GENERAL HOSPITAL & PERSONAL USE DEVICES PANEL

OPEN SESSION

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Rockville, Maryland
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**PROCEEDINGS**

**WELCOME AND INTRODUCTORY REMARKS**

MS. O'LONE: Good morning. Welcome to the General Hospital and Personal Use Devices Panel for the open session. Thank you for coming. If you have not signed in for this meeting, please do so.
I am Martha O'Lone, the executive secretary of the General Hospital and Personal Use Devices Advisory Panel. And before we have panel introductions and turn this portion of the meeting over to the panel, I have two items of business that I have to read into the record.

The first is a conflict of interest statement. It goes like this. The following announcement addresses conflict of interest issues associated with this meeting and is made part of the record, to preclude even the appearance of any impropriety. To determine if any conflict existed, the agency reviewed the submitted agenda and all financial interests were reported by the panel participants.

The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employer's financial interests. However, the agency has determined that participation of certain members and consultants, the need for whose services out-weighs the potential conflict of interest involved, is in the best interest of the government.

Full waivers have been granted for Dr. William Rutala and Ms. Marcia Ryder for their interest in firms that could potentially be affected by the panel's decisions. The waivers permit them to participate in all matters before the panel. Copies of these waivers may be obtained from the agency’s Freedom of Information Office, Room 12A-15 of the Parklawn Building.
In the event that the discussions involve any other products or firms not already on the agenda for which an FDA participant has a financial interest, the participant should excuse him or herself from such involvement and their exclusion will be noted for the record.

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

And the second item of business is appointment to temporary voting status. Pursuant to the authority granted under the Medical Devices Advisory Committee Charter dated October 27, 1990, as amended on April 20, 1995 and October 10, 1997, I appoint the following person as a voting member of the General Hospital and Personal Uses Devices Panel for the duration of the panel meeting on August 2, 1999. In addition, the following person will act as panel chair for August 2, 1999, and that’s Charles E. Edmiston, Ph.D.

For the record, this person is a special government employee and is either a consultant to this panel or consultant or voting member of another panel under the Medical Devices Advisory Committee. He has undergone the customary conflict of interest review. He has reviewed the material to be considered at this meeting. And it’s signed David W. Feigal, Jr., M.D., director, Center for Devices and Radiological Health on the 21st of July 1999.
And the only other piece of business is that the future tentative date of this panel would be potentially November 16 for this year. We don't have any other dates set aside at this time as tentative dates. And to find out if we're having upcoming meetings, the phone number of the hotline is 800/741-8138 and the code is 12520. That helps to get right to the General Hospital Panel to determine if there are any new messages on that line.

I'll now turn the meeting over to Dr. Edmiston and we will begin the open session of the 34th General Hospital and Personal Use Devices Panel meeting at this time. I'll introduce him. He is an associate professor of surgery at the Medical College of Wisconsin and has been a consultant to our panel for quite some time and thank you very much for acting as chair today.

DR. EDMISTON: Thank you very much.

At this time I'd like the rest of the panel members to introduce themselves, starting with my colleague on my right.

DR. FOWLER: Dr. Joe Fowler, a dermatologist at the University of Louisville, Louisville, Kentucky.

MS. RYDER: Marcia Ryder. I'm a nurse consultant in vascular access and a doctoral candidate at the University of California at San Francisco in the Department of Physiological Nursing.

DR. RUTALA: Bill Rutala. I'm director of hospital epidemiology, occupational health and safety at the University of North Carolina Hospitals and professor in
the School of Medicine.

MR. PALOMARES: Salvodore Palomares, manager of regulatory affairs at ICU Medical.

MR. DACEY: Robert Dacey, consumer representative from Boulder and Longmont, Colorado.

MR. ULATOWSKI: Tim Ulatowski, director of Division of Dental, Infection Control and General Hospital Devices, FDA.

DR. EDMISTON: Thank you very much.

Now at this time I'd like to invite Mr. Larry Kessler from the FDA to give us an update in postmarketing surveillance.

POST MARKET SURVEILLANCE

MR. KESSLER: Good morning. I want to thank Dr. Edmiston and Martha O'Lone for having me here. Let me tell you how this little presentation happened.

About two years ago Dr. Alper asked me, as the director of the Office of Surveillance and Biometrics in the Center for Devices and Radiological Health, to talk a little about postmarket surveillance in front of a meeting of the entire panel chairs in this very room. At the end of that meeting, the panel chairs asked that we give such presentations to all the panels, to give you our perspective on postmarket surveillance, because you will see postmarket surveillance issues from time to time, even in your premarket review.

I'm going to give you our perspective on how these relate to some of the work that we think you can play
a very important role in helping us with the FDA mission.

In the next 10 to 15 minutes I'll describe a few methods of device postmarket evaluation at the Center, present challenges in accomplishing postmarket evaluation, and describe the pivotal role that advisory panels can play in postmarket evaluation of medical products.

This schematic is a fairly brief overview of the way in which we generally perceive our overall role at FDA. From the left-hand side of the chart here--this is a time chart basically--design modification happened basically at industry and with the clinical community and patients telling industry what new products they need, what clinical needs need to be met.

FDA gets more and more involved as we travel from design modification through testing and clinical testing to review. On the right-hand side of the chart you'll see, under the postmarket evaluation part of this, at least five different mechanisms we have at our disposal to help evaluate and monitor products as they live and breathe on the market. We have the Medical Device Reporting Program and two postmarket surveillance authorities--Section 522 in the postapproval or PMA authority. I'll talk about these three in some detail.

I won't today, because of time, talk about our epidemiology program or the large field inspection force we have running out of ORA with our contacts through the Office of Compliance, but they are a very critical part of postmarket evaluation. I just won't get to talk about them
While we're doing review and after we do postmarket evaluation, the FDA should have constant contact with the clinical community to find out what's going on and to communicate our findings and problems, something we need to improve on. One of the ways in which we do contact the clinical community is our contact with advisory panels, and I'll say a little bit about how postmarket evaluation and advisory panel work should meet.

Well, why bother with any of this at all? Well, because there are a series of questions that we find often need to be asked in the postmarket period. First and most obvious is long-term safety. A number of products that reach the market do so on the basis of fairly modest or short-term studies. Rather than wait for long-term studies to prove complete safety or effectiveness, some products will make it to the market where we will not have complete long-term data.

This may be particularly true in terms of long-term implantables, where we would hesitate to wait, say, 10 years, which is what we might want to see for certain kinds of implantable performance, and we don't want to do clinical trials that last for 10 years, so we'll let something on the market based on a shorter period of time data and then look at it later.

Other important questions come up often in the postmarket period. For example, performance of device in community practice. Often you will see products for review
that are done in carefully designed clinical trials but products then move to community practice and we won't see the same effects and we will often see different patterns of adverse events that you will see in the premarket review.

Sometimes effects of changes in user setting are important in product evaluation. For example, a larger number of products than ever before are leaving the hospital doors and winding up in out-patient clinics and at the bedside at home. Some of those products need professional training to be used properly and we get adverse events on a daily basis that show serious injuries, illness and death from products that went from the hospital to home either without adequate training or labeling or other kinds of problems that can be sometimes avoided.

I'll talk for just a minute about the Medical Device Reporting Program because a number of people who know a bit about FDA and postmarket evaluation think MDR is where our postmarket evaluation begins and ends, and that's not the case at all but it is one of our most important programs.

Since 1984, manufacturers must by law report deaths and serious injuries as well as malfunctions or near incidents to FDA. Since 1990 with the Safe Medical Devices Act, all user facilities--every hospital, nursing home, ambulance, surgi-center--must report deaths to the FDA and serious injuries to manufacturers.

Unfortunately, the User Facility Reporting
Program in the country does not work nearly as well as it should. The number of reports we get per year from manufacturers is roughly in the 80,000 to 100,000 range and only 5 percent of those reports of our total MDR system come from user facilities.

Beginning about 1992 we were receiving over 100,000 reports of adverse events each year. Information should include device specifics--the event description, event date, patient characteristics--with which we could see if there's a potential problem that needs rectifying in the postmarket period. Unfortunately, reporting in the MDR program is often very limited--limited information. It sometimes provides critical signals to FDA but sometimes we miss things because the information is poor.

Part of this comes from the unfortunate litigious environment that we all practice in. Often we'll hear manufacturers around this room tell you the reason our data are limited is when they call a hospital after a hospital has told them that their device may be involved in a death or serious injury, the hospital will say, "That's all I can tell you. My lawyers tell me to give you no other information."

Part of this has to do with the vast number of reports which are associated with use error, and hospitals are nervous about reporting out of their facility problems where their users may not have read the instructions, may not have followed the instructions so carefully or chosen to use products in ways that the manufacturer did not
initially intend.

But we do get a lot of mileage out of the 100,000 reports we get per year and here are some examples of things that reflect adverse event reports and actions taken prompted by the MDR program, related to products that involve this panel.

For example, we get directed inspections of a manufacturer this year for blood leukocyte filters and hypotension and released a public health advisory related to leukocyte filtration.

We've done product recalls in the past few years. In fact, one explosion of an infusion pump puzzled one of our analysts. We had outstanding collaboration from our Office of Science and Technology staff, who looked into the problem with us, and eventually convinced the manufacturer to do massive, 15,000 pump recall and reserving.

In the recent past infusion pumps have presented a lot of problems with free flow and we put out patient notifications about this problem. This problem continues with a lot of pumps and we do all we can to try to minimize the problems that we see in free flow with infusion pumps, but it's a constant problem.

I want to talk for just a couple of minutes about these two authorities because this is where you as panel members can be most influential and helpful to the FDA.

Postmarket study authorities--there are two of them that we can invoke. One is postmarket surveillance Section 522 and the other is the Postapproval authority.
Section 522 was originally mandated in SMDA '90 and changed in FDAMA '97. And the changes were to reduce some of the scope of the original 522 act.

Postapproval refers to PMA products only and is also sometimes called condition of approval studies. Section 522 covers only Class II or III products whose failure may present a public health problem. The language in the statute is more specific but this is the basic essence of that language.

We see both authorities as a complement to the premarket role of the FDA and the role that you play.

The criteria that we use for postmarket surveillance study in the requirements for manufacturers are whether we can figure out what the critical public health question is, and it can result from for-cause situations, new or expanded conditions of use or other reasons. We have to consider whether other post-market strategies, such as the MDR program, give us enough information without requiring manufacturers to do additional study on their product in the postmarket period. And we have to consider practicality and feasibility of the conduct of studies.

We also try to figure out how will the data be used? And I'll come to that in just a minute.

Postmarket surveillance studies have a wide variety of approaches. Our early foray into postmarket, earlier in this decade, was heavily weighted toward studies at the bottom end of the more rigorous type--randomized
trials or case control studies. However, recent guidance that we've published this year on postmarket surveillance studies suggests that we will be expanding the kind of approach that we would require manufacturers to apply, including detailed review of complaint history or the literature or nonclinical testing of the device, to help us resolve potential postmarket problems.

But postmarket studies are challenging. First of all, the rapid evolution of technology makes studies obsolete. It is indeed wonderful that the medical device community revises their products on almost a weekly basis but it makes a postmarket study a particular challenge because by the time a study protocol is approved, fielded, data are collected and analyzed, it is often the case that the product is no longer marketed. So is it still relevant? It makes it a challenge.

Second, in truth, there's a lack of incentives for the industry. It is a rare situation where a postmarket study is going to give great good news to a company, so they're not excited about doing these, frankly.

There's also a lack of interest in the clinical community. Very few postmarket studies are sexy enough to be publishable, like the premarket stuff with the hot new technologies. So that presents a big challenge.

But by far we think the biggest challenge that we have faced, both in postapproval studies and in Section 522, is a lack of a clearly specified public health question. What are we going to do with the data once it
arrives? Are you going to suggest a relabeling? Are you going to suggest expanded or restricted indications for use? Would you consider advising us of a product recall?

If one of those actions doesn't occur to you and you're just interested in the question, then it probably isn't a good candidate for a postapproval or postmarket study. But if you can help us with a clearly specified public health question and what you think you might do with the answer to that question, it'll help us formulate the appropriate protocol and hold the manufacturer responsible to conduct that protocol and bring results here back to the panel, which we rarely have done.

So that's my challenge for you. When considering a postmarket study, whether postapproval or 522, and that's an issue that we can work out at FDA and you needn't be concerned with, please ensure that the question you're asking is of primary importance, help specify that question and note the clinical or regulatory relevance of answering the question. What will we do with the data? That'll help us formulate the question; it'll motivate the company; it'll motivate the clinical community to contribute data, answering the question; it'll help us address potentially important postmarket surveillance problems.

The 100,000 events that we get every year represent thousands of deaths and scores of thousands of serious injuries that occur because of medical devices sometimes being used improperly, being handled improperly or sometimes failing. Our job is to try and minimize that
and we hope you'll help us in that mission.

   Thank you very much. I'd be glad to take any questions.

   DR. EDMISTON: I think in the interest of time, we're going to move on. Thank you very much, Mr. Kessler.

   Our next presenter will be Mr. Charles Ho, who will give us a presentation on Y2K.

   Y2K INFORMATION

   MR. HO: Good morning. I'm Charles Ho. It is my honor to be here to talk before the General Hospital and Personal Use Devices Panel to discuss with you the year 2000 problem.

   Yes, medical devices are subject to the year 2000 problem. Susceptible devices can be found in the microprocessor or PC-controlled products, software applications, device interfaces to databases and recordkeeping systems and also in embedded chips for date display or recording.

   What is the year 2000 problem? It's the failure of a computer system to properly process a display face due to representing the year using only two digits or other date-related problems, such as failure to recognize the leap year. For example, list of confusion between the 2000 and 1900.

   An example of a year 2000 failure. A chemical in a clinical laboratory test has an expiration date in the year 2000. However, the testing device reads this date as in the year 1900 and did not allow the test to proceed,
since the testing device thought the chemical was out of date.

So how do we define the year 2000 compliance? For the purpose of a database, year 2000 compliant means, with respect to medical devices and scientific laboratory equipment, that the product accurately processes and stores date/time data, including but not limited to calculating, comparing, displaying, recording and sequencing operations involving date/time data during, from, into and between the 20th and 21st centuries and the years 1999 and 2000, including correct processing of leap year data.

So what is the FDA requesting of the panel? Please provide us with advice regarding problematic devices from the panel's domain of expertise. Please identify types of devices which because of their use of dates, could present risks to patients if not addressed. Please provide suggestions to CDRH regarding actions to reduce risks from year 2000 problems.

What has the FDA done regarding the year 2000 problem? Since 1996 we have made internal assessments of potential impact and vulnerable devices. In June 1997 we sent a notification letter to manufacturers to advise them of the problem. FDA will address the year 2000 problem in premarket reviews. New submissions are not required for repairs which are only date-related. Repairs/updates before impact will not be classified as recalls.

In addition, we are also participating in the Biomedical Equipment Working Group. This is a group of
federal users of devices and scientific equipment. The work group is chaired by the Department of Health and Human Services. We send a consolidated request for information in January 1998. We think that the public and the private health care organizations have the same information needs.

We established a website in the spring of 1998. We sent out a guidance on FDA expectations in June of 1998.

The address of the FDA product database can be found at www.fda.gov. Please select the year 2000 item.

The Biomedical Equipment Database. This is an FDA-operated World Wide Website. The data are provided voluntarily by the manufacturers. It is a certification by the manufacturers. The data are continually updated, searchable and downloadable.

What does the project database show us? Well, many companies have not yet reported. Presumably assessments are still in progress. Most noncompliant products involve date display or date recordings. They usually record date-stamping.

A limited number of products have significant operational problems, such as the problem of the expiration date that I talked to you about. PC-based problems and PC-type problems, such as recording and date-stamping.

Manufacturers are providing a number of solutions, such as software upgrade, patches or complete replacements.

Major additional letters to manufacturers. In January 21, 1998 we sent out a letter on the year 2000
impact on biomedical equipment. This was followed by the June 29 and September 2, 1998 letters. Then September 21, 1998 we sent a letter on manufacturing process concerns. May 26, 1999 we sent a guidance on MDR reporting. June 18, 1999 we sent out a year 2000 readiness survey.

Major additional communications to health facilities and consumers. December 29, 1998 we sent a letter on computer date problems on medical devices on January 1, 1999. This is about the rollover from 1998 to 1999. May 26, 1999 we sent a guidance on MDR reporting. And most recently, on July 16, 1999 we sent out a Y2K planning.

The future CDRH/FDA activities. We have already established a Biomedical Equipment Clearinghouse. We are expanding the database to include complaint as well as noncompliant devices. We are continuing to do outreach communications with industry, clinicians and consumers. We are pursuing rigorous action on products which present significant risk. We increased inspectional emphasis on Y2K.

Health care facilities. We recommend that health care facilities do the following. Inventory and assess devices used; obtain information on device status; test devices for Y2K compliance; check interconnected or networked devices; check device information system connections; plan for or develop workarounds, upgrades or replacements; and finally, develop contingency plans.

If you have any comment, please give your
comments to the panel executive secretary or to Dr. Tom Shope at the address listed. You can also send comments to him via e-mail at Tbs@cdrh.fda.gov.

DR. EDMISTON: Thank you very much, Mr. Ho.

At this time we'll move into the main presentations but before we do that from the FDA I'd like to make a statement.

The charges of this panel today are twofold. This morning we're going to discuss guidance for review of needleless systems and this afternoon we're going to discuss and make recommendations to the FDA for guidance in the development of jet injectors. That will be the focus of today's presentations. We will try to keep on task and try and keep on time. These are two extremely important areas that need to be discussed.

I also want to point out again that anyone who comes to the podium, please speak directly into the microphone. Identify yourself and your affiliation.

For those members in the audience, representatives from industry and from private organizations, we would like you to state not only your name and affiliation but we wish you would also state what, if any, financial interest you may have in the medical device industries.

At this time I would like to ask Mr. Tim Ulatowski, the division director for Dental, Infection Control and General Hospital and Personal Use Devices, to provide an overview of this morning's topic.
MR. ULATOWSKI: Thank you, Mr. Chairman, and welcome to the panel. Thank you for taking the time out of your busy schedules to come in and have this discussion with us today about these important devices.

There's somewhat of a misnomer in the agenda this morning. We're discussing protected sharps devices, not needleless systems per se.

But at any rate, today's discussion is a somewhat different panel session for a panel session. Usually we discuss premarket submissions, premarket approval applications, investigational applications in closed session or sometimes premarket notifications, so-called 510(k)s. But today we're having a discussion about guidance documents, either current ones or future ones, and there will be no voting today, as there usually is when we talk about a premarket submission.

We are talking about different devices from the morning to the afternoon, somewhat different--protected sharps devices in the morning and jet injectors in the afternoon. Certainly they're somewhat different but they're related in terms of the problems they're trying to address.

In the morning session we are revisiting our 1996 guidance on protected sharps and what we intend to do is to update the guidance based upon your comments and post it
under our new good guidance practice procedure, which came into effect a couple of years ago.

Now we're not here to discuss worker safety policy or current events that are driving an interest in protected sharps per se. That's certainly an important issue. We're here to talk about a guidance document and how to update that guidance document to the benefit of the agency.

This guidance we're talking about does not address some devices that fall under the aspect of worker protection, sharps containers and some other devices. We are talking about primarily protected syringe devices, but there are many other devices that come under the purview of our guidance that we'll be discussing today.

As I was considering having this as a discussion item, I think one of my concerns, my critical concerns was as we move forward with clearing products, as FDA moves forward and people are relying upon our clearances across the country, we want to make our evaluations of these devices certainly up to date and pertinent, relevant to what's going on today in terms of what people think we ought to be doing in terms of product evaluations.

I think some people out there think we get products and we're fidgeting with them and testing them on ourselves, trying to stick ourselves and what-not. We don't really do that. We do get samples and we do fiddle with them, as we are engineers and nurses and what-not and physicians, and we love to fiddle with things, but
primarily our focus is upon the documentation contained in the documents and the testing that's done by the manufacturers or the people they bring in to evaluate the products or to whom they send products for evaluation.

I'm primarily concerned about the clinical survey aspect in our guidance document as we discuss things this morning. I know that there's various organizations and institutions who have their own surveys for their purchasing purposes or whatever, and each has its own scheme of questions and answers and approaches and how many products are tested and what controls are run.

I think there's a place for everyone doing their own thing to a certain extent but as far as FDA's purposes, I want to try and reconcile some of those differences in approaches and see where we need to be doing perhaps a more comprehensive job in some cases and where we can leave some other evaluations as people feel it's necessary in their own institutions.

So that's my reflections today and Irene Naveau is going to bring us up to date in a little more detail on the guidance document.

DR. EDMISTON: While we're waiting let me ask Mr. Ulatowski one question. Do you prefer that in the course of this morning that when we refer to these systems we refer to them as protected sharps systems? Would you prefer that?

MR. ULATOWSKI: I think that's more generally the scope. There are some needleless or blunted needle-type
systems but more generally it's protected sharps.

DR. EDMISTON: Fine. Thank you.

MS. NAVEAU: Good morning. The guidance document under discussion this morning is entitled Supplementary Guidance on the Content of Premarket Notification Submissions for Medical Devices with Sharps Injury Prevention Features. The document is intended to assist manufacturers, distributors or importers in preparing 510(k) submissions for medical devices or accessories with sharps injury prevention features, as well as to facilitate the 510(k) review in a consistent manner.

I plan to include in my discussion today a brief background of the existing guidance document, as well as a review of working definitions of those types of medical devices to which this guidance document pertains. The desirable performance characteristics of these devices will be identified. Elements of the guidance document will be addressed and then a brief summary.

Finally, I'd like to present a list of questions that were previously submitted to the panel to review for subsequent discussion and recommendation.

The earliest medical device with a sharps injury prevention feature was reviewed in 1984 as an accessory to an IV administration set. In 1985 a shielded syringe was reviewed.

Since that time, the General Hospital Devices Branch has reviewed over 225 sharps injury devices with safety protective features, with the largest number of

It should be noted here that other divisions in the Office of Device Evaluation also review various medical devices with safety features. Therefore a comprehensive list of these devices is not currently available.

In 1994 a supplementary guidance document, the precursor of the guidance for review today, was presented to panel. At the conclusion of that particular panel meeting, we acknowledged the comments and recommendations of the panel, as well as the public, specific to the performance data section and sample size recommendations for studies being conducted. The revised draft supplement guidance in effect today has been used by the agency and industry since March 1995.

