Workshop Discussions

Introduction

The workshops detailed below were held as a continuation of the symposium. The resulting discussions of the participants are divided into two parts. Part 1—Graft Characterization Measurements and Retrieval—deals with subjects covered in Plenary Sessions 1 and 2, while Part 2—Standards Development—addresses subjects covered in Plenary Session 4.

These discussions are presented here in their original form so that the reader may be aware of the verbal interchange involved when the participants discussed vascular graft technologies at the workshops. These discussions were not peer reviewed, and therefore, are separated from the main body of the volume.

Part 1: Graft Characterization Measurements and Retrieval Workshop

B. Whalen, B.S. (Whalen Biomedical, Inc.)—It was suggested that I could ask some of the presenters what their feelings on the need for particular standards might be. Remember we are here to assist the Food and Drug Administration (FDA) in formulating a Class II performance standard for vascular grafts. Vascular grafts, after all, are already a commercial product, even though the development of vascular grafts has proceeded in a rather empirical fashion. Nevertheless, devices have been developed which are apparently quite effective to the extent that over 300 000 implants per year take place in this country. However, that is not to say that standard development is inappropriate.

In organizing this afternoon's session it was clear that we were putting manufacturers in a somewhat unusual position. After all, manufacturers are in the business of producing these grafts. I appreciate their cooperation in discussing their methodology, and at this point I would like to ask any of the presenters if they feel a particular need for performance standards, or for that matter, if they feel that performance standards for something like a Class II vascular graft, already in widespread use, is appropriate at this point in time. Given the fact that it is so difficult to perform prospective, randomized, controlled studies, is it possible, or can no one afford it?

I realize that writing performance standards is not an exciting thing to do. They are a lot of work, and as I said much earlier today, it has been difficult in the past to get interest and participation. Now I think we have the interest and the participation because the FDA is sponsoring this activity, and I hope that most of you will attend this workshop tomorrow on performance standards and give us

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some help because it is going to be a difficult process. I think you realize from the presentations today that there is a spectrum of clinically available vascular prostheses. Thus, it is unlikely that we can think of a simple performance standard. So the performance standards are going to be involved. There are going to be performance standards for bioprosthetic grafts versus synthetic grafts, and as you heard this morning, there are new technologies on the horizon and presumably new standards will be developed for them.

S. Brown, D.Eng. (Case Western Reserve University) —I am Stan Brown, I'm one of the people who is running the workshop tomorrow on performance standards. I have been involved in ASTM Committee F-4 on Medical and Surgical Materials and Devices for about ten years and have been heading up the biocompatibility section. We have been able to make a lot of progress in the whole issue of biocompatibility. Initially, by ignoring the question of what is biocompatibility, we did not even bother to try and define it. We figured what we really needed were methods of assessing biocompatibility, as a way of beginning to get or to take steps towards the performance of materials from a sort of histocompatibility point of view.

What I heard this afternoon were a number of speakers talking about prototype test methods. Some of the issues that came up were absolutely what we are trying to get at in Committee F-4 in terms of the rationale for suture retention strength. You do not take a big suture and a 4-mm bite because that isn't what the surgeon does. You take the 1-mm bite and you take a 6-0 suture because this workshop is trying to get at the performance, the kind of characteristics that we are really interested in.

We talked about mechanical properties in different directions of testing. We heard about porosity testing and methods and the types of porosity tests that can be done. I'd like to see these questions answered because these are methods that we very easily within ASTM could come to grips with. I think we could get a consensus. We could actually get some working documents out of test methods that could then be used as references for describing the performance characteristics of vascular grafts.

I would be interested in hearing views from the surgeons, the speakers this morning, the inventors, and the users on the history of vascular prostheses and their evolution. Then I would like to look into the future at potential problems we might see that we would like to avoid. I would like to hear what sort of test methods would be appropriate for them to have, so that they would then know what the material is, and the devices that they are considering using.

J. Anderson, M.D., Ph.D. (Case Western Reserve University) —If we are after performance characteristics of vascular grafts, why don't we all go to the bar now and forget about tomorrow because you are not going to get it. I don't think you are going to compile the type of data that is going to enable you to really make judgment calls. I don't think that is really what you want to say. If so, then I don't think that you are going to accomplish it. The first thing that we have to

address is the material characteristics of vascular grafts. That is, the physical, chemical, mechanical, and other types of properties of these materials in their finished ready-to-use state. Once ASTM has accomplished that, they can move on to perhaps other questions. But I don't think you are going to get performance characteristics.

S. Brown —I think we are going to get characteristics, and as you say, of the materials that we can ultimately use. That is different, in a sense of material, isn't it?

J. Anderson —That is different. We have to be very clear about what we are asking for, and what we would like to obtain, especially because we are dealing with an interdisciplinary group ranging from chemists to surgeons. We all have to talk the same language.

S. Brown —I think we are saying the same thing, Jim. Part of what I am looking at is, if you can begin to come to terms with it, then we can begin to make progress, can get people involved, and can get things going. If you look historically at the orthopedic arena, Committee F-4 started in 1962 with people like Jonathan Cohen and Pat Laing as orthopedists who wanted to discuss with the orthopedic manufacturers some of their common problems. In 1972, the first biocompatibility test method for metals, implants in bone and muscle came out. We now have something that is making good progress as a performance standard on the total hip. Basically, it is saying, "well, things that have the strength of this and less seem to break, so maybe that can set a lower limit of strength for the material that is to be used in the manufacturing of the device." That is now 20 years later, but yes, they are material descriptions. What I am driving at is, particularly for the surgeons, if we could get some input today as to what they think would be helpful from the user point of view of material test methods and material descriptions in getting a better understanding of what they are going to have to deal with when they are considering a patient problem.

M. McClurken, Ph.D. (IMPRA, Inc.) —As a manufacturer, I deal with physicians quite often and I think there is a problem right in front of us in that every major manufacturer is currently making and selling grafts well below 6 mm. And from what I heard from Mr. Britain that will continue for the foreseeable future. The surgeon must be confused because on one hand it's being said that these are a different class and very dangerous, but there seems to be no systematic way for him to make a decision amongst these prosthetics. Just a bare beginning is an open discussion of test methods. You don't have to have the same method for a biologic or PTFE® or Dacron®, you just have to be specific so that if somebody else wants to come along with a contrary point of view, you at least know what you are talking about. But often, the specimenship gets pretty tough out there in the marketplace, and like I said, good intentions of the FDA looking five years down the line are not helping the physician today who is trying to say "I'd love to use this 4-mm graft." I'd say I can make it and I know this and I know this. You can't have it. I think we should put the decision-making back into the hands

of the surgeon and give him true honest information regardless of whether the tests are uniform or there is a minimum or a maximum. Just give the surgeon good information.

A. Kantrowitz, M.D. (Sinai Hospital of Detroit) —I appreciate Dr. Anderson putting the surgeons at the top but that is really not true. It is myth that we would like to continue to propagate, but unfortunately, the surgeons are not capable of the answering the question that was just asked. And I can speak for my colleagues because I know them. They have no idea about the physical properties that are required in order to obtain the end result they are interested in. The end result that concerns the surgeon is what percentage of grafts in a fairly standard test pattern—in a reasonably standard aorta, aorta-iliac, or a femoral popliteal bypass, for instance—will be open, patent, and functioning five years down the line. The surgical community is just now in the process of gathering that information. We have no idea what physical properties will assure a particular clinical result; and I do not think you have either. It is well established that the healing process in humans is totally different from that in animals and we really do not have a good animal model. It is difficult to use an animal like a dog, which is a traditional, experimental model, to test the kind of subtle qualities that you are interested in; and I honestly do not think that the surgeon can answer the question. It is a joint decision that all of us must come to as best we can.

