do this, we looked at the published

1 literature and we wanted to see in the papers if there was a  
2 common thread as far as the adverse events are concerned; if  
3 there was something we could point out and say, okay, this  
4 is where the problem is, and to see what can be learned from  
5 this review.

6 [Slide]

7 A search was done at the National Library of Medicine  
8 Medline and different sponsors provided bibliographies. The  
9 journals included surgical, medical emergency medicine and  
10 pathology journals. There were 17 reports which included 18  
11 patients. One of the reports had 18 patients. There is a  
12 table that we have given you that includes all of these. We  
13 reviewed these papers.

14 [Slide]

15 This is an example of one of the patients included in  
16 the tables. The first column is the clinical presentation.

17

18 [Slide]

19 The next one shows the complications that occurred and  
20 how the diagnosis was made. In this particular instance,  
21 the patient died with a large tear in the root of the  
22 mesentery near the ligament of Treitz. I imagine he was  
23 pressed very hard, with blood in the abdominal cavity.

24 [Slide]

25 The next column shows the outcome. In this instance

1 the patient died.

2 [Slide]

3 The next column shows the assumed pathogenesis. In  
4 some of the articles there were some useful comments. This  
5 is an instance that was very appropriate and shows the need  
6 for proper training.

7 [Slide]

8 We also tried to find out, based on the published  
9 papers, whether or not the patient needed a maneuver -- some  
10 patient who has a problem swallowing a piece of meat that is  
11 stuck in the esophagus and somebody jumps on them. The last  
12 column is the reference.

13 [Slide]

14 The results obtained are shown on the next two slides.  
15 The maneuver was successful more often than not. Seven of  
16 these patients died. Other than the seven, one of these  
17 patients who was actually a near-drowning victim, went into  
18 a vegetative state; and one patient who was a rather older  
19 gentleman needed continued assistance.

20 [Slide]

21 There were various types of injuries, which is quite  
22 remarkable. Most of the injuries were in the hollow  
23 viscera, tears in the stomach and the esophagus and  
24 gastroesophageal junction. There were two instances where  
25 the aortic valve was ruptured. One patient had a

1 preexisting aortic murmur with aortic stenosis, and after  
2 the procedure the murmur became more pronounced. The other  
3 patient had a bioprosthesis which was totally torn by the  
4 procedure. There was an abdominal aortic aneurism in one.  
5 It went on to thrombose. In the other patient the thrombus  
6 was displaced and caused an obstruction to the common iliac  
7 artery. There were instances of mesenteric root tear, which  
8 occurred more often when the pressure was applied above the  
9 xiphoid rather than correctly. There were instances of  
10 diaphragmatic hernia, with the colon being pushed up with  
11 ischemic infarction of the colon.

12 [Slide]

13 So, we concluded that serious injuries do occur with  
14 the conventional abdominal thrust maneuver, and some of the  
15 patients may not have needed this procedure.

16 With the device-assisted procedure there is going to be  
17 greater pressure applied, and it is entirely possible that  
18 there may be more injuries associated with this. When this  
19 does occur, it may be rather difficult to tell whether the  
20 injury was caused by the procedure alone versus the  
21 procedure with the device.

22 [Slide]

23 We learned that continued training is essential for  
24 people to use this. Very often the procedure was done by a  
25 big, burly person, who would squeeze him and this would

1 result in tearing of the stomach, or something like that.  
2 It would be very advisable for a patient to be seen by a  
3 physician in follow-up. And, the old adage still holds,  
4 "primum, non nocere," which roughly translated means don't  
5 do something standing. I shall leave you with a quotation  
6 from T.S. Eliot, "now you are left to your own devices."  
7 Thank you.

#### 8 Questions to the Panel

9 DR. CURTIS: Thank you. We will be moving on to the  
10 panel discussion now. Our lead reviewer is Dr. Becker.

11 MS. O'NEILL: Before that, Anne, could we go over the  
12 questions again we would like you to consider?

13 DR. CURTIS: All right, go ahead.

14 [Slide]

15 MS. O'NEILL: We would like you to look at the  
16 indications and see if you agree. It is pretty  
17 straightforward.

18 [Slide]

19 What type of bench testing or other evidence would be  
20 necessary before beginning use in humans?

21 Third, what type of data, if any, should be obtained  
22 from human volunteer studies? That means if you think we  
23 should be doing human volunteer studies once a sponsor has  
24 provided clinical measurement of the time course of the  
25 pressure-generated with their device and that during the

1 unassisted Heimlich.

2 How might we determine an appropriate range of energy  
3 which would be safe and effective? How might we address  
4 concerns of patient positioning, sitting or standing versus  
5 supine victims, and patient size?

6 [Slide]

7 Fourth, what types of evidence should be required to  
8 assess the risks and benefits to permit clearance of a  
9 device prior to commercial distribution?

10 How do we assess complications associated with  
11 performance of the assisted Heimlich? What about children,  
12 the frail elderly, the seated or supine patients? How do we  
13 assess benefits associated with performance of the assisted  
14 Heimlich maneuver?

15 [Slide]

16 Is use data, clinical evidence, necessary prior to  
17 commercial distribution? Is it possible?

18 [Slide]

19 If needed, what are some alternatives to gathering use  
20 data? Can labeling, instructions for use, and hands-on  
21 training mitigate some of the risk?

22 How might uses of such a device be trained? Should  
23 different techniques be used for victims who are unconscious  
24 versus conscious? Should different techniques be used for  
25 victims who are sitting or standing versus supine?

1 [Slide]

2 What kind of data, if any, should be obtained after  
3 commercial distribution, if these devices are approved  
4 eventually?

5 [Slide]

6 Are there roles for professional societies in training  
7 users and assessing outcomes, if these devices are approved  
8 for marketing?

9 [Slide]

10 Would basic life support and advanced life support  
11 training need to reflect use of such a device if it were  
12 cleared for marketing?

13 Thank you. These are the questions we would like you  
14 to help us with.

15 DR. CURTIS: Thank you. Dr. Becker?

16 **Panel Review**

17 **Lance B. Becker, M.D.**

18 DR. BECKER: Well, thank you, and I would like to thank  
19 the presenters as well. As I reviewed a lot of this data, I  
20 came with perhaps just a slightly different perspective. I  
21 do look at safety but I now began to look at something that  
22 I call efficacy, and then looked at something I call  
23 effectiveness, and differentiated those two based on  
24 efficacy being does the device work for the particular  
25 patient, and effectiveness being a big more general

1 question, does it work when it is then disseminated out into  
2 the community? In other words, does it finally affect  
3 outcome if one looks at survival?

4 The reason why I think that is sometimes a useful thing  
5 to do is because one thing that we have learned in looking  
6 at a lot of sudden death type of data is that there is a  
7 terrific difference between what I call process outcome  
8 variables and outcome variables that involve things like  
9 survival. A good example in this presentation is that we  
10 have seen a lot of data presented on pressures that were  
11 generated, and I think that those are probably some very  
12 good process variables but the final pudding is in how it  
13 tastes, and does it save people's lives has to be a critical  
14 issue that we get to at some point.

15 Obviously, this is a very early part of the sort of  
16 discovery of the usefulness of these type of devices, and  
17 so, you know, I think in a very general way what I am seeing  
18 as I go through a lot of the data that has been presented is  
19 that there seems to be reasonable data sort of on safety.  
20 There is probable some kind of data that seems to be  
21 emerging on the efficacy. The effectiveness, I haven't  
22 really seen any data on that yet.

23 So, I guess I would just open by saying that I hope  
24 these things will continue and that we will talk about so  
25 that there is really compelling data, particularly because I

1 would guess that as device manufacturers you may eventually  
2 want some other organizations to include your devices in  
3 guidelines and, clearly, as we talk about national  
4 guidelines and things like that, the effectiveness data will  
5 be what is really going to be scrutinized the most  
6 carefully. Just as an example, if you wanted an  
7 organization, like the American Heart Association, to review  
8 these types of things, I would say that that kind of data  
9 will have to be presented.

10 Now, in terms of some of the questions, I am not sure  
11 that I offer a lot of answers on this. One concern that I  
12 had in going through it where I saw an opportunity for some  
13 additional data is in the issue of how much strength is  
14 really required to use the device. The scattergram that I  
15 think Dr. Spyker put up showed that in the volunteers there  
16 was really a very broad range of force that people seemed to  
17 apply as they were using the device. If I understood that,  
18 my interpretation would be that that gives me a bit of  
19 concern. If you just want to address that?

20 MR. WHITBECK: I think that is a very good question,  
21 and I just want to make the comment, as we are moving  
22 through this important issue, that the data that was there  
23 was the pressure at the mouth and was not necessarily -- it  
24 is an indication of the pressure applied to the abdomen but  
25 the condition, the age, the bones of the rib cage and the

1 anesthetized subjects done by Gordon -- many people feel  
2 that being anesthetized changes the costal muscles and gives  
3 you much more pressure at the mouth so it is an indication  
4 of the pressure, but not necessarily the pressure applied to  
5 the abdomen.

6 DR. BECKER: Thank you for the clarification on that.  
7 Yes, it is hard to get volunteers to be anesthetized these  
8 days. Medical students just aren't as committed as they  
9 used to be --

10 [Laughter]

11 But I think that is going to be very important  
12 information that actually could be gained in terms of what  
13 average individuals are capable of doing because it raises  
14 the question of who can use these devices. So, is this  
15 something that a kid can use? You know, about how much  
16 force is required to produce the needed amount of force to  
17 expel sort of a typical object, or something like that? I  
18 just raise that because I think that is information that  
19 could be ascertained, and probably not at terrific expense.

20 Another thing that I am kind of looking for is some  
21 information on the learning curve to become familiar with  
22 the use of these devices. We know that in CPR there is  
23 quite a learning curve and, again, this is something that I  
24 suspect would be kind of readily amenable to providing  
25 pretty good information. How long does it take a person to

1 learn how to use this device in a reasonable way? I haven't  
2 seen that information yet, and that is the kind of  
3 information that I think is going to be useful. It gets  
4 into training issues, which is something that is part of the  
5 questions, and it, again, gets into the overall cost/benefit  
6 kind of analysis that will ultimately have to take place to  
7 determine if these types of devices are really worth being  
8 broadly disseminated.

9 I also wanted to just raise another issue. It is  
10 probably a labeling issue. I am always concerned when I  
11 read something -- and I don't mean to pick on any  
12 manufacturer -- where it says to use the device "quickly yet  
13 cautiously." I don't know what that means. So, I am going  
14 to presume that other people wouldn't know what "quickly yet  
15 cautiously" would really mean.