The guidance document is used in our review for various types of safety devices and include the blunt or blunted needles of stainless steel or a plastic material, the prepierced septum devices of various configurations, reflux valves, which are sometimes referred to as bidirectional valves, vial adapters, those devices that provide needleless access to a drug vial for reconstituting and withdrawing medication, retractable needles, shields and guards associated with syringes, and recessed needles.

These devices are integral components of an existing device or may be marketed alone. For example, a reflux valve can be marketed alone for use as a heparin lock type of device used in conjunction with an IV catheter, an IV administration set or a syringe.
What are we talking about when we refer to devices with safety features? There are any number of definitions for devices with safety features but for our purposes today I'd like to read two working definitions of these devices.

A medical device with a sharps injury prevention feature is a device designed with a component or attachment, either active or passive, that protects the user from a sharps injury.

Sharps injury prevention features are found in devices such as but not limited to piston syringes, hypodermic single lumen needles, IV administration sets, intravascular catheters, vacuum tube holders, as well as blood collection devices.

These features can be a component of a finished device, such as a sheathed or shielded syringe, while some safety feature products are marketed separately as accessories that are attached to devices by the user at the time of use.

For regulatory purposes, accessories to a device are classified in the same class as the devices to which they are assembled.

The second definition: a needleless system is one that provides repeated access to a patient's vascular system without the use of sharps. Fluid flow through the system may be unidirectional or bidirectional, with the latter allowing the user to administer or withdraw fluids or medications.
An example would be a prepierced septum and blunt canula. With this type of septum, a blunt canula connected to a syringe or secondary IV administration set can be inserted into the prepierced septum on a Y site of an IV administration set, an adaptor or other secondary IV or extension set.

Another example is a valve connector, sometimes referred to as a reflux valve. It prevents fluid flow through the device in either direction when not activated. However, when a male or mating lower connector is inserted into the prepierced septum at the end of the valve's housing, the valve is activated in various ways, depending on the valve configuration. This activation opens the fluid flow pathway for the infusion of IV solutions or medications and for the withdrawal of blood samples.

In the next two slides I've listed a number of desirable performance characteristics that we believe should be considered by industry in conducting their simulated clinical and actual clinical studies in the evaluation of safety devices. Evaluation of these characteristics may require actual use of the device and by targeting questions to health care workers who may or may not have had any experience with the device.

These characteristics can usually be assessed with visual inspection of the device or by simple manipulation of the mechanism and should include: hospital personnel are shielded from the needle before, during and after disposal. The protective mechanism can be used
equally well, regardless of hand preference or for hand size, for that matter. If additional steps to the usual procedure are necessary to activate the protective mechanism, they would be few. And they do not interfere with the usual nonprotected procedure.

It is not necessary for the user to place either hand near the needle during a procedure and the hands should remain behind the needle at all times.

In addition, the protective shield or retracted needle reliably locks securely into place with little effort. The protective mechanism is designed in such a way that the user is always aware of its status; that is, whether or not the device is engaged or locked into place.

The design of the protective mechanism allows appropriate visualization during device use. The user is not exposed to the needle during disassembly and the mechanism is compatible with the sharps disposal system used in the facility.

In September 1998 OSHA published a request for comments from a number of health care organizations related to occupational exposure to blood-borne pathogens due to percutaneous injury. The FDA responded by submitting the preceding list of desirable performance characteristics that are found in the guidance document.

Five similar performance characteristics were listed in OSHA's recent executive summary as suggestions from researchers for selecting safer medical devices. However, it has not yet been determined how OSHA will
incorporate these suggestions in their revised standard.

This may be an opportunity for FDA to meet with OSHA and consolidate recommendations regarding the characteristics of devices with injury prevention features.

The performance characteristics on the previous two slides are listed in this table. They were compared with those characteristics outlined in the evaluation forms the three other organizations use; that is, the Service Employees International Union, the SEIU, from their guide In Preventing Needle Stick Injuries in 1998; the New York State Department of Health, the NYSDOH, from their study of needle stick prevention devices in March of 1992; and the Training for the Development of Innovative Control Technologies, the TDICT, from their Safety Feature Evaluation Form found on their website.

The results of this comparison indicate that similar evaluations are being used by these organizations and in most cases concur with our characteristics. For instance, we all agree that the user should be protected from needle stick injury before, during and after use, that the safety feature may be activated with either hand, and the user be able to visualize the fluid and the fluid level during preparation and use.

We have included a statement indicating that the device with safety features should be compatible with the sharps disposal system in the facility. The statement may be included in their evaluations, but it was not evident in the material that I had access to.
The guidance document does not include a list of targeted questions, as do these organizations, but it does contain recommendations to industry regarding their report forms that would include this information.

Apart from the section that addresses appropriate device description and labeling, much of the guidance is directed to device specification and performance test specific to sharps injury prevention. What it does not address are sharps containers which are addressed in their own guidance document and needle recappers.

In essence, the guidance provides overview information to applicants to aid in the analysis of performance characteristics of these devices and contains recommended types of tests that can be performed. Again only recommendations are suggested to industry. Therefore the document does contain a checklist or a to-do list for manufacturers to follow.

In this document we refer to five main types of performance testing for devices with sharps injury prevention features. Those include bench testing, biocompatibility data, preclinical, simulated clinical and actual clinical studies.

The guidance also contains factors that should be considered before conducting a simulated clinical or actual clinical study; for example, how a device is equivalent to other similar devices, and microbiological issues.

Typically, needleless systems present a contamination concern addressed with simulated testing in a
microbial challenge test, whereas the sharps devices present a needle stick concern addressed with simulated clinical and actual clinical study data.

In summary, we have established that the 1994 revised draft guidance document has served as a working document for FDA reviewers and industry alike for the past five years. The document includes recommendations to industry, especially related to design features and performance characteristics that should be included in their studies prior to 510(k) submission.

Several types of surveys are in progress by industry during their preparation in introducing their safety devices into the marketplace and by organizations dedicated to the protection of health care workers and others that use devices with protective features.

In light of public health issues that have arisen and emerging new technology, we are revisiting our document. We recognize that it may need revision for the following reasons: for consistency in our reviews and to assist the manufacturer in assembling scientific information, especially microbiological and performance data to determine substantial equivalence. There may be other areas in the guidance, as well, which you may offer your suggestions for change.

I'd like to read now the following questions that were previously submitted to the panel. I understand that the questions will then be considered separately for discussion and recommendation.
Number one, "Our current guidance document allows sponsors to perform either a simulated clinical use study or an actual clinical use study to evaluate the performance of the sharps injury prevention feature. In most cases, sponsors have provided information from simulated clinical studies. When would it be appropriate for FDA to consider data from actual clinical use versus simulated clinical use?

"Are there minimum criteria in terms of sample size, independence of the evaluators and number of sites that FDA could consider for both the simulated clinical and actual clinical use studies?

"In addition to the survey format, are there any other methods that the FDA should consider when evaluating the performance of these types of devices?

"Are the evaluation criteria listed in the guidance document appropriate and inclusive?

"How could the results of these evaluations be presented to users? Should the results be included in the labeling?"

And two, "Currently sponsors submitting applications for needleless access devices are asked to demonstrate that their device is substantially equivalent by providing nonclinical bench data to demonstrate that their device does not increase the risk of microbial contamination of the fluid pathway, validation of the cleaning method, and instructions for use. What additional types of information should be considered for our premarket
review?"

Three, "What mechanism does the panel recommend to the FDA to increase user awareness of the safe use of these devices?"

And four, "Is there a need for educational programs for the use of sharps injury prevention devices? If so, what content should be included in the educational programs to encourage the safe and effective use of these devices?"

And five, "Are there other areas of the guidance document that should be revised?" Thank you.

DR. EDMISTON: Thank you very much. Do the members of the panel have any questions for Ms. Naveau?

[No response.]

DR. EDMISTON: That being the case, I'd like to invite to the podium Dr. Joseph, director of the Office of Health and Industries Program at the FDA.

DR. JOSEPH: I'll say good morning while we get ready and we appreciate your being here and thanks to the division for including us today.

As was stated, I'm Dr. Joseph, the director of the Office of Health and Industry Program in the Center. The office has several activities in which we engage on behalf of the Center, one of which is outreach and educational activities.

What I'm going to talk about today is a little bit about to put our educational activities in a context.
I think it's really important to briefly review what our mandate is in terms of the FDA mandate relative to devices. And because there are other sister agencies who also, as Irene said, have an interest in this area, I thought we'd briefly take a little snapshot of what OSHA's mandate is and see how we can blend our activities and then get your advice on that.

Okay. The mandate of the FDA in terms of medical devices is to really focus on our regulatory activities on the product features and product aspects, and that's again to ensure the safety and effectiveness of those devices. So we pretty much look at the labeling requirements, the performance test methodology, good manufacturing practices and quality systems.

Whereas the Occupational Safety and Health Administration has a deep interest in sharps injury prevention devices, as well, and from their mandate you can see that they're tasked with ensuring that workplace conditions are safe and healthful for employees, and they do this by enforcing their standards developed under their act, as well as collaborating with the states to ensure that those conditions are met and providing research, information, education, training in occupational safety and health.

And as Irene said, recently OSHA issued their request for information and comments on a number of items to reassess their blood-borne pathogen standard. They asked specifically for information on 16 items. I've just
listed three here, which has sort of some interesting possible overlap with where our interests are, and that's in training and education in the safe use of medical devices and any effect on reducing injury rates and the impact on the delivery of patient care.

But we've, as I said, we do have a role and there are things we can do. Irene mentioned we cleared in excess of 200 devices with some sharps injury prevention features. We have cosponsored several meetings with CDC, OSHA, NIOSH, NIH and the most recent one was last August relative to the prevention of transmission of blood-borne pathogens.

We have issued three safety alerts or notices, all of which went to the health care community, two of which pertained to recommendations on the safe use of safety prevention technology relative to administration sets, and most recently, the one we issued in February of this year, on capillary tubes. I think that was probably the first alert that we issued that was jointly sponsored by OSHA, NIOSH and ourselves.

We've also issued eight guidance documents on injury prevention aspects, of which three were directly related to sharps prevention devices, the primary one being the one that you'll be discussing the morning; the other two are supplementary to it.

Irene mentioned we responded to the OSHA request for information by providing them with the human factors desirable performance characteristics that we look for and feel would assist and go a long way in preventing any
injuries.

And I failed to mention under the safety alerts that we also are currently developing a new notification on use of devices with sharps injury protection features and we're just now trying to determine the direction or if those will be interval notices.

But we've also been planning an educational teleconference with several federal agencies on sharps injury prevention activities and devices. We've been communicating with OSHA in trying to determine if they're willing to take the lead in this venture and we certainly are willing to collaborate with them on that.

And as Irene read to you, there are three questions that we would appreciate response from you as guidance for the future, since the office has been tasked with doing some additional educational or outreach activities and before moving too much further along, we thought it would be helpful if we could get your guidance on the mechanism that the panel could recommend for us to increase user awareness of the safe use of devices.

If indeed there is a need for educational programs for use of sharps injury prevention devices, should you respond in the affirmative to that, then what should the content be included in those programs that would encourage the safe and effective use of those devices?

And in the interest of being very brief, that's all I'll say this morning. And I look forward to whatever information or guidance you can provide us. Thank you.
DR. EDMISTON: Thank you very much.

Are there any questions from the panel members for Dr. Joseph?

[No response.]

PRESENTATIONS BY USERS OF PROTECTED SHARPS SYSTEMS

DR. EDMISTON: That being the case, we're going to move on to our presenters, the users of protective sharps systems.

Before I do that, I'd like to reiterate again when you come to the podium, please speak clearly into the microphone. Also it's very important for you to identify the organization you're part of. We need to know what, if any, financial interest you may have in the medical device community.

And I should also emphasize that we're trying to run a tight schedule today because we're going to have some significant discussion regarding this particular guidance documentation. I want to encourage our next presenters to limit their comments to 15 minutes.

The first person I'd like to call to the podium at this time is Dr. June Fisher, who's a clinical associate professor of medicine at the University of California and is director of training and development for innovative controls and technology. Dr. Fisher.

DR. FISHER: I would like to make the comment that I am thankful for the invitation to speak here today and that I really am very excited to see that the FDA is addressing the issue of health car worker health and
safety.

I know there's a mythology out in the general community that there's an oppositional thing between patient safety and health care worker safety and I know that in institutions these are weighed. I think that this has been proven repeatedly that this is an erroneous approach to patient care.

As a clinician, that is my primary concern but I do know that the health care worker who has a safe environment can provide much better care. The most obvious example is if you think about in terms of back injuries. I do not want to be lifted in a hospital but if I had to be there, by somebody who has had a back injury and is not supplied with the appropriate devices to lift people.

I think that this certainly goes for the needle stick area and I really welcome this kind of--the FDA is vigorously approaching the issue of health care worker safety in their desire to improve patient safety.

I am not going to talk specifically about needleless systems. It'll be a little bit more of an overview, which will be consistent with some of the presentations that went a little earlier.

[Pause.]

I have a lectureship in engineering but I must say that I'm totally baffled when we have anything like this. I think it's every speaker's nightmare to not have your slides available. Since your time is a little pressed, I will try to speak a little extemporaneously and
then hopefully the slides will be projected.

The Training for Development of Innovative Control Technology is a program that was started in 1989 and has been funded for almost 10 years by the National Institute of Occupational Safety and Health and it's a program that brings together product designers, industrial hygienists and users. And most of my discussion will be really based on user-driven technology.

You're going to have to bear with me. They were organized.

This is our logo for our slide. I hope I'll have a few more minutes.

DR. EDMISTON: Of course you will.

DR. FISHER: As all presentations that I do around this topic, I always use this dedication slide. This is a group of health care workers who--the first group are still alive and the bottom group are people who have died from occupational exposure to blood.

I have to make the point that these are all in one city. And when I do speak around the country, I hear from many people that probably the same numbers do exist, so that as important as the CDC numbers have been, most of us feel that these numbers are very, very limited. And I don't have time to discuss that, so we have to remember that there is a real human face and there are serious outcomes for this.

I was asked to talk a little bit by people earlier today so I put this slide in. Coming from
California, we have a particular circumstance that we now have legislation mandating the use of safer devices, which will change the whole direction in California and will have impact or already has had impact nationally.

We have the blood-borne pathogen standard, which is OSHA. We have a Cal/OSHA standard now, which is working under an emergency order, which mandates the use of engineering controls. If this is not passed by the board, the emergency standard will continue so that this will be in effect regardless of what--in California we have a political board. The assumption is that they will pass this.

There's legislation in Tennessee, Maryland and I think in 20 other states--somebody may speak for that--and there's federal legislation pending on it. So we have, although we don't want to deal with the political issues, we do have a political driving force.

As I said, our project is a project that brings together the industrial hygienists, product designers and health care workers. And, as far as I know, this is unique for any area in health care. And I would certainly recommend that this kind of collaboration exist for many areas in device development.

I do know, as an aside, because I have a lectureship in engineering, I have 48 product designers usually a year running around the hospital and there are major, major issues that need to be addressed, not just in these devices, that could be improved by bringing together
the user and the product designers.

Why bring the health care workers to it? This is from a modification of Warren Estrine from HEMAS because they have a familiarity with new existing devices, the knowledge of the medical device procedure and protocol and an understanding of the environment in which the devices will be used and intimacy with the concerns of the actual user and an advocacy that goes on.

The manufacturers do try to have this but in my only experience with them, they really don't fully understand the line user. I suppose the best example is when I was a resident at Stanford. The hospital was built by talking to the chiefs of medicine. The building didn't work, and it was the first instance we made it very clear that you have to go to the person who's doing the job.

Our project involves a large group of institutions and this is an old slide and it can be expanded now because we have national involvement with both dental areas and with some of the other hospitals in the country.

This slide, and it's upside down and it's supposed to go later--it's showing you when we do simulation studies. I think we'll have to forego that.

Our methods developed our review of data on needle stick injuries, an appraisal of the health care workers who are doing the observational studies, failure analysis of devices. And I really want to emphasize that that is very important, to do failure analysis and
simulation studies with the devices and joint brainstorming sessions and multi-center health care worker testing.

One of our first things we did was to provide a tool for health care workers to assess devices and you got some of that when the chart was presented before. If there's a consistency with the SEIU it's because they adapted their devices from ours, so I wouldn't say that independently this occurred.

And we have now 14 devices where we have the tools--I don't know if I can focus this any better--and you can get these tools on our web page, which give guidance to the health care worker in evaluating the device. And I chose the one for needleless systems for IV connectors today.

The interesting thing about these devices, I'm not going to go over the specifics within 15 minutes but we can provide you with those, all of them. I don't know Martha, if you were able to get that off the web. We could provide that for the committee. I have a copy here.

These were the first written criteria for now 14 types of safety devices. They provided a means for involving health care workers and most of these have been validated in multiple institutions. This is an old slide. The 14 are now in the 1999 AHA document.

And while they were originally used for a tool for health care worker evaluation and selection, it became the industry benchmarks. So it is very important to
develop these criteria that are user-based because it does drive the industry.

That was the surprise to us, a picture showing--this is when our team was living down in the emergency room. Here is a product designer actually who is now trying to do laboratory failure analysis of the device. This is a picture--actually the woman in white is a product designer, industrial hygienist and nurse who is guiding another nurse in testing of the devices, using the criteria sheets.

One of the things that we did is also we do design evaluation courses for nurses. When you're talking about education, this is one of the things that actually we want to include. We're hoping now to be able to develop a program with the American Nurses Association where we will hope to develop 400 master trainers around the country so that we could emphasize the training.

Training is essential. When the question was asked for health care workers, you cannot just coldly go in. This is one of the slides for our course. We're not expecting the nurses to be product designers but we were trying to help them develop a language so they could talk to product designers and manufacturers in a constructive way.

The importance of it is that out of this course, not only did they learn something but we learned a lot. And what we got out of that course was a user-based performance standard for design evaluation selection of
medical devices.

And a performance standard is different than benchmarks and it should not stifle innovation. We were very aware that the manufacturers have to have that kind of freedom where they can develop new devices.

We are still in the early stages of development. It should be user patient-based. You give a framework for evaluation. And we need a national task force to develop consensus on performance standards and this is one of the things that I was talking about with Tim for a long time, that if the FDA could take the lead in promoting this kind of census, it may not be something that you can do yourself but if you develop that national consensus, that will be furthering things.

And performance standards versus criteria performance are generalized. It's procedure-based and encompasses the product life cycle versus the point of use only. Before, I was talking about the specific criteria.

It's a rather extensive document. We can also give you copies of that that can be made, but these are the areas that they cover. Obviously patient care and quality care came first. User safety, user fit and satisfaction, we felt, came before patient fit and satisfaction. And product life cycle, which we're talking about sharps boxes, administrator's fit and satisfaction.

One of the other things that came out of there was the issue of scenarios, which you call simulation and we're calling them scenarios. It's the ability of the
actual user to test-drive new products and it approximates real-life situations and it draws attention to unforeseen difficulties. It's a very systematic way of doing that.

These are the variables that we identified and that impacted on the use. Some of them may sound silly to you. Why lighting? Well, that's labeling and packaging. Noise? Why noise, people ask us, because a lot of the engagement of the devices depends on sound. And crowding, condition of hands, visibility. Some of these, I think, are included in your document, also. So we feel these are the variables to be considered for the sharps devices.

And here is the way we rank them. You choose what is applicable to your clinical situation and then develop the device. This chart shows how you put them all together.

And, as an aside, I just have to say we tested that at UCSF and I think the system works because a door was open in the room when we were doing the simulation and one of the nurses was acting as a patient who was having some difficulties and the intern ran in and said, "Can I help you?" So I knew that we had a good scenario. We just closed the door.

What came out of that is that we needed a user-based design and that users should be involved from the very beginning of need-finding and they should be involved throughout the whole process. Rarely are they. This is really the process that goes on. If you don't believe me you don't have to, but we've gone to manufacturers who've
all told us this is, in reality, what happens. And we would push that the user be involved from the beginning.

One of the other things I just want to put in, what we really are aiming for is to have the PEST. That is passive, easy, simple and throughout. That's the summary of what we think is desirable in a device.

I would like to go over briefly the overheads. I have to apologize for the overheads because they're handwritten. There was a power failure as I was trying to use my computer and I couldn't wait any longer because I had a plane waiting for me. As a physician, my handwriting is not very good but I think you can read that.

These are the recommendations for FDA, to participate in the promotion of primary prevention of occupational exposure to blood. I know that there's a lot of emphasis and there should be and people do get stuck but I think we have to think about primary prevention so we don't even have to think about post-exposure treatment.

The first thing, some of these are very specific and some are more general. One is labeling of all sharps devices. At present, the only sharps devices that are labeled are those that have the safety feature. We believe that the ones with nonsafety features need to be labeled, also, and they clearly need to be labeled.

There are going to be instances where you have to use a standard sharp device but you should be very aware that it is a standard sharp device, so we think that they should all be labeled. They should not be treated
differently.

I think it's interesting that previous speakers from FDA brought this up, to actively solicit device failure inadequacy from end users. I think you may have to redefine things. I don't want to think about death or serious injury. I think any needle stick, and we have probably 900,000, should be analyzed and FDA should be having their handle on. I'm not asking you to look at all 900,000 but that there should be more awareness of what's going on there.

There should be promotion of criteria for systematic pilot-testing of market-available devices. I didn't talk about that because of the time but what I presented before, we consider are just screening tests. That pilot testing systematically is a very urgent issue. And from my experience, both in my institutions that I've been in and now I've been in many institutions talking around the country, pilot testing is--at best I could call it a joke.

Generally you give the device to people and you come back two months later and ask them, "Did you like it or you didn't like it?" That is not pilot testing. There needs to be a very systematic approach to doing it and to actively collecting the data.

And I think if there were criteria for this that you would be getting better pilot testing and actively collect failure inadequacy data obtained from pilot test. If you had good pilot tests, that would really give you
postmarket data that is really not available now. So we're recommending that there really be an emphasis on the pilot testing.

And there should be expanded requirements for simulation testing. From what I can gather, the simulation testing is left to the manufacturer to define what they are and I think that that causes a great deal of variability. There should be standards. I'm not saying that you specifically say you have to do this and this and this, but put the benchmarks out there, the standards for the variables to be included in that testing.