R. Whalen —And yet, Dr. Kantrowitz, wouldn't you as a surgeon like to know what is meant by low porosity, high porosity in terms of degree of leakage, for instance, that you might expect with the vascular graft? I mean, not all users of vascular grafts are surgeons, and in my own work with circulatory assist devices we found that these are very qualitative terms that mean nothing. It has been extremely frustrating to try to evaluate these grafts—we don't feel that we should have to test these products through in vivo experimentation, when for instance, there should be a standard test where porosity among these different grafts can be related. Water porosity may not be sufficient for us.

A. Kantrowitz —That is reasonable. I think that some kind of a physical criteria for porosity is something that not only could be formulated but also would be useful to the surgeons.

P. Sawyer, M.D. (Interface Biomedical Laboratories Corp.) —It's not all that bad. We're not ignorant. We've been playing around with vascular grafts for 35 years now. I made a preserved homograft. I watched that homograft go down the tube. It should have gone down the tube. It had, ultimately in the final analysis, inadequate tensile strength to survive more than three years implanted in humans. But it served its purpose saving the arms and legs of wounded men in Korea in 1951. And then Voorhees made cloth grafts the same time that Adam Wesolow and Lester Sauvage and everybody else started to experiment with a whole series of different prostheses. We crushed and mishandled veins. The veins survived our aggression because they are part of the gold standard. We had one problem—they are not big enough for vascular reconstruction of large vessels.

But everyone in the room has implanted big pipes. You can use any big 16-mm porous pipe you want and basically, it will survive 10 to 15 years. If you are going to use a knit pipe you use one 2 mm smaller than a woven pipe because you know its going to be 2 mm bigger than it was when you implanted it in 12 to 14 h.

The basic problem that we have to face is what to use for small pipes.

Adam Wesolow and I have been discussing going to smaller than 6 mm since 1957. He was putting in compound prostheses in 1958. He didn't solve that problem but it is rapidly being solved now.

Dardik's graft is a pretty good graft. I have a graft which is not the ultimate. However, in 4-mm sizes it has been in humans for seven years; it has somewhere between 40 to 60% long-term patency.

We are gradually zeroing in on a problem that we found in the beginning was pretty horrendous. Initially we did our experiment by trial and error. But there are after all only 1000 surgeons in the United States that really do vascular surgery. There are 3000 to 5000 general surgeons who occasionally do vascular surgery. We frequently redo what they do. There are 2000 maybe 2500 thoracic surgeons who do a limited amount of vascular surgery and do it very well also. You have no idea how penetrating the grapevine is. The information that the PTFE graft could clot reached everybody in the United States within 48 h of the time the first papers and the first presentations of the Society for Vascular Surgery were discussed. If we are just a little more patient, possibly within the next 5 years, there will be about 6000 new grafts coming down the pike and of those 6000, 1 or 2 will turn out to be pretty good and we'll have another period of progress.

R. Whalen — The problem is, of course, that the FDA is going to proceed with the Class II standards and it is going to be really difficult, if not impossible, to do prospective randomized studies. The standards will occur. And while the communication network does work, we also heard today about the pseudo positive reports, and it takes a long time for things to sort themselves out. And the FDA is going to act independently of whatever we do.

P. Sawyer — The patient we implant the graft into is a much greater variable than the graft itself today. Also, all these patients who produce their disease by smoking, they don't quit smoking when we put the grafts in them. We all know that now.

Y. Nosé, M.D., Ph.D. (Cleveland Clinic Foundation) — I think I know both Adrian Kantrowitz and Phil Sawyer so I can say for and against the votes. And I think both of them are partly right. And I think surgeons are not stupid but sometimes very dogmatic. This is why we have problems. And so if we have an accepted exact same graft given to three surgeons, one says it leaks too much, one says it is too tight, and one says it is just right. So for them the concept of porosity is different with each surgeon, no matter from which school he's trained, which city he comes from, which nationality he is. So this is why I think Dr. Brown's point is try to establish some common numbers so we understand each other. Also

the suturabilities for Denton Cooley, one says it's great to suture, and for a certain individual it is impossible to suture. So if you take that one graft to one vascular surgeon, you are told this graft is terrible but for the other it is excellent. So at least we need some common expression. Kinkability is the same. Some individual would say this is terrible, it kinks too much. Some would say it is just right because he cut the length of graft just right. If you cut it wrong, you will get in trouble. So I think from that point of view Stanley is right and Jim is wrong. And one more important thing is that all the grafts presented today are excellent grafts. For some situations and patient populations it does not show a good result, but at least it is as durable, well developed with long history and work study as qualified vascular grafts. I'm sure all of us, the manufacturer, FDA, regulatory agents, and users, would like to make things easier. But make sure it will be good for the patient. To make our life more complicated is not the purpose of us meeting together here. To make our life easier, please give some guidelines for the very strongly opinionated surgeons and a certain common number. Also, give certain minimum safety requirements so that the regulatory agent and surgeon are happy, and the manufacturer can make a product much easier.

G. Hargens, Ph.D. (Franklin Research Institute) —I feel something's missing here in the discussion of mechanical properties. I was a founding member of the ASTM Committee F-4 20 years ago, and I was very much disenchanted then because we talked mainly about steel for the orthopedic replacement. Finally, after 10 years or so, we began to talk about soft tissue. Now I feel today we're really talking about something that I worked on for many years, that is, the measurement and description of human tissue mechanical properties.

Some time ago when I worked with ocular tissue, the ophthalmologist didn't know what I meant by viscoelastic properties. So I became hopeful today, in fact gratified, when one slide, just one slide, had the word "viscoelastic" on it. That's the key because human tissue is viscoelastic, very nicely divided between viscous and elastic moduli. I think we'd like to have the prosthesis, the graft, look something like, or feel like, mechanically the thing it replaces. That's rather essential for mechanical compatibility. So I hope tomorrow we will get into the viscoelastic properties and describe those characteristics in their proper terms. That is essential for our description of whatever we come up with.

R. Whalen —Well I do suppose those topics will be covered in terms of specifying mechanical properties for graft materials. However, there are some characteristics of these materials that are controversial in terms of their importance, even something as basic as compliance. We heard papers that talked about the compliance of natural vessels, but of course, we don't replace healthy natural vessels. So it may be that we should be talking about the compliance of diseased vessels in achieving the compliance value to match. There are many similar questions, and it's not to say that this forum was meant to resolve issues such as these. We are here to define the common areas for which it is possible to write some sort of a standard.