16 So, one of the things that occurred to me is would  
17 there be a training model that could be worked up that a  
18 person could try the device out on, that would have some  
19 kind of a pressure gauge that would actually show how much  
20 pressure they were exerting on the device.

21 I don't know how practical it would be but, you know,  
22 for training courses you could somehow rig a pressure  
23 transducer into this that would give some feedback to the  
24 user because one thing that these devices share in common  
25 right now is that they provide no feedback really. Have you

1 used enough force? Have you used too little force? Have  
2 you not used enough?

3 As we look at devices, a good example might be one that  
4 is no longer in trials in this country -- I guess I can't  
5 even say the name of it here, but it did have a built in  
6 pressure transducer that provided some feedback when  
7 compressions were being performed on the chest. So, I would  
8 just raise the issue that these devices right now don't have  
9 any feedback link so that the user can know if he has  
10 generated enough force or not. So, those are some of my  
11 preliminary comments.

12 Another concern that I have is that I think some of the  
13 answers to this could be done in animal studies. There are  
14 good animal models, since we can't use medical students the  
15 way we used to -- you know, there are good animal models for  
16 some of this, particularly since presumably whether the  
17 airway is open or closed is not the issue.

18 I will back up for just a second. The big criticisms  
19 of lots of CPR research is that the airway is often open in  
20 an animal but close in a human. There is a lot of  
21 controversy about it. It is not an issue for this. So,  
22 animal models would likely be appropriate for some of this  
23 pressure force type of exploration, and you would be able to  
24 show really in much more detail I think the ability, for  
25 example, of these techniques to expel something from the

1 trachea using some animal models. Some of that, I think,  
2 would be useful.

3 The usual progression that I see in devices is that  
4 first there is sort of the theoretical background for it.  
5 Then it is tried out in animal studies. Then, with some  
6 successful animal studies, it gets moved on into human  
7 studies. I just note that what I have seen here is that we  
8 have gone to some human volunteer studies but I think there  
9 is a role for some animal studies within some of this work,  
10 and I would encourage at least a discussion of what might be  
11 useful for that.

12 My final comment, because I don't really want to wander  
13 on here too much, is that I do think that the postmarket  
14 surveillance issue is probably, in my mind, the most  
15 important issue of all, which is that there simply has to be  
16 some way that when the device gets used we can keep track of  
17 its success, its complications, and whether or not it can be  
18 improved.

19 Now, all of the criticisms that I have laid out here,  
20 they apply to the Heimlich maneuver as well as this device.  
21 So, I don't think that this should be seen really as  
22 anything other than a step forward in terms of what we are  
23 trying to do in terms of documentation. I wouldn't want any  
24 of the device folks to go away feeling that they have been  
25 beat up on because if we were here, talking about the

1 Heimlich maneuver, many of my concerns would be just exactly  
2 the same concerns. However, as we move into this I do think  
3 that we are not setting the threshold higher in terms of our  
4 levels of evidence that we expect for things that are going  
5 to move out there. So, I think that these are important  
6 considerations and I think the postmarket surveillance is  
7 just going to be a key piece of data that many of us will  
8 require. I don't know if I answered any of the questions.

9 **Panel Discussion**

10 DR. CURTIS: We will get to that later. Dr. Roberts?

11 DR. ROBERTS: Well, I think that these devices present  
12 a very difficult problem for the FDA and for all of us.  
13 That is, I think you can only do a certain amount of testing  
14 of these devices, and you can only try and simulate the  
15 real-life problem of someone choking. I think it raises a  
16 big issue because if you are going to turn these devices  
17 loose to be used in the general population, how do you have  
18 any idea whether they are safe and effective? You really  
19 don't until you have them out there and people are using  
20 them.

21 I think that this is a major issue and I think that the  
22 agency has done a very nice job of trying to address the  
23 concerns and the questions about how to do this, but I  
24 think, honestly, when it comes right down to it, I am not so  
25 sure that there is going to be a great animal model for

1 using this on. I think animals are constructed differently  
2 than humans, and it is going to be a little hard. You can  
3 do some things with animal models but I don't think you are  
4 really going to be able to demonstrate it as well as you  
5 would like to in order to really know whether or not this is  
6 going to be useful in humans.

7 I was actually quite amused that there were actually  
8 anesthetized, apneic, standing people that they did some  
9 kind of testing on. I find that almost incredible. Anyway,  
10 I think those models are going to be very hard to come by  
11 these days.

12 I think that there are some very important issues with  
13 this. I must say that I think one of the biggest things is  
14 that there needs to be good training. I would certainly  
15 agree that one of the things that we need to work on with  
16 these types of devices is how the training is going to be  
17 carried out, and is there a possible sort of a resuscitation  
18 model, like the "Rescucie Annie" model that is used for  
19 training people on how to do CPR, and actually is used for  
20 sort of demonstrating the Heimlich maneuver? Is there a way  
21 to rig up such a model that would sort of give people an  
22 idea, either with a standard Heimlich maneuver or using one  
23 of these devices, how much force one needs to apply in order  
24 to, hopefully, be effective? I think that is hard because I  
25 don't think that there is any particularly great data about

1 how much force that is. But I think that is something to  
2 work for.

3 I think that one of the crucial issues is the case  
4 study report form which has been started. I think there are  
5 some things that it needs to get into in a little more  
6 detail, but I think that is the way that this needs to go,  
7 and we need to figure out some way to try and get people to  
8 report in, in terms of what their success or failure has  
9 been with this. I suspect that finding the failures isn't  
10 going to be that big a deal and, quite honestly, when you  
11 look at some of these papers that describe failures, I think  
12 it is probably fair to say that the successes are never  
13 reported because someone has a success, goes on with their  
14 life and doesn't go running to the emergency room or to  
15 anyone else reporting the fact that they have had a success.  
16 But I think it is very important to try and get some of this  
17 information.

18 The other thing that I think is absolutely crucial is  
19 that when one of these devices is hung up or, you know, kept  
20 somewhere, that right above it or with it is a description  
21 of how to use it. What is even more important is to have  
22 that description describe how to do the Heimlich maneuver  
23 if, in fact, this device is not readily available. I think  
24 that needs to be number one because in a panic situation  
25 someone is going to remember that there was some device, but

1 not where it is but, hopefully, if they have reviewed the  
2 information at least they have had the opportunity to maybe  
3 know how to do the Heimlich maneuver themselves. I think  
4 that is very important.

5 I think one of the most important things that has been  
6 stressed is the fact that, if for no other reason, I see  
7 these devices being helpful to the community at large just  
8 because it increases the awareness of the problem of choking  
9 and that there is something that can be done about it. You  
10 know, whether these work a hundred percent or not is  
11 probably not the issue. It is just that, particularly in  
12 certain areas such as restaurants, or nursing homes, or  
13 whatever, people will have this brought to their attention  
14 and that may, you know, diminish the problem right off the  
15 bat. Those are my comments.

16 DR. FREISCHLAG: I agree with everything that Dr.  
17 Roberts said. Certainly, if it is hanging on a wall in a  
18 restaurant I would go over and see what it was. I know in  
19 CPR classes, when it gets time to do the Heimlich they sort  
20 of have you pretend on each other. You really don't do it.  
21 You sort of put a fist on each other and say, "yeah, I know  
22 how to do it." I have done it a couple of times when I was  
23 a waitress and, therefore, know how to do it but it  
24 certainly didn't come from my medical training whatsoever.

25 The only thing I have to add is that I have a concern

1 about the use of these on children. I guess I would want  
2 that explored a little bit more. These look actually like  
3 the size of a 1-year old or a 2-year old child --

4 [Laughter]

5 -- I have a very large 3-year old child and this looks  
6 bigger than him. So, I guess my concern is the use on  
7 children. I am not sure they should be used on children for  
8 all the reasons you are telling us we need these. I can't  
9 imagine a smaller rescuer than a 2-year old and, therefore,  
10 being sort of a small person myself, I don't think I would  
11 go get this for a child. I think on the couple of children  
12 that I have done, if the thrusts don't work you can really  
13 beat them on the back and they tend to be very manipulative;  
14 you can move them around. So, I am not sure children is  
15 something that I am interested in, or I would have to have a  
16 little bit more proof with these devices.

17 DR. FIELDER: I was watching your video, and in the  
18 video they reenact successful uses of the Heimlich maneuver,  
19 once with a grapefruit and other times just with hands. As  
20 I was watching I was thinking about myself being in this  
21 position because it is reenacted in a restaurant and  
22 suddenly the person stands up and, having a vivid  
23 imagination about these things, I imagined myself sitting  
24 there, eating my onion soup and thinking, "oh God, now what  
25 do I do?"

1 I did a book on the VC-10 some years ago, and became  
2 much more aware of safety in flying. So, I sit in those  
3 exit rows and I look at the windows that you can open for  
4 escape hatches. I try to imagine myself doing this. They  
5 give you helpful information, like this thing weighs 55  
6 lbs., but it is also a big, awkward thing and you wonder if  
7 you are going to get out without broken fingers or if you  
8 are going to screw it up because it is so heavy, or  
9 whatever. And, I would love to practice sometime, just to  
10 see how much force; do you jerk it; do you pull it; is it  
11 easy; is it hard? And, I would feel a lot safer sitting in  
12 an airplane if I had a chance to do that.

13 I think the same thing happens here with this Heimlich  
14 maneuver. I imagine myself being in that restaurant and  
15 thinking, well, how hard do I squeeze this person? I don't  
16 want to rupture anything inside. And, I would like to have  
17 some descriptive language to tell me how much force to use,  
18 even if it was in pounds, because knowing that the airplane  
19 door weighs 55 lbs. tells you that this is a pretty good  
20 sized object and you are really going to be braced and ready  
21 to do something interesting.

22 So, I agree with the panelist who suggested we need  
23 some kind of pressure measurements, some kind of feedback,  
24 some way to tell those untrained users how much force to  
25 apply.

1 I also imagine myself as the choking victim, and at the  
2 table next to me is a linebacker for the Philadelphia  
3 Eagles, who jumps up, grabs one of these things and ruptures  
4 all the things that we saw in the table --

5 [Laughter]

6 -- I would like for that person, when they pick it up  
7 and look at it, to have some idea of how hard to squeeze me  
8 to help me out.