And to require, before you even do the testing, a user-based work task analysis. Define what variables you want in that test. If you're going to go in the emergency room and you're going to use some standards that you devised for the out-patient department, that doesn't give you much detail. Or if you just bring a group of people together that doesn't represent the spectrum of work and say, "Well, try this," and sit in the room, which has no clinical bearing at all, so I think that you should have user-based work task analyses and require testing for failure.

That sounds very strange but in our own experience if you just go to a naive health care worker, they know what their problems are but they don't know how to look at it. They're so grateful that you have a new device that they say, "Oh, it's fine." And you look at them and you say, "That is fine?" So they have to
understand how to go to failure, to do all those mistakes.

Our trained users will throw things on the floor, will do bad practice because they know that's what they have to look at, because that's what you're going to get in reality. And to require the inclusion of trained users in the testing process. This is why we're excited about our collaboration with the ANA, to train these kinds of resources around the country, but I think that should be required by the FDA in your simulation testing, that you've had some trained users who can foresee.

And my last slide is that our performance standards and our criteria and some discussion scenarios are all available on our website, which is here. Thank you for allowing me to speak. I think I've covered the 15 minutes.

DR. EDMISTON: You're right on time, believe it or not. You're right on time.

Are there any questions from the panel for Dr. Fisher?

[No response.]

DR. EDMISTON: Dr. Fisher, I have one question. When you use the word "pilot," are you referring to bench testing or to simulated clinical testing?

DR. FISHER: No, I'm actually--thank you for asking that. I think they should be bench-tested. I think there should be evaluation before you even do a simulation, at least for the evaluation. For the manufacturers, they should then go to simulation.
And then the pilot testing is actually postmarket pilot testing by the institutions. And I think most places say they do that. They're going to decide if they're going to buy a device or not and they bring it on the unit and look at it.

DR. EDMISTON: So you're defining pilot testing really as product evaluation within the institution.

DR. FISHER: Yes. And I think that that's a very valuable area that FDA could use for a postmarket details without having to wait for the death, which may come a year later. So I think that that data could be extremely valuable.

DR. EDMISTON: Well, thank you very much.

Our next presenter is Ms. Toni Hughes, a perioperative nurse who is representing the Association of Operating Room Nurses.

MS. HUGHES: Good morning. Thank you for the opportunity to submit a statement on behalf of AORN to this Federal Drug Administration advisory panel.

My name is Toni Hughes. I'm a registered nurse with a bachelors of science degree in nursing and a certification in operating room nursing. I'm a perioperative nurse at Anne Arundel Medical Center in Annapolis, Maryland. I have been a perioperative nurse for 19 years and a surgical department manager for the past two, a member of AORN since 1981. I was the chair of the AORN National Practices Committee from 1998 to 1999 and am an active member of the Maryland Nurses Association and the
American Nurses Association.

Organized in 1949 with a current membership of 43,000, AORN, the Association of Perioperative Nurses, is the professional organization of perioperative registered nurses, whose mission is to promote quality patient care for providing its members with education, standards, services and representation.

AORN supports the development and use of products, such as safe needle devices, to prevent unnecessary exposures of perioperative personnel to hazardous blood-borne infections. Perioperative nurses are acutely aware of the potential dangers associated with use of needles and other sharps in caring for perioperative patients. Although only 13 percent of the sharp injuries in the operating room are due to hollow bore needles, needle stick injuries are even more significant risks than the preoperative and postoperative patient care arenas.

Eighty percent of all blood-borne exposures are the result of needle stick injuries. One study has found that a needle stick injury prevention strategy eliminating 100 percent of needle sticks and not costing more than 36 percent of the cost of needle devices would not increase overall costs.

As participants in product evaluation and purchasing teams, perioperative nurses recognize the complex challenges encountered when trying to identify the most effective and affordable products available.

As health care employers begin to acknowledge the
hazards and risks associated with direct delivery of health care services and begin to seek safe needle devices for workers, manufacturing standards should be established to ensure that truly safe and effective devices are available in the marketplace. The FDA's role in supporting the development and manufacturing of high quality, safe, affordable and effective devices is critical to achieving a truly safe working evidence. AORN supports the FDA's efforts in collaboration with manufacturers and users to build a safer health care working environment.

DR. EDMISTON: Thank you very much.

Does the panel have any questions for Ms. Hughes?

[No response.]

DR. EDMISTON: In that case, thank you very much.

Our next presenter will be Ms. Mary Alexander, who is the past president of the Intravenous Nurses Society.

MS. ALEXANDER: Good morning. I'd also like to thank the panel for allowing INS to make a statement.

My name is Mary Alexander. I'm the chief executive officer of the other INS, with the Intravenous Nurses Society. We're a national nonprofit member organization that was founded in 1973. INS is the largest organization for the IV specialty and exists to promote excellence in intravenous nursing through standards of practice, education, public awareness and research. The organization's ultimate goal is to ensure that patients receive safe, high quality, cost-effective nursing care.
The Intravenous Nurses Certification Corporation is also affiliated with INS. However, it is a separate corporation established in 1983 to ensure the clinical competency of intravenous nurses. INCC achieves this goal by administering certification exam and recertification programs.

A registered nurse who passes the certification exam and meets the experience criterion receives the certified registered nurse intravenous credential. This credential is maintained by continuing to practice the IV specialty and completing continuing education requirements or retaking the exam.

INCC exists to benefit and protect the public through assessment, validation and documentation of the clinical eligibility and continued competency of nurses delivering intravenous therapy in all practice settings.

INS understands the inherent dangers involved in administering IV therapy. Vascular access devices, needles and sharps are fundamental to the practice of IV therapy. INS members are the frontline health care workers who provide IV therapy to patients in a variety of practice settings, which are now extending beyond the acute care setting and including but not limited to the home, physicians' offices, skilled nursing facilities, subacute facilities and ambulatory infusion centers. As well as our members, more practitioners are involved and their competency and skill levels differ widely.

INS supports engineering and work practice
controls that eliminate or minimize exposure of the health care worker to blood-borne pathogens. In 1997 INS wrote a position paper on safety products which appeared in the Journal of Intravenous Nursing.

INS supports research and development activities on IV products and medical products and devices to improve patient care and protect the health care worker, education and compliance with commonly accepted principles of infection control and basic practices, choice of products based on engineering design that accomplishes the prevention of transmission of blood-borne pathogens and improvement in patient outcomes, safety and risk management based on professional responsibility and clinical standards of practice, and blood collection design characteristics which result in effective safety device, which include the elimination of the need for the clinician's hands to be placed in front of a sharp needle tip, integration onto the device's design and not an accessory, activation before disassembly in that it remains in effect after disposal, and simplicity in utilization, preferably a passive system.

Requiring all health care facilities to use needleless systems and sharps with engineered protections, such as retractable needles, and instituting training and education in the use of safer medical devices provides an effective means of preventing percutaneous exposure incidents and reducing the needle stick injuries each year.

INS contends the best way to reduce the risk of accidental needle sticks to health care workers is through
ongoing education, training and competency testing, use of vascular access devices that minimize the risk of needle stick injuries, in compliance with OSHA's blood-borne pathogen standards.

Frontline health care workers should not have to risk their lives while saving the lives of their patients. INS applauds and supports your efforts to positively impact health care worker safety. Thank you.

DR. EDMISTON: Thank you, Ms. Alexander.

Are there any questions from the panel members?

[No response.]

DR. EDMISTON: Thank you.

Our final presenter will be Susan Wilburn, the president of the American Nurses Association, who will address the panel.

MS. WILBURN: Good morning. Thank you very much. It's a pleasure to be with you here today and thank you for taking a look at this issue that is of critical importance to the American Nurses Association and the two and a half million registered nurses around the country that we represent.

My name is Susan Wilburn and I'm the senior specialist for occupational safety and health at the American Nurses Association, so my work is to work with you to protect nurses from needle stick injuries and the subsequent illness and death, as Dr. Fisher described. And I wanted to start today to talk a little bit about our members and the impact in recent years of needle stick
injuries on their lives.

The American Nurses Association is the professional association representing nurses in the United States with our 200,000 members and as the professional association, we develop the code of ethics for nurses; we establish standards of practice; we develop standards for certification and certification testing of basic nurses and nurses in specialty practice, including advanced registered nurse-practitioners. And as the largest union representing nurses in the country, we also, in 28 states across the country, represent nurses for the purposes of collective bargaining and the advancement of the economic and general welfare of registered nurses. And my role as the occupational safety and health specialist falls in all of those areas.

Our members are all too often the victims of needle stick injuries. This nurse, Linda Arnold, that many of you may have had the opportunity to hear from and have known about over the past four years, had a needle stick injury after she finished an IV insertion of a patient with AIDS. Linda is a nurse from Lancaster, Pennsylvania, a small community hospital, and most people in that community not only were unaware that the community had any patients with AIDS but the first time they learned about it was when one of their own, a very young nurse who, at the time of her needle stick was 23 years old and had only just come out of nursing school about three years prior when she had her needle stick injury.
As a result of her needle stick injury, she did develop HIV and subsequently AIDS; in fact, in very short order. And as a result of her injury, Linda did a great deal of research on her own, working in collaboration with ANA, with a number of other organizations, including SEIU, and worked with the International Center at Charlottesville, Virginia for Health Care Worker Safety.

Linda decided that she wanted to start an organization that would prevent, for all nurses, what had happened to her and the tragedy for her family. She founded in 1996 the National Campaign for Health Care Worker Safety. And part of the goal of her campaign was to get institutions around the country to implement and use safer needle stick devices, as well as to educate nurses and other health care workers about the importance of working together with their employer to evaluate, select and implement these safer devices.

But one result or lack of result during the many years of Linda's work, as well as work for many years by a number of us, even following the FDA advisory in 1992 about IV needleless systems, is that this is data from November '98 from the American Hospital Association consultant, Gina Pugliese, that across the country, the percentage of use of safer needle devices is abysmally small. You can see the largest use of safer devices in needleless IV access, and most of us believe that it is not coincidental that this has occurred in the years ensuing since the FDA advisory in 1992.
But for hypodermic needles and syringes, the most common use of injections, there's less than 10 percent of the hospitals around the country, as of last November, had implemented safer devices. November was immediately following the California legislation and then subsequent to November, last spring there's been a number of other states.

So this number will be increasing rapidly and there also with come with it a need from the FDA and the other organizations responsible for worker health and safety, as well as consumer health and safety, to assist these institutions as they implement their new regulations to be able to provide education to employees and to choose the right devices.

Another of our members, Karen Daley, who is the president of the Massachusetts Nurses Association, had a sharps injury last summer. And I know that you're not talking about sharps injury containers; however, if the needle that was in the sharps container that stuck Karen--she was working in the emergency room, she was working on the day shift, she had taken care of a patient and had administered a medication, had taken the sharp that she was using, put it in the sharps container and in the top of the sharps container the previous needle that had been dropped had not dropped down into the box. It was a mailbox kind of drop container where the weight of the sharp itself is supposed to drop that sharp down below.

It did not do that and even though in the
previous five months the nurses in Karen’s institution, who are represented by the Mass. Nurses Association for collective bargaining, had repeatedly gone to the employer and labor-management committees and said, "Get rid of this container; it's not safe," well, the day after Karen got her diagnosis of HIV and hepatitis C, all of those sharps containers were removed, but too late for Karen.

What happened is as she dropped her sharp in, there was a needle already in the top. She got stuck about a millimeter and a half into her index finger. And nine months later--and most of you know that six months following a needle stick injury, 95 percent of all seroconversion to HIV will occur. With coinfection with hepatitis C, that seroconversion can be extended. And I just heard of another nurse in the last month that it was 11 months before she came back with a positive HIV test.

Karen Daley is a tremendous leader within the American Nurses Association and you can barely imagine the devastating effect its had on our entire organization. And the way we all learned about Karen's illness was because the Massachusetts Nurses Association had introduced legislation in the State of Massachusetts to require safer needle stick devices and Karen, on the day they introduced the legislation last spring, spoke on the steps of the State House and her story was featured in the front page of the Boston Globe.

Now the issue here is not sharps containers. The issue is that if the device that was used by the nurse or
whoever had used the device previous to Karen had a blunting, retractable or sheathed feature, Karen wouldn't have been stuck.

And I think what's happened is that even though I live in Seattle, I'm less familiar with Power Point than I am with WordPerfect presentations and I think this is what happened in the translation to Power Point.

I wanted to just mention quickly the hazards to health care workers and the kind of situation that nurses and health care workers face on a daily basis in the institution.

We are subject to various biological hazards. You can see HIV, hepatitis B, hepatitis C, tuberculosis and many others.

Chemical agents, and ANA has had a great privilege to work over the past few years with the FDA on the issue of latex allergy and the teleconference a year and a half ago on that subject. Another chemical hazard to health care workers, glutaraldehyde, ethylene oxide.

Ergonomic hazards--back and upper extremities.

Physical agents like sound and radiation.

And then what has been lumped together in the category of psychosocial hazards are stress, violence, shift work, shift rotation.

So it's not just needle stick injuries that we need to worry about.

Health care workers, with occupationally acquired HIV, Dr. Fisher mentioned the CDC data for confirmed cases
of the HIV virus from a needle stick or other blood-borne exposure. As of December '97 there were 54 documented cases and 132 possible cases that didn't meet all the criteria but are very likely to be occupationally acquired HIV.

And as Dr. Fisher mentioned, with the number of cases you saw just from one hospital in California and the fact that in March of this year I learned about two nurses, Karen Daley and one other who I'll mention in a minute, who were notified that they had become infected with both HIV and hepatitis C, two in one month, all of us that are involved in this field of occupational safety and health believe that these estimates are very, very low.

And if you take prevalence data from the CDC and from the Hospital Association, who has said that 16,000 of the 800,000 to 1 million needle stick injuries per year, 16,000 of those are needle stick injuries from patients with HIV, and then you add onto that the .03 seroconversion rate, that will bring you to a number of between 10 to 35 occupationally acquired HIV infections per year. And with only 54 since 1985, we know that this is an underestimation.

I also wanted to note that of the 54 documented cases, 87 percent were from percutaneous injuries and 89 percent from hollow bore needles, so we can hone down the area of the greatest risk.

Then the risk from these needle stick injuries. I mentioned HIV .03 or 1 in 300 risk, but the risk from a
needle stick injury sustained from a patient infected with either hepatitis B or hepatitis C is so much greater. And as a result of the blood-borne pathogen standard that was implemented in 1991, we have reduced the death rate from hepatitis B from thousands per year to a negligible, less than 10 per year, as a result of the requirement for immunization.

The problem with hepatitis C though, is that there is neither an immunization nor at this point a reliable cure.

The data is all across the map in terms of hepatitis C. We at the American Nurses Association believe that we have only begun to see the needle stick injuries that have seroconverted to hepatitis C. We know that there is as long as a 10-year lag time between infection to illness and we know that it was only in the last year, in 1998, that the CDC began to recommend that health care workers be tested for hepatitis C following a needle stick injury. So that we don't know how many people have developed hepatitis C and we're going to be seeing this tidal wave over the next number of years.

This was a scan that didn't work. I'll go on.

Now when we talk about needle stick injuries, of course we need to find out whether there is a way that we can reduce the number of needle stick injuries, and this is a slide that demonstrates the data from the CDC case controlled study from '93 to '95 in Minnesota, New York and California. That's the starred percentages.
For butterfly or wing steel needles there was a 23 percent reduction in needle stick injuries following the implementation of safety butterflies, a 76 percent reduction with blunt needles, and a 66 percent reduction in needle stick injuries with a hinged recap IV needle. And the last 84 percent reduction from IV safety catheters is data from the University of Virginia Charlottesville trial. So we know that there is great benefit from the implementation of safety devices.

ANA's recommendations to the FDA and in general to institutions as we look at safer devices are to incorporate user training and in-use testing by users and evaluation by health care workers to implement safer devices.

Our main goal is to remove all barriers to implementation. And as many of you know, we've been working in a coalition to pass the Pete Stark legislation which would require the implementation of safer needle stick devices on a federal level, as we've been working state by state.

There are some folks that say that there should be no unsafe devices on the market, that every device that is on the market should have a sharps injury prevention feature. We know as nurses that there are uses for what are less safe devices or unsafe devices.

And I have a question for you, for the panel, and the question in general is do we need a supplemental premarket review for devices with sharps injury prevention
features or should all devices undergo the same kind of testing and that any device that increases the risk of needle stick injury to either the health care worker or, of course, to the family member who is at home taking care of that patient and may be administering diabetes, may be administering some other medication at home, that any device that is being used by any consumer or any health care worker should be a safer device?

And as Dr. Fisher mentioned, we have begun a process to develop experts across the country in device evaluation and selection and our first training will be in Massachusetts since, of course, the state is very, very eager for this not to happen to any other nurse, and that will be in November.

And last comment, the family at home that's taking care of the patient, I talked to a nurse the other day in Wisconsin about the issues related to needle stick injuries and she said, "Well, you know, the other day I walked"--pediatric nurse--"I walked into a patient's room and there was a baby in the bed that had a needle stuck in its stomach." This was a syringe that had been inadvertently left in the baby's bed and the child had picked it up, as children do, to play with it and when the nurse came in to observe the child, this was a syringe stuck in the baby. And we know that you will join with ANA in wanting that not to happen to any baby but also not to happen to any other health care worker, either. Thank you.

DR. EDMISTON: Thank you, Ms. Wilburn.
Are there any questions by panel members? Yes, Dr. Rutala.

DR. RUTALA: Yes, I have one question. You mentioned some data from Gina Pugliese November 1998 where there was some market data where health care institutions were not implementing various engineering controls.

Certain professional organizations have believed that engineering controls should be implemented when there is a demonstration of efficacy; that is, actual clinical efficacy. And certainly we've heard this morning that these devices should be safe and efficacious. How do you feel about the issue of actual clinical efficacy versus simulated efficacy testing?

MS. WILBURN: In the questions I noted that most of the manufacturers have been doing simulated testing instead of actual testing and we believe that not only should it be actual testing but it should be actual testing with an educated group of trainers who, like the group that Dr. Fisher has worked with, can really put a device through its paces and not just be thrilled with a new bell and whistle that is much better than what we've had before.

I also wanted to add that Dr. Kessler earlier was talking about the use of medical device reporting and we've learned at ANA how unsatisfactory medical device reporting has been for incidents that occur to health care workers. When I've gone around the country to talk to nurses about medical device reporting, specifically about the issue of latex allergy, they say, "Well, we know all about MedWatch.
We know that we're supposed to use it when there's a patient incident. We are unaware that it applies to health care workers."

So there needs to be an additional education and advisories from the FDA to reinforce to end users that it is not only the consumer or the patient but it's the user of the device that should be reporting an incident.

DR. EDMISTON: Thank you very much.

I want to thank our four presenters. This ends our formal scheduled presentation portion of the morning.

Before we move on to the open public hearing session, Martha O'Lone has a statement she needs to read.

OPEN PUBLIC HEARING

MS. O'LONE: Actually this is part of the open public hearing. I have two statements that I promised if people were not able to attend that I would read into the record for them.

The first is from the Department of Health Services Sharps Injury Control Program at the State of California, from Dr. Cone and Martha Davis. They said, "Since we may not be able to attend the meeting, would you please accept and read into the minutes the following comments?

"Recent legislation in California, AB1208, added Labor Code Section 144.7 that required the Division of Occupational Safety and Health, Cal/OSHA, to revise the blood-borne pathogen standard. The revised standard requires California health care workers to use needles with
engineered sharps injury protection and needleless systems
to reduce the risk of sharps injury and potential
transmission of blood-borne diseases.

"In addition to the requirement for a revised
standard, Labor Code Section 144.7 also directed Cal/OSHA
and the California Department of Health Services to jointly
compile a list of needleless systems and needle devices
with engineered sharps injury protection to assist
employers in complying with these new requirements.

"Within the California Department of Health
Services, the Sharps Injury Control Program has proceeded
in the development of this list. We make no claims to
evaluating devices placed on this list.

"Now that other states have passed similar
legislation, the impact and importance of this California
safety device list increases. As the FDA is a federal
organization which approves medical devices and associated
safety claims and labeling, it is our hope that the FDA
will take the lead and establish a process which
standardizes the product safety claims across all states
with similar legislation.

"In developing the list, we requested the
assistance of the FDA in identifying needles with
engineered sharps injury protection and needleless systems.
We were told that the FDA could not provide a complete list
of FDA-approved needles with engineered sharps injury
protection and needleless systems. We could, however,
begin to develop our list by searching the Releasable
510(k) database for antistick syringe, which has a product code 80meg.

Only a small subset of devices making safety claims are available with "meg" codes. As of July 6, 1999, there were only 17 products listed with the product code "meg." We are aware of piston syringes not on the "meg" list that are available on the market that make safety claims. We also understand that there are not similar anti-stick or safety device codes for blood-drawing devices, for needleless intravascular administration set, safety catheters, for safety lancets, for blunted surgical needles or for hemodialysis needles.

Please provide a way for us to identify safety products. You may wish to consider providing a way to search the Releasable 510(k) database for engineered safety products in all categories mentioned above or consider new product codes specific to identify needle devices with engineered safety component. Alternatively, once safety claims are approved by FDA, could FDA maintain a list of these safety needle products?

"Additionally, we would like to know what are the criteria, if any, for making safety claims, above that of 'not significantly different from existing products.'

"The following comments refer specifically to the Supplementary Guidance on the Content of Premarket Notification 510(k) Submissions for Medical Devices with Sharps Injury Prevention Features.

"Currently a device manufacturer of a piston
syringe makes the following safety claim: 'Once sealed, works like a built-in portable sharps container' and provides 'sharps container savings. Can eliminate the need for containers in patient rooms.'

"Are these claims reviewed when the FDA reviews a product as a medical device with sharps injury prevention features? The Supplementary Guidance on the Content of Premarket Notification 510(k) Submissions for Medical Devices with Sharps Injury Prevention Features should incorporate specific safety criteria for what constitutes a safe sharps disposal container.