Part 2: Standards Development Workshop

S. Brown — What we've been able to accomplish in the past with some of the symposia and workshops is basically a starting point upon which to build some working documents and end up with some standards as the final product since ASTM's interest is in standards. And as we heard from Charlie MacNeill, the FDA has been mandated by the Federal Government and Congress to write standards. Either we're going to do it as a consensus group or the FDA will have to do it for us. For those of you who are visitors, I'd very briefly like to go through a little bit of what ASTM is about and how it functions, vis a vis writing standards. We are a so-called voluntary consensus group, which means we're all paying our own way. We are made up of manufacturers, users, and general interest people, which usually means academics. The rules are that there will never be more than 50% ballots cast by manufacturers on any given issue to maintain a balance between vested interest and nonvested interest. When need be, manufacturers' ballots are lumped as one company rather than as individuals who are representing the company. The idea is that we, by working together, starting in many cases with the way we have had an information exchange in the last two days, can come up with documents describing methods to test devices, or devices and products themselves that the manufacturers can live with and the users can understand, and satisfy the needs of both parties. In terms of the Committee F-4 on Medical and Surgical Materials and Devices, there are a number of subcommittees, Cardiovascular being one, Orthopedic being another, which are basically the surgical specialties with the intent they would be producing the end product, the device standards, and the performance standards for devices. There is another subcommittee, Resources, and in the subcommittee are the material task forces on metals, plastics, ceramics, composites, biocompatibility, and implant retrieval analysis, and usually they act as a resource for the device specialties. I think within the cardiovascular scenario it probably makes more sense to get within cardiovascular sections that would have the expertise in test methods for cardiovascular devices. Probably some of the biocompatibility test methods would be developed within the auspices or under the auspices of the cardiovascular section rather than under my biocompatibility section per se. What is important is that we are ASTM. There is no ASTM to which you can give a test method and say do a round robin. It's we who get together within the umbrella of ASTM and say we will do it. But it doesn't get done unless we do it. So the point of today's discussion really is, now that we've heard some of the issues and have been asking some of the questions, what are we going to do to write standards for describing initially the test methods that describe the component, this tubular thing, that we're calling the vascular prosthesis? What are the methods that we will use to generate the data that describe them? Once we have effective methods, then we can put numbers on and attach ultimate performance criteria. One comment that I would like to make that I think is particularly germaine to the ASTM methodology is there was a comment made earlier this afternoon implying that suturability in a device standard assumes that there will be no improvement

in the techniques of suturability throughout the life of the standard. I would hope that people would keep in mind that standards are by definition revised and reapproved every five years. Most of them are now all in a constant state of flux. About every time you get a standard finally on the books, we start the revision committees. Putting a suturability statement in a standard simply states the current state of the art and it's revisable at any point. I think we all need to keep in mind that we are not de facto limiting our ability to new advancement simply because we've written a standard on either a test method or on an end device. I will close my introduction on that.

Y. Nosé —I think this meeting was cosponsored by FDA, so let's hear from Mr. MacNeill on what the FDA would like us to do and let's start from that point. He has made a presentation that is so editorialized and I do not know really what we have to do. If you would give us some insight as to the Priorities 1, 2, and 3, then we'll do it.

C. MacNeill, P.E. (FDA, Center for Devices and Radiological Health) —I can wear two hats, that of FDA and my own, so what I think I would rather do here is wear my own hat. Probably the best thing to do would be to put together a team to make an offer to develop a mandatory standard. When the invitation for offers is published in the *Federal Register,* the team should submit a response to develop a proposed mandatory standard for publication in the *Federal Register* as a regulation. I think that is what needs to be done. Otherwise, we at FDA, who do not have the expertise that you people do, will be writing the standard. I don't know whether you'd like that or not.

Y. Nosé —If it is so, AAMI (Association for the Advancement of Medical Instrumentation) has done it, what's wrong with it? Why do you need it? Why do you need an ASTM standard in addition? What is wrong with any standard?

C. MacNeill —Under the law, the FDA has been required to put out an invitation for offers to develop a standard or to submit an existing standard for consideration as a performance standard. If somebody submits the AAMI or other standard the FDA will review it and make a decision on it on an official basis.

A. Wesolow (S. Wesolowski), M.D. (VA Medical Hospital —I think it's an unfair question to ask the FDA representative, because by law he cannot speak in those terms.

Y. Nosé —I know that, that's why I did it.

A. Wesolow —From my point of view as a participant of 30 years in research and 20 years in this arena, this is the first time where all the elements are there which will allow a voluntary body, such as ASTM to offer standards to the FDA. There's no question in my mind that if we structure this committee correctly and if we do what's necessary (what the work, what the research, what the data tell us should be done), there's no question that the FDA will accept it. Now the FDA representative can't say that because this would be collusion. I mean, we're not

the only ones that keep looking at the FDA individuals, unfortunately. They have everybody looking at them. But from my point of view, I'm really thrilled.

Y. Nosé — Is there anybody who opposes having an activity of standardizing vascular prosthesis if it is in the freeze state?

P. Sawyer — I'd like to make a motion. Let's face it gentlemen, if we don't do it, somebody's going to do it for us. Based on reality, I make a motion that we ask Drs. Nosé and Wesolow, our FDA representatives, can you act — are you formally permitted to perform on a panel? Are you permitted to act in an advisory capacity, Mr. MacNeill?

C. MacNeill — No.

P. Sawyer — Can you perform on a panel?

C. MacNeill — I can sit here and make some comments.

P. Sawyer — Ok, I make a motion that we select a committee. I guess that's probably the wrong way, maybe three working committees, who will ultimately produce an overriding committee. The three working committees should be purely scientific. Their job is to monitor what goes into the written document, regulations. The committees would include members from the FDA or the regulatory community itself who will tell us what we can and cannot go into, to a degree at least, and manufacturers who can tell us what can be put in that relates to reality. We have to then indicate who is going to be empowered to select those committees and I would like to suggest Dr. Nosé, Dr. Wesolow, Mr. MacNeill, and Dr. Mortensen. I guess we have to also include Dr. Anderson because he's the repositor for all the pathologic and historical specimens that have been collected by all of us since 1950. The manufacturers have to select people to represent them too. Who do you think?

Isn't that what we and the FDA want?

A. Wesolow — This is not a business meeting where we make motions. It is a work conference where we can make resolutions which will then be presented at subsequent business meetings. On Friday morning, Committee F-4 has a business meeting and we can make suggestions to them as to how we carry on.

J.D. Mortensen, M.D. (MIDMID, Inc.) — Before we get much further into the discussion, with Dr. Nosé's permission, I think we should consider a factor that hasn't been vocalized. I'm sure it's been on everybody's mind the last two days. There are many factors operating to achieve the aim for which we're here and for which most of us have dedicated years of life and activity. That aim is to make safer and more effective vascular grafts. When we get in a meeting of this type or have a panel of this type we somehow assume that's not going to be done unless a regulatory standard is perfected and put into action under the aegis of the Congress as has been described. I submit that about ½ million grafts of various types are successfully implanted annually and that very few patients are injured by the vascular grafts. The tremendous strides that have been made in the lifetime of most people in this room in respect to vascular grafts have been

accomplished without regulatory standards. We are all interested, the users primarily, but also the patients and developers, in good results.

Most developers have done a heroic job in monitoring their own work in producing good grafts. The culprit, the bad graft, the dangerous graft, has long since disappeared by good research and development, not forced by regulation, but by the marketplace. So what I'm saying is not to be construed as an argument against the development of mandatory or regulatory standards but to put them in their proper perspective. All the other factors, science, altruism, desire to help patients, marketplace profit, will continue to operate to make better and better grafts, irrespective of regulatory or mandatory standards. It needs to be looked at in its proper perspective. In this day and age there is always the chance that a bad graft will get out and be put in people who will end up with a serious complication or dying. Therefore, Congress is correct and should be commended for instituting some type of regulation. But that regulation need not take the position of controlling the direction of research, or controlling the work of the users or the work of the manufacturers. All these parties are interested in improving the safety and efficacy of vascular standards. I think we need to look at that perspective as we go about the deliberations of this particular session.