9 Just a couple of other comments, Dr. Spyker said we  
10 should brain-storm an free-wheel here. When you are  
11 creating a model for developing pressure or testing this  
12 device, could you use cadavers? I mean, is it possible to  
13 try to get some initial data through cadavers? The consent  
14 factor is not there. I would not recommend apneic,  
15 anesthetized medical students, or any other kind of  
16 students, even law students --

17 [Laughter]

18 -- so I think that this particular application might be  
19 an inappropriate risk and if I were on an IRB I would  
20 scuttle it immediately.

21 The other thing related to children -- there are also  
22 pregnant women who are going to choke and, clearly, you  
23 should not use this device for pregnant women. So, in some  
24 way, you have to indicate to people that this is a no-no;  
25 that you can cause injury to the fetus by using the device

1 in a way you would with someone who is not pregnant.

2 Finally, I was thinking about labeling as these devices  
3 were being passed around. It seems to me that if untrained  
4 folks are going to use them, the labeling ought to be right  
5 on the device. It ought to be pictorial so that you don't  
6 have to interpret the text. It ought to be painted on there  
7 large enough so that folks like me, whose eyes are quietly  
8 going bad, can see it and read it pretty easily. As I think  
9 of myself in a restaurant, rushing up there, I would like to  
10 see it on the device so that I would know what to do and  
11 have some kind of idea about what kind of pressure to use.  
12 That is all.

13 DR. SIMMONS: First of all, trying to look at this  
14 logically, you know, the FDA has posed some very hard  
15 questions here. They must have sat around for hours trying  
16 to think of all these very hard questions. As I was trying  
17 to look through and come up with a logical answer for a lot  
18 of them, what I actually came up with is that the science  
19 really isn't there to answer the questions.

20 As I was looking through these articles, some of them  
21 are actually more on the level of high school science  
22 projects and some of the science that I have actually seen  
23 presented here and other types of projects, and whether it  
24 is the peak pressure, or the pressure time curve, or the  
25 area under the curve, or is it the FEV-1? Maybe there

1 should be an FEV-0.2 or something like that. And, you know,  
2 the time for the amount of volume being expelled -- I don't  
3 know that you know the answer for what is the most effective  
4 thing to expel a piece of food stuck in somebody's throat.  
5 To try to make up a logical, scientific answer to the  
6 questions just may not be going to happen.

7 I saw at the end of Dr. Subramanian's slide that the  
8 first rule is to do no harm. So, in something like this  
9 maybe the logical thing to do is try and find out, first of  
10 all, is the device going to do any harm and then, second, is  
11 it logical. Then, if it is logical and it is not going to  
12 do any harm, maybe the benefits are going to have to come  
13 from the postmarketing surveillance.

14 So, I was unconvinced, looking through the book, that  
15 the devices adequately prove, from what I have seen, that  
16 they will do no harm. I mean, the Heimlich maneuver has  
17 been around a long time and it may only have a 78%  
18 effectiveness rate, but it actually has a very low incidence  
19 of reported harm, and I don't know what the harm from one of  
20 these devices is in somebody's hands.

21 So, I would say I would like to see some more real data  
22 that it is not going to do any harm because, logically, I do  
23 think they are going to generate more pressure. You are  
24 going to generate more force. Logically, it should expel  
25 food better. I just don't know how you are going to prove

1 that in a reasonable amount of time that is going to do  
2 these companies any benefit. So, maybe if you can design  
3 some experiments to better prove that it is not going to do  
4 harm, then if the device seems logical ask them to do  
5 postmarketing surveillance. And, I think that the idea of  
6 putting a 1-800 number on the thing, "if you ever use this  
7 thing, call me and I'll pay you back for using the device,"  
8 is a good mechanism.

9 I did have some other questions I wanted to have the  
10 reviewers ask, but I will leave those for later. Those are  
11 my comments for now.

12 DR. CURTIS: Dr. Vetovec, will you introduce yourself  
13 and then make your comments?

14 DR. VETROVEC: Yes. I am George Vetovec. I am from  
15 Medical College of Virginia, campus of Virginia Commonwealth  
16 University in Richmond. I am chairman of cardiology there.  
17 I apologize for being late.

18 I guess when you are nearly last there aren't too many  
19 things to be said, except to perhaps support some of the  
20 things that were said. One of the things that bothers me,  
21 and this is probably true of the Heimlich maneuver itself as  
22 well as any device, is the marked disparity between body  
23 habitus. That may be a major issue in terms of injury and  
24 in terms of how you apply the force, and maybe even where  
25 you apply the force and how effective it is, and what the

1 risk of injury is. So, while the "Rescucie Annie" idea is  
2 clever and might be useful in some basic studies, I am a  
3 little concerned that it might not deal with the reality.

4 I really like the cadaver idea. I don't know what the  
5 logistics of that would be. Maybe one or two studies with a  
6 very limited number of cadavers might at least get some  
7 general information.

8 We are dealing with a terribly inexact science, and I  
9 think it is going to have to involve some type of  
10 postmarketing survey. One thought that I had that would  
11 control this a little bit better is, rather than releasing  
12 this to be used in restaurants and homes and a lot of  
13 uncontrolled areas where it would be hard to get data back,  
14 if I read the data correctly here, about 50% of these events  
15 occur in hospitals and nursing homes. So, one interesting  
16 question would be to tie this in some way to professional  
17 training related to CPR, through the American Heart and so  
18 forth, and to first only release it to be used within the  
19 hospital or nursing home setting where you would be much  
20 more likely to get forms filled out and back on the efficacy  
21 of this and the complications. That might be a way to  
22 gather science on the run. I don't know, that is my best  
23 thought.

24 DR. ROBERTS: Yes, actually that was my idea too. I  
25 made a note that maybe the best place to release this is

1 nursing homes and let it be used there. At least, if it  
2 doesn't work, you would have people that may be able to  
3 respond in other ways and it might give you some  
4 information.

5 DR. CURTIS: I think this would be a good time to take  
6 a break since we are scheduled for one anyway. We will  
7 reconvene at 3:15.

8 [Brief recess]

9 DR. CURTIS: I think it is probably my turn to go ahead  
10 and make a few comments. One of the things that we were  
11 kind of discussing is the fact of the pressure generated by  
12 these devices. We don't have a whole lot of data from here.  
13 Basically, the data that is available so far has to do with  
14 things like the cast of the larynx and how much pressure it  
15 takes to pop out a piece of meat or a piece of orange out of  
16 it, and then the volunteers and how much pressure was  
17 generated using standard Heimlich versus the assisted  
18 maneuver. Who were these volunteers, and what were they  
19 told to do, you know, in terms of doing this? The results  
20 show that there is more pressure generated by the assist  
21 device than there is by the Heimlich itself, but what kind  
22 of instructions were they given, and how was it done?

23 MR. WHITBECK: The volunteers, both victims and  
24 volunteer rescuers, were asked to stand in a relaxed manner  
25 and to breathe normally. Because the spirometer that we

1 have gave us the tidal volume and how they were breathing,  
2 we just tried to relax them to begin with. You know, "this  
3 is no big problem; just relax." So, they would be standing  
4 like this as if they were choking. They would have the  
5 spirometer in their mouth, and then after we thought that  
6 they were relaxed, we just told them we were going to do the  
7 Heimlich maneuver on them. We didn't say anything else, and  
8 they were familiar with what the Heimlich maneuver was.

9 DR. CURTIS: I think you probably need to be speaking  
10 into a mike.

11 MR. WHITBECK: Thank you. We got different rescuers,  
12 as shown in the data, and showed them, first of all, this is  
13 how you position the device, with one hand on the xiphoid --  
14 "can you feel it?" "Yes." -- put the device below that,  
15 grab both handles and pull back with two or three very hard  
16 thrusts. That is it; it was that simple.

17 At the time we did those tests we did not know what the  
18 literature pressure values were. I looked them up later and  
19 thought it was pretty good; they seemed to agree. The  
20 reason we were doing it in that order is that we were trying  
21 different shapes, trying to see what was the most  
22 ergonomically comfortable, what is the most effective shape  
23 and with how much stiffness. So, we were doing product  
24 development while we were testing these.

25 DR. CURTIS: Thank you.

1 MR. FUNK: I am Charles Funk with the Heimlich Helper.  
2 The only thing we tried to do, we picked up on Dr.  
3 Heimlich's research and our main attempt was to duplicate  
4 that. Our device comes close to the Heimlich maneuver or  
5 how Dr. Heimlich performed it, and our tests showed that it  
6 did. Basically, our people started exhaling and, as they  
7 exhaled, we performed the maneuver and then looked at what  
8 the difference was. That is exactly what Dr. Heimlich did.

9  
10 DR. CURTIS: Were the volunteers used in the studies  
11 employees of the company?

12 MR. FUNK: Yes.

13 DR. CURTIS: Thank you. One of the things I would  
14 wonder about, I mean, the Heimlich maneuver works but it  
15 doesn't work all the time. So, the issues here are weighing  
16 whether the increased pressure you can generate by this  
17 thing is going to give you a higher success rate. That  
18 would be one thing you would want to demonstrate, a better  
19 success rate. Secondly, can you do that but not have the  
20 expense of a higher complication rate? So, those are the  
21 things I think you are going to have to try to get at.

22 MR. WHITBECK: I just want to make a comment about  
23 that. I think it has a lot to do with confidence in  
24 performing the maneuver, and I think the device gives the  
25 person more confidence.

1 DR. CURTIS: Okay.

2 MR. WHITBECK: That would then, in general, create a  
3 better success rate.

4 DR. CURTIS: Which is a good hypothesis, one that you  
5 would have to seek to demonstrate eventually.

6 MR. WHITBECK: Right.

7 DR. CURTIS: One of the concerns I would have is how  
8 much pressure is enough. I think there is a big difference  
9 between a volunteer situation where you are measuring  
10 pressures and you are getting people to stand up, and you  
11 know that you are about to pull on this thing on a conscious  
12 volunteer who really isn't choking but you are just trying  
13 to see how much pressure is generated, versus a real-life  
14 situation where you suddenly realize that somebody, honest  
15 to God, is choking to death. People panic. We were even  
16 told that the first few thrusts are the most important ones  
17 and that, you know, several minutes later it is going to be  
18 too late. There could be a real tendency to pull the heck  
19 out of it and possibly generate even more pressure than was  
20 in any of the tests that you have in here because people are  
21 really doing it as absolutely hard as they can.