"Lastly, to protect the safety of our health care providers, FDA should make readily available results from Medical Device Reporting System that is device-specific. We encourage product users to report to FDA MedWatch on injuries involving device failures with potential for blood-borne pathogen exposure. It is important to know which devices have had failures resulting in injuries and the frequency of occurrence. Users of products need to know the risk associated with each device. We would like to see FDA prescribe specific test methods to assess safety performance of a needle safety device or other medical device product that manufacturer claim will be 'safer' to use than a 'standard device.' How safe is safer and what are the risks associated with a 'standard device?""

It ends with "Thank you for allowing us to submit comments."

DR. EDMISTON: Thank you very much.
MS. O'LONE: And we have one more. The second one that I have is from a manufacturing firm and our purpose is to go over some things to add to the guidance, and this goes through actual line deletions, so it may not make as much sense if I read all this comment on the second page, but I'll begin with their first page and then try to address what they've listed as revisions. Those would be addressed also as written comments in the draft that goes out in the Federal Register in the future.

This is from Biomedical Disposal. It was written by Cathryn Cambria, who's the director of regulatory affairs and quality assurance. Its subject is suggested changes to the guidance document.

"In developing these comments we were guided by the belief that this guidance document should reflect changes in technology, regulations, and the marketplace since March 1995 when this guidance document was issued; allow and encourage new technology as it becomes available; and include clarifications to avoid potential misconceptions. Separately, making the guidance document for needle destruction units available via the Internet would additionally help reduce confusion."

They have on here, "Biomedical Disposal is a private company located in Atlanta, Georgia, which markets products designed to make the health care workplace safer. Specific products for needle safety include the SharpX, a FDA-approved needle destruction unit." And they state that they also recently acquired a patient for safety syringe
technology.

Their main comment that they made that I'll share now, in the interest of time, is that they felt that the guidance should be amended to say that it's for the review of 510(k)s for devices with built-in sharps injury prevention features, and also to reiterate that there is a separate guidance document for needle destruction units.

And that's the end of the comments that they have that are pertinent to read at this time.

Well, now that we are in the open public hearing portion of this meeting, let me read a statement. This next half hour or so will be available for members of the public who would like to address the panel. Please raise your hand so we can determine the number of speakers that are present who may be interested in addressing this panel.

I am aware at this time that we have a representative from the Service Employees International Union. Could you raise your hand please?

Do we have any other individuals who would like to address this panel? Could you please come forward? One more? We have two individuals. Could you come forward, please, state your name, your affiliation?

MS. GOODENOUGH: Good morning. My name is Laurie Goodenough. I'm a registered nurse and a member of Local 200A, Service Employees International Union, AFL-CIO. Service Employees International Union has 1.3 million members, including 675,000 health care workers. It's the nation's largest organization representing the interests
and concerns of our nation's caregivers.

SEIU has been a leader in fighting to protect our members from a wide range of workplace hazards they face. In 1986 SEIU originally petitioned OSHA for the blood-borne pathogen standard that was eventually completed in 1991. Understanding the important role of FDA regarding the safety and efficacy of needles and other sharps, in 1991 we petitioned FDA to better regulate conventional needles and other sharps which can occupationally transmit hepatitis and HIV.

While FDA largely denied our 1991 petition, the agency has cleared well over 200 safer devices with integrated safety features. Unfortunately, however, fewer than 15 percent of needles and other sharps purchased by health care facilities today use these potentially life-saving devices. Most health care workers have never seen these safer products. In other instances, lack of proper training has led to resistance to adoption of safer products by the health care workers themselves.

On behalf of SEIU, I offer our experience on what we have found to be the critical elements necessary to achieve success at the work site level during the conversion from conventional to safer needles and other safer sharps.

Education and training must be coordinated with the manufacturer of the device and the education staff of the facility before the device is put into use.

Training must be mandatory for all staff using
the new device.

Training should include a review of the manufacturer's written program, as well as a video program, on the use of the device for the initial training and ongoing training.

There must be assurance that the manufacturer's representatives have clinical experience and are available on-site or on-call for 24-hour coverage during the initial implementation and use of the new device.

There must be an opportunity for a performance test on the new device, including three return demonstrations; at least one return demonstration conducted with the manufacturer's representative and at least one return demonstration conducted with the facility's educational services coordinator.

There must be allowance for extended training for workers who fail initial performance tests or are uncomfortable with the new device.

There must be follow-up testing within a 30-day period on the implementation and use of the new device.

Education must include a review of the risk of exposures to blood-borne diseases from needle stick injuries and how these injuries can be prevented through the use of control technology.

Education must be provided on OSHA blood-borne pathogen standards that require the use of feasible safer devices.

Education must be provided and disincentives
removed on how to report a needle stick injury.

There must be the provision of easy, visual reference material--an example would be a poster--that can be posted throughout a facility that can provide key points on the use of the safer control technology.

As a part of any effective program to implement safer devices, there must be an ongoing monitoring of surveillance data regarding needle stick injuries before and after introduction of the new control technology.

Thank you for this opportunity to suggest actions by FDA to stem this epidemic of 600,000 to 1 million needle stick injuries which affect our nation's health care workers each year.

DR. EDMISTON: Thank you. Before you go, are there any questions from the members of the panel?

MS. GOODENOUGH: You mentioned our book as part of this checklist and I didn't know if I can offer you one of these to add to--

MS. O'LONE: We have that as a resource already.

MS. GOODENOUGH: Okay, thank you.

DR. EDMISTON: Thank you very much.

Could the second speaker come forward please and identify herself?

MS. DUCMAN: Thank you very much. My name is Kathryn Ducman. I'm a registered nurse and the director of clinical services with Retractable Technologies Incorporated. We are the manufacturers of safety medical devices. We have a retractable syringe, Vanish Point
syringe that has been on the market since 1997, as well as a blood collection device that has been on the market since September of 1998.

I appreciate the opportunity to speak and certainly am in great agreement with the previous speakers. I again would like to reiterate that all devices with the potential for sharps injury and/or blood-borne pathogen exposure undergo the same rigorous testing and standards that safety devices must go through, so that frontline health care workers are protected from those injuries.

I also would like to see some type of criteria that assesses the length of exposure that these safety devices do protect health care workers from. I think there's an enormous difference between a device that offers instantaneous or in-patient safety as compared to those that must be activated manually outside the patient, which does create an exposure to that sharps injury. So in-patient versus out-of-patient and the length of exposure is a criteria that certainly needs to be included in that.

Also safety post-assembly of any safety product needs to be looked at quite stringently. Blood collection devices pose an enormous risk to health care workers because they are large bore hollow needles filled with blood. Many, many of the safety devices on the market, once disassembled, present a nonsafe contaminated needle on the back end phlebotomy needle that is not addressed in any of the labeling. So once that is disassembled, they are exposed to a risk.
Also some criteria for the products that are on the market and have had some history if they are creating sharps injuries because of their design, and looking at that criteria that would go back and assess them accurately.

Thank you very much for the opportunity to speak.

DR. EDMISTON: Thank you very much.

Are there any questions from the panel?
[No response.]

DR. EDMISTON: Thank you.

Is there anyone else in the audience who was not scheduled or is interested in making a presentation to this panel?
[No response.]

DR. EDMISTON: If not, at this time I'd like to close the open public hearing and take a break. Let's meet back here at the top of the hour, 11:00.

[Recess.]

PANEL DISCUSSION/RECOMMENDATION

DR. EDMISTON: Thank you for coming back promptly. At this time the panel will address the questions that have been presented. We will discuss these questions in detail and make recommendations to the FDA.

It is possible during the discussion of these questions that we may ask for assistance from members of the FDA, OSHA or NIOSH, who I suspect are still available in the audience.

Could we get the first question up on the screen,
I should also point up before we get started that we are not voting today, although I may poll the panel members to arrive at a consensus for the recommendations which we will be giving to the FDA.

I will read the first question. "Our current guidance document allows sponsors to perform either a simulated clinical use study or an actual clinical use study to evaluate the performance of the sharps injury prevention feature. In most cases, sponsors have provided information from a simulated clinical study."

Question one: "When would it be appropriate for FDA to consider data from actual clinical use or simulated clinical use trials?"

I'd like to open this up to the panel for discussion. Dr. Rutala.

DR. RUTALA: I'll begin by commenting that I believe that the demonstration of actual clinical efficacy should be required for any claim, suggestion or hint that a device will reduce sharp injuries. That is, if a manufacturer claims, suggests or hints that a product or a device will reduce sharp injuries, then I believe that clinical efficacy data should be required.

The manufacturer should first perform simulated use studies. If the device fails that, additional testing is unnecessary. However, all devices should be tested under clinical conditions.

In all such cases, a comparative group must also
be studied in order to determine efficacy; that is, the added benefit from the new device. For example, the frequency of injuries from a blunted suture needle should be compared to similar surgeries using standard sharp needles. The usual guidelines for study design should be followed, such as adequate power, objective outcome measures and randomization.

If a manufacturer is going to claim the device will reduce needle stick injuries, then this claim must be verified in actual clinical studies. For example, a self-sheathing IV needle device should be tested using pigskin by an IV technician. However, lack of injury in this simulation may not predict lack of injury when used by ordinary personnel on live, moving patients.

So in summary, if there is a hint, claim or suggestion that a device will reduce sharp injuries, I believe that not only should the manufacturer do simulated use tests but also actual clinical use studies.

DR. EDMISTON: Marcia, do you have any comments?

MS. RYDER: I am in complete agreement with Dr. Rutala's offerings. The only thing I would add in regard to the actual clinical study would be the suggestion that not only would these devices be incorporated into health care worker review but also those devices that are used by patients and nonprofessional people also be included in those trials.

DR. EDMISTON: Mr. Palomares?

MR. PALOMARES: Personally, seeing how the
products are used, I don’t think it would be feasible to actually conduct clinical studies. You’re talking about very low effect size—not effect size but incident rate here. And to actually conduct a study along this nature to develop the information to determine whether it's beneficial or not, basically like was said earlier, the technology just overrides it. By the time the study is done, there’s already new technology available and that product is nearly obsolete.

DR. EDMISTON: But for instance, if a claim is made that the device will prevent infection or prevent contamination of a line or device, that really needs to be validated; don’t you agree?

MR. PALOMARES: I agree with that and what I think needs to be done is that there should be a standardized protocol to follow. Right now manufacturers are left open to determine the protocol, the sample size, the challenge organism for a needleless system on microbial challenges. And at that, the FDA doesn’t have an adequate benchmark to say did this product perform as good as its predicate?

And really that’s what we’re here to talk about. Is it as good or better than what was previously on the market, to get it cleared?

DR. EDMISTON: Mr. Dacey.

MR. DACEY: I have to, from a consumer perspective, agree with Dr. Rutala. I’m especially concerned when a product works down the line to where it’s
in the hand of the consumer or consumer-patient. I was
going earlier that I've self-administered insulin for 20
years and I've stuck myself I can't count the number of
times inadvertently, but it's my own needle.

But I did a little research with our local
hospital--I serve on the ethics committee--just to get
their perspective in a generalized way around this subject.
Again from a consumer perspective it was a case of I didn't
know a problem existed until I started asking questions.
And I was very impressed with the hospital's response in
that they had been tracking these sharps stick incidents
and knew what the costs were and I was very impressed with
the problems that they were confronted with in this. Then
I tried to project that down into home care and it got to
be pretty awesome. So I definitely favor more actual
clinical use study.

And one of the comments I got from the staff
people was that they felt at the mercy of manufacturers,
that they didn't have a role in the product design. That
resonated over and over again.

DR. EDMISTON: Dr. Fowler.

DR. FOWLER: I agree entirely with Dr. Rutala. I
think we might have to make a distinction of the idea of
simulated studies versus clinical use studies, however, in
that the type of study that Dr. Fisher described earlier,
to me is essentially very close to a clinical use study and
that sort of study certainly may well be valuable. A
controlled situation using humans rather than artificial
limbs or animal testing or what have you, that sort of evaluation I think in some situations certainly would be a valid clinical use study.

I also agree and understand the difficulty in performing open-ended long-term studies without proper guidance, so I think there should be criteria developed to specify the types of work that needs to be done on a particular product under those controlled conditions.

DR. EDMISTON: I think one of the concerns that I have, and if someone from the FDA could jump in and give me some assistance on this, in terms of the 510(k) submission, a device that's submitted to the FDA, even if it's an invasive device, that device is significantly dissimilar or similar to previously marketed devices. That has a major impact, does it not, on how it's perceived by the FDA?

MR. ULATOWSKI: That's true. There's two primary methods of getting to the market and all the devices that have been cleared, I believe, have been cleared through our 510(k) process, which is a determination that the product is as safe and effective as a legally marketed product already out there that is also subject to the 510(k) process.

That has its benefits and its problems. The benefit is in some cases if the product is sufficiently similar to one that's already legally marketed, in fact identical in some cases, one can rely upon certain what we call descriptive information--dimension specifications, certain bench specifications--to clear the product, and
only go to other tests as necessary to evaluate differences.

The down side is we've been working with a technology here for 15 years plus, perhaps, where the earlier technology may not be the best thing on the block but yet it remains substantially equivalent and legal. And I think one purpose of the guidance and the discussion today from the public and from the panel is to kind of draw a line in the sand, to say these are the features that are appropriate, these are the ways one should evaluate them. And those that would by some chance get some older technologies that don't meet these expectations really should fall by the wayside now.

I'm giving a long answer but the short answer is our process constrains us in some respects.

DR. EDMISTON: There's no doubt that failure of a device can, in part, be documented by benchwork that occurs in the laboratory. The issue that Dr. Fisher brought up, postmarket evaluation, we really don't know what's going to happen to these devices once they get out into the public, the public domain. We see that with anti-infectives. We see that with a variety of compounds that within the clinical trial period of numerous patients we find no adverse effects; it's when the compound or the device is out in the hands of the public that we do see these problems.

So I think we need to separate this postmarketing and I don't want to forget about it; I want to come back to
it. I really think the postmarketing surveillance part of it is extremely important.

Going back to Dr. Rutala's statements, I am also in line with his comments concerning these devices, especially these devices representing new technologies. And many of these devices do represent new technologies. And to adequately demonstrate that these devices are safe, there's no doubt that simulated studies can demonstrate that within a very defined environment.

What I'd like to do is that as we move through this, let's try and arrive at a consensus on each question rather than going back to them all at the end.

Martha, could you read the very first response that Dr. Rutala gave us?

MS. O'LONE: Well, I know that you started out with some information about clinical efficacy. I didn't quite get every word. I might ask Dr. Rutala--did you have your remarks prepared?

DR. RUTALA: Yes, I do. I can give you a copy of them.

MS. O'LONE: If you would like me to read them, I can do that.

DR. RUTALA: Or I can just reiterate--

DR. EDMISTON: We're particularly interested in the first two sentences.

DR. RUTALA: That's exactly what I was going to repeat. My comment was the demonstration of clinical efficacy should be required for any claim, suggestion or
hint that a device will reduce sharp injuries. If a product does not make a claim, suggestion or hint, then a clinical use study may not be necessary, but a clinical use efficacy study would be required for any claim, suggestion or hint that a device will reduce sharp injuries.

DR. EDMISTON: Is there any comment from the panel? We're talking about claims specifically that are made with these devices that may impact on patient care or health care professional caregiving. Yes?

MR. PALOMARES: How would you capture that data? When you talk about--

DR. EDMISTON: Actually, Dr. Rutala answered three questions in his commentary. I think the issue that's at hand here is that devices that make specific claims--anti-infectives that make specific claims, they're approved for indications. And while these may not be approved for indications, the broad indication is that they're safe devices, that if a specific claim is made, that needs to be validated for the consumer and for the health care professional.

So should the panel be in agreement to enter in Dr. Rutala's first two sentences or two and a half sentences as a response to question number one?

MR. PALOMARES: I believe in the guidance document it talks about devices that don't--let's say, for example, don't have a needle in it. It could still say it's for the prevention of needle sticks, since it does not have it; it's passively performing that function.
DR. EDMISTON: Well, if you make a specific claim, I think it still falls under that purview.

MR. PALOMARES: I would not agree with that. I understand that the panel is trying to make what’s best and safe for the general public--

DR. EDMISTON: I think you just answered that, in terms of the safety perspective, that it would be prudent if the claim is made with that device, to enter into some type of clinical evaluation.

Let me summarize this first question, then, the response to this first question. Clinical use efficacy studies should be required for any specific claim regarding sharps injury protection features. All right?

The next question, "Are there minimum criteria in terms of sample size, independence of the evaluators, number of sites, et cetera that the FDA could consider for both the simulated clinical and actual clinical use studies?"

Mr. Palomares, I'll let you speak first.

MR. PALOMARES: Well, understanding if we are going to go in the direction of having clinical studies, how do you determine--

DR. EDMISTON: Correct me if I'm wrong from the FDA. We're just making recommendations.

MR. ULATOWSKI: That's right. You're providing recommendations and we'll think about what you said in total.

MR. PALOMARES: That's fair.
DR. EDMISTON: There will also be an opportunity for written comments, both from the private sector and the public sector.

MR. PALOMARES: What are you deeming as an acceptable sample size? As well as what level of improvement in safety are you looking for if we make claims along these lines?

DR. EDMISTON: I think if you read the guidance documentation under statistical evaluation, they make a lucid argument for the use of confidence intervals. And I think if you look at the confidence intervals, if you had X number of devices in which you're testing in multi-centers, and multi-centers could be two centers, with independent investigators, because obviously you want to have as many users, as Dr. Fisher indicated, as many users looking at these devices on the front end, that an N, in my perspective, an N of 500 is not reasonable considering the number of these devices that are used, even within a single institution.

Marcia, do you have any comments?

MS. RYDER: Well, certainly as identified, I would agree in terms of the confidence interval perspective and certainly, again because of the scope of the problem and numbers and spectrum of users, that we certainly, as scientists, should require the scientific rigor that is suggested in the document.

DR. EDMISTON: Dr. Rutala?

DR. RUTALA: Yes, I'm just going to refer to
possibly five minimum criteria that could be used in doing a clinical use efficacy study.

One is that the body sites tested should conform to the expected use of the device. For example, a peripheral IV should be used on a patient's arm and hands.

Two is that the sample size should be based on a clinically meaningful reduction in needle stick injuries. A reasonable number might be greater than or equal to 10 percent reduction, but that is debatable. The exact percent reduction should be reported in the manufacturer's package insert.

Three, as with drugs, manufacturers should provide data demonstrating efficacy and the study should be properly performed or performed by impartial outside investigators. When observer bias may influence results, observers should be masked as to the intervention.

Four, appropriate populations should be studied. That is, the study should have internal and external validity.

And five, the device studied should be the actual device to be sold, not a prototype to the device being sold.

DR. EDMISTON: Mr. Palomares, how does that sound? Does that sound reasonable?

MR. PALOMARES: I agree that it should be the final device. I know a lot of manufacturers try and use prototypes. It's not the best way to do it. I believe most of them don't do that but I know there are some that
have done that.

I believe--can you repeat those?

DR. RUTALA: The first was the body sites tested should conform to the expected use of the device.

MR. PALOMARES: I believe that's true.

DR. RUTALA: The second was sample size should be based on clinically meaningful reduction in needle stick injuries. A reasonable number might be greater than or equal to 10 percent reduction.

MR. PALOMARES: I'd agree until about the 10 percent.

DR. RUTALA: That is just a proposal.

DR. EDMISTON: Actually that's an interesting argument. What we're talking about is the power, the power of statistical tests.

If you're working on a urinary catheter you're going to decrease the urinary infection rate, the nosocomial urinary infection rate from 2 to 1.5 percent, that would involve thousands of patients.

However, as you determine what would be an appropriate reduction--5, 10, 15 percent--impacting upon your power actually decreases the number of individuals that you would need in your data pool.

I think it's reasonable, from my perspective, that if you're going to manufacture a safe device, it should reduce needle sticks and there should be some documentation of this.

Dr. Fowler?
DR. FOWLER: I agree. I think the statistical methods, as you say, will require varying numbers of subjects, depending on what you're trying to achieve and that is something I think that might have to be a joint decision between the regulators and the industry or manufacturer wanting to make a particular claim. Obviously, as you say, if you want to claim your product is 10 percent better than what's out there, you have to have a certain number of subjects in order to do that and that certainly can be come up by any statistician.

I think the independence of the evaluators is, of course, critical and I would also speak to the use of multiple sites, whether that be at least two, perhaps more. Knowing that products of this nature will be used in many, many different sites, having the testing done at multiple sites. It would somewhat increase the variability of the users and would be a more realistic assessment, I think, of the product in its final environment.

DR. EDMISTON: Mr. Palomares and members of the audience, I understand that when you're talking about reduction, especially if you're making a claim for a device that it's equivalent to what's already on the market, you may not be looking to demonstrate that the advantage is there's a tenfold or a 10 percent reduction. You're looking for equivalence because this is what you submitted to the FDA.

However, getting back to the earlier statement that Dr. Rutala made, if you're going to make a specific
claim, then you're looking at more than likely having to provide a statistical argument for that claim.

I don't think the FDA is going to hold us to what we're saying in terms of a number because they realize the subtleties that are involved here.

MR. ULATOWSKI: As we approached the guidance document back in the mid-'90s, we understood that claims being made and how one approaches clinical evaluation would be a very difficult situation. And we indicated in our guidance that fundamentally everyone's making a baseline claim that you're trying to provide a safe device that's going to help prevent needle stick injuries.

And then beyond that, people may want to, for whatever reason, want to make some other disease prevention claim or something else that might incur additional requirements.

I think with the discussion I heard this morning and from your response, although it's not a question, it's kind of the coming together of the need for data and is it pre- or postmarket? And what are the numbers?

I think in terms of numbers, if the idea is it's preventing needle stick injuries, well, to be able to show that statistically in a significant manner would, depending on your institution, may require some big numbers. And we realize that, so we went to a survey, rather than calling it a clinical study, with the type of traditional clinical end points that one might see in studies, but rather look at a survey and a user familiarity, user confidence sort of
outcome, rather than hard and fast incidence differences.

That may not be totally satisfactory and it has not been, I think, for every institution because then they'd move to do their own additional studies and collect more data in their own institution. But I hear the interest in clinical information, in following up on claims being made, and that's very helpful.

DR. EDMISTON: Let me tell you where I'm coming from. When a new product comes into my institution, as it does into all of our institutions, before we accept that product as part of our inventory we go through our product evaluation committee and at some step there's evaluation that occurs of that product.

I can tell you with the sharps issues that quite often we don't have enough information to make that evaluation. So it's been very difficult to get that information.