R. Whalen — Somehow I really feel that these discussions on standards get far out of scope. We've heard at this meeting a great deal of practical information as well as a great deal of information that really relates to current research. There is no way that the current research and some of the more questionable aspects — I mean we can't decide, for instance, on the basis of anything that was said at this meeting whether porous grafts are better than nonporous grafts. The standards that we're talking about are really very simple performance standards. The other thing is that an FDA representative said at the outset of this meeting that the FDA was going to begin formulating Class II Performance Standards for Vascular Grafts. Now, we can set up committees to set up committees, but I think the FDA may act first if we take too long.

C. McMillen, Ph.D. (University of Akron) — I've been here for two days listening to this, and this is the first time I have heard Dr. Nosé mention that AAMI has developed a performance standard for Vascular Prosthesis. Could you tell us in just two or three sentences what types of things they're trying to classify?

R. Snyder, Ph.D. (Advanced Vascular Technologies, Inc.) — I'm also co-chairman on the AAMI committee. Basically, there is a draft standard in existence which currently covers biological material, polymeric material specifically, PTFE, and textiles. That standard lists what the committee believed to be the key characteristics of grafts: porosity, physical dimensions, labeling, and strength and specified some test methods to be used for determining what those characteristics were. The standard then goes on to state that those characteristics will be provided in the labeling, will be made available to the user. I think the other thing is that there are also some test methods in regard to incoming materials to specify that a particular material that is listed on the label is in reality the material that was used. The standard does not develop any specific number such as what porosity

you should have for a graft or what strength you should have for a graft, but rather how those parameters should be measured and how those parameters should be communicated to the user community.

S. Brown —Roger, would you proceed with some sort of analysis of what you think of that standard; where it's deficient or from your point of view what you see as reasonable objectives that ASTM should try to meet.

R. Snyder —That's a tough question. I think a couple of things—one of the areas of deficiency in the standard or one of the areas of difficulty in the standard that I think any standards organization has to address is the wide variety of products that are available to answer the same problem. Dr. Mortensen has shown a list of applications for vascular grafts and they are quite wide. The number of grafts that work for certain applications differ. It is extremely difficult to write a single test that will apply to PTFE as well as it will to a textile graft. Porosity is just one key issue. The water test has been well accepted by the surgical community. I think most users have a grasp of what those numbers mean in terms of what difficulty they will encounter in using a graft whether it has to be preclotted or not preclotted, but that test will not apply to a PTFE graft, for example, because it's hydrophobic. So a second method of describing the porosity of PTFE had to be developed and that's the biggest thing that particular organization faced.

Another thing that obviously happens with any standards group, particularly when you have a number of manufacturers on board, or a number of users with differing viewpoints, is that you end up with two or three tests that may do the same thing. That particular standard as I described in my talk yesterday as well as the standards being written internationally contain four methods of determining the strength of a product. In my personal viewpoint, stepping outside of my role on the committee, I think that's excessive. However, it's difficult to get a consensus opinion among a number of people that need to use those standards on how you're going to measure particularly the strength of a graft. So I think the two areas are the multiplicity of testing for strength and the multiplicity of grafts that that standard tries to cover.

We have the same basic characteristics for grafts. You need to know if the material is porous; whether you're going to get blood leakage through it. You need to know if the suture is going to pull out of it, you need to know if it's going to last 20 years, and you need to know whether it's going to occlude immediately. Those are basic features that you need to know, but how do you measure them for a biological material on one hand and a textile on the other hand that has a 2500-mL/min/cm^2 porosity? That's a wide range of products all of which according to the data that we've heard in the last 2 days function reasonably. So that's been the main problem.

As far as suggestions which ASTM might consider, I personally think there is a big lack in the areas that are probably already ongoing in determining biocompatibility. Most of what you see from the manufacturing point of view uses the U.S.P. packaging test for biocompatibility. There's a lot in the literature that's better than that. Other areas include: what are reasonable types of tests to be

performed while developing new products, what type of animal study, what type of animal model, and what type of clinical studies that one should undertake to determine that your graft functions at least as well as what is already commercially available which is normally the standard.

C. MacNeill — I think that there may be a problem between ASTM and AAMI that probably needs to be resolved to find out whose going to do what, so that's something that ASTM could consider talking to AAMI about.

Y. Nosé — I think if AAMI has done it we have to strengthen it and make that document more meaningful. However, there are many other areas to be covered. I believe that to make one document on a vascular prosthesis standard is an impossible task because there are all kinds of different devices, all kinds of different approaches, and porosity is a big issue, maybe, but some devices do not have porosity at all. So I think that what AAMI tried to do was an extremely difficult task which they did extremely well. However, to make a document you have to make everything vague, not specific. This is why that particular document served some usefulness. However, there is another type of documentation — a standardization that is necessary. For instance, component characterization and terminology characterization test methods. Both of these standards will supplement each other and will make everybody happy. I think as far as ASTM is concerned, we do not wish to have a similar approach because we have to do some work in areas that the AAMI standard did not, or could not cover.

D. Lyman, Ph.D. (University of Utah) — Your comment, Dr. Nosé, that there are all kinds of different devices is very important. For example, when Roger Snyder mentioned that the graft should last 20 years we must contrast this with the excellent paper that Dr. Griesler presented this afternoon which showed his graft does not last 20 years. Yet, the biological response of the graft we hope will last 20 years. If a graft had to withstand hydrolytic stability of x number of months or days under what accelerated tests, this graft probably would not pass. Yet this might be the ultimate type of graft for certain uses when we get a controlled regeneration. So we have to watch what we are specifying. The characterization of the material to make sure we have a good reproducible material and that the fabrication technique has not adversely affected it should be our major concern. Unfortunately, this has been abused many times in implant development. We must be specific enough to control the polymer in use, but not use it to exclude new materials which function differently.

Y. Nosé — If you make it too specific you put yourselves in trouble because if we specify that a vascular prosthesis fabric has to be this and this way, then all the manufacturers are stuck. I think sometimes accidentally fabricated graft is one of the best grafts, so it's very difficult to specify in detail. I would like to hear some manufacturers' opinions.

D. Lyman — We do this after the fact. Then we can begin to specify some of these parameters so we can repeat our experiment.

Y. Nosé — That's quality control, and that and the standard are two different things.

D. Lyman — They are quite interrelated. Because if we're looking at the molecular structure as the standard we are trying to achieve, the QC (Quality Control) tells us if we have achieved or maintained this structure.

A. Wesolow — Dr. Nosé, I think in these days of litigation, if a standards body such as ASTM does elaborate a series of quality control standards and good manufacturing practices this is a protection for the manufacturer.

Y. Nosé — I would like to hear from manufacturers.

E. Friesch (Dow Corning Corp.) — I am at somewhat of a disadvantage because we do not make vascular grafts, but I can comment from our rather broad experience with a wide variety of other implants. Probably, the existence of standards and adherence to good manufacturing practices alone do not adequately protect manufacturers in litigation. It is often difficult to know what will happen when you get into court in front of a jury who may have little appreciation for the value of standards and the manufacturing of medical devices. Having done appropriate product testing and process validation prospectively probably provides the best protection. Testing should include biocompatibility and biodurability studies, and process variations validated to assure the important characteristics of the product are reasonably duplicated. In medical device litigation, it often seems that "guilty until proven innocent" applies.