22 MR. WHITBECK: If I may comment on that, that is pretty  
23 much the intent when you have a choking victim, to give it  
24 all you have. Of course, if you are not successful with the  
25 Heimlich, that will be what any rescuer will be doing very

1 soon if they don't get success on the first one. Two of  
2 three Emergency Cardiac Care experts and Dr. Patrick himself  
3 told me, "now, Wayne, when you're telling people how to do  
4 this, tell them to give it all they have. You've only got a  
5 few seconds. They've got to get that food bolus out of  
6 there." So, when we designed the device, we said we can do  
7 something here. We can put an upper limit on the pressure  
8 that can be exerted by the ballplayer that is sitting beside  
9 you at the restaurant because as his arms come back he  
10 cannot develop as much strength, plus he has the seat belt  
11 aspect because he's pulling back there with probably 50 lbs.

12

13           When the back slap was removed from being appropriate,  
14 and Dr. Koop, of course, in 1985, in health reports did  
15 that, the reason that it was taken out was because of the  
16 scientific research that showed that a food bolus or  
17 substance needed two things to remove it, and the back slap  
18 didn't do a very good job. It did some. The reason was  
19 that the peak only lasts for one-hundredth of a second but  
20 the Heimlich maneuver lasted for about 70 times that amount  
21 of time. So, that was entered into the argument which the  
22 National Emergency Cardiac Care reviewed, as well as the  
23 peak pressure.

24           Now, Dr. Patrick integrated, found the area and said  
25 that we have to look at energy because in physics it would

1 be energy or the ability to do work that would move a  
2 substance which is restrained. There is a force there. You  
3 need to have a pressure on it for so long, pressure to be  
4 significant enough to move it out. What they showed was  
5 that the back slap had lots of pressure, even more than the  
6 Heimlich, but it didn't last long enough. So, if the food  
7 bolus came up towards the mouth it stopped; it didn't get  
8 any further. So, I hope that is helpful.

9 DR. CURTIS: Thank you. I think most else that really  
10 needs to be discussed has to do with the questions. So, I  
11 am going to stop now and ask you, Mr. Jarvis, if you have  
12 any comments.

13 MR. JARVIS: No, I don't.

14 DR. CURTIS: Dr. Altman?

15 DR. ALTMAN: I should have gone first because I changed  
16 my mind after each speaker. You know, I have been a dentist  
17 for 15 years and I have, luckily, never had to use the  
18 Heimlich. I have no idea how much pressure I would use, any  
19 more than I would know how much pressure I would use with  
20 this. I think in an emergency situation I would probably  
21 push a lot harder with my hands than 35 lbs. of pressure  
22 with each arm. I don't know. I suppose if somebody was  
23 trying to save me, I would rather they pushed hard enough  
24 and risk tearing something inside and not dying, right there  
25 at the table. So, as a consumer rep. I am actually sort of

1 quite in favor that it would help as an adjunct. I think it  
2 is a great idea. This one scares me. It doesn't bend.

3 In restaurants, I know that we are dealing with people  
4 that come and go rather quickly, and I have seen posters in  
5 kitchens talking about how to save somebody that is choking.  
6 I wouldn't imagine that these kinds of things would ever be  
7 placed some place without instructions as well. I applaud  
8 you guys that did this. I think this is great. I think  
9 they should all include an 800 number on here. I think the  
10 diagrams are good. I do think there needs to be some  
11 warning and contraindications. I agree with my colleagues,  
12 I don't see a use for this in children because I don't see  
13 that you couldn't put your hands around a child; and a space  
14 above a pregnant lady's stomach is difficult to find and  
15 small.

16 But I do see an advantage, and, you know, I would  
17 rather have an 18-year old waitress with long finger nails  
18 grab one of these than trying to grab me from behind and  
19 dislodging whatever is in my throat. So, I guess I am less  
20 concerned about the data than most people are here because I  
21 think for small people and people who aren't strong this  
22 would be a great adjunct, and I have no doubts about where  
23 my hands go on this and, while I train in CPR every two  
24 years, I am not sure in a panic situation where my thumbs  
25 and my hands would go. I think it is going to be a risk. I

1 have no doubt here.

2 So, I think this is good. I am concerned about the  
3 contraindications, and I do think that training is important  
4 but, again, I have been trained every two years and I am  
5 still not sure, you know, if I would do exactly what I am  
6 supposed to do when it comes to the Heimlich. But I would  
7 rather somebody do something, or somebody have something,  
8 than to do nothing.

9 DR. CURTIS: Thank you. We need to have another open  
10 public hear. That will be now. Does anyone in the audience  
11 want to make any comments about these devices? Yes?  
12 Identify yourself, please.

13 **Open Public Hearing**

14 MR. SALAZAR: Good afternoon. My name is Jose Salazar.  
15 I am here on behalf of the American Red Cross. I can look  
16 at this as an educator. I am also a field provider or  
17 paramedic. So, I just wanted to share some things after  
18 looking at the presentations.

19 First of all, as far as the training and the numbers  
20 that were put up regarding training with the Heimlich  
21 method, the question that we may ask is if you haven't  
22 reached significant numbers with the traditional Heimlich  
23 maneuver which doesn't require any device, will you actually  
24 reach more numbers with a device that you are talking about  
25 with time and also cost. I am not sure about that. Maybe

1 it will make people more apt to react or maybe not.

2 One of the things that has to be looked at is not only  
3 just using the device but also in a real situation, as  
4 panelists mentioned, and the fact of will someone step  
5 forward and actually act in an emergency. That question is  
6 always being asked with other devices that are out there  
7 now. Would it be easier with the device or would it be  
8 simpler just using your hands?

9 The other concern that we have to look at, and one of  
10 the things that I was real concerned about is the safety. I  
11 know we have been talking about that. With the use of the  
12 traditional method, with your hand and your fist you can  
13 control placement as far as feeling the xiphoid or ribs. I  
14 am not sure whether with a device of this type that would be  
15 the same.

16 Controlled studies are great. What was mentioned also  
17 is the panic situation of a real situation. I have been on  
18 a lot of scenes where people do a lot of strange things, and  
19 you put a device in their hands and you never know what is  
20 going to happen. So, I think those things need to be looked  
21 at.

22 The other thing is that I just want to make sure that  
23 people are aware that, like with any device, it is very  
24 important that the traditional method is still used because  
25 what happens when this device doesn't work? For example, if

1 you just use this device as the only way to save people,  
2 what do we do with the pregnant patient? What do we do in a  
3 situation where you really cannot even get that device  
4 around them? There are some very big people out there.  
5 Would it be good to use this device, or would it be easier  
6 to tell people to lay on the ground real quick and then to  
7 an abdominal thrust with them laying down? Because, if you  
8 have a real small person with a big person trying to use  
9 this device, well, if that person becomes unconscious they  
10 might fall on top of them. So, while these devices might  
11 have a lot of merit and make it easier for some people, I  
12 think we need to think at those situations also. Thank you.

13

14 DR. CURTIS: Anyone else?

15 [No response]

16 Thank you. Do any of the panel members have any other  
17 general comments they want to make before we start going  
18 through the questions?

19 [No response]

20 There are a lot of them so why don't we start doing  
21 that? The first question we have been asked to address is,  
22 the FDA considers device safety and effectiveness for  
23 particular intended use. Would the following indications  
24 section be appropriate for such a device? It says the  
25 device is intended for use as an adjunct in the performance

1 of the Heimlich maneuver rescue technique for the relief of  
2 acute foreign body airway obstruction.

3 Any comments about that indication statement? It seems  
4 very appropriate to me. I am not sure how else I would word  
5 it or what the concern would be.

6 DR. SPYKER: After speaking with Dr. Becker, it is not  
7 clear to me whether we would like to use abdominal thrust or  
8 Heimlich maneuver. The generic term is probably  
9 scientifically sound; the Heimlich maneuver is probably more  
10 recognizable to the lay person. So, I suppose both, but  
11 probably include the generic term.

12 DR. CURTIS: Include abdominal thrust? Okay. I think  
13 that point is well taken because I think when people say  
14 Heimlich maneuver most people would have some clue as to  
15 what that is. You are right, it is a little more specific  
16 than the general term, abdominal thrust.

17 I thought that was kind of an easy one. The second  
18 one, what type of bench test data or other evidence would be  
19 necessary before beginning use in humans? This is a little  
20 tougher. Anybody, jump in there.

21 DR. SIMMONS: Maybe you can break that down, the bench  
22 testing, into safety and effectiveness.

23 DR. CURTIS: All right, bench testing for safety.

24 DR. SIMMONS: Yes. If you break it down to bench  
25 testing for safety, then I think probably something more

1 needs to be done than what has been done now. I would  
2 endorse this suggestion, if a model can't be satisfactorily  
3 developed such as "Rescucie Annie" or something of that  
4 nature, then at least some human data on pressures in the  
5 intraabdominal cavity in cadavers, or something, would be an  
6 appropriate first step in trying to decide if it is a safe  
7 device.

8 DR. CURTIS: I think some of the issues with bench  
9 testing, like dropping it and pulling it, and all the rest  
10 of that, some may be necessary to some limited extent, but I  
11 would surmise that most of the panel is not too worried  
12 about that. This is not an implantable device. It is  
13 something that is going to sit on a wall some place, and if  
14 it were eventually to crack you would replace it. So, I  
15 think probably the major safety issue you would worry about  
16 is can you jam this thing into somebody's abdomen and hurt  
17 them.

18 So, there has to be a model. There were discussions  
19 about what could be an appropriate model. It is hard to  
20 come up with what a good answer for that is. Cadavers would  
21 be one answer; something to say really what kinds of  
22 pressures were being generated by these things.

23 DR. ROBERTS: I am assuming that what the FDA is  
24 looking for is sort of a general approach for any devices,  
25 not necessarily for these devices per se. One thing that I

1 think has been done to some degree with these devices is to  
2 look and see whether or not you can change the airway  
3 pressure since, it looks like from the literature, I think  
4 that is something that may have some correlation. I guess  
5 at a first go-around you would want to be able to see that  
6 you can do that.

7 I don't know the ways for testing these, but there must  
8 be a way to develop some kind of a model in terms of how  
9 much force you can generate with this, whether it is some  
10 kind of a strain gauge, or something, so that you would have  
11 an idea of really how much force, and I think you would want  
12 to try it at least in the worst-case scenario with someone  
13 who is a fairly muscular, strong person, a linebacker or  
14 whatever, who goes and works out, and how much force can  
15 they generate versus someone else. So, we had some  
16 information in terms of the height and weight of some of the  
17 people that were doing the testing, but we ought to have a  
18 little bit more information in terms of a muscular person  
19 doing this so that we can get some feel as to how much force  
20 you can actually generate with these things so that you know  
21 that you are not going to, hopefully, overdo it and cause  
22 injury and, yet, be able to generate enough force that you  
23 can, hopefully, create an appropriate response, if we are  
24 assuming that airway pressure gives us some kind of an  
25 appropriate response.