This is a very, very difficult issue in terms of designing appropriate trials that encompass enough warm bodies so that we can reach levels of significance, even within multi-center institutions. But I think if specific claims are made--it may be best from the manufacturers' perspective never to make a specific claim but if claims are made, this is going to impact on our presentation or how we view that device.

So on one hand, if you're presenting a device and you're saying it's equivalent to what's available but we're cheaper, that's one issue. On the other hand, if you're
stating we're equivalent but we're going to reduce your nosocomial bloodstream infection rate, that's another issue.

So I think you have to be very specific from the manufacturing perspective what you're saying in the labeling.

So from that perspective, if the device can be demonstrated to be equivalent to devices that are currently being marketed and there's no significant change in technology, I think more than likely we can defer to the historical data on that device. But if a specific claim is made, then we need to be more probing in terms of what we expect in terms of the data to evaluate that device as a health care professional or as a consumer.

MR. ULATOWSKI: That clarification is helpful. Thank you.

DR. EDMISTON: All right. Do we have enough information? Yes, Marcia?

MS. RYDER: I just wanted to reiterate the comment and concern that I made earlier in terms of the design of these studies, the incorporation of patient users and not simply multi-center hospital institutions in that evaluation. Is there some way we could interject a comment in those recommendations?

DR. EDMISTON: You mean working with, for instance, the phlebotomists?

MS. RYDER: To be very specific, home care.

DR. EDMISTON: Oh, yes. That's a difficult nut
to crack right there, yes.

MS. RYDER: Because we need to be assured that they're safe not only for professional users but, as we all know, that the home care arena is huge in terms of patient users, as well.

DR. EDMISTON: I think the real problem with home care, home care environment, is trying to document what occurs within that environment and trying to develop a study where you can actually have the appropriate controls and know what's going on in that environment. Home care is a very, very difficult issue.

I think unless someone out there knows something I don't, most of these devices are going to be evaluated, if they're evaluated, in institutions that have health care professionals who are used to using them and they will be the end users. But I think it would be tough to deal with that home care issue, especially the way it's structured currently.

Any other comments or questions?

MR. DACEY: On that home care issue, despite the fact that it is so terribly difficult and clearly the user, in perhaps most cases, would be a non-health care professional, I too would like to see some effort made, some diligent effort made to examine in a clinical setting, and again I don't have expertise on how to do this, so that there is some feedback statistically on what happens when these things are in the hands of a person at home. Eventually some of them are going to be there.
DR. EDMISTON: One of the questions that's going to come up is in terms of education and I think in terms of home care, that's an area where we need to strengthen our education.

MR. DACEY: Absolutely.

DR. EDMISTON: We may be able to get toward that issue by looking at it from the educational perspective.

MR. DACEY: I certainly can accept that.

MS. RYDER: I would just reiterate in terms of your comment then, you're saying that we are going to be able to make the huge assumption that professional workers, if we're able to demonstrate safety and efficacy, that we can assume that it will also be safe for a patient user. I think that's probably a huge leap but also I agree that the ability to be able to study that in a home care environment would be very difficult but it's something that is here and it's something that we're dealing with every day as nurses, and even on the educational basis in talking about educating the health care worker, but they also have to have the ability to educate the patient. And that hasn't been really addressed, either.

DR. EDMISTON: Marcia, could we reach some of those conclusions by doing more intensive surveying of that home care environment?

MS. RYDER: That could be a start.

DR. EDMISTON: That may be it.

MS. RYDER: Through the home care professionals.

DR. EDMISTON: Home care agency, to try and
assess precisely what is going on because you know and I know this is a very aberrant environment at times. It's hard to get a handle on what exactly is going on.

MS. RYDER: Well, of course, because we certainly don't even know the scope of husicomial infections, as well as other types of injury.

DR. EDMISTON: All right, Ms. O'Lone, what have you come up with over there?

MS. O'LONE: Jeez. No, that's your job.

DR. EDMISTON: All right, this is my job. This is what we have here. Bear with me for a second.

We should get Dr. Rutala to read his third and fourth sentences. Could you read your third and fourth sentences? I think you really hit on those areas. We will amend those sentences.

DR. RUTALA: I think we agreed on the body sites tested--

DR. EDMISTON: Yes.

DR. RUTALA: --should conform to expected use of the device.

DR. EDMISTON: Yes.

DR. RUTALA: I think the issue of a reasonable number as it pertains to meaningful reduction was an issue but the comment was sample size should be based on a clinically meaningful reduction in needle stick injuries.

DR. EDMISTON: We're talking, in part, about devices that are making a specific claim.

DR. RUTALA: That's correct. That's correct.
Very important distinction.

DR. EDMISTON: So devices that are making--


DR. EDMISTON: All devices, if they involve puncture of some type, should be tested on appropriate tissues or simulated tissues.

In terms of the sample size, if a specific claim is made, then an appropriate sample size should be determined.

DR. RUTALA: That's correct.

DR. EDMISTON: I don't think we have to determine that sample size.

DR. RUTALA: Or the percent reduction.

DR. EDMISTON: Or the percent reduction. No, we don't.

DR. RUTALA: The third point was as with drugs, manufacturers should provide data demonstrating efficacy and the study should be properly performed or performed by impartial outside investigators.

The fourth point was appropriate population should be studied. And the fifth is the device study should be the actual device used.

DR. EDMISTON: Are we all fundamentally in agreement with those principles?

[Nods from the panel members.]

DR. EDMISTON: And you indicated that you wanted independent investigators, that it was appropriate to have
independent investigators and that there should be at least two or more sites involved in the clinical evaluation of those devices in which a specific claim is made. Is that what you're saying?

DR. RUTALA: I didn't say two or more sites but I will accept that.

DR. EDMISTON: Actually Dr. Fowler said that. Sorry about that.

Martha has indicated that it might be appropriate to indicate what type of patient population or end user population that we would be studying and I think based on our discussion that we'd have a difficult time really—I have a difficult time and I'm not sure how the rest of the committee feels, the panel feels, but in terms of providing some rational way in which we can get to that home health care population, I think we can agree that it would be appropriate for a manufacturer to develop a reasonable protocol which then is available, farmed out to two or more investigators, who can do the studies. I don't think that can be done per se for home care because it's just not been studied very well in the past.

MR. ULATOWSKI: You raised a point to consider and I think we can put our minds to it and get additional comment from the public and maybe there's an approach to be taken there.

DR. EDMISTON: Let me at this time ask Dr. Fisher, would she be willing to come to the podium and make a comment specifically addressing this home health care
population?

DR. FISHER: We are currently doing a study with home health care and the problems are enormous but I think that they're solvable.

One of the things we've actually done is do a needle box for home health care because we found that it just didn't hold in the situation.

As I was hearing the discussion I was thinking again that if you have trained users, they can not only deal with the issues for the health care worker and the home care but they can be the resources for getting the other data.

I think we do have to separate the issues into three components. One is the health care workers themselves being exposed. Now, one of the issues that they brought up is that if the user, the patient is going to use a nonsafety device and they have to demonstrate that, that they can't use that safety device. They don't have a safety device in demonstration, so that they have a loop that you have to think about.

And I know that there are issues and costs, that you would want a diabetic not to have to buy the more expensive devices but how are you going to demonstrate that for that person or the lancets?

So you have that component. How can they do that kind of teaching and demonstration if they're not using a safety device? Hopefully the market will come down and we'll be able to have the safety device but that's an
When they do their own procedures, what kind of technique? And I must say that I was rather staggered to find out what people are doing in the home. What three years ago would have been done in an ICU, at least in the Bay Area is now being done at home, so that there are very complex procedures that are being done there.

The problem also that goes on in there is that the patient may come home from the hospital with one device or one system, certainly with a needleless system, and then the whole thing has to be changed, so you have more complexities there.

Then the issue that of nonhealth care people administering techniques. I do know in my own family that my young nieces were administering to their 88-year-old father complex procedures because they wanted to keep him at home. So I was somewhat staggered at what they were using. So the protection of that, the nonhealth care worker provider.

And then the issue of the protection of the patient, which may be different, as was pointed out before, having a stick from yourself. It may be painful but it is another--you don't have the kind of risk. So you're faced with that problem.

I would think that the examination of this issue is of a high priority and there is virtually no data available. And I think that that would be something that both in terms of FDA and the Health and Human Services
should be putting in quite a bit of resources to research this area because it is the booming area and I think it presents an enormous risk.

I think that the approach that we've taken is applicable because we saw that. In fact, the pictures that you saw about the design course was a design course for home health care providers.

DR. EDMISTON: Thank you, Dr. Fisher.

Could I have the speaker in the back, please?

Would you please identify yourself, please?

DR. FARRELL: I'm Dr. Farrell from CDER. Seven months ago I left my hematology-oncology practice and I will tell you that there is a CALGB protocol randomizing febrile neutropenic patients to home care versus hospitalization and sometimes the administration of the second drug that day is done by family members. I think home care studies have been done and are successful.

DR. EDMISTON: Please identify yourself.

DR. WENIGER: Thank you. I am Bruce Weniger from the National Immunization Program at CDC and I wanted to just follow up on a point that Dr. Fisher mentioned about the absence of data.

I understand that the California sharps safety legislation is going to require every hospital and clinic to maintain a log of needle stick accidents, which I think is going to be very, very important and useful. And yet if we use the analogy to the systems that we have for monitoring adverse events of vaccines, we mandate that
adverse events believed to be associated with vaccines are reported to some central place, the Vaccine Adverse Events Reporting System of FDA and CDC.

But, at the same time, the FDA also receives data from the manufacturers on the number of doses of vaccines in every lot, so that they can put denominators under those numerators of adverse events.

So two issues to consider are should FDA consider requiring the reporting of this information from those logs in some way? And secondly, should FDA consider receiving from the manufacturers of this safe needle or old needle devices the number of products within each lot distributed in the United States so that they can eventually put denominators under them and then compare the rates on a national basis of these accidents? Thank you.

DR. EDMISTON: Thank you. I think your comments really speak again to the postdischarge nature of this.

Let me see if I can encapsulate this a bit and I want comments from the panel. Would it be appropriate for the panel to recommend to the FDA that efforts be taken under way to investigate the optimal means by which devices such as these can be studied in the home health care environment and to start this as a discussion process with public comment, comment from industry, but not per se make this as a mandate from this panel? Is that appropriate?

[Nods from the panel members.]

DR. EDMISTON: Does FDA agree with that?

MR. ULATOWSKI: That's just fine with me as far
as the recommendation is concerned.

DR. EDMISTON: Okay. I think that takes care of question number 2.

Question number 3, "In addition to the survey format, are there any other methods that the FDA should consider when evaluating the performance of these types of devices?"

I think I'll ask my colleague to my right if he has any comments regarding that.

DR. FOWLER: Well, I think we've already really spoken about that, the comment about the clinical use studies. I think the survey format can provide good postmarketing data, which should probably be looked at. And, in fact, a clinical use study may involve, to a greater or lesser degree, a survey format.

DR. EDMISTON: When you talk about survey format, you're talking about survey format from the end user, correct?

DR. FOWLER: Well, my understanding of a survey format would yes, that the company, for instance, in a clinical study would obtain the information from the end user of the product, yes.

DR. EDMISTON: Well, this is information that would occur prior to marketing, so it doesn't really correspond to postmarketing, correct?

DR. FOWLER: I'm not sure it would necessarily apply to one or the other. It could be both.

DR. EDMISTON: Marcia?
MS. RYDER: Could you repeat the question?

DR. EDMISTON: "In addition to the survey format, are there any other methods that the FDA should consider when evaluating the performance of these types of devices?"

MS. RYDER: I concur. I believe we've already covered that.

DR. EDMISTON: Let me just make one interjection here. I think that the activities that we've seen today from Dr. Fisher's group, from the Service Employees International Union, the surveys that they've developed, these also might be appropriate for consideration on the part of the FDA in looking at some of these guidance criteria.

There's a wealth of information that these organizations have already developed and I think it would be appropriate to at least look at this in developing future guidance documentation.

MR. ULATOWSKI: I think people put a lot of time and effort to creating the sorts of reporting forms that are used today and I'd be perfectly happy to entertain a 510(k) that had data submitted using one of these mechanisms, these instruments, if you will.

So I applaud June and other of her coworkers' efforts in this regard.

DR. EDMISTON: Mr. Dacey, do you have any comments?

MR. DACEY: No further comment.

DR. EDMISTON: So I suspect what we would
actually propose is that in addition to the surveys currently in place, it would be appropriate to incorporate data from TDICT, SEIU and what was the other organization? The New York State? New York State Department of Health--these types of vehicles as surveys.

Yes, Dr. Fisher?

DR. FISHER: As flattering and validating of our work are those comments, I think we have to be realistic. We can't even get people to report needle sticks. And I have some suspicions that surveys are not going to--I would be encouraged but I'm not optimistic that we're going to get that kind of data.

And I would like to suggest that we think in more formalized outcomes. That was why I didn't go into the whole issue of pilot testing because I didn't have enough time, but I think if you would establish standards for pilot testing which could be done premarketing and that we develop ways that we can easily get material.

One of the things we were talking about, developing a little Palm Pilot type of thing so that you instantaneously can enter in that you used the device, that the device was adequate or you have maybe four or five different parameters that you can just--because otherwise in an environment which Susan Wilburn described where people are very, very busy and they're running around, you're just not going to get that data that we need to get.

So there has to be attention directed to formalized studies and that formalized studies have great
specificity. In fact, we submitted a graph and I don't know if it's going to be funded, to NIOSH or not, to have a user-based design pilot study, to come up with a national agenda where we poll people who are interested and develop some criteria for what pilot testing should be, what should be included in pilot testing and, when you give that, to test it with a group of users and with a control group, to see if you can get better data and to have some kind of way that you can quickly get that data, that you don't put a burden onto people who don't even have time for reporting.

We did not bring this up but reporting goes from 30 percent to 60 percent. No matter what efforts you make, you can't get--the most common one, besides which some people are discouraged because in some hospitals your pay, your merit pay will depend on whether you have a needle stick or not, is "I don't have the time to do that."

So I think we have to be realistic and try to--I'm not saying we shouldn't do it but we should be more creative in trying to get that data.

DR. EDMISTON: I think your survey data, even though you found limitations in it and we all recognize limitations in this type of data, still is valuable in that it recognizes the problem and it addresses the problem.

As Mr. Ulatowski indicated, there was a lot of work involved in these studies and I think they're a valuable format. I think that in terms of--when would you anticipate that this document would be revised and available for public comment?
MR. ULATOWSKI: That’s always a good question. Probably sometime in the fall.

DR. EDMISTON: Yes, I think it would be very difficult to implement the technology and the research methodology at this stage, to try and address this particular issue.

DR. FISHER: I was giving that as a perspective—

DR. EDMISTON: As a perspective. But my feeling about this is that this probably won’t be the last revision of this document, that this is going to be an ongoing process until we essentially reach a zero state.

So does the panel feel comfortable in using the previous survey vehicles and also incorporating the work that’s been done by other agencies in surveys to assess the risk?

[Nods from the panel members.]

DR. EDMISTON: Okay.

Number 4, "Are the evaluation criteria listed in the guidance document appropriate and inclusive?" Mr. Palomares?

MR. PALOMARES: I have no comment at this time.

DR. EDMISTON: Let me get a little help from the FDA. Can you review this particular aspect in terms of the evaluation criteria? Off the top of your head.

MR. ULATOWSKI: Well, we showed a couple of slides of elements of the guidance document in terms of the bench testing, biocompatibility, preclinical, clinical, simulated and clinical.
The panel, though, is primarily concerned—typically any panel that we bring here is concerned with the clinical aspects of guidance documents and not the engineering aspects so much.

I think we have all seen some different things presented or in front of us here and if there's one or two noteworthy items that seems to be worth mentioning to us, then that would be acceptable to us. I don't expect you to go down and try to catalogue, compare and contract everything on those lists.

DR. EDMISTON: When I look at those guidance documentation and evaluation criteria, as you go from bench to a full blown clinical study, if indeed a clinical study is warranted, and in most cases it probably won't be warranted, I think from an engineering perspective you hit that from the bench studies and you can also hit that in the simulated studies, too.

So my take on this is that the evaluation criteria that are currently in place have been well conceived and documented and we can fine-tune these in terms of the type of end users we're studying and eventually with postmarketing types of surveillance. But I'm personally happy with the evaluation criteria that are present in the document.

MS. RYDER: A question for you. Are the current items in this document in compliance with AMMI and ISO standards today?

MR. ULATOWSKI: Well, there is no specific
standard that speaks to the safety features. There's
discussion of development of standards. There are
standards for syringes and needles, those types of things,
but not for these additional features.

MS. RYDER: Okay. I was specifically referring
to the bench testing and the biocompatibility--

MR. ULATOWSKI: Oh, yes, there's adequate
standards with regard to biocompatibility and engineering
tests that can be applied in this instance.

I think one thing with a guidance document, we
try not to be too prescriptive in our guidance document on
how one may approach a certain area of interest. There may
be more than one approach to an engineering test, for
example. I've heard comments about, well, you need to
provide a little more information and end points and
criteria. There's pros and cons to that. You don't want
to box technology in. But I understand the need for people
to get more information sometimes.

DR. EDMISTON: Mr. Palomares?

MR. PALOMARES: To the degree of testing, whether
it's bench, simulated clinicals or clinicals, I agree and
disagree with the panel to a certain extent and I'll work
with the panel here. However, one thing as a manufacturer
that we see is we want to be working off the same playing
ground. What I mean is on microbial challenges--

DR. EDMISTON: Could you speak into your
microphone, please?

MR. PALOMARES: Excuse me. With regard to
microbial challenges, right now most manufacturers use that as the benchmark for getting a needleless system approved, because that's what ODE has been asking for.

However, when you're looking at the various tests that the manufacturers perform, you don't get a consistent result. Sample size, challenge organism, number of activations, point of use—all of those come into a factor of whether this product is safe and effective.

I think from an industry standpoint, we're looking for something more standardized. That way we can always give something where ODE can review it and say this is an apples to apples comparison and this product is equivalent or not equivalent to what's existing on the market.

DR. EDMISTON: Well, that's an appropriate comment and I think what we could propose is that the FDA entertain the development of standardized testing protocol specifically in microbial challenges so that you're right; your competition or whoever is not doing less than you are to demonstrate the efficacy of your device.

Dr. Rutala?

DR. RUTALA: No questions.

DR. EDMISTON: So with the evaluation criteria in place, we feel comfortable with the evaluation criteria, with the caveat that the panel recommends that the FDA look at the development of standardized testing protocols, specifically in microbial challenge protocols, in comparing these devices. Inclusion.
Is the panel in agreement with this?

[Nods from the panel members.]

DR. EDMISTON: Thank you.

Final question for the first response. "How could the results of these evaluations be presented to users? Included in the labeling?" I think Dr. Rutala, that was his last two sentences. That's also been echoed for the past half an hour by the various panel members.

Dr. Rutala?

DR. RUTALA: Let me make a couple of other comments regarding labeling criteria that could be considered.

Of course, labeling should consider intended use, as well as unimproved uses, training required for use, disabilities which preclude use, potential dangers with using the device, and a range of expected reductions in injuries compared to the standard device.

And, of course, we also talk about the labeling issue as it pertains to demonstrating efficacy when there is a hint, suggestion or claim of efficacy in reducing sharp injuries.

DR. EDMISTON: I think your last statement, the expectation of reduction of injuries? There should be a reasonable expectation?

DR. RUTALA: A range of expected reduction.

DR. EDMISTON: A range of expected reduction.

DR. RUTALA: Compared to standard devices.

DR. EDMISTON: Compared to standard devices.
DR. RUTALA: That's correct. Again we're talking about the device that has a claim of efficacy.

DR. EDMISTON: And the benchmark for that could be what's current in the literature.

DR. RUTALA: That's correct, or a comparison with the standard products.

DR. EDMISTON: Do we have an OSHA representative in the room? Could you come to the podium, please? I was told I can't torture you.

Let me ask you a question because we all deal with OSHA.

MR. ULATOWSKI: He needs to identify himself.

MR. LANDKRON: I'm Kevin Landkron with OSHA.

DR. EDMISTON: We understand what our obligations are in terms of training our employees, whether they're full, part-time or contract employees, as they come into our institution, especially in terms of blood-borne pathogens.

Tell me how does OSHA perceive labeling of equipment that we are using within the institution? Do you care about that or are you more interested in what we're doing on our end to ensure the equipment is being used appropriately or safely?

MR. LANDKRON: As far as labeling of a device, I wouldn't think that we would come into that per se. I can't answer definitively. I know in blood-borne we have, as far as contaminated medical equipment, we require that to be labeled. Sharps containers, we require those to be
labeled.

So we do have some labeling requirements, but as far as the labeling of the device prior to it getting into the workplace, I don't know what role we would play in that.

DR. EDMISTON: All right. So I think it gets back almost to the first--very similar to the first question in that if a claim is made, that claim needs to be documented in some capacity so that the user is able to see that claim, either as an insert or through the educational materials that are presented to him by the company.

Does that sound reasonable, Mr. Palomares?

MR. PALOMARES: It does sound reasonable. Unfortunately, the perspective from industry is that your directional insert that comes in with your case of product usually ends up on the floor of central supply. It doesn't get to--

DR. EDMISTON: Oh, you're right. You're right. You're right. There is an onus on the institution in terms of ensuring that, but that's not the FDA's venue.

MR. PALOMARES: No, it's not.

DR. EDMISTON: That's why I brought up the OSHA guy.

So you're right. Compliance is an institutional issue, from our perspective. But you're in agreement that if claims are made, or even if claims aren't made, if this is a technology that requires education on the part of the
handler, and virtually all of these devices do, that this is clearly spelled out—it's reasonable to have this clearly spelled out within the product, either as an insert or as a poster, as Dr. Fisher has indicated, or some type of educational aid.

MR. PALOMARES:  It is reasonable to expect that, yes.

DR. EDMISTON:  Does the panel have any other comment?

DR. RUTALA:  The only other comment that I would make is that this question seems to go beyond just the efficacy issue and I was wondering if we should consider other issues, such as intended uses, unapproved uses, training required for use and disabilities which preclude use, such as a sight-impaired person to use the device, or potential dangers with using the device.

So beyond that issue of efficacy for a device making a claim.