M. McClurken — I forget who made the point, but there may have been almost a million PFTE grafts implanted thus far, so obviously the problem isn't the past, it's the future. I think it would be a shame if we look at this as an opportunity to write one bad document and all go back to work. I think we ought to be looking for a way so that on an ongoing basis we get more people involved with the basic level of test methods. We've seen test methods described wherein everyone can be manipulated by any party, a doctor, a manufacturer, a lawyer. I think everybody's motives here are very fine, but I think what it's going to take is manufacturers are going to have to take time out of their work and the academics will have to take time away from their lab and actually address these nasty little problems of how fast, how big a sample, a standardization of this and that, but keep at it for the foreseeable future because the problem isn't particularly my graft or his graft. It's the guy in the garage somewhere in Southern California who is under financial, legal, and time pressure to get something on the market. He hasn't got time to come here and he can't afford to stay here but he's the one who is going to cause Congress to say "why didn't you stop this guy." The only way you can stop him is if we get not just us but these guys involved, and that's the future. It's almost silly to look back.

Y. Nosé — Are you sure it's a problem? You know maybe the big company was the small garage operator ten years ago. We allowed them to do it. Many innovations come from the garage operation. Some of them are very good.

P. Sawyer —Every major manufacturer of grafts in the United States started in a garage. Every single one of them. One of them in a very small garage.

Y. Nosé —I think our obligation is not to kill the garage operators, but to try to encourage them. Try to make more innovative devices in the market which are effective and safe and at least we have to give them a guideline. These guys just do not know minimum guidelines. If they did know they would become more confident to produce them. Then the entire job can be done by an American-made medical product.

M. McClurken —I talked a little bit about PTFE. The early aneurysm problems with PTFE were a very simple problem of undersuturing. This was known to Du Pont scientists for 20 years before that probably. Why did two companies, one very large and one very small, both miss this? There was absolutely no standard, there was nobody they could turn to. I'm talking about privately held companies. This is obviously a difficult problem, but I want to focus on the future and I want to focus on specifics. I think materials composition is important, but I think small subcommittees have got to start somewhere and saying this may not be the minimum or the maximum it's just a way of doing it.

P. Sawyer —Did you notice how fast they were self-correcting?

M. McClurken —Certainly.

P. Sawyer —Yes, you bet your life.

I could tell you three or four other stories not from this podium, but I'll tell you in private, about how fast crimping and compacting techniques which proved to be very dangerous in biological systems were corrected within days. Everything that had gone out and they returned to a classic ancient slow technique for crimping, namely, steam.

S. Weinberg, Ph.D. (Biomedical Device Consultants) —One of the problems of a small starting manufacturer entering into the graft business relates to making judgements as developers as to which test criteria and test methods to utilize, and in particular, what type of criteria the regulators and the surgical community require. Finally, what criteria will be used to make the judgment that we have completed our development work? Once we are prepared to submit data to the FDA, we need substantial confidence that the data will be accepted by them assuming we did our work properly. In the past, I have been involved with many submissions to the FDA and the thing that continually frustrates me is that we'll put together a series of test methods, information, and other data which are based upon the state of the art and should be all that's necessary for us to get approvals, but one time after another both in my company, and others, we get comments and requests for information on issues that have never been raised or are totally off the wall in terms of their relevance to the specific application of the device. Materials that have been used and have 20-year plus histories in vascular grafts all of a sudden come under question. For us as developers and especially in a start-up environment, it would be a great advantage to sit down and be able to

predict and to plan for our development in programs in a way that would allow us to submit data to the medical community and the FDA with a fairly high confidence level that assuming we do our work right, it will be accepted. This will allow us to plan for a particular marketing date and develop an effective strategy. Investors which invest in companies like ours want to know when we are going to have the products in the market and when we are going to start generating income. An effective vascular graft standard would help us and I'm 100% in favor of this effort. I'm also glad the issue of the AAMI standard has been mentioned since many man-years of work were put into the AAMI international standards effort. As an improvement on the AAMI standard, I would like to see one test method for each test including measurement of textile graft porosity. Even today, a graft was introduced by a new company with a porosity measurement based on a new improved porosity test. The porosity value was totally out of phase with all values that were measured by competition and resulted in a confusion in the medical community which ultimately resulted in clinical problems. These are the kind of problems which could be avoided with an appropriate standard.

Y. Nosé — Katherine, do you agree?

K. Botzko, M.S. (C.R. Bard, Inc.) — Yes, I agree 100%. I think that a little bit of what Dr. McClurken said is also very applicable in this area. You have a lot of new people coming into the field and a lot of people looking in the vascular area. When they look for test methods, there aren't any standardized test methods so they develop a brand new way to measure porosity, a brand new way to measure strength, and that really does confuse the issue because as surgeons go out and look at this information they have no way of telling whether the numbers they're seeing compare in any way to the number they've seen for different vascular prostheses. I think it would be an aid both to existing companies and to newer companies in the field if they had some standardized test methods and knew that what they were producing met at least the same types of quality tests that are met by existing prosthesis.

Y. Nosé — So that means all manufacturing companies, all test methods, all different, all accepted, and you select one as your company's method.

K. Botzko — What I'd really like to see in an ideal world is some kind of testing on various test methods to see which ones gave the best reproducibility and pick that one.

Y. Nosé — What's wrong about everybody's methods. I can find five different methods that are used — all acceptable.

K. Botzko — Well that's what the current standard that's put out by AMMI and ISO has. It lists the four different methods and says basically we don't know which one is best so use whichever one you want. It would be nice to know which one is the most accurately reproducible.

P. Sawyer —I submit that the water used and the dirt in it produces a greater variation than anyone of those four test techniques.

K. Botzko —So everybody whose doing that now is using clean filtered water so you filter out the particulates to start with although the people working in England tell me that the water that they get up in Scotland produces the porosity results.

E. Murphy, Ph.D. (Consultant) —I'm a retired bureaucrat, editor, and assorted other things—I think one of the problems is that we have talked as if there were a single standard that somehow we would produce. We should recognize that ASTM uses "standard" as a modifier. It speaks about standard specifications, standard test methods, standard definitions, standard recommended practices, and so on, not about a standard as a document solely in terms of dimensional or numerical data. So there are a number of possible documents that this group might very well develop. Many of them initially perhaps might be tentatives to be used (and debated) for running further animal or clinical trials so that the results reported will be comparable with everyone following the same protocol. In this way, the results are much more useful for all concerned and data from many different laboratories or clinics can be lumped together.

It does not follow that we have to develop instantly a document. Development of a good document may well take a decade or several decades of debate and trial and hammering out before it becomes useful.

This Committee F-4 was started in 1962. I was involved in the early days. There was great wringing of hands about what to do. The participants concentrated, I think wisely, on orthopedic implants where it looked as if there were some possibility of progress. It still took many years to develop even the beginnings of documents for the orthopedic metals and for the various uses for those metals. The activities gradually broadened to other specialties, materials, and aspects. There are a variety of documents not only on the basic materials and their properties but on the dimensions of the various kinds of plates, screws, hip replacements, and so forth. So we should be looking forward to developing a volume of documents, not a single so-called standard.