1           So, those are two bench testing things that I would  
2 suggest.

3           DR. CURTIS: I was concerned with the issue of the cast  
4 of the larynx and then the food stuck in it. There is a  
5 suggestion from that in vitro testing, non-human testing,  
6 that very large pressures were necessary to dislodge the  
7 meat, greater than 74, and, yet, the Heimlich maneuver,  
8 which generates less pressure than that, is effective most  
9 of the time. So, that may be a false indication as to how  
10 much pressure is actually necessary. So, I am not sure that  
11 has given us the best idea of what is really necessary. You  
12 want to know how much you need to have, and how much more  
13 than the unassisted Heimlich would be useful. So, I think  
14 that that cast by itself is probably not the best way to go.  
15 The question is, in a better simulation of a human model,  
16 what kind of pressures would be necessary to dislodge a  
17 piece of meat or something that is a more typical thing that  
18 we get. I am not sure what the answer to that is, but in  
19 those particular tests it looked like a lot of pressure was  
20 necessary and, yet, it can't really be true since the  
21 Heimlich doesn't generate that.

22           DR. VETROVEC: Going back to the safety issue, I am  
23 perplexed as to how you would set up a model but it just  
24 occurred to me that there may be a whole body of information  
25 on it related to crash test dummies. There may be an

1 existing series of data related to something like that that  
2 might be a good basis to start with from an injury  
3 standpoint.

4 DR. BECKER: One thing on models, the idea of cadavers  
5 -- I would be concerned about that as a model for this kind  
6 of thing because the changes in the pulmonary vasculature  
7 and compliance, specifically, are just so intense after  
8 death that, you know, you wouldn't have a fully expanded  
9 thorax. I don't think it would be a very good model. You  
10 know, I do think that there should be some consideration to  
11 some other alternative, some kind of model.

12 DR. SPYKER: Looking forward to the next question, it  
13 is clear that we meant for you to consider animal models in  
14 that question and other evidence -- that is a politically  
15 correct description of the term animal model.

16 DR. CURTIS: Do you have a comment?

17 MR. WHITBECK: Yes, I would just like to ask Dr. Becker  
18 and Dr. Roberts, when you are thinking about the pressure  
19 that should be measured, what pressure is that that should  
20 be modeled by the test design that would be given to the  
21 FDA?

22 DR. BECKER: Well, I am not an expert on pressure, but  
23 I would think some type of other strain and, you know,  
24 pounds of pressure being exerted by the rescuer --

25 MR. WHITBECK: On the abdomen?

1 DR. BECKER: Not on the abdomen, on the device, and  
2 then something that would say something about the type of  
3 pressure that the device exerted on the abdomen. I think  
4 that both of those would be things that would be fairly  
5 straightforward to measure and would provide important  
6 information because they are going to be different. You  
7 have two handles so the amount that you put on the two  
8 handles is going to be quite different than the amount of  
9 force that there is going to be on the abdomen. But you may  
10 eventually decide to change the device based on some of  
11 those characteristics. You may have data already on those.  
12 But I think that those are the things that I had implied.

13 MR. WHITBECK: So, it is force on the handles of the  
14 device, as well intrathoracic pressure or pressure between  
15 the device and the abdomen?

16 DR. BECKER: I mean, I am not absolutely sure. I would  
17 think just the pressure on the abdomen and as soon as you  
18 get into intrathoracic pressure or intraabdominal pressure,  
19 you know, you just open up an incredible can of worms. I  
20 mean, if you could go that way, great. But I would think  
21 the simple thing would be just the amount the contact area  
22 places on the abdomen. It may have something to do with the  
23 kind of injuries that are seen.

24 The other thing that may happen with a decent animal  
25 model is that you could get an idea of the type of injuries.

1 It is a very standard type of thing for CPR literature. You  
2 know, nobody tried out the various adjunct devices that are  
3 being proposed without showing that the vest and many of  
4 those other devices were at least comparable in terms of the  
5 intraabdominal injury they create.

6 MR. WHITBECK: Thank you for that clarification.

7 DR. CURTIS: It has been brought to my attention that  
8 there is some information on the Internet regarding the use  
9 of the Heimlich maneuver for asthma because of mucus plugs,  
10 and that it can be effective for that.

11 The indication as proposed right now is talking  
12 specifically about foreign body airway obstruction. Would  
13 you be looking for anything beyond that?

14 MR. WHITBECK: No.

15 DR. CURTIS: Okay, because there are more people with  
16 asthma, obviously, than have problems with foreign bodies  
17 stuck in the throat.

18 Maybe an animal model for this really is a way to go.  
19 You have a dry cast of a larynx or something, and you get  
20 something stuck in it and you are trying to generate  
21 pressures. It is really not a very lifelike or realistic  
22 situation. It may be more straightforward than trying to  
23 develop something brand-new, to have an animal and be able  
24 to measure intraabdominal pressure and create a situation of  
25 a foreign body obstruction and see what the pressure is and

1 the success rates that are generated with the assisted  
2 devices versus unassisted. That might be more realistic and  
3 a lot easier to accomplish than to try to generate some  
4 brand-new kind of non-animal model or something that  
5 simulates a real situation.

6 Let's talk about number three, what type of data, if  
7 any, should be obtained from human volunteer studies? We  
8 have three sections to the question. One, sponsor has  
9 provided clinical measurement of the time course of the  
10 pressure generated with their device and that during the  
11 unassisted Heimlich?

12 How might we determine an appropriate range of energy,  
13 pressure and duration, which should be safe and effective?  
14 How might we address concerns of patient positioning,  
15 sitting or standing versus supine victims, and patient size?

16  
17 DR. VETROVEC: It is going to be hard to do things with  
18 real live patients where they are going to simulate this. I  
19 think the safety issue that is another issue. No one knows  
20 if there is a continuum of force. You can think of  
21 designing something at lower forces to get measurements that  
22 you then extrapolate in some way, but I don't think you have  
23 any idea whether that works. I would be reluctant to do  
24 this.

25 The other issue is that you are going to do it on

1 normal volunteers who are otherwise healthy, and the  
2 injuries are going to be more likely to occur in elderly  
3 people with lots of other vascular disease. So, it may not  
4 even be equivalent. So, I am not sure that is going to be  
5 helpful.

6 DR. SIMMONS: I guess I agree. I can remember when we  
7 were talking about the BLS and how you had to at least show  
8 how you do that. Then, when that partner comes around you  
9 with his fist in your solar plexus, I think there is a lot  
10 of -- I don't care how much you like the person behind you.  
11 I am just not sure that the volunteer data was very  
12 meaningful. I don't know, I just can't imagine getting  
13 consistent results that are going to be meaningful.

14 DR. CURTIS: And, I think too that we would all be  
15 willing to accept the idea that there is likely to be a  
16 higher risk of rupture of one of the intraabdominal organs  
17 with use of this, but if it is a patient who is choking,  
18 that is very acceptable when the alternative is death. And,  
19 in a human volunteer you don't even want to think about  
20 risk. So, the question is how could you somehow get a  
21 handle on that, short of doing that? I don't think you  
22 could do it with a human volunteer and get meaningful data  
23 that wouldn't risk the volunteer.

24 DR. BECKER: I would agree with that. I would be very  
25 concerned with anything that was realistic with humans. I

1 have reviewed some of the cases where the Heimlich maneuver  
2 has actually been performed and, you know, I would have to  
3 say that in a vast majority of those cases it quickly earned  
4 another name, which I am not going to say right here, but  
5 there was projectile vomiting that occurred with the use of  
6 the technique, and that is almost uniform. So, I think we  
7 need to be pretty careful about human volunteers for that  
8 kind of force.

9 DR. FIELDER: I agree with those comments because one  
10 of the things that is happening in this kind of volunteer  
11 study is that the volunteers aren't getting anything out of  
12 it. It is not a therapy that is being tried for an illness  
13 or condition that they have and, so, subjecting them to  
14 anything more than a minimal risk I think would be  
15 inappropriate.

16 DR. CURTIS: I think that the issues that are up there,  
17 at least in (a) and (b), probably could be reasonably  
18 addressed by an animal model. We are talking about time  
19 course of pressure generated. I think it would have to be a  
20 fairly large animal model because you are trying to simulate  
21 something that would happen in a human size person. But an  
22 appropriate range of energy and pressure it would take to  
23 dislodge a foreign body, you know, I don't see how it could  
24 be done in humans.

25 In terms of positioning, probably also that could be

1 dealt with animal testing. I don't see how you could do it  
2 in a human volunteer before you went ahead and actually used  
3 the device. Any other comments on that?

4 DR. ROBERTS: I guess I just have some questions about  
5 how applicable the animal model is in this. It would be  
6 wonderful to get some information from something other than  
7 a human, but I am just wondering in terms of the size and  
8 the anatomy. I mean, what you are really trying to do is  
9 simulate someone with something stuck in their throat, and  
10 how exactly you would get something shoved down an animal's  
11 throat so you can push it out, I don't quite understand how  
12 you would do that. I mean, if anybody can come up with a  
13 great animal model, that is good but I have a hard time  
14 trying to imagine how that would be done effectively.

15 DR. CURTIS: I think you would have to have an animal  
16 that is anesthetized and shove something down its throat.  
17 Then you would have to use your device to measure pressures  
18 and actually attempt to dislodge it, and see what kind of  
19 pressures you generated and see what it would take to  
20 actually dislodge it. I can't think of a better way. I  
21 can't think of something mechanical that would work. I  
22 think it would have to be something like that.

23 All right, let's move on to number four, what types of  
24 evidence should be required to assess the risks and benefits  
25 to permit clearance of a device prior to commercial

1 distribution?

2 a) How do we assess complications associated with  
3 performance of the assisted Heimlich maneuver? What about  
4 children, the frail elderly, the seated or supine patient?

5 b) How do we assess benefits associated with  
6 performance of the assisted Heimlich maneuver? Any  
7 comments?

8 DR. BECKER: Well, it would be wonderful if there were  
9 a way to even assess the success rate of the Heimlich  
10 maneuver right now. One of the things that makes this whole  
11 thing rather dreadful is that we have no really good data on  
12 how often the Heimlich maneuver is used successfully and not  
13 successfully, and that makes it very difficult for a device  
14 to come and either meet that standard or be different from  
15 it.