DR. EDMISTON:  Since I'm one of those individuals who's never read one of those inserts, explain to me. Is it clearly defined in the inserts the intended use of the device?

MR. PALOMARES:  The device usually has its intended use on the directions for use or its package labeling. So it states what it's used for.

DR. EDMISTON:  Okay. I think in terms of—well, within an institution in terms of visually impaired individuals, I suspect the greater onus is placed upon the
Marcia, how do you feel, in terms of the education of that person?

MS. RYDER: Indeed, but once again it goes that we need to begin thinking beyond the institution and into the home care setting.

I believe, if I'm not mistaken and we can certainly address this, that many of the things that Dr. Rutala detailed are already part of requirements of labeling. Is that not true?

MR. ULATOWSKI: Well, there's labels for products, syringes and that. A lot of the instructions for use that were mentioned are not included because they're commonly understood sorts of provisions.

But for safety devices, I would not consider them commonly understood and would expect more information in labeling.

DR. EDMISTON: Yes? We have a volunteer from the audience.

MS. DUCMAN: Again my name is Kathryn Ducman, registered nurse, director of clinical services with Retractable Technologies.

My question on this issue pertains to products already in use. As you mentioned, standard syringes that have such an historical perspective implied uses but, for example, they are labeling as nonreusable products when they are inherently reusable.

I direct you to remember that reusability is
certainly an issue of safety, whether that reuse is intentional or inadvertent.

And when you put that in perspective with the clinical situation, a very volatile and uncontrollable setting, to label something as nonreusable might be physically impossible. And how will the FDA regulations back-track and look at that issue in regard to standard products as it does to safety products?

MR. ULATOWSKI: Well, that's a whole other issue for another day, actually.

DR. EDMISTON: I think that takes on two issues. First of all, we're talking about sharps instruments and the issue today is not--

MR. ULATOWSKI: That's reuse of single use only instruments and we're addressing that separately.

DR. EDMISTON: Right.

MR. ULATOWSKI: We do have a policy forthcoming.

MS. DUCMAN: But as the reuse pertains to sharps injuries. I mean reuse is either inadvertent or intentional and how can you label something as don't reuse when it is inherently reusable, whether that reuse is the inadvertent stick that occurs in an uncontrollable setting, clinical setting, or an intentional use, which is often what is thought of in opposition to sharps injuries?

MR. ULATOWSKI: I understand what you're saying. It's somewhat outside the purview of exactly what we're talking about today but your point is well noted and we are considering that aspect in terms of safety with reusable
products or single use only products.

MS. DUCMAN: Thank you.

DR. EDMISTON: So let me poll the panel. In reference to Dr. Rutala's statement, your statement in terms of labeling, in terms of the criteria for labeling, intended use must be thoroughly documented and present on the insert and available for the user.

Also, how do we make this information more presentable to the user? I would suspect that we could propose to the FDA that we look at strategies either educational, tapes, because I know some of these devices--I do look at the tapes--some of these devices do come with tapes, that these types of educational tools are inherently valuable to our health care professionals and we use them for in-services.

Is the FDA in agreement with that?

MR. ULATOWSKI: [Nods.]

DR. EDMISTON: Okay, let's move on to question number 2. We have 20 minutes left and let's try and move along here. This is the toughest part of the whole format and I think we'll move quite rapidly now.

"Currently sponsors submitting applications for needleless access devices--intravenous systems that do not require the use of a needle--are asked to demonstrate that their device is substantially equivalent by providing nonclinical bench data to demonstrate that their device does not increase the risk of microbial contamination of the fluid pathway, validation of the cleaning method, and
instructions for use. What additional type of information should be considered for our premarket review?"

And this we've already addressed in terms of the FDA should attempt to develop standardized testing protocols for microbial contamination. Is the panel in agreement with that?

[Nods from the panel members.]

DR. EDMISTON: Number 3, "What mechanisms does the panel recommend to the FDA to increase user awareness of the safe use of these devices?"

Now let me ask the FDA on this. You're proposing, the FDA is proposing that they would provide documentation to the public in terms of the way in which these devices should be used, when they should be used?

MR. ULATOWSKI: That's all part of it. And perhaps Dr. Joseph would want to add to that.

DR. EDMISTON: Could Dr. Joseph give us a brief synopsis.

DR. JOSEPH: As you say, that is indeed part of the it but also we were thinking in terms of mechanisms, and you touched on some of them--tapes, posters. You know, what vehicles would be most effective to the users of these products that we would be able to get the message to them?

And I think in terms of the message, that's part of another question.

DR. EDMISTON: So we're proposing multi-media type of documentation.

MR. ULATOWSKI: We haven't been as broad-based as
you're discussing now in our evaluations, but we incorporate an expectation in regard to these aspects.

DR. EDMISTON: It always amazes me that the OSHA guys never want to get involved in this part of it. I'm picking on you; I'm sorry about that.

So how does the rest of the panel perceive this? Let me ask Mr. Palomares first, representing industry.

MR. PALOMARES: Well, as a member of industry, what we try to provide is adequate information such that a user facility can train their personnel, whether that's adequate directions for use, whether that's having a product specialist on site during the trials and conversions period, whether it's tape, whether it's demonstrations. That all does occur.

DR. EDMISTON: So you think anything that would enhance the appropriate use of your devices, even on the part of the FDA, to demonstrate how these devices should be used, that would be reasonable?

MR. PALOMARES: I think it already occurs. I don't think it needs to be part of the regulatory process simply because in order for a facility to take on this, they're asking the manufacturer to provide this information. They're asking to train us, demonstrate how this product is used, give us some support.

To have FDA now regulate and saying this is adequate support or not, does it provide a benefit?

DR. EDMISTON: As part of your marketing of these devices, you actually provide in-service for most of these
devices, correct?

MR. PALOMARES: That is correct.

DR. EDMISTON: Marcia, as a user, how do you perceive that? Is the in-service usually appropriate? Is it comprehensive enough?

MS. RYDER: For the most part, industry does assume a large responsibility for doing that and in most good companies I would have to say it's done pretty well. Otherwise if they don't educate properly, their device doesn't work. So I think they do take a major step in doing that.

Again back to the home care issue and the end user, because the scope here is so huge, perhaps a suggestion to the FDA would again consult with patient educators in terms of studying and look at those mechanisms by which patients learn best and perhaps incorporate some of those systems into the pieces that you develop.

DR. EDMISTON: Mr. Dacey, I haven't forgotten you.

MR. DACEY: That's fine. You touched on an area I only have 100,000 words on.

After years in the world of preparing patient education materials and test-driving many, many formats and mediums and also studying the whole world of marketing, in fact, I think it would behoove the FDA to look at the private sector to see how they strive to influence consumer decisions.

And I've even come to the point, after all these
years, of questioning the term "patient education." Are we really educating or are we influencing? We're seeing shorter attention spans. We're seeing, when you get into the younger generation, what I call Generation Extreme, you see a whole different demographic profile.

So people, especially when you get into self-care issues, when they have the need--they aren't even aware of these issues until they are confronted with it in their personal lives. That is the same with their families, who may be operating in the home care setting.

I think there is no well defined, totally effective medium for communicating to all patients and to all caregivers the information that you want to provide. I think you've got to almost customize it. And very often it becomes essential to do it on a one-on-one basis.

My book shelf is crowded with instructional videos, some of which I haven't even gotten around to seeing yet. And now with the Internet and DVD and all the other stuff that's coming down the pike so rapidly, all I can do is urge you to look at the private sector, find out what they're using, what works, and consider, seriously consider customizing communication to providers who are, in this case, self-care perhaps, and consumers.

DR. EDMISTON: Dr. Fowler, do you have any comments?

DR. FOWLER: I would suggest that FDA leaves any requirements very, very broad-based. And while the concept of requiring appropriate training and education I think is
necessary, the specifics of that training and education, I think, should be totally left up to the--I think a recommendation should be that whatever appropriate training and education vehicle the manufacturer chooses, if it appears appropriate to FDA, would be allowable. I would think that overregulating or overspecifying requirements in this area would not really be of any benefit.

DR. EDMISTON: Dr. Rutala?

DR. RUTALA: Yes, just two comments. First, I do agree with the preceding comments but I would like to possibly allow the panel to consider a variation of a couple of the comments.

First, the issue of training, user training. I was wondering, like what is done for the OSHA blood-borne pathogen rule, where there are certain criteria that must be met to essentially achieve training on an annual basis, if there isn't some indication here for the FDA to consider some minimal criteria as it pertains to user training, minimal criteria such as how to use the device, the indications, the contraindications, the hazards, the material incompatibility issues, things such as that.

I agree that that should not be very prescriptive, it should be broad-based, but the criteria should possibly be considered.

The second point is the issue of competency testing of users. It's becoming very common now in health care to recognize the need for competency testing. That is, we can train persons by showing videos and by asking
them to listen to a slide presentation but very commonly, that does not result in a competent person, a person capable of performing a task.

So there's more commonly now competency testing to ensure that the person performs the task after hearing the user training.

So the two points that I would like to bring up are the issue of considering minimal criteria, and I don't know that we decide what they are—we've addressed a few of them but minimal criteria for user training of these needleless devices or protective sharps.

And the second, when indicated, competency training, so that it's not merely a matter of seeing it done but actually performing it and ensuring that the person knows how to perform it properly.

DR. EDMISTON: In reading through this, it's obvious that 3 and 4 really run together. Let me read 4. "Is there a need for educational programs for use of sharp injury prevention devices? If so, what content should be included in educational programs to encourage the safe and effective use of these devices?"

I think in terms of your comments that the FDA's position should be that the information, the insert information provided by industry should describe the intended use of the device in which it should be appropriately used and also should address, as you've indicated, the competency, the potential competency of those individuals who are using the device.
Now in terms of how this information can get across, I think there is some area of debate—whether it's part of an in-service by your colleagues in the industry or is there some formal mechanism by which the FDA puts together a series of educational tapes and then provides those to the end user?

I don't know if that format needs to be completely worked out but it sounds to me, from listening to Dr. Joseph, she is addressing this particular area in terms of education. Is that correct?

DR. JOSEPH: That's correct.

DR. EDMISTON: I would like to say one more thing. The home health care area is extremely important and it's come up several times. And I think the level of sensitivity should be such that that also should be an area of priority for the FDA.

DR. JOSEPH: We have certainly heard it.

MS. RYDER: Again one more comment in regard to the home care area. I would suggest that one would be careful at how those requirements are placed on the manufacturer or the institution in educating the home care patient. And the reason for that is because we're all very much aware of the reimbursement issues, which are getting much worse instead of better.

So the time that nurses have to spend in educating patients becomes less and less and less. And now we're suggesting that—I'm suggesting that we be careful on where we put that responsibility.
DR. EDMISTON: I think this whole issue of home health care is really a black box that's not going to be clearly defined by this criteria document, but I think we need to be thinking about it in the work that Dr. Joseph and Dr. Fisher and others in the audience are alluding to needs to be considered, especially in future revisions of this documentation.

Is the FDA in agreement with our comments?

MR. ULATOWSKI: [Nods.]

DR. EDMISTON: Number 5, "Are there other areas of the guidance document that need to be revised?"

I keep hearing very clearly that we need to have a mechanism for postmarketing surveillance. We've heard from Dr. Fisher that pilot testing as she defines, which I really look upon as product testing within the institution, is defined as postmarketing. She suggested there should be a premarket-type pilot, and we've talked about that.

But in terms of this particular question, I really feel there should be some mechanism in place to look at postmarketing surveillance for these various devices.

Now will we get 100 percent compliance? Unlikely. But I think this should be a consideration that is entertained by the FDA.

Let me panel the panel.

MS. RYDER: No added comments.

DR. EDMISTON: Dr. Rutala?

DR. RUTALA: [Nods.]

DR. EDMISTON: Mr. Palomares?
MR. PALOMARES: [Nods.]

DR. EDMISTON: Mr. Dacey?

MR. DACEY: I agree.

DR. EDMISTON: Terrific. That was painless.

Yes? We have a guest.

MS. WILBURN: Susan Wilburn from the American Nurses Association.

I wanted to add an additional example of information that's available, a database about device-specific injury rates. That is a database called Epinet that is available from the University of Virginia in Charlottesville that is complementary and incorporated in some ways in the CDC database.

I wanted to reiterate what the doctor from the CDC was talking about—the Cal/OSHA standard for needle stick reporting will provide device-specific data and the medical reporting guidelines that have been proposed and will be finalized this year, according to OSHA, also will include a change in needle stick reporting.

So the federal OSHA blood-borne pathogen standard will include all needle stick injury reporting, not just those needle sticks that went on to cause an infection later.

DR. EDMISTON: Thank you very much. We can't forget Jeanine Jacgertz's contribution to this field. That's an absolute benchmark for many of these future studies.

MS. WILBURN: As you've been referring to what's
happened in the health care field in terms of downsizing and really tightening up of budgets, one of the things I've heard in the last couple of months from institutions related to manufacturer-provided education on new devices is that I've had nursing administrators say that the manufacturers have told them that they have to pay for that kind of education.

So I think that clarifying recommendations for education for manufacturers is very important.

DR. EDMISTON: Does the panel have any more recommendations or--oh, we have the OSHA fellow. She says round three.

MR. LANDKRON: Just very quickly, 3 and 4 are about educational programs and formats and things of that sort. We do have training requirements in the standard. Dr. Rutala makes a good point, where we spell out certain criteria that we expect to be met in that training.

DR. EDMISTON: I knew you guys were in there somewhere. Thank you very much.

Are there any final comments from our panel members?

[No response.]

DR. EDMISTON: If not, I'd like to ask the FDA if we have addressed the questions sufficiently.

MR. ULATOWSKI: [Nods.]

DR. EDMISTON: If so, I will now close this part of the meeting so that we can break for lunch. We will reconvene at 1:30. Thank you very much.
[Whereupon, at 12:30 p.m., the meeting adjourned for lunch, to reconvene at 1:30 p.m. the same day.]

AFTERNOON SESSION

[1:35 p.m.]

MS. O'LONE: I think we'll go ahead and start for this afternoon, in the interest of being on time.

I'm Martha O'Lone. I'm the executive secretary of the General Hospital and Personal Use Devices Panel and I'd again like to welcome the audience to the afternoon portion of this meeting.

And again for the purposes of transcription I will ask all persons addressing the panel to identify themselves and their affiliation and if they have any interest or direct involvement in medical devices.

I would now like to reintroduce the chair for the panel, Dr. Charles Edmiston, who's here on my right. He's a professor of surgery and he's also a hospital epidemiologist at Memorial Lutheran Hospital at the Medical College of Wisconsin, Milwaukee, Wisconsin.

ISSUE: GUIDANCE DEVELOPMENT FOR JET INFECTORS

DR. EDMISTON: Thank you very much.

We now would like to begin the afternoon portion of the 34th General Hospital and Personal Use Device Panel. This afternoon we're going to discuss guidance documentation for jet injectors.

And for those of you who were not in the audience this morning I would like my colleagues on the panel to
reintroduce themselves, starting with my colleague on the right.

DR. FOWLER:  Dr. Joe Fowler, dermatologist, University of Louisville, Louisville, Kentucky.

DR. RUTALA:  My name is Bill Rutala.  I'm director of hospital epidemiology, occupational health and safety at the University of North Carolina Hospitals and professor in the Department of Medicine.

MR. PALOMARES:  I'm Salvodore Palomares.  I'm industry representative.  I'm the manager of regulatory affairs for ICU Medical.

MR. DACEY:  Robert Dacey, consumer representative from Boulder, Colorado.

MR. ULATOWSKI:  Tim Ulatowski, director, Division of Dental, Infection Control and General Hospital Devices, FDA.

DR. EDMISTON:  And we have one more panel member who is MIA, who I suspect will be here momentarily.

This is a great entrance.

MS. RYDER:  I'm Marcia Ryder and I'm a nurse consultant in vascular access and I'm a doctoral candidate at the University of California San Francisco in the Department of Physiological Nursing.

MS. O'LONE:  Okay, and now we'll have Tim Ulatowski, the division director for Dental, Infection Control and General Hospital and Personal Use Device Division provide an overview on the topic for this afternoon's session.
MR. ULATOWSKI: Thanks again, Martha, and welcome back to the panel for the afternoon session.

Like this morning, we are not doing a premarket evaluation of any devices. Rather, we're having a discussion regarding a technology and obtaining opinions and recommendations from the panel on a particular type of device, generally called, for the afternoon, jet injection technology, which has quite a long history in regard to the fundamental technology, which I think will be touched upon, but also some interesting new technologies coming along that fall within the general umbrella, I'll call it, of jet injection technology.

Within this large grouping of current or future products, we do have different types of injectors that a subsequent FDA person will talk about, and delivery of different products, FDA-regulated products by these injectors, both drugs and biologics.

This being a drug and biologics delivery device, we are not alone in this Center in the evaluation of these products, typically. When the need arises, we will obtain the opinions of our drug or biologics centers on drug or biologic aspects with the injectors. And in fact, some of the products that may be touched upon today are, in fact, primarily regulated by our Center for Drugs and Center for Biologics, those injectors that may be prefilled with a biologic or a drug when it's sold to an end user.

There are some significant safety concerns that
you hear about with these products and a very great potential future need for new technologies.

We intend to develop a guidance document based upon what we hear today and what we have heard already in other forums. I think there's a definite need for guidance in this area and we intend on moving forward.

We also intend on incorporating as much as possible any standards that might be created to address this technology, of which there is some activity now.

As with this morning, I have a particular interest as the director in regard to these products. We deal with quite a range of manufacturers in the medical device area, from very large manufacturing facilities with hundreds, even thousands of employees and regiments of people who are in the regulatory affairs area down to very small operations who create and develop and try to finance their operations.

And that's really the challenge in front of us. As a center, we have to deal with both ends of the spectrum in the device area. One of the critical areas that we have to deal with with this technology is when clinical data are needed and providing some criteria along those lines, of when more than just bench or engineering information is necessary.

So we'll consider your recommendations, comments, reflections today and those of the public and we intend on publishing a guidance through our good guidance practice procedures, in which we post a draft on the website and
obtain public comment for a period of time and then we finalize the document.

So without further ado, I'd like to introduce Von Nakayama, Captain Nakayama, who will talk about this technology from our perspective in a little more detail.

CAPT. NAKAYAMA: Thank you, Tim.

It's my pleasure to give you a background on jet-injected devices. The terminology jet injector is, and I think Dr. Weniger will discuss this in a little bit more detail, is under a little bit of debate. Some people may prefer to call it needleless injector systems or needle-free injector systems.

In any event, as I progress with my overview, I'd like to remind you that this is a very important topic, although it is quite pointless.

[Laughter.]

CAPT. NAKAYAMA: A jet injector is a preamendment device that's an alternative means to administer a drug or biologic. Jet injectors can be labeled for the specific administration of specific compounds, such as insulin, or for general purpose use, such as IM injections of vaccinations. Jet injectors are designed for personal use or multi-patient use.

The prevalence of jet injector use may increase due, in part, to increased public health awareness of needle stick injuries, sharp disposal, reuse of single use needles, and the possible cost-effectiveness of mass immunization programs.
Two things jumped out at me over the weekend that I just want to interject here. Malaria infects 275 million people a year. TB deaths account for 1.5 million deaths a year. Treatment of these epidemics may be most effective, cost-effective, using jet injectors rather than a traditional needle and syringe.

The classification of device. Currently a jet injector is defined as a nonelectrically powered fluid injector and classified in 21 CFR 880.5430. I will get to the definition on the next slide. Jet injectors are Class II devices and subject to regulatory controls that are identified in 21 CFR 860.3.

Part 21 CFR 880.5430, nonelectrically powered fluid injector--the jet injector that we're talking about--is a device used by health care providers to give a hypodermic injection by means of a high velocity jet fluid. This fluid penetrates the surface of the skin and delivers a fluid to the body.

As a Class II device, the jet injector is subject to both general controls and special controls. General controls include items such as registration and listing, reports and records, and conformance to the general provisions of the Food and Drug and Cosmetic Act, such as prohibitions against adulteration and misbranding.

There are special controls and the type of special controls that may apply to Class II devices include performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines,
including guidelines for clinical data, and other actions deemed appropriate by the agency.

Jet injectors themselves are complex and have designs ranging from the relatively simple to highly sophisticated. There are two broad categories based upon the intended user. The first is a personal use device designed to be used by a single patient in the treatment of a disease or health condition.

The second is for multiple patient use, where the device is used by a health care provider, generally for public health initiatives like immunization programs, and can be categorized into three types: low, medium and high workload devices. High, medium and low workload devices are terminologies recognized as developed through various CDC-sponsored conferences on jet injector devices.

Jet injectors can be used to administer different forms of a drug or biologic, including liquid doses, powered formulations and coated particles. The dosing sites or target tissues can be mucosal membranes, the skin, epidermis or dermis, subcutaneous tissue, and intramuscular tissue.

The mechanism of action of a jet injector is the acceleration of a drug or biologic using spring or compressed gasses to high velocity that will deposit the drug or biologic into the tissue without any part of the device penetrating the tissue. Jet injectors use nozzles instead of needles and may have a single nozzle to inject a single injectate in a single stream or an admixture in a
Multiple nozzle designs, on the other hand, can inject a single injectate or admixture through several streams or simultaneously inject several different injectates in one action.

There are several important review issues in the evaluation of a jet injector for safety and effectiveness. The first is the identification of an appropriate legally marketed device to which a jet injector device can be compared. The CFR definition of a jet injector is--I'll repeat it again--a device that injects fluids to the body through the skin. We have used an elastic interpretation of "substantial equivalence" to include injectors that inject solids--powders and particles--not only through the skin but in some cases to the skin.

Advanced technologies, new medications and emerging concepts of immunization may require rethinking of how the jet injectors are to be reviewed and evaluated.

The second issue is that a jet injector is reviewed in three distinct parts. One part is on the physical and mechanical properties of the device--its physical specifications, materials of manufacture, biological and chemical compatibility, cleaning, disinfecting and sterilizing of the device, and the human factor issues that affect its proper use.

The second review concern on this three-part review looks at the performance characteristics of the jet injector and is an evaluation of the data that has been
provided to establish the performance specification of the device. Data may include nonclinical data, such as bench testing for functionality, reliability and appropriate conditions for use, and simulated use studies, or valid scientific data that comprise evidence to support the safety and effectiveness of the device.