C. Biggerstaff, M.S. (W.L. Gore and Associates) —We didn't start in a garage. We used a basement instead, but it all turned out pretty well. My concern about standards is that we don't end up with a standard developed that becomes law that would restrict innovation, restrict research, and restrict new products coming on line. Especially if it takes five years for a standard to get revised and changed. New products could come and go within that time very rapidly. Vagueness maybe is not a good term for a standard, but standards that are general enough to not restrict research, that would be a main concern.

Y. Nosé —It reminded me that about ten years ago when we started the polymeric section standard there was several years' debate. The question was that we could not standardize polymeric plastic materials. At that time, Dr. Horowitz

asked me to chair that session. I said, "ok, let's make a generic standard which defines what is a polyurethane and what is a polyethylene." Starting from that point, now everybody is making hundreds of different standards. I think we should apply a similar approach, starting the simplest, easiest possible way, so that we understand first what we're talking about, then go further.

E. Horowitz, Ph.D. (The Johns Hopkins University) — As I've listened to the discussion here, I'm reminded of some of the history of Committee F-4 in the early days and the arguments, particularly in areas that were as controversial as biocompatibility. I know that we struggled for five years before we even formed such a session. Dr. Nosé and I have been talking about cardiovascular standards now for at least five years and perhaps longer. I am strongly convinced that such standards have a very important place not only in the industrial sector, but in the medical and in research sectors as well. It's there that protocols, definitions, test methods, and test procedures are organized in a coherent way. We heard earlier that standards may not be important in the courtroom. I think, on the other hand, you can find cases where, particularly, ASTM standards have influenced the decision made in a court case. The important part that I feel we have to play is to select problems that we can deal with. This means from the manufacturing point of view, from the academic point of view, and from the government's point of view. As Eugene Murphy pointed out, we should try not to write the single biblical document, but to define different aspects of the problems beginning perhaps with generic definitions, with defining some particular test that is an obstacle to progress. In those cases, as for example, with the porosity where we have four tests on the books without any correlation factors, there is an important role for this committee to establish round robin tests that can begin to evaluate the individual tests and to begin to correlate them so that there is some meaning to the test data. If you've done this in the past in your own career, you'll find that several of the tests will be meaningful, that there can be coefficients established to correlate them, and some of them will be meaningless. These can be determined this way and be discarded. So I am all in favor of a very strong program to develop standards. I believe it will help the medical community and I think it will strongly help the manufacturers. It will also uncover new areas of research for people in academics, in industry, and in the government as well. When you talk about the material itself, the field of characterization of materials is moving much more to the atomic, molecular, and surface science areas. We're learning each day how important the surfaces of these materials are, and with the modern tools of characterization, we are in a better position now to define composition and concentration profiles along the surface, and physical defects which may affect the performance of the materials and devices. I think that the standards work will stimulate additional research and I encourage you all to partake in this and to be active. Let's have your ideas.

C. MacNeill — Let's call it the rule of reason. Food, Drug, and Cosmetic Acts talk about reasonable safety and efficiency, they don't talk about minimum or

perfect safety and efficiency. A device does not have to be perfectly safe and perfectly effective. There's some degree of in-between those two extremes, something that's reasonable, and this is what we should look at. I'm not a vascular surgeon, I'm just an engineer, but, if I was a surgeon and I was getting a vascular graft, I'd want one that has some identified resistance to burst strength under blood pressure. I'd also like to know what the dilation would be when the blood starts flowing again so I can get a match between the device and artery vein in the pulsation. As a surgeon, there are certain things I would like to know. Some of these can be set as a real specification, and other items can be considered in the labeling, identifying the degree of porosity and the degree of dilation under given pressure so that the surgeon can do his job and have enough information to do it in a safe and effective manner.

Y. Nosé —I think that this particular point is extremely important. If it was necessary to develop a hemodialyzer with a perfect safe standard, I do not think we would have a hemodialyzer now. It is still not a good device, but still we use it. Another good example is immune adsorption agents such as protein A which is released experimentally. It is not a good system. When we connect it to the patient who has cancer, the patient has a fever, chills, shock, everything, and the people think it is not good. We have to improve it. But my opinion is that effectiveness of this protein A has nothing to do with removal of immunocomplexes or antibodies or whatever, but gives the patient a controlled, frequent shock. I still remember what my old professor said during his lifetime practice of stomach cancer surgery. He had three cures for inoperable cases. All three had mistakes. He had a mismatched blood transfusion and the patient was in shock, but this immunological shock actually removed the cancerous tissues. I think that sometimes if we look at the one side and try to provide a safe device, probably there is not such a thing. I bet if you try to make that device purified and make it complication free or side effect free, probably that protein A does not work, that's my personal bias. I have nothing to do with protein A, but I never use it because it is very dangerous. I believe the key is the side effect, so I would try to really encourage you. You should not be worried about side effects or complications, especially if it is not really life-threatening.

R. Snyder —First, I didn't want to be misquoted. There are not four tests for porosity in the AAMI standard. There are only two, one for PTFE and one is based upon the Wesolowski Water Method for Textiles. Those are two distinct products and so those require two distinct methods of testing. It's in the strength area where there is confusion. Second, I think to a certain extent we're really talking about two different things at the same time. One, we're talking about establishing some sort of performance for the product. On the other hand, we start talking about testing methods. I think those are two distinct things and we have to keep that in mind. In the line of testing methods, I think one area in which AAMI has been deficient and other groups have been deficient, and in which this distinguished panel could really help, is how do you test a vascular prosthesis in

an animal model. Yesterday we heard about goats, pigs, rabbits, dogs, and baboons. The only thing we didn't hear about was the rat which other people are using. We heard grafts all the way from 1½ cm in length to 24 cm in length. Iliac, cross carotid, all sorts of models, and this data is all reported in the literature. A surgeon gets this data and he's asked to evaluate whether this graft is worthy of a clinical trial. Yet he can't compare it to the data over in the other literature because it's a totally different model. I think there is one area where there's a crying need so that people can evaluate whether or not a particular product is likely to function.

A. Wesolow — I have a bank of over 360 materials you can match it against in the growing pig if you so desire.

R. Whalen — I guess I've been coming to these meetings now for about seven years and sometimes I really have this sense of deja vu. We seem to do a lot of talking and I get concerned that we're not doing anything. I'd like to ask if we are going to do anything or are we going to indulge in philosophic discussions. I think if we are going to do something, we have to do it fairly quickly. As far as these test methods go, I don't think the goal should be for us to develop standard articles that will identify safe products and safe vascular prostheses, but rather simply to establish whether people are comparing apples and oranges. We don't seem to be able to agree upon how we can measure the porosity of a piece of cloth if that's what we're choosing to do. The task really, I think, is much simpler than we're making it out to be, and unless we simplify it we're not going to achieve anything today.

Y. Nosé — What do you suggest to start with?

R. Whalen — Well, I suggest that if we are talking about performance standards, there are three basic categories, PTFE grafts, polyester fabric grafts, and bioprosthestic grafts. There should be separate test methods, perhaps, suggested for each of these types of vascular prostheses. Now, a concern I have, however, is that we don't want to have any performance standards act as an impediment to the use of new materials and new types of technology. I mean, smooth surface polymeric grafts are coming along and I really wonder if the performance standards that we might identify for these other types of grafts would be appropriate, but we have to do something.

Y. Nosé — Performance is very big. Nobody understands what the performance is and I think we have to reduce it down to a more specific expression such as porosity, flexibility, durability, or compliance. Maybe something like this is a starting point, and I believe in each area that we have expertise to cover it at this symposium. Probably, let us ask the individual to cover that specific area to get some recommendation.