16 I guess I would suggest that there needs to be some  
17 kind of database created, and I would just wonder if there  
18 wouldn't be a way to do that. That would essentially be a  
19 terrific service to the resuscitation field because for this  
20 whole issue of airway obstruction there is just no data that  
21 is really worth anything out there. It has been a very  
22 difficult thing even for Dr. Heimlich who has presented  
23 three or four cases at times, and then requested various  
24 revisions in guidelines. I mean, there is a real paucity of  
25 data.

1 I guess I would just throw out to the committee if  
2 there is any possible way of some kind of a database, either  
3 through postmarket type of surveillance. I wonder if there  
4 would be a way if you grabbed this thing off the wall, you  
5 know, if it could ring a bell or something like that, or  
6 record something, or be hooked to a cellular telephone or  
7 call 911. I mean, I could imagine a few things that could  
8 be integrated into the device, but I think the key is that  
9 we have to get some data on this. I think we are all at a  
10 terrific disadvantage, the company and the committee as  
11 well, with where we are right now -- pretty smack-dab in the  
12 darkness.

13 MR. WHITBECK: May I make a comment on that? I  
14 couldn't agree more. If we can get to the point of approval  
15 and getting to the market, we are planning to strongly  
16 incent [sic] any use of the device and a third party to  
17 screen it, and make that data available because it has been  
18 frustrating for us in some of the areas where we would have  
19 liked information, such as you must mentioned, Dr. Becker,  
20 that isn't there, other than Redding's data and also  
21 Patrick's and Heimlich's. But we suspect there is more.

22 There is one possibility, and that is the original  
23 death certificates where choking was cited. Those have not  
24 been collected from the states. We understand now how those  
25 data are collected. There could be some work a priori done

1 on that, but we are not sure how successful it would be  
2 because we don't know what is on the death certificates, but  
3 there may be height, weight -- any of those demographics  
4 that we would like to s\get.

5 But I just wanted to say that we are certainly willing  
6 to do two things, strongly incent, third-party to review  
7 whether this case actually happened or whether somebody just  
8 wanted their money back on a Choke Reliever, and then make  
9 the data available to the medical community. We would want  
10 to do that because we have suffered frustration ourselves  
11 from not having it.

12 DR. CURTIS: I think in terms of types of evidence,  
13 there is some reference in the panel pack here about data if  
14 somebody crashes, that sort of thing, and I think a lot of  
15 that must be available. How much pressure does it take, on  
16 average, to rupture an aorta, intraabdominal blood vessels?  
17 There must be some ball parks that. If we could compare  
18 that kind of data to what the maximum pressure possibly  
19 could be generated from this thing, we could see how much  
20 overlap there is and that would give some ability to assess  
21 the relative risk and benefit prior to commercial  
22 distribution.

23 I think one of the comments that was made before by Dr.  
24 Vetovec maybe is really worth reiterating, the issue about  
25 a lot of these problems occurring in hospitals and nursing

1 home. Would that be the place to go first to use that? If  
2 there is an 800 number that you can call afterwards to say  
3 what kind of experience there was, we may learn. I mean, if  
4 a visceral rupture happens in a hospital situation, there  
5 may be some differences in terms of what the ultimate  
6 patient outcome would be compared to if it happens in a  
7 restaurant or some place. So, maybe not having widespread  
8 distribution at first would be the way to go, but maybe more  
9 limited and then try to gather some of this information.

10 Another issue too though is the whole issue of  
11 children. I think all of us have the sense that we are not  
12 so sure it would be as safe to use it in children as it  
13 would be in adults, but what if the child is choking? Would  
14 you not give it a shot if you had it available? Would you  
15 want it to be? Or, should it be limited to adults only? I  
16 am not sure I know what the right answer is about that  
17 either. I have a feeling that if there was a child I had in  
18 front of me and I tried the Heimlich and I couldn't get the  
19 thing out, I would use whatever I had in front of me.

20 DR. VETROVEC: Well, I think that is a different issue  
21 though than using it first. I mean, it could be for  
22 children, approved for failed Heimlich. I am still in favor  
23 of not over-scientifically working this out because I don't  
24 know how to advise anybody, nor how to even study it, but  
25 getting it out into hospitals and nursing homes where,

1 hopefully, you would get decent follow-up and better  
2 understanding of what has happened because all the patients  
3 are there and they are not going anywhere presumably, in the  
4 next 12 hours. So, you are going to know what the  
5 complications are. But for children it would probably be  
6 reasonable to approve it for failed Heimlich.

7 DR. ROBERTS: I think the nice thing about putting it  
8 in the nursing homes and the hospitals to start is that you  
9 may, in fact, answer some of these questions in terms of the  
10 frail elderly and the seated or supine patient. If you find  
11 that there is a big problem, for example, in the frail  
12 elderly, then maybe you don't want to even try it in the  
13 kids. But I think that it may be a reasonable thing to try  
14 it in that sort of controlled setting and then, once you get  
15 some data from that, then maybe have a better feel for what  
16 you should do for later on.

17 DR. BECKER: I think I have a little bit of a problem  
18 with trying it in a hospital setting. The nursing home  
19 setting may work. But, you know, the place where people  
20 choke is really not in the hospital. I am just thinking  
21 that you may get into a numbers kind of thing. I don't know  
22 how well it has been studied, but realistically the data  
23 that I have seen on choking is that you combine usually meat  
24 with alcohol, and that is really what it comes down to. We  
25 don't serve alcohol in the hospital any more --

1 [Laughter]

2 -- a lot of our patients might prefer it, and who knows  
3 what they get in a nursing home. But, really, most adults  
4 that do choke are intoxicated.

5 DR. VETROVEC: I don't know how realistic this is, but  
6 the data that I have been using is Eckberg's data which is  
7 quoted here, on page 8, and that lists only 24% occurring in  
8 restaurants and bars, and it lists 24% occurring in nursing  
9 homes and 19% in hospitals. So, you have about 40% of the  
10 events --

11 DR. BECKER: The problem is that I wonder if those are  
12 really food boluses or are those aspirations. I think what  
13 you are seeing there are the stroke patients and other  
14 patients who are just having trouble with their airways. I  
15 mean, I would be happy to take a quick poll here, but I have  
16 not see very many food boluses in my hospital. I have seen  
17 it in restaurants. I just would hate to hamstring sort of  
18 the development of it because the numbers were smaller. I  
19 would think if the numbers were there to support it, it  
20 might be a way to go.

21 DR. VETROVEC: I don't know, I always assumed it didn't  
22 happen in my hospital because the food was so bad nobody was  
23 eating it.

24 [Laughter]

25 DR. CURTIS: I think one of the other things that you

1 can think about with this is -- I may be repeating myself,  
2 but as a last resort in children, certainly, if nothing else  
3 works you are going to grab the thing. I could very easily  
4 understand that this could be life-saving and you are  
5 willing to accept a lot of risks with something that is  
6 potentially life-saving. The question though is if we let  
7 this out into general distribution, how does the public  
8 handle that? Who does the Heimlich? Is it more likely to  
9 be somebody who knows something about CPR, who is trained  
10 and who knows? Is one of these things going to be something  
11 that everybody can grab and use?

12 And, it is going to be used when people aren't choking.  
13 You know, that is another thing. Some of the ruptures and  
14 things that were described in here were in people who had no  
15 foreign bodies in the airway. So, you may have somebody who  
16 has a ventricular fibrillation and collapses and somebody  
17 may grab one of these things and start pumping on his  
18 abdomen instead of doing CPR. I think there is a very good  
19 chance of that sort of thing happening. Then you have  
20 complication risks with no benefit whatsoever. So, I think  
21 public education is going to be very important as we get  
22 around to distributing this.

23 MR. FIELDER: I want to add a note of caution here,  
24 that the folks in hospitals and nursing homes are not just  
25 useful resources for us to test our gizmos on. And, I think

1 it is a good idea to start with a population like this where  
2 you have that control, but also I would expect them to have  
3 some sort of a consent and the usual ethical protection for  
4 people who are actually subjects trying out a new device.  
5 So, I just wanted to add a note of caution that there are  
6 other kinds of considerations that you need to plan for when  
7 you do this type of study.

8 DR. CURTIS: The other thing too though is that the  
9 first time one of these things gets used in a restaurant and  
10 it works dramatically well, and it gets picked up and  
11 publicized there could be a real stampede for people wanting  
12 those and not wanting them to be limited. So, that is  
13 something to think about too.

14 DR. ALTMAN: Dr. Curtis, it seems to me that we have  
15 lost the fact that it really is an adjunct. It doesn't say  
16 that it is to replace the Heimlich. It seems like we keep  
17 losing that fact. Nobody is saying don't do the Heimlich;  
18 use this apparatus first. In fact, the literature says  
19 don't go out of your way to get this. But it seems to me  
20 that if you were a small lady with a pretty large husband  
21 who had trouble swallowing, this would be a nice thing to  
22 have at your home, readily available. But I do think it is  
23 an adjunct. They are not proposing that these things  
24 replace the Heimlich. Your comment about somebody having  
25 cardiac arrest, or whatever, that is off-label usage --

1 [Laughter]

2 -- so we can't control that sort of thing.

3 DR. CURTIS: I think in general for this question, for  
4 the most part the complications and the benefits is  
5 something -- the way you would actually get that information  
6 would be after the device is out, postmarketing or that sort  
7 of thing; you know, call the 800 number if you used it, and  
8 collect information on how many complications there are and  
9 how many times it is used beneficially on people. I  
10 certainly don't see how you could get that cumulative  
11 information beforehand. Any other comments on this?

12 DR. ROBERTS: There is a problem, I mean, I think it is  
13 reasonable to bring up this consent issue but, honestly, I  
14 don't know that you can consent everyone as they walk in the  
15 door that you might use this device on them at some point  
16 during their stay in a nursing home. Certainly when they  
17 are choking you are not going to ask them to sign a consent  
18 form to let you use this device. So, I think we would  
19 definitely have a problem with that.

20 On the other hand, I think, and someone from the FDA  
21 can correct me, there have been devices that have been  
22 approved and, yet, only allowed to be distributed in a  
23 limited way, which in the case of one device that I am  
24 thinking of was very beneficial because it actually turned  
25 out that there were problems with the device that were

1 picked up in that limited release and then the device was  
2 basically redesigned and released again. But it wasn't  
3 being used as part of a study at that point, it was just a  
4 limited release. So, I think you have done that kind of  
5 thing before -- I think.