Valid scientific evidence is defined in 21 CFR 860.7(c)(2). That section also defines what valid scientific evidence is not. And I have some slides for that if you want to review those items. They're the last two slides in my presentation.

The third issue is the evaluation of the jet injector as a combination project, a device with a drug or biologic component. There can be questions as to whether a drug or biologic can be jet injected and if the jet injection of that drug or biologic could cause a physical change to the drug or biologic through incompatibility with the device or denaturing of the drug or biologic when subjected to high pressures, high velocity forces.

There's also a question as to whether or not the drug or biologic will have stability issues when the drug or biologic is incorporated as part of the device, either through a modification of the original container closure system--the vial--or as it's put into the vial of the device.

Then there's the issue of mutually conforming labeling. Is the device labeling consistent with the drug and biologic labeling, and vice versa? Are there possible
conflicts that could arise from the use of the device with the drug or the biologic? Most drugs and biologics are labeled with the route of administration, such as subcutaneous, intramuscular IV. The method of administration is generally not specified.

The development process of a drug or biologic might have included dose administration only by needle and syringe. These data may not be sufficient to conclude that the drug or biologic is suitable for administration by jet injection.

This is of particular concern because of the significant differences between a dose administered by a jet injector as opposed to one that's been delivered by a needle and syringe. A jet injector, for instance, uses nozzles instead of a hypodermic needle. The injection pressures are high, with high velocities, whereas with the needle and syringe, it's low finger pressure and slow flow.

A jet dose is all or none versus the dose control that's available through a needle and syringe, including partial dosing.

A jet dose is dispersed. The analogy is it's like a shotgun, compared to the concentrated dose, a single bullet, that is evident from a needle and syringe injection.

The jet injector can involve multiple tissue dosing versus single target tissue from needle and syringes. Various dose forms can be administered through a jet injector. The needle and syringe will inject a liquid.
There are also multiple fluid paths and multiple drugs that can be administered in a single jet injection. The concomitant dose is a single drug and fluid path.

I hope I haven't used my Andy Warhol 15 minutes, but this concludes my overview. You'll receive additional information about jet injection devices from the speakers who will follow me but I hope that this overview has provided you, the panel, with a foundation upon which to consider the three questions which were mailed to you and on which guidance is solicited.

The first item is, "What are the key issues that should be considered in the premarket evaluation of jet injectors?"

Number 2, "What data could be appropriate to address each of the above issues?"

And 3, "If and when clinical data are appropriate, what are the panel's general recommendations regarding the form and content of the studies to derive the clinical data?"

And while that's up, I think what I will do is just flip through the next two slides to show you what, as you think about clinical data, what valid scientific evidence comprises.

Well-controlled investigations, partially controlled investigations--I can read that but you can read it as well as I could.

And this is what they're not.

And with that, unless you have any questions, I
will defer to Bruce.

DR. EDMISTON: Thank you.

MS. O'LONG: And our next presenter is Dr. Bruce Weniger from CDC, who will present on needle-free technology.

DR. WENIGER: My name is Bruce Weniger and I'm with the National Immunization Program at the Centers for Disease Control and Prevention.

I want to thank Martha O'Lone and the other staff of the FDA for inviting this presentation. And there are hand-outs of my slides on the table outside that were put out during the lunch hour.

In addition to the dangers of needle stick injuries that were the subject of this morning's discussion, in much of the world needles and syringes pose a serious threat due to their improper recycling and reuse without proper sterilization.

WHO estimates that upwards of half the injections in the developing world, including for vaccines, are unsterile and thus unsafe, resulting in major burdens of iatrogenic disease and WHO estimates in the world there have been 8 million infections caused in this manner for hepatitis B, 2 million for hepatitis C and 75,000 HIV infections.

In addition to transmitting blood-borne diseases, needles also pose obstacles to immunization, which is one of the most cost-effective interventions to prevent disease. Just a decade ago in this country, to fully
vaccinate a child in accordance with the recommended immunization schedule required only eight injections. Today is requires a minimum of 14 injections, and this number will increase to 16 injections next January when the oral polio vaccine is entirely replaced by the injected polio vaccine.

And many wonderful new vaccines for diseases not yet vaccine-preventable are in the pipeline to be added to this schedule. But as those of you who have taken your children for their vaccinations know, doctors and nurses are uncomfortable, as well as parents and children themselves, administering multiple vaccines or receiving multiple vaccines, as documented in various studies from which 20 percent to 80 percent of the respondents either objected or deferred some vaccinations, which may result in costly repeat visits or even missed protection.

We believe that needle-free injection technology presents a practical solution to overcome this and the other drawbacks of needles and syringes that I just mentioned.

Jet injectors are devices to administer drugs by shooting through the skin a fine stream of liquid under high pressure through a small orifice. The first commercial needle-free injector in the United States was the Hypospray shown here, developed in the late 1940s, and this first model was developed primarily to reduce needle phobia among diabetic children.

Over the decade since that first indication, a
variety of other needle-free injectors targeted for insulin users have been developed into a very small but established niche in the diabetes market. Since insulin injectors are usually owned and used by only one patient, there’s little concern that some have permanent middle nozzles, as shown here in this AdvantaJet.

More recently developed models for insulin users, such as this Vitajet, have begun using disposable cartridges made of clear plastic to hold the drug. To save on costs, such cartridges are often reused up to several weeks by the same patient before replacement. This late model Medi-Jector is another injector which uses a disposable cartridge.

Another recent entrant into this market is the Injex, also with a disposable cartridge. It’s smaller than the previous injectors you saw because the heavy and sturdy spring cocking mechanism has been off-loaded into a separate item.

Unlike the previous devices shown, this J-Tip is unusual as a completely disposable single use only device. The user loads the drug through the orifice, through this protective cap into the chamber, and pressurized gas stored here drives the drug into the tissue.

Now let’s turn away from devices oriented to the insulin market, even though they also deliver other drugs subcutaneously, as well. This Biojector 2000 is the first injector with a single use disposable cartridge marketed for immunization and it also has other indications. It is
sold primarily to clinics and doctors, rather than to individual patients.

Another device still in research and development is also aimed for use in immunization. The SensaJet is now undergoing clinical vaccination studies in Cuba.

This Intraject device still in development is similar to the J-Tip that you saw earlier in that it is completely disposable and operates by a charge of pressurized nitrogen in here. What is novel about this Intraject is that it contains a borosilicate glass liner held within the plastic nozzle here. It will be prefilled at the factory with vaccine or other medication.

Thus the Intraject steps beyond the realm of a device and really represents the primary packing of a drug or biological. Use of the more common glass liner instead of polypropylene may facilitate satisfying packaging regulations.

This PenJet model, also in development, is designed to administer drugs or vaccines in cartridges also prefilled by the pharmaceutical company but unlike the Intraject you just saw, this injector device would be reusable.

Another example of a prefilled needle-free cartridge for use in a reasonable device was brought to an advanced stage of development with several published clinical trials by Pasteur Merieux Connaught. This Imule cartridge is about the same size and shape as a standard unit dose vaccine vial.
Now almost all the previous devices I showed you have the disadvantage of requiring the health worker or end user to fill them by manually transferring the vaccine or drug from another container. This is inconvenient, takes time, and often expends a needle and syringe or some other transfer container.

CDC, WHO and PATH strongly believe that the prefilling of a small, simple needle-free vaccine cartridge that would serve as its own primary packaging would represent a tremendous advance for immunization practice in both developing and developed countries. The cartridge would be included in the vaccine price, thus offsetting the cost of a standard vial.

We are working to promote a universal, open standard and source for such cartridges to be available to all pharmaceutical and jet gun manufacturers on an equal basis.

The universal standard for 33 millimeter film cartridges has been a boon to both the makers of cameras and film. And the VHS standard has been a boon to both movie studies and VCR manufacturers and video rental stores. Similarly, a common standard for needle-free cartridges ought to help the now-struggling cottage industry of jet injection manufacturers while, at the same time, improving compliance with vaccination and thus hopefully getting more vaccine used.

I would like now to focus on a different category of jet injector--the high speed devices used for mass
immunization campaigns, controlling epidemics, and vaccinating large numbers of soldiers. But first I'd like to credit Dr. Robert Hingson, who contributed so much to the science and development of this field, including the early low workload models I showed you earlier, as well as the high workload models to follow. Dr. Hingson was a uniformed Public Health Service medical officer early in this career, like many of those in the room here today. And this is the New York Times obituary in 1966 of this father of jet injection.

The most common high workload device in the world today is the Ped-O-Jet type device, which is being used here by Dr. Hingson to immunize patients against polio and measles in Costa Rica in 1967. That one campaign in that one small country immunized in one year over 800,000 persons.

Since the early 1950s, such high workload devices have been used around the world to deliver hundreds of millions of vaccinations, if not billions by now. For example, in the early 1990s Brazil purchased 10,000 of these Ped-O-Jets and immunized 50 million children up to age 15 in mass campaigns to control measles.

In the last five decades, such devices have been made by a variety of companies, such as these Hypospray trade name devices. High workload devices usually accept multi-dose vaccine vials and automatically refill an internal injection chamber between each injection. They're often powered by foot pumps or pressurized gas or
electricity and springs and can vaccinate hundreds of patients per hour. Here are some Dermo-Jet high speed models.

One distinguishing feature of existing high workload devices is that they have reusable metal nozzles and internal fluid pathways that are reused and not ordinarily sterilized between consecutive patients.

Another common model is this Med-E-Jet shown here. One Med-E-Jet device, however, was implicated in the first and to date, only known case of blood-born disease transmission between patients. Before getting into the issues raised by this, let me briefly review some clinical aspects of jet injectors.

Over the years, a variety of medications, such as those listed here, in addition to vaccines, have been reported in the scientific literature to be successfully and safely delivered by jet injectors. The published data for this are contained in a bibliography on needle-free injection that we maintain and a somewhat mistaken website address. We're now posting this bibliography to make it more convenient for people to obtain it and we'll be periodically updating it. If you'll send me an email--my email address is in the hand-out--I'll be glad to give you the current website address to get that bibliography.

Focussing just on the immune response to vaccines, jet injectors have usually been found to be as good as and often better than the immune response achieved with traditional needles. There's no good data on why this
immune response is often enhanced but it may be due, if we may speculate, to the somewhat different dispersion of the vaccine compared to needle vaccination or perhaps because some of the dose is always left in the skin, which is rich in antigen-processing cells.

You can see here the wide variety of both live and inactivated vaccines which have been successfully demonstrated effective with needle-free injectors.

On the safety side, controlled clinical studies of jet injectors have often found somewhat higher rates of local reactions, both immediate and delayed, compared to needle and syringe.

The pain issue is not as carefully studied and the results are mixed. Despite the claims of reduced pain in early and often poorly controlled studies, I'm not yet convinced that they always have less pain. In any case, it seems to depend on both the device and the vaccine used.

Adjuvant vaccines more frequently seem to provoke immediate pain compared to needle and syringe. Other local adverse events include occasional blood at the injection site and rarely, laceration and other traumatic injuries are reported, but probably no more commonly than with needles.

Tissue deposition tends to be diffuse, in a generally conical shape with the apex at the skin. The drug tends to follow the path of least resistance, often glancing off muscle fascia, especially if the angle of penetration is not perpendicular.
Where the drug ends up depends on a variety of factors, as listed here, related to the device or to the operator or to the patient. In actual reality, it's hard to predict precisely where a dose is going to end up.

But is this really much more different from with needles, in which a nurse must estimate the thickness of the patient's fat for at least an IM injection and then decide how long a needle to use and occasionally may misjudge the proper angle and depth of penetration?

The devices listed here in this bullet have sufficient power for IM injection but it's not certain that they always achieve it. But as long as the dose works empirically, does it really matter? Good results have been found for several IM vaccines, even hepatitis B. And you may recall that hepatitis B had a problem when it was being delivered with needles in the gluteus. It was believed the lower seroconversion that was found was due to the occasional deposition into fat and it wasn't really getting into the muscle. And yet hepatitis B is documented to have high seroconversion rates when delivered with jet injection.

This is an x-ray of a living human biceps, comparing simultaneous intramuscular injection between a needle, which is the upper contrast injection, and the Hypospray injector, the lower contrast one, and you can see how the contrast appears to spread along the muscle fibers, with perhaps the Hypospray dose spreading a bit faster. And by 45 minutes later, most of both injections have
This is more recent magnetic resonance imaging of simultaneous subcutaneous injections in a living human thigh. The needle dose in the upper left position of these four shots is the needle dose and the jet injector dose is the one in the central right.

When the volunteer walked around between the initial dose at 2 minutes here and here at 48 minutes, you can see that most of the dose was gone but when the patient was immobilized, most of the doses remained in place.

This cadaver injection photograph was kindly shared with me by Weston Medical. It illustrates a somewhat conical and diffuse distribution of the dye, which was injected from the center of the black circle marked here on the skin. Note that it doesn't appear to penetrate the underlying muscle, perhaps only 2 centimeters or so underneath the skin.

This illustration from the Lancet was from injection of dye by a J-Tip device in vivo into breast tissue prior to a mastectomy. In addition to coloring the fat below it, which is a bit difficult to see, notice how well the blue dye diffused laterally and superficially to permit its visualization through the skin.

Now the great variation in where jet injector doses end up is revealed in this product brochure and the next slide I'll show you for the Biojector 2000. Bioject varies the syringe size and thus the orifice size as a means of achieving different depths of penetration. Based
on magnetic resonance imaging this data was obtained and it found that almost one-third of the number 3 syringe here, only 29 percent of the injections went into muscle or actually got into muscle, even though they were intended for subcutaneous use.

Now let's look at the intramuscular injections in the next slide, please. Here you see the various syringe sizes intended for intramuscular injection and you can see that for only one-half to two-thirds of the time did these various orifice sizes actually deposit their dose intramuscularly. In other cases it was left on the surface of the muscle.

So once again I would ask if the clinical results are good from controlled trials, does it really matter where the dose ends up? I wonder if we had done similar studies of multiple IM injections with needle and syringe, how often we would find that the intended target tissue was missed.

Let us now return to the issue of the safety of multiple use nozzle jet injectors. In the mid-1980s one Med-E-Jet device, as I mentioned earlier, was documented to cause a hepatitis B outbreak in California. Several dozen confirmed cases were identified who had received multiple hormone injections in one weight loss clinic. There was no evidence of problems in other branches of this chain of clinics using similar devices for similar injections. As part of the investigation, CDC did laboratory testing of the Med-E-Jet.
The Ped-O-Jet device, another device I showed you, was also tested as a control and most of the results were reported in this 1990 Archives of Internal Medicine article.

First, a chimpanzee carrier of hepatitis B surface antigen was inoculated with both jet guns and in several cases visible blood appeared at the injection site. Nevertheless, when they looked at subsequent fluids ejected from that jet gun into vials, they could not detect hepatitis B surface antigen.

These are close-ups of the nozzles of the two devices, the Ped-O-Jet on the left and the one implicated in the outbreak on the right.

After failing to detect contamination with hepatitis B antigen in the downstream ejectates after injecting the infected chimpanzee, they then intentionally contaminated each nozzle of the device with infected serum, serum containing HBsAg, and then looked in subsequent fluid ejected from that gun, as well as various parts of the gun.

After intentional contamination of the nozzles of the two devices, the Ped-O-Jet and the Med-E-Jet, in both devices hepatitis B antigen was detected in from 6 percent to 80 percent of the samples of the next discharge into the vial. Swabbing, whether swabbing the vials or not swabbing the vials, reduced but did not eliminate the contamination rates, at least in the case of the Ped-O-Jet. It reduced it in the case of the Ped-O-Jet but not in the Med-E-Jet.

Also in the Medi-E-Jet, the external
contamination somehow made its way into the nozzle interior, but this was not found with the Ped-O-Jet.

Now despite these findings, the California outbreak represents the only documented case of blood-borne disease transmission from the use of jet guns, despite hundreds of millions of injections delivered over five decades.

In deriving some hypothetical cut-offs for how much blood or serum might transmit disease if transferred between patients via jet gun, hepatitis B virus is a good agent to consider in a conservative, worst case scenario because of its extremely high infectivity. Needle stick accident surveillance indicates hepatitis B is 100 times more infectious than HIV, for example.

Given chimp studies indicating that carrier blood may contain 100 million chimpanzee infectious doses per milliliter, this calculates to a theoretical single infectious dose of 10 picoliters of blood, and this is an extremely small volume that challenges detection methodologies.

A few years ago the U.K. Public Health Laboratory Service and the Global Program on Vaccines at WHO pioneered an animal model to evaluate the safety of multiple use nozzle jet guns. They used calves and developed an ELISA assay shown here using serum albumen as a blood marker and diluted blood to generate various standard calibration curves, as you see in the example illustrated here.

Now we at CDC are collaborating with the
University of Florida and Small Business Innovation Research Contractors to duplicate and extend that model in both calves and pigs. We're discovering some problematic nonlinear behavior of serum albumen at extremely low dilutions and we're not getting this straight line you see here from the London study.

You can see here the overlap between totally negative controls, the optical density of totally negative controls, and some of the lower calibration positive controls. And this is hampering the achievement of consistent results and good specificity close to the target of 10 picoliters, but we're hopeful that we can work this problem out.

This is a photograph from our injections of anesthetized pigs in Florida. After various control specimens are collected, including mock injections in the first boxes of this injection grid, 100 real injections of phosphate-buffered saline are given in each series.

Immediately after these injections, the next ejectate is fired into a specimen vial representing the fluid that would have been injected into the next vaccinee in a typical use scenario. Despite the assay problems that I mentioned, on at least some occasions among 100 or more specimens, for each of several guns tested, both in the U.K. and in Florida, we have detected contamination well above currently levels that we would consider indeterminate or uninterpretable.

And now in 1994 a similar study in Brazil used a
procedure of using urine dipsticks to measure blood and they found an alarming rate of from a little less than 1 percent to up to 6 percent positive after routine vaccinations of human beings. And they observed that the health workers were negligent in not swabbing the head of the device with alcohol between each vaccinee.

Now various gun manufacturers are planning engineering changes in these multiple use nozzle devices, such as disposable spacers and covers, to see if they can pass this test. But our biggest challenge is how to prove safety from negative results in such an evaluation model.

If 100 consecutive specimens are clean, what would happen on the 101st? Or if we had 1,000 consecutive injections that were clean, can we be sure the 1,001st wouldn't be contaminated? And thus how many samples are really going to be necessary to satisfy regulatory review?

As a result of the 1980s outbreak and these recent lab tests, WHO policies over the last few years concerning multiple use nozzles and reusable fluid path devices have become increasingly restrictive. I won't take the time to read these policy statements because you have them in the hand-out, but currently WHO does not recommend their use, even for emergency campaigns where the use of conventional needles and syringes might also impose some burden on unsafe injections in iatrogenic disease.

Now CDC currently still recommends weighing the risks versus the benefits of using jet guns versus needles and syringes which, as I mentioned, have their own risks.
However, the Department of Defense in 1997 withdrew these devices from their routine use, despite their reliance on them for decades to immunize soldiers.

So now existing high workload jet injectors are in a state of limbo. This means the world's population is more vulnerable to the threat of pandemics and bioterrorism.

Now in 1976, upwards of 75 million Americans were vaccinated with these devices in a short space of time in order to protect them from the swine flu. But now with these devices in limbo, we lack any alternatives means to quickly vaccinate large numbers of persons with limited manpower.

And it is not a question of whether the deadly 1918 swine influenza pandemic will recur but really a question of when it will recur. The recent H5N1 fatal influenza cases in Hong Kong were perhaps a warning of this vulnerability.

Let me conclude on my last slide here with some key questions I hope will be addressed in today's discussion. First consider needle-free injectors as simply drug delivery devices sold empty. Should the device manufacturer be required to furnish data on clinical efficacy for each and every medication that might possibly be administered with them?

That might be a burdensome obstacle and would be inconsistent with how new needles and syringes are licensed, perhaps.
Obviously if they're sold for diabetes there ought to be clinical data on their use with insulin. If they're sold for vaccines I could understand the need for perhaps some representative, a live vaccine or an inactivated vaccine, as markers for all the many possible vaccines.

Instead however, recognizing the public health advantages of needle-free injection, the clinical data on efficacy and safety for specific vaccines delivered by jet injector might properly be a part of the license application for the biological because currently the manufacturers really only provide data on vaccines delivered with needles.

However, for the device developers it might be reasonable to require animal and clinical data on where the dose is deposited and with how much variation. And this ultimately would leave to the end user, the physician, to decide which drugs or vaccines are acceptable to use in the device based on published data and ideally relevant information in the drug labeling.

Second, let's consider the issue of prefilling vaccine into cartridges at the vaccine manufacturer that I mentioned earlier. Now regardless of whether the cartridge is going to be of glass or new polypropalene, routine stability and potency studies will be required, of course. But if the same drug has already been licensed in similar material as the primary packaging, such as prefilled syringes, could not the needle-free packaging application
refer back to that other data and avoid starting at square one in the process of regulation?

And finally, let's ask if it would not be reasonable in determining the safety and efficacy of common vaccines that were prefilled into such cartridges to use relatively small clinical studies for reatrogenicity and serologic response with jet injectors. And then bridge from those studies to perhaps the large field trials that may have been conducted in the past with needle and syringe and show comparable rates of immune response.

And finally, in terms of the issue of the multiple use nozzle jet injectors that I mentioned earlier, what type of safety evaluation should be applied for them? And how many negative results in an animal model will demonstrate sufficient safety? No contaminations out of 100 shots or 500 shots or 1,000 shots or 10,000 shots, et cetera?

Now some might argue that such jet gun designs are inherently unsafe if they use the same nozzles between patients, but given the inherent risks of needles, is it fair to apply a zero risk standard to jet injectors, regardless of the results of such safety testing? These are some difficult questions to address. I do understand. Thank you very much.

MS. O’LONE: Thank you. Now we're going to have some presentation by industry and professional organizations. And again we're requesting that all persons making statements disclose whether they have financial
interests in any medical device company and also please state their names as they come up to address the podium, and their affiliation.

PRESENTATION BY INDUSTRY

DR. EDMISTON: Our first presenter will be Mr. Glenn Austin from PATH, which is the Program for Appropriate Technology in Health.

MR. AUSTIN: Thank you. I'll start with one of the first slides of my presentation telling you a little bit about my affiliation and who PATH is.