R. Whalen — We choose these individuals as a group and certainly these individuals are all associated with companies currently manufacturing vascular prosthesis. Remember there are 350 000 implants a year now of these devices.

P. Sawyer — 500 000.

R. Whalen — 500 000. Well then, let's see — we're not talking about something new. All we need to do is to identify test methods to characterize these materials so that if we look at Devices A and B we're not using different methods. That's what I see as our task.

P. Sawyer — If we just want to address standards, doesn't the AAMI protocol do that for us? It sets certain measurement standards. It doesn't lock us in, it doesn't cast us in concrete, but it establishes certain minimum criteria to permit us to measurably determine the safety of at least the more porous prosthesis, PTFE, and I guess probably the grafts of biological origin which have measurement standards of slightly different character to determine their functional stability and their ability not to clot.

S. Weinberg — Let me raise a final point. Most of us in the room now have been involved, know of, or have lived with the AAMI or the International Standards on vascular grafts. This document basically defines the labeling requirements and subdivides the test method into three primary graft types. It seems to me now that we have a whole new set of players involved in this process and I would suggest that some new faces and some of the old faces, who have been involved in the standards, first get together, form an official group, and review the standards that exist so that people who aren't aware of what's been done in the past can be brought up to date. Once this is done, deficiencies in the current draft standard can be identified and then the new faces in the group can move ahead to fill those gaps. It just seems to me that we've been working on this effort for the last five years and now we have a new organization involved. Much of the expertise and effort of this new organization could be focused in areas where our standard is deficient and incomplete. It seems simple to me — pick a group, let's get started, using new and old faces, take the old standards that exist, and use those as a basis for the new and move ahead. It doesn't seem that complicated.

R. Whalen — I agree with that totally.

A. Wesolow — This probably would be a very productive approach. If we had the vascular standards people from AAMI together with the vascular standards people from ASAIO (American Society for Artificial Internal Organs) with a group from here, which will be very long on materials specifications, and could sit down jointly with representatives from NIH and FDA, we could get the first draft out in a day. I propose that Committee F-4 consider doing something of this sort: this is the first time that I'm aware of in 20 years that it is possible to make this proposition with a likelihood that all of the groups concerned might listen and be willing. Because if we don't do it, the FDA is going to. I think everyone finally recognizes this.

J. D. Mortensen — It seems that our direction is being focused, which I suppose is the prime purpose of this workshop. A couple of divergent thoughts,

however. We act as though this is a new ball game and new project. I'd like to point out that the FDA has recognized this problem and spent many thousands of dollars already in pursuing vascular graft standards. They didn't just come into this field today. They have financed a Phase I study which many of you know about and have read thoroughly. We're not starting from scratch. The Phase I study has been completed. The fact that we've discussed in some detail testing methods and the need for better tests are direct outcomes of the Phase I study which identified one of the more serious problems. Testing methods for vascular grafts were largely in an undeveloped state until recently. So I think we do have a basis on which to proceed. The suggestions that we get off the dime and proceed are very worthwhile, but let's not forget that we're not starting from zero. Furthermore, the AAMI draft standard (it's a working standard and it's in draft only), has been reviewed carefully in the Phase I FDA study and has been compared to international standards from standards from several countries. Those comparisons are available for review by this new working group. So, we don't need to start completely from scratch. It is time now to proceed. A recommendation from the FDA study was that the AAMI standard is the best work that's been done to date and it should be used as a guideline to build on it. We don't need to invent the wheel all over again. Some of the most important problems and issues have been identified and attacked by that standard. I think the many people in the audience and on the stand who have worked on that AAMI standard shouldn't go away with the idea that their work has been lost. Also, we shouldn't go away with the idea that the FDA is just now beginning to look at this. This has been their commission now for 8 years and they've been active. I believe the current status of regulatory standards and voluntary standards and guidelines for testing and labeling instructions owe a debt of gratitude to the FDA. They shouldn't always be cast as the sheep in wolf's clothing trying to do us harm, but in many instances are benevolent in their efforts if we'll work at it in the right way.

B. Hargens —I think from what I've heard in the last two days that vascular people have been talking exclusively to each other. Now perhaps some of the rest of us, who are working in other areas of biological materials, might have some contribution. I would hope that whatever procedural mechanism you set up you will somehow make it possible for those of us who came here thinking we did have a contribution to make, maybe from a life work, to have some input and that you could let us know what you're writing.

For example, I've heard the testing described and I felt it was rather limited and narrow. I want to say that there are many other excellent procedures in studying tissue properties and making your prosthesis all you want it to be. We've made excellent prostheses for other parts of the body. I would think that perhaps you could somehow extend an invitation to us at some point in your deliberations to make a contribution along with lines.

C. McMillan —If I could suggest an action item, perhaps the group could circulate to all the attendees of this meeting a copy of the AAMI proposed draft standards and you could then include with that a card that people could send back

either with suggested comments or interest in participation in smaller subgroups to work on these standards.

J. Doyle (Canadian Standards Association) — Dr. Mortensen made a comment earlier on perspective. In listening to his comments, it would seem that there has been speculation on the perspective of the FDA. What type of data is acceptable to the FDA? I think as a further suggestion to what the two previous speakers have said on this topic, that FDA should take a look at the two or three existing standards in this area and let us know exactly what the deficiencies are. I know they can do this because they certainly comment on the Canadian standards.

On the second point, what is the cost-effectiveness of what Committee F-4 is proposing. If drafting a performance standard will lead to safer or more effective grafts, then we probably should proceed with its development. By safer in this case, I am referring to lowering the risk of failure of these devices. However, a standard should not be looked upon as the only solution, nor even the best one, if the problem is the failure of these devices. For example, it may be more profitable to develop new suturing techniques. In any case, a standard if developed should serve the needs of all concerned including industry and the FDA.

E. Horowitz — You know there is an important lesson to be learned by looking at some of the older ASTM committees, particularly the metallurgical committees, the stainless steel committees, and so on. If one asks the question, "What is the prime purpose of that standards activity?," it is really to control the quality of the product in the steel mill. Those test methods, if you look at them in terms of chemical composition, mechanical properties, and the other attributes of the metallurgical material, even before it's made into a product, are the keystones of the standards. As I hear the conversation today, and try to put this problem in that perspective, I see two parts. One is what you would call the intrinsic qualities or characteristics or properties of the materials. One of our basic problems is that with each manufacturer and with each different processing technique, we have generic products with different properties. Dacron is not necessarily Dacron, it's a whole variety, a whole set of different subspecies. Likewise with your other polymeric materials and your other composites and metallurgical materials. So one part of this problem is how do we define the material that is ultimately going to be made into a medical device or a medical product. That somewhat simplifies the approach. It gets away from the performance problem which is extremely complex. The other part of the problem is clearly the performance. Now that we have very well characterized the basic materials so that we can compare a product from a manufacturing Site A and B or even within the same manufacturing site, how will that product perform in service? That to me is at another hierarchical level of difficulty and work. So my own view would be to see if one could establish some task forces, maybe even within the existing audience to obtain some names to get started on several of the tasks I have mentioned. I think if we adjourn this meeting without having some names on pieces of paper where people have agreed to interact with one another, to accomplish something, there is going

to be a six-month hiatus before anything gets done. That's number one, and my suggestion would be to deal with the lowest common denominator problem, that is, to deal with the simple part. You alluded to this earlier. Define one or two problems that could lead to a test method or a characterization procedure that we consider to be important and proceed along those lines.