6 DR. CURTIS: I think some of the next questions are  
7 actually kind of what we have been talking about. Number  
8 five, is use data, or clinical evidence, necessary prior to  
9 commercial distribution? I think we have been discussing  
10 that already. I think that has been covered.

11 Number six, if needed, what are some alternatives to  
12 gathering -- I am sorry?

13 DR. SPYKER: Before we go on, could you summarize what  
14 you think the consensus is on number five? Please.

15 [Laughter]

16 DR. CURTIS: I think in general what we are saying is  
17 that, I mean, to me, clinical evidence means you have used  
18 it in humans in a clinical setting and seen how it works. I  
19 believe we are all saying that it is hard to see how you  
20 could do that. I think the only way you are going to get  
21 data on how it works is to use it on a choking victim. Now,  
22 whether you limit distribution and collect some information  
23 -- there is no other good way to do that. So, if you want  
24 to gather data on the use of the device, benefits and  
25 safety, you would have to let it out even if you called it a

1 study, a clinical study, and actually gathered some data on  
2 choking victims and see what happens. That is the clinical  
3 evidence we have been talking about. That would be the only  
4 way you would have some real hard data on that.

5 I think we have all agreed that getting a bunch of  
6 volunteers to have this thing held up to them and see how  
7 much pressure comes out of the mouth really doesn't tell us  
8 a whole lot about what would happen in a clinical situation.

9  
10 DR. VETROVEC: Anne, can I just go back? We kind of  
11 passed off the issue that the FDA asked about, the breakage  
12 of the device and so forth, but it does occur to me since it  
13 is a plastic device that there might be need to be some  
14 recommendations regarding storage related to temperature and  
15 analyte expectancy. I don't know if this plastic dries out  
16 in two years and cracks, and it may not get used for four  
17 years and then it doesn't work. So, there might need to be  
18 some information provided based on just the plastic and the  
19 properties of the material.

20 DR. FIELDER: I want to go back to the clinical  
21 evidence issue because basically what people have been  
22 proposing here is a kind of clinical trial flying under a  
23 different flag, where you find a population in a nursing  
24 home or a hospital. It is almost like you are giving them a  
25 device exemption to test it and see if it works. When we

1 test things to see if they work, we have to have patient  
2 protection. I don't think it would be difficult to get  
3 consent from the people who live in a nursing home. They  
4 are usually around; they come to stay; and they give consent  
5 for other procedures, and I don't think it would be  
6 difficult to get volunteers who would be willing to have  
7 this device used on them should they have a choking episode.

8  
9 But I would say that if you are going to use human  
10 volunteers, you are really doing something that is analogous  
11 to a clinical trial and you need to have some patient  
12 protection measures put in there.

13 DR. VETROVEC: I might say I looked at some of this  
14 from an entirely different standpoint. We started out with  
15 the concept that we would potentially release this to  
16 everybody and ask for information back so that it would be a  
17 global clinical trial, if you will. It was my idea of  
18 limiting it to the nursing home and the hospital, not to  
19 take advantage of these patients in the sense of  
20 experimenting on them, but limiting the exposure of the  
21 world at large in a circumstance where you would get data.  
22 We are assuming that at the point we say it can go out to  
23 the market it is safe, as best we can tell, based on animal  
24 or whatever model information at that point. So, it is not  
25 like we decided that we are going to see what is going to

1 happen. We have decided that, to the best of our knowledge,  
2 it is safe but to be absolutely certain we want to gather  
3 data. It seems to me that is a little bit different than  
4 the clinical trial where you don't know whether it is going  
5 to work at all.

6 DR. FIELDER: I am not suggesting it is the same thing  
7 as a clinical trial. It seems to me that if there is a  
8 question of risk and you are limiting the distribution to a  
9 certain population because you are not sure about the risk,  
10 then that is analogous to a clinical trial in the sense that  
11 you are testing something on somebody; there is an unknown  
12 risk, and in a circumstance like that I would expect some  
13 kind of patient protection measures to be in place. I am  
14 not sitting here, thinking that you are, you know, evil  
15 people, looking on these nursing home residents as useful  
16 fodder for your invention. I am not saying that at all.  
17 But there is a parallel to a clinical trial when you have  
18 any kind of human volunteers, and you need to think about  
19 protecting those patients if you are putting the at more  
20 than an insignificant risk.

21 DR. CURTIS: I think one of the issues is if you are  
22 not going to distribute it widely, how could you most  
23 efficiently distribute something like this? You want to put  
24 it where it is more likely to be used and so in a nursing  
25 home, that is where the issue comes up. Another possibility

1 could be patients with neurological diseases where choking,  
2 that sort of thing, is more of a risk. I mean, you are  
3 faced with getting a consent for something that might happen  
4 sometime in the future. You usually think of informed  
5 consent as something for a procedure or something that is  
6 going to happen fairly soon but you can't predict this sort  
7 of thing.

8 DR. FIELDER: If the Food and Drug Administration  
9 decided that this was a safe and effective device, you could  
10 use it anywhere and you could take it to a nursing home for  
11 the purpose of gathering data or whatever. That would be  
12 fine. If you are using it where there is risk, and you are  
13 subjecting a population to risk in order to find out how  
14 this thing works and if people get hurt, then these are  
15 patients in something like a trial. It is true that usually  
16 in informed consent somebody is sitting there, waiting for  
17 their invasive procedure, but there is a lot of testing and  
18 a lot of research where people give consent to participate,  
19 not knowing exactly what is going to happen to them but  
20 knowing what kind of risks they are consenting to.

21 I don't see this as a big problem if you would like to  
22 do this. My preference would be to decide whether this thing  
23 was safe and effective or not and then use these areas to  
24 try and get some data about it.

25 DR. VETROVEC: How often would the patient have to

1   reconsent?

2           DR. FIELDER:   Why would they have to reconsent?

3           DR. VETROVEC:   For instance, in the current rules in  
4   our hospital, a patient who gives consent to have blood as  
5   far as regular dialysis has to renew that once a year, even  
6   though they presumably still know they need blood.

7           DR. FIELDER:   This is an administrative detail.   I  
8   don't know the answer to that.   But once a year doesn't seem  
9   like a horrible burden either.

10          DR. BECKER:   I guess I would just ask the question if  
11   this situation isn't really more analogous to emergency  
12   conditions, like cardiac arrest?   I am just wondering if  
13   that is really not the more appropriate way to look at this,  
14   and for that there is really a different set of consent kind  
15   of considerations.

16          DR. FIELDER:   Well, people don't choose to go to the  
17   emergency room.   They show up because they are in big  
18   trouble.   The people in the nursing home are there because  
19   they are sick and frail and needs to be taken care of.   They  
20   are a population that is being studied.   When they choke you  
21   have an emergency situation, but it seems to me that if you  
22   are using them to gather data on your device, and that  
23   involves risk that you are trying to find out about, that it  
24   is more like a clinical trial.

25          DR. ALTMAN:   I understand the controlled environment of

1 a nursing home but I hope we wouldn't think whatever data  
2 could be collected on the frail elderly could be used for  
3 the rest of the population. I think there would probably be  
4 more problems associated with something in the frail elderly  
5 because they, in fact, are frail and elderly than Gary and  
6 me having dinner in a restaurant. So, you are going to get  
7 data on the frail and elderly but data for nothing but the  
8 frail and elderly.

9 DR. FIELDER: I am not a scientist but I would say,  
10 yes, that probably is data on just the frail elderly but  
11 they are also the ones who are the most susceptible to these  
12 kinds of complications, it seems to me from the literature  
13 that I have read. I don't know how good this data would be  
14 for the general population.

15 DR. ALTMAN: Do we have data on the Heimlich maneuver  
16 in the frail elderly to show that, in fact, that frail and  
17 elderly person would have died? So, I am not sure what good  
18 the data is going to do us.

19 DR. SIMMONS: Also, somebody has to go out and get  
20 these, and I can tell you there is going to be a significant  
21 percentage of persons who won't sign it, or their family  
22 members won't sign the consent form. Then you are going to  
23 have people in blue wheelchairs and yellow wheelchairs, and  
24 if they are choking in a yellow wheelchair you have to do a  
25 Heimlich --

1 [Laughter]

2 It is going to be a nightmare to do a study like that,  
3 and you would have them last for years looking for  
4 something. I am not saying you are wrong; I am just saying  
5 given that kind of a situation, I would think it would be --  
6 ooh!

7 DR. FIELDER: Well, consent does complicate scientific  
8 inquiry because people might decide not to participate, and  
9 that is their right, and that is absolutely primary. So,  
10 there is no way you can get around that. I am not trying to  
11 make your life more difficult here, it is just that I was  
12 thinking if my mom was in that nursing home and a bunch of  
13 people showed up without asking my consent or her consent to  
14 try out this device that might have some risk with it, I  
15 would want a chance for her to think about it and say yes or  
16 no.

17 DR. CURTIS: I think we have gotten a little bit off  
18 base here. I think the original idea of the nursing home  
19 was that it was just more likely to happen, and not that we  
20 were picking on a group of people as guinea pigs, which is  
21 what it is making it sound like.

22 I have an idea and I would like to throw it out. What  
23 would be the worst case with these devices? The worst case  
24 would be if it doesn't add anything, doesn't help any more  
25 than the regular Heimlich maneuver but it is more dangerous.

1 So, you are much more likely to cause, say, a rupture of the  
2 aorta or something like that and, yet, you don't get any  
3 benefit out of it. How do you get around that? You know,  
4 maybe we want to distribute the device widely but recommend  
5 that the unassisted Heimlich be tried first, one or two  
6 thrusts that sort of thing, and that if it pops out the  
7 foreign body the situation is over with, but if it doesn't  
8 pop it out, if you still have an obstruction, what are you  
9 going to lose by trying it? You could have the benefit of  
10 seeing if there is any efficacy over the unassisted  
11 Heimlich, and if there are complications everybody would be  
12 more willing to accept that because of the fact that you  
13 were unable to dislodge the foreign body with the unassisted  
14 maneuver. It might be a way of satisfying everybody about  
15 distributing the device widely and then following what  
16 happens afterwards, or in designing a clinical trial if you  
17 wanted to do that before you had general release of it. The  
18 one thing I am worried about is if you have 5% benefit from  
19 popping out foreign bodies but you have 20% of the patients  
20 having serious complications, maybe that is not a good way  
21 to go, and it could be one way of approaching this issue.