S. Brown —Manny, I would like to follow up on your suggestion about some specific names. Mike McClurken from IMPRA has presented yesterday a very nice paper on mechanical test methods of the components with suture pull-out tests, burst strength—anyway, basically with the concept that their functional test of that are appropriate for the way they are going to be used. I mean you test with a 6-0 suture because that's what the surgeon uses and if the suture breaks, as engineers and materials scientists, we'd say it was a lousy test, but for the kind of in-use we're interested in, we would say the device is stronger than the suture and that in itself is a valid result. I've talked to Mike and I think we have an agreement that at this point the way to start is to start and he's agreed to sit down and write up a couple of draft methods and circulate them before the next meeting. So we can actually get things going. My feeling is that the only way we're going to get going is as you say is to get going and if we can get a document or two out in the mail, then we'll find out who is really interested in getting involved because they will take the time to write positive or negative comments. Then we can get a meaningful mailing list and really proceed from there.

M. Helmus, Ph.D. (Arthur D. Little, Inc.) —It seems to me that we need to get a perspective on the particular graft design and decide what are the parameters that are important for the graft to function properly. Rather than talk about specific test methods, let's go back and first look at the graft and decide what it needs to do, and what the surgeons need to know. After these properties have been listed, then the proper test methods for these parameters can be determined. In this process, accepted test methods that are familiar to the user and manufacturing communities need to be factored into the recommended test procedures. Once, again, we need to go back and look at the device. We are talking about test methods but what is it that we need to know about the device—suturability, conformability, compliance, kink resistance, porosity, and then the biological properties. I think this is quite an important issue. You have to look at these issues in terms of what some people have said. There are three basic graft materials—PTFE, Dacron, and biologics—but a test method for, as an example, suture pull-out in PTFE materials may not be suitable for woven Dacron materials. We need to keep our perspective and develop test methods safe, effective, and useful to the surgeon.

S. Brown —Well, I'd like to say that I think we've spent the last two days looking into that mirror. In many respects we've been doing it for five years or twenty years and I don't think we really need to start all over and as Mike was saying pick a method. The other thing is that I don't think anybody has said implicitly or otherwise that a suture pull-out test method that is going to be written

by this committee is going to be exclusive for one type of material. Clearly, that's a critical issue. We're going to talk about developing maybe a Type A/Type B method that, depending on the nature of the material out of which the tubular segment has been fabricated, you would select Type A or Type B, not trying for exclusively woven or expanded PTFE, and that's what makes a good test method. And that's what make the consensus system work. That somebody from a company that makes a kind of material might start by writing a method that is very appropriate for their type of material and somebody else on the committee says now wait a minute, we need to put a variation in so that it's appropriate for our type of material. If there was iteration and some consensus in having some documents to work with, we could then produce a meaningful test method.

R. Snyder —Stan, in all due respect, this has been done. Those types of test are written in the AAMI document. Not all surgeons, by the way, use 6-0 sutures for grafts. An unfortunate comment was made, a lot of them use 3-0, particularly for the larger diameter grafts. My point is if you want to circulate a document that has tests written in it why not circulate that document that's already had something like seven years of work put into it. This document specifies suture pull-out tests, although my competitor may disagree with the test method that's in there, but he's free to comment on it. It specifies porosity tests, specifies unfortunately too many strength tests, but those tests have been written. They've been detailed as to how to perform them in that document. Why not have that document circulated if you want to write something. If you just want something written, we can all sit down and write something but it's already been done.

Y. Nosé —That's good. We certainly do not like to reinvent the wheel or duplicate the effort.

W. Colone (IMPRA, Inc.) —I disagree with Roger. They have basically defined the test methods. You need to get exact sample sizes, test rates, everything, or it's meaningless. I know as an engineer you can take longitudinal tensile strength and raise it or lower it by 50 to 75% just by changing the size of the sample and the rate of the test method. AAMI does not list anything that says what a longitudinal test is and that you grab a graft and pull it in this direction. That's meaningless, it doesn't do anything for anyone. You have to say take a whatever inch sample, pull it at this rate, then when everybody tests the same way, we can get something done. You can start comparing Gore to IMPRA, to Extracorporeal, as PTFE grafts can do the same thing for Dacron grafts and biological grafts.

Y. Nosé —That's my frustration also and I think FDA's frustration might have been the same. This is why ASTM who knows exactly how to make standard for each test method, the procedure, and so forth is necessary to supplement the AAMI's write up.

W. Colone —Right, I completely agree with that, that is all it would take. Everybody's making this more difficult than it really is. The PTFE graft manu-

facturers have to sit down together. If you lock them all in a room one day for four or five hours, they will know how to test their grafts. I know Gore does the same tests we do. There are slight variations, but I can't count their suture retentions the same as ours if they're going through two walls with a different size suture. Or I can't count their longitudinal tensile tests as compared to ours if they're doing it faster or slower using a different sample size. Those are the only things that need to be ironed out. It's not that difficult. Same for the Dacron people. They all do similar tests right now. Just get together, hash them out, write it up. It's very simple. The basis is already there with the AAMI standard. They've already defined it and explained what it means but they don't give any test methods. So it's very simple.

P. Sawyer —OK, Dr. Nosé, how are you going to do it administratively? That's what has to be decided.

Y. Nosé —I believe Adam Wesolow is most experienced in this field and should take a lead.

P. Sawyer —I just told him he had to do it.

Y. Nosé —He should recruit the most qualified individual from a surgical society, from a manufacturing organization, or other society and draft it. I think he should approach from the global point of view and which area he needed to fit in and then get everybody — whoever's name is on the computer. I think Adam is going to call you up and demand your service and I think it will be good for the sake of everybody. We've got to do something at this time and eventually what we do is a help to our patients. Also you can make more money and so make sure whatever is involved are not really expensive tests. Anybody can do it, the minimum, bare bones basic required test method. This is the key. And of course, in addition, there are various test methods, whenever you feel it is right to use them — whatever test method we created is all right, but make sure we don't make our life more miserable right now — right now it is terrible. Think about 20 years ago when Adam Wesolow and Phil Sawyer brought the tube from somewhere, not specified, we don't know where it is from and implanted it in the patient. I think we have to make sure Phil Sawyer can be able to prepare his innovative devices in that patient and he's showing excellent results. We should not discourage that innovative scientist, innovative vascular surgeon, small garage operator.

I think we will inform all of you concerning the procedure we should follow. If you have any suggestions, any recommendations, any distinguished names you believe should be recommended for the job that are not listed here, please recommend them to us. I think we should recruit the best manpower available, best organization available, and with the leadership of Adam Wesolow I am sure we can do it.

E. Horowitz —I will just say one thing. The administrative task as Dr. Sawyer has pointed out is formidable. What needs to be done at this meeting is that there

has to be a conversation with Pat Laing who is chairman of Committee F-4 and then I think there could be made available through ASTM Headquarters some logistical and administrative help to make this process possible, otherwise, it is going to be very difficult.

Y. Nosé — We would like to express our sincere thanks to the FDA, particularly, Mr. Britain, Mr. MacNeill, and Dr. Sung, the International Center of Artificial Organs team, particularly Helen Kambic, and also the team of the staff of the International Center and many others who helped make this symposium possible. I believe it is a starting point.