22 DR. VETROVEC: I kind of like that, and the advantage  
23 of that is that for a restaurant to go look for the device  
24 or a nursing home, you are going to lose time and if you  
25 just tried the Heimlich you may avoid some problems. The

1 flip side of it is that the picture I got here was that the  
2 first try is kind of the most important. So, if this is  
3 somehow better you might be biasing yourself against this  
4 device. That is the only downside I see here. It solves a  
5 lot of other problems and it does solve the temporal  
6 problem.

7 DR. CURTIS: The other thing too is that maybe this  
8 would be an initial way to approach it, and if you did you  
9 could say, "well, gosh, it's been used on a hundred patients  
10 who were choking and nobody ruptured anything or was any  
11 worse than before," then you could liberalize things and  
12 start getting it earlier toward a first response type of  
13 thing. I don't think we are going to know the answer to the  
14 risk of this thing until it is used, and the more necessary  
15 it is to take that risk the more we accept it.

16 DR. ALTMAN: I guess it gets back to my statement when  
17 you talked about the indications. It does say it is an  
18 adjunct in the literature. It doesn't say it is to replace  
19 it. If I was really large and you couldn't do the Heimlich  
20 because you couldn't get around me, then trying to do the  
21 Heimlich when you know you can't is a waste of time.

22 DR. CURTIS: Yes.

23 DR. ALTMAN: That is really what they indicate it be  
24 used for. So, it is a matter of wording but, truly, that is  
25 what they are getting at. It is just maybe not worded that

1 strongly but they do say adjunctive and they do say don't  
2 run off and get it; do the Heimlich.

3 DR. CURTIS: And that could be handled simply by saying  
4 if the Heimlich maneuver fails or can't be done, and leave  
5 that open -- if the patient is too big or I can't get my  
6 arms around -- leave that a little more general.

7 Maybe we can move on now? Comment? Yes?

8 MR. WHITBECK: Thank you, Madam Chair. The issue that  
9 you have been discussing -- I know that your job is to come  
10 up with the right criteria to test all devices, not just  
11 ours. We have told you about ours but there was another one  
12 today. Of course, we are thinking a little more narrowly  
13 than you are. We are just as concerned about complications  
14 but our thinking is narrower.

15 Looking at our device and our testing from our  
16 viewpoint, we see that the maximum force has been limited  
17 with our device, which it isn't in the Heimlich. Also we  
18 see from seat belt testing that you can go up to 700 lbs.  
19 without problems, and our device basically works as a seat  
20 belt although it has an 1 7/8 in. impeller in the middle.  
21 So, it has a safety advantage that the Heimlich does not  
22 have. The Heimlich does not limit the upper stress. It is  
23 only limited by the person. But our device limits it by its  
24 flex. It cannot give more than 90 lbs. So, might that not  
25 provide some safety assurance to the committee? No?

1 DR. CURTIS: Not possible. Thank you.

2 [Laughter]

3 All right, number six, if needed, what are some  
4 alternatives to gathering use data? Can labeling  
5 instructions for us and hands-on training mitigate some of  
6 the risk? I think we have discussed some of these  
7 alternatives.

8 DR. VETROVEC: We have also said that they ought to  
9 have instructions on this device, or a card over where it  
10 is, or a combination of all of those things.

11 DR. CURTIS: Yes, I think we would all like that right  
12 on there, or right on the wall. Something like that would  
13 be helpful. Hands-on training, I think it comes up a little  
14 bit later but the issue of incorporating it into PCLS  
15 training is kind of a nice idea. Any time people have some  
16 instructions on how to use something or get some opportunity  
17 to try it out before it is a real situation always mitigates  
18 risk.

19 DR. ALTMAN: I guess I would relate this to CPR. If  
20 you ever have one of these, this is how to use it. They can  
21 do the same thing with this. If you have one of these, this  
22 is how to use it.

23 DR. ROBERTS: I would point out though, especially from  
24 looking at this literature, that it took a while for the Red  
25 Cross or whoever is doing the PCLS to buy into the Heimlich.

1 So, I am not sure that you are going to get them to buy into  
2 this thing right off the bat. As a matter of fact, I would  
3 sort of doubt it. But that doesn't mean that there  
4 shouldn't be some kind of training. I think, unfortunately,  
5 it is going to fall on the people selling this equipment to  
6 provide some indication of what kind of training people  
7 should have in order to use it, but I am afraid you are not  
8 going to get the Red Cross or somebody else to incorporate  
9 this right into their training right off the bat.

10 DR. CURTIS: I am sure they won't.

11 DR. SPYKER: I guess when we wrote this question we  
12 were wanting rousing endorsement of the importance of this.

13

14 DR. ALTMAN: Is there some reason why a videotape  
15 couldn't be sold with the machine?

16 DR. CURTIS: I would imagine it likely would be. You  
17 said you were looking for rousing endorsement of this  
18 statement? Is that right?

19 DR. SPYKER: I just wanted you to say of course these  
20 are very important.

21 DR. CURTIS: Of course they are very important.

22 DR. SPYKER: Thank you. If you have anything more  
23 specific to suggest, that is really what I meant.

24 DR. ROBERTS: It would be ideal if you could find some  
25 type of model, as I said, to show people how to use this and

1 give them an idea of how much force they are generating. I  
2 would hope that something relatively simple would be able to  
3 do that. Some kind of a strain gauge or something like  
4 that.

5 DR. CURTIS: If you can't generate too much force, if  
6 you pulled as hard as you possibly can and that is not too  
7 much by the pressures that are generated when this is tested  
8 for use, then it is not really an issue of training.  
9 Training would come in if you had to put moderate but  
10 cautious amounts of force but you could do too much. If  
11 that is not true, then I don't think it is so much a  
12 training issue. It is really where to place it and then  
13 push hard. So, I think there is some training that would go  
14 along with it, and I do think eventually, if it proves to be  
15 good, that it should be incorporated into CPLS training even  
16 if not immediately because we want that knowledge  
17 disseminated.

18 DR. SPYKER: When this was discussed earlier I think it  
19 was mentioned that the measurement of force in the handles,  
20 flexion and strain gauge would also answer Dr. Fielder's  
21 interest in having some way to try it and find out really  
22 what an appropriate force is, or what would happen when he  
23 gave it maximum. Maximum for him might not be for someone  
24 else.

25 DR. CURTIS: Number seven, how might users of such a

1 device be trained? Should different techniques be used for  
2 victims who are unconscious versus conscious? Should  
3 different techniques be used for victims who are sitting or  
4 standing versus supine?

5 I don't know that I see how there would be a difference  
6 in how you would use the device in a conscious or  
7 unconscious patient. I mean, a conscious patient would be  
8 more likely to be standing than sitting. An unconscious  
9 patient would be slumped over possibly. I guess the  
10 question would be whether it would be better to have such a  
11 patient on the floor or let them be slumped over in a  
12 sitting position and trying to use this thing. The trouble  
13 with being slumped over is that you give yourself less room  
14 to position the thing. It might be logical to get a patient  
15 on the floor and then apply it.

16 DR. VETROVEC: I can imagine a patient lying on their  
17 back, however, and somebody trying to apply it front-wise.  
18 There probably needs to be some description that it has to  
19 be applied from the back. That might need to be in the  
20 labeling. I think all bets would be off if you tried to  
21 force this down in front of somebody.

22 DR. ROBERTS: On the other hand, what you might want to  
23 do, particularly since this is considered to be an adjunct  
24 you might, is to basically use the same procedures that one  
25 does for the Heimlich if someone is unconscious and just

1 recommend that those be the same as you would do with this  
2 device.

3 DR. CURTIS: If most of the devices were actually  
4 market released, I would imagine that the Red Cross would  
5 have a problem with incorporating that into their training  
6 and, if not, then how else would we go about having people  
7 trained with it? It might be that the video should go out  
8 with every one of these and you can make a recommendation  
9 that people watch the video. If they don't, I am not sure  
10 that you could force that to happen or how you would. Even  
11 if you sent the video ahead of time and said let me know  
12 when you have finished watching it and I will send you the  
13 device, that still doesn't guarantee that people would watch  
14 it. But having people have a video available to look at  
15 with the purchase of it might be good, because it really is  
16 fairly simple to use. I think the major issues would be  
17 things like conscious versus unconscious and sitting or  
18 supine. The standing and sitting I think are handled fairly  
19 similarly.

20 Number eight, what kind of data, if any, should be  
21 obtained after commercial distribution, if approved? I  
22 think we would like to know what kinds of complications  
23 there are; we would like to know what kind of a success rate  
24 there is. So, the ability to gather data by strongly  
25 encouraging a phone call in when the device is used would be

1 one way of gathering that information, and that probably  
2 would be the most important thing that could be done. I  
3 don't think anything else would be necessary.

4 DR. ROBERTS: I kind of looked over this case study  
5 report form and thought it looked pretty good, although I  
6 would certainly suggest that some things, such as the height  
7 of the rescuer -- they ask you the weight but the height  
8 would certainly be important. Was the victim standing,  
9 sitting, lying down at the time of the rescue so you would  
10 get that kind of information. Was the victim seen after the  
11 rescue attempt, you would want to know that and, of course,  
12 any injuries that occurred due to the rescue. You would  
13 want to know those as well. Those are things that were  
14 missing, that I saw in a quick run-through that were missing  
15 from this report form.

16 DR. CURTIS: Other comments? All right, number nine,  
17 are there roles for professional societies in training users  
18 and assessing outcomes, if approved? I think the answer  
19 would be yes.

20 DR. ROBERTS: A resounding yes.

21 DR. CURTIS: A resounding yes.

22 [Laughter]

23 If this were proved effective, I would think you would  
24 want that incorporated into all CPLS kind of training. If  
25 it were approved effective, I think it would be a very easy

1 thing to accomplish.

2           Number ten, would basic life support and advanced life  
3 support training need to reflect use of such a device if it  
4 were cleared for marketing? I think that is a resounding  
5 yes.

6           Other comments?

7           [No response]

8           Is there anything else that you wanted us to address?

9           DR. SPYKER: No.

10          DR. CURTIS: Okay. Well, I think we are finished for  
11 today. All the panel members need to leave their panel  
12 packs here on the desk, and we will reconvene tomorrow at  
13 9:00 a.m. Thank you, all.

14          DR. SPYKER: Thank you, all.

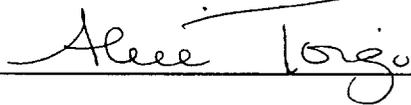
15          [Whereupon, at 4:40 p.m., the proceedings were recessed  
16 to be resumed at 9:00 a.m., Friday, April 24, 1998.]

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*C E R T I F I C A T E*

I, **ALICE TOIGO**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.

  
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**ALICE TOIGO**