Since I didn't know what else was going to be covered, and this is a very diverse and complex set of issues, I prepared about three presentations worth of information and I thought maybe the panel could help me select what to emphasize here this afternoon.

I'm going to give you a little background on PATH whether you want to hear it or not. We can cover some needle-free fundamentals, which I think were already covered to a good extent and if you don't need to really look at the dynamics of the needle-free injection or jet injection, there's been some recent discussions with the ISO working group that I could share with you on standardization and regulatory issues, talk a little bit about variation among devices. I think Bruce has covered that and the earlier FDA presenter covered that but there is some level of detail.

Also, we've done at PATH about 11 years worth of functional and safety testing that might be of interest.
Are there areas that are of particular interest to the panel?

DR. EDMISTON: Your ISO information would be extremely interesting to this particular panel.

MR. AUSTIN: All right, we'll emphasize that, then.

As you said, PATH is the Program for Appropriate Technology in Health. We're actually not an industry representative. We're a nonprofit, nongovernmental organization. We've been around now about 22 years and we're an international organization with field offices around the world.

However, we work very closely with industry and with the public sector to try to ensure that products that otherwise might not benefit underserved populations are made available. That's our mission--to improve the health in underserved populations, especially women and children in developing countries.

This is basically a reiteration of some things that were covered very well by Bruce. There are many good reasons to be considering needle-free injectors, especially reduction of sharps injury and reducing the hazardous waste.

When you're talking about those campaign-type injectors, it can lower the cost. The Ped-O-Jet style injector has been the very lowest possible way to deliver vaccine in developing countries for many, many years.

We also have a special interest in eliminating
unwanted reuse, and this is, as Bruce said, a very common problem in developing countries.

I'm going to skip over some of these. I don't want to give you whiplash here from going through the slides quickly but we'll go through these rather quickly.

Jetstream quality is an important issue. It can be measured. This diagram shows on the right side a laminar or coherent flow and on the left side, a turbulent flow. And this gives you a photographic representation of the kinds of differences you see in commercially available jet injectors. I think this also represents a range that you would see in jet injectors that have demonstrated good immune response or good response to the drug delivery.

This is a simplified diagram addressing what Bruce talked about in terms of the site and dispersion of the injectate delivered by jet injectors. It depends a lot on the operator's pressure against the skin and site selection and in the underlying tissue orientation. As you can see, the jetstream in the upper left diagram, you can see the jetstream is oblique to the muscle fascia. That's going to deposit over the fascia.

If it's normal to the fascia and there's a shallow subcutaneous overlying tissue, it will typically penetrate the muscle fascia. If it's deep subcutaneous tissue, you get a wide dispersion in the fatty tissue. And, of course, the needle is going to deliver at the tip of the needle primarily.

Also along the injection track in each case it is
depositing, as Bruce indicated.

Well, as was mentioned earlier, the world of needle-free is expanding and I think it's going to expand beyond these current uses because of reduced dose forms, the nonliquid forms that were mentioned, which as far as I know are not in current commercial use, and a new emphasis on intradermal or subdermal delivery because of new findings for improved immune response, smaller, low energy requirements for the devices themselves, and we're likely to see these first bundled with new drugs. It's also a possible answer for simultaneous multiple injections, which would reduce the number of immunization shots that a child might have.

As I mentioned earlier, the ISO Standards Working Group had their first discussion on June 3. This is an ad hoc group. It's a spin-off of the Pen Injector Group that's been working for eight years to develop standards for pen injectors.

If you're familiar with those, those have a needle. They're self-contained. They're typically for the delivery of insulin to diabetics. They're very popular, much more popular in Europe than they are here in the States.

They did establish this working group and timeline. It has representation from ANFIM, which Bob Harrington will talk about in a minute. And they are addressing sort of the typical starting point of standards--the physical dimensional characteristics, safety
I don't think they're yet addressing all of the aspects that are unique to jet injection, although I hear there's been some follow-up discussions about the effect on the drug in terms of the sheer and the high pressure exposure.

So what I'm going to do now is show you slides that alternate between capsulizing what the ISO discussions consisted of and then some of the pieces that might be missing from those discussions. I was not there so I lifted these from the minutes.

The drug compartment could contain liquid or powder. This might also be called a syringe or cartridge, depending on the manufacturer. That can be single dose, multi-dose or refillable. It can be disposable or reusable. It has to have some sort of power source, typically spring, gas or compressed air. There's also patents on ballistically driven jet injectors.

The nozzle can be either multi-use, durable or disposable.

I think one of the things they missed in the basics that is not present in the pen injector is the activation means or the trigger that is used, and this has some safety implications.

I would add that some jet injectors are being designed now with autodisposable features so that the nozzle or cartridge cannot be reused. This is of particular interest, as I said, in developing countries but
Hybrid devices have some reusable portion of the fluid path but also have some disposable portion and this is to add a margin of safety, and I'll talk a little bit more about that in a minute and show you some cut-away views.

There's the distinction between prefilled, as Dr. Weniger mentioned, and filling on site. If you fill on site, you then incorporate another subsystem or another device to transfer the drug, and this might be on board the injector, as in the case of the Ped-O-Jet or the campaign injectors or it may be a separate component which is common to all of the nonprefilled, hand-held devices that Bruce showed you.

There are considerations about the fluid path, as well, particularly if you're considering contamination. How much of the fluid path is reused? How much is exposed to potential blood being wicked back up into the system after exposure to the nozzle face? And is the dose adjustable or fixed?

ISO group captured the same safety aspects that they had been using for pen injectors. So in fact you can see here even from their transcript that they're still using pen injector, mostly having to do with dose accuracy.

I think there's quite a few other safety aspects that should be considered—freedom from cross-contamination, as Bruce said, both blood-borne pathogens but also skin-borne pathogens and environmental
contamination, especially of a concern if you have an exposed drug or vaccine transfer system that has a needle or sharp that could be left on a table top or whatever. That portion of the fluid path is not always considered.

There’s also the consideration of when the device is safe when used as directed, complaint versus noncompliant use. A lot of the tests that were done in London and safety tests that were done in Brazil were in a noncompliant mode. That is if you had visible blood on the nozzle, the device would be reused or it would be sampled downstream for contamination. And, of course, that would be noncompliant.

In fact, the Med-E-Jet Corporation has just now changed their instructions and has sent out copies to all their customers and to us, trying to find a safer way to use that device that was implicated in the weight loss clinic hepatitis B outbreak. There is a distinction there and that's something for the panel to consider.

I think that compliance can be assured partially with good design, and that's something that can be tested, particularly in the kinds of user tests that June Fisher was talking about.

Additional safety aspects. Unlike a pen injector, if you accidentally fire this, this can do some damage from several inches away, so it's not something you'd want to accidentally fire into the hands or the eyes.

Some injectors that autodose from a vial may occasionally provide a short dose. This could prevent
adequate response to the drug or vaccine.

Of course, any injector that causes more bleeding and adds blood to the work environment can pose a risk. And poor maintenance, such as leaving it soak in a mild disinfectant for too long, that sort of thing, can lead to other infections.

ISO's initial statement about quality aspects describes things like dose accuracy and then how durable the device is. There are some other quality aspects that might be worth considering. The dose accuracy, as set, is something that ISO is already considering directing themselves toward.

The dose accuracy as delivered. In other words, is all the dose delivered into the tissue or is some left on the surface of the skin? This is something that we frequently observe with jet injection. Not all jet injectors are able to deliver the entire dose into the tissue.

Efficacy. I think Bruce has already addressed this very well. There’s a very good history of efficacy in commercially available jet injectors now.

Stream quality, as I mentioned, and pain or bleeding rates, which may be something that could be addressed.

I'm going to talk about some variation in the fundamental part of the jet injector, the part that's of most concern for cross-contamination. This very simple diagram shows the fluid cartridge or fluid container. This
is the piston here. It's driven forward by some force. These are the reaction forces or the pressure forces inside. Those arrows will stay on subsequent diagrams. They're really just to show that this is a pressure vessel during the use of this container. It's driven out the exit orifice and this would be considered the nozzle face.

So there's another picture of that. The items you see in red are now additional device components that become incorporated, depending. These are all variants within reusable nozzles and there's many different subflavors of this that are either in development or in commercial devices.

The fluid path with autofill--this is very common to campaign-style injectors--has an inlet that allows fluid to come into this chamber, typically with a check valve, and then also a check valve at the outlet, and this offers a potential sequestering site for contamination. And there are injectors with this design that stay largely free from contamination but it does complicate the fluid path. It does add something to the fluid path.

There are a number of injector designs where the nozzle front or face is disposable, but the rest of the fluid path is reused. The piston and the cylinder walls, if they were to be exposed to contamination, would then still be reused in subsequent shots.

And there's new designs now with a space-backed nozzle and a protector shield in front where the jetstream actually goes through the air and the protector shield is
meant to catch any contaminants and is the surface that is in contact with the skin.

At first you might think that disposable cartridges would be guaranteed safe because you're throwing it away and if you throw the whole thing away, that's likely true, but there are different subsets of this, as well.

The cartridge might have a reusable piston so the drive rod and the piston face may be tied together and you throw away the front portion only, so that piston can carry contamination to subsequent patients.

Some designs have a soft plastic cartridge that is not fully supported, so it has to be supported by a metal outer shell that's depicted in red here. If that design allows the fluid to pass very close to the shell opening--in other words, the orifice is near--then you're going to have the same situation that was found with the Med-E-Jet. You have sequestering sites there.

There's also partial cartridges with a separate nozzle face and if that nozzle face were to be reused, obviously that's a potential carrier for contamination.

User interface issues are very important. Particularly in our constituency with low literacy users, the device must be easy to learn to use and learn to use properly.

I think one of the most important things is assuring compliance through good design. And if we're talking about disposable cartridges, this new family of jet
injectors, we want to watch out that we're not introducing another means of contamination through handling.

This is one design actually that I was involved in that if you were to reload the cartridge with bloody gloves, you'd want to have an overcap over this, as an example. That's hands-on.

Getting back to the autodisposable features, just like with the syringes, there's active versus passive. Obviously whenever possible, passive is the preferred.

And then there's some kind of interaction with the device. The device has to participate with the cartridge usually in order to result in a disabled cartridge.

There are other standards that probably at some point will need to be discussed about disposal, reuse. Is it sterilizable or disinfectable, as most of the current campaign injectors are? What are the methods used? How often is it done? Are there cold liquid disinfectants allowed?

And then what is the wear life over multiple uses, including exposure to things like steam sterilization and liquid disinfectants?

Again there's the difference between a prefilled unit dose, which does become a package, versus filling on site, which then has to be compatible with some sort of intermediate filling mechanism.

I'm just going to show you a couple of quick pictures. We've done developmental tests for about 11
years. They're not meant to develop standards. They're not guaranteeing performance. However, they give you a little bit of insight into the sort of dynamics that are going on when a jet injection is given.

The three tests that I'll talk about are a combination of target photography test, force test and penetration test.

Target test is very simple. We're shooting through a thin piece of plastic and looking at the resulting hole. It does tend to correlate, at least in our limited human and porcine studies, to the trauma of the entry puncture hole and it does very strongly correlate to the jetstream quality.

Again reviewing this picture, you can see these would make quite large targets and we double up and do this photography test because a substream like this is too weak to penetrate the target and that would result rather than in a rough trauma at the entry or puncture wound, it would result in undelivered injectate.

We also test the force. These nice neat bell curves are not an exact representation of what's happening because the test mechanism has some mass and it smooths out and slows down the bell curves. However, as a comparative test, there's some value.

Mostly I wanted to show you this to show you how wide a range efficacious injectors cover, more than a factor of 2 in terms of peak force and length. This is all half-cc shots. This is all the same volume.
We use a foam model that was developed originally for training people to insert Norplant capsules as a test for penetration. This shows the sort of thing we would observe with human subject tests—a very small amount of residual fluid, a few drops, and this actually depicts a running liquid down the arm. And this is the range that you would see with human subjects, as well.

We tried to develop a gel penetration test. It's become part of the nomenclature or discussions among the industry. We're now recommending that this not be pursued until someone finds a gel that actually simulates human tissue better. This is something we worked on for nearly 10 years and have now abandoned.

I think that's my time, unless you'd like me to discuss the safety tests. I think I should stop.

DR. EDMISTON: I think we're going to move along.

Do the panel members have any questions at all for Mr. Austin?

[No response.]

DR. EDMISTON: Thank you very much.

Our next speaker is Mr. Bob Harrington, who is here to represent the Association of Needle Free Injector Manufacturers.

MR. HARRINGTON: Good afternoon to the panel. I think I'm the last speaker so if you want to run early, you can run, and if I keep you too late, boo at me or something.

I would like to thank Von and Dr. Weniger and
Glenn for talking about jet injection and giving you some background. Unfortunately, they used probably most of my material so I'll be quite quick through my slides and I will eliminate some that I already have prepared.

My first presentation today is about ANFIM, the Association of Needle Free Injection Manufacturers. The second presentation is about the Ped-O-Jet, since I was president of Vernitron and currently owner and president of American Jet Injector, and I'll talk a little bit about the truth and the myth of high workload injector contamination.

ANFIM was an association that was created to promote an understanding and advancement of needle-free injection technology through the world, to develop common standards that facilitate invention and progress within the field of jet injection—needle-free injection, I should say.

We want to represent industry as a unified group when dealing with regulators like yourselves, standard-setters, government agencies and other organizations and the general public. We're trying to disseminate information to the common benefit of all members.

We want to act as liaison between PHRMA and IPPMA or the pharmaceutical equivalents of our organization.

There are four classes within our organization: needle-free manufacturers, needle-free developers and related industry members, such as pharmaceuticals or vaccine manufacturers, and then observers from the public health community.
We have five board members that are actually voting and two nonvoting board members: myself, Linda D'Antonio and Valerie D'Antonio from DCI, John Lloyd, who is head of the Program for Expanded Immunization at WHO, and Ralph Bitdinger from Becton Dickinson.

We have two liaisons to the board, one from Center for Disease Control, Dr. Weniger, and the other is Pat Cricenti from FDA Center for Devices and Radiological Health.

I'm here to talk a little bit today as an industry about regulatory fairness. According to Congress, a vibrant and growing small business sector is critical to creating jobs in a dynamic economy. Small businesses, however, bear a disproportionate share of regulatory costs and burdens.

According to reputable sources, there are about 12 billion vaccine injections in the world each year on an annual basis. The needle industry is made up of multinational million dollar if not billion dollar corporations with tens of thousands of employees. Unsaid, however, is they have significant dollars available for PR and lobbying efforts.

The needle-free industry, on the other hand, is made up of small businesses with less than $10 million in sales and less than 50 employees. So we need to have some regulatory fairness here as a small business.

Why is ANFIM here? Because we want to deserve a federal regulatory enforcement process that is reasonable
and predictable. We want a common sense to problem-solving and a strong voice in the federal regulatory process.

Congress has mandated that small businesses should have this by passing Public Law 104 to 121 or known as SBREFA, the Small Business Regulatory Enforcement Fairness Act. This act makes certain that small business have a voice that will be heard by the FDA or other federal agencies as they go through the rule-making process. It gives small business expanded opportunities to challenge a federal agency's final regulatory decision.

The bill makes the Small Business Administration, the SBA, responsible for giving us the tools to do that. According to Congress, these boards will shoulder much of the responsibility for making regulatory fairness a more integral part of government.

There are six aspects of this regulation and I will not read them to you. I'll just paraphrase the top. It's regulatory compliance simplification. It should be comprehensive; it should be in plain English.

Equal access to justice. If we go to court and challenge an agency that has made regulations that we think are unfair, we are able to have court and attorney fees returned to us.

There's a congressional review process. Congress is authorized to review each major rule promulgated by any agency before it becomes regulation.

There's enforcement reform. Within one year of a new regulation, the FDA shall establish a policy for
reduction and, in some circumstances, the waiver of civil penalties for violations by small businesses.

There's an advocacy review panel. There's an oversight of regulatory enforcement. All of these things are part of the law and we're just asking please that they take effect on regulations within the needle-free industry because we are a cottage industry.

Under judicial review and a new act, the RFA, Regulatory Flexibility Act, we have an opportunity to seek review of federal agencies' compliance with the law through the SBA if you fail to meet the required analysis and disclosure obligations. We can ask the chief counsel to file a friend-of-the-court brief on our behalf, appealing any ruling or violation of RFA by a federal agency.

My basic message under the ANFIM message is simple. The children of the world need needle-free injection products. The entire world and the environment we live in need needle-free injection products.

We, the citizens of the developed world, have an obligation to the less fortunate inhabitants of the developing world. We cannot continue to pollute, contaminate and infect the developing world by a policy which recommends disposable needles, all the time knowing that they routinely are reused dirty or are improperly disposed of.

ANFIM and the FDA perhaps have two choices. The FDA can either allow this technology and our industry to grow, prosper and flourish by providing reasonable
direction, guidance and support or create a burdensome bureaucracy that unnecessarily overregulates needle-free products, with the end result of potentially forcing all of my member companies out of business.

Three questions deserve answering in this process. Are new regulations economically justified? Are the safety issues associated with needle-free products real or perceived? Do needle-free products really require regulations? If we have the answer to those three questions, I think we have a significant step forward.

We must remember that in hundreds of millions of injections by jet injectors, there has only been one documented case of a contamination in the entire world, yet as the result of reused, dirty or improperly disposed of needles there have been millions of unsuspecting and undeserving children throughout the world that have been needlessly infected with hepatitis or HIV.

Okay, that ends my ANFIM presentation and I will change hats here and become an entrepreneur and a businessman and a member of the industry community.

As I said, my name is Bob Harrington. I'm president and CEO of American Jet Injector. It's an entrepreneurial company that began in 1995. Prior to forming Am-O-Jet I was president and CEO of Vernitron Medical Products. Vernitron, together with Walter Reed Army Hospital, developed and patented the most widely used high workload jet injector device in the world, known as the Ped-O-Jet.
Today Am-O-Jet, a company that I formed, manufactures under FDA 510 approval two high workload jet injectors. One is a foot-powered and one is an electric-powered.


There are prior immunization programs of note. My numbers are conservative by nature in the terms of what they really did.

The US DOD, from 1965 to 1980, did 35 years of continuous service, to include the Vietnam and the Gulf War build-up, on 20 to 40 million military personnel, which each were injected on multiple times.

CDC, WHO and U.S. AID sponsored the smallpox eradication program, 50 to 100 million people around the world.

Swine flu in 1976, according to Dr. Weniger, did 75 million injections. Conservatively, I was 20 to 50.

The Brazilian African meningitis program in 1988-1998 did 80 million injections in 60 days. The Brazilian measles eradication program did somewhere between 60 and 80 million in 60 days.

Numerous CDC, U.S. AID, WHO--name is all--sponsored routine vaccination and/or emergency epidemic immunization programs over the last 30 years--100 to 500 million injections.

Conservatively there are more than a half a
billion, roughly, shots in the world, all without a reported contamination.

We've talked about the CDC MMWR article in 1986. Thirty-one cases were confirmed with the Med-E-Jet. Unreported in the CDC MMWR article was that the other injector tested, the Ped-O-Jet, the leading injector in the world, in all cases tested negative for any traces of hepatitis. And if you go to the article you can see it on page 375, line 21.

What has happened as a result of that one contamination is the axiom that says that all injectors are unsafe. Since there has been one reported contamination of a jet injector, it is theoretically possible to contaminate all jet injectors.

As a result of the MMWR article and the Med-E-Jet contamination, the Journal of the AMA, Newsweek and Middle East Health all reported this contamination, saying that prior to it, jet injection had been considered a safe method of inoculation.

WHO and their policy--Dr. Henderson came out with a policy that said we are strongly recommending that jet injectors should not be used if alternative methods are available. He further explained that in the past, jet injectors were always used for mass immunization programs when large numbers of people needed to have quick inoculation.

Ironically, he added in the same press release, "For such emergencies, however, we are still saying that
jet injectors should continue to be used."

"All jet injectors should be used only as a last resort for mass immunization epidemics until studies under way at Centers for Disease Control show whether a design of a jet injector needs modification." Very quickly, after eight or ten or 12 years since that time, the policy remains in effect today with very, very minor modifications.

The problem is that CDC had no opportunity or no plan to go further with any hepatitis evaluations. They were very content with the fact that the leading jet injector was not and could not be contaminated in their previously run hepatitis positive chimpanzee experiments.

The myth continues in 1996 when WHO and Public Health Laboratory in Kings College do a study. They tried to simulate the infection of hepatitis in calves in a scenario.

The first information coming out of the study said all but one injector was shown to be easily contaminated when evaluated. They developed a new optically read ELISA assay, 10 to the minus 9, designed to simulate hepatitis.

The net result of this PHL testing was issued in a work in progress report 1998 was to reaffirm the theory that high workload jet injectors, those with reusable fluid paths and reusable nozzles, were easily contaminated and therefore not acceptable.

All the time, however, WHO continues to recommend
an enlightened policy of one needle/one shot, utilizing disposable needles and/or an autodestruct needle, knowing full well that they are used dirty in 70-90 percent of the developing world, that the developing world simply can't afford autodestruct syringes and that the resulting sharps from either type are improperly disposed of and routinely left unprotected on the street or in a dump to easily infect unsuspecting men, women and children.

The facts of this whole scenario say that the contamination study has not been replicated at an independent laboratory; nor has it been subject to any peer review.

In an ongoing CDC public-funded SBIR phase 1 research project that Dr. Weniger talked about, my company, Am-O-Jet, the University of Florida, Kings College and an independent U.S. laboratory, we think that the findings of this WHO study are seriously flawed. I'm not as tactful as the public health community because I'm paying the bills on this one and I do not see the replication of the data.

Of importance and for the record for the FDA when we start looking at these studies that people begin to make up and say, "This should be the standard," it is not one of the three approved tests for FDA for hepatitis. The test method may not be scientifically valid. And there is no indication that this test method will be acceptable to the FDA for any future device submission.

The myth continues. In a steering committee on jet injection in Geneva, Glenn Austin from PATH gave a
Subsequently, WHO issued a report and this report was used by Keystone Industries, the purchaser of the Ped-O-Jet assets and trademarks out of a bankruptcy sale in 1995, as the basis to write a letter to the Department of Defense informing them that the product Ped-O-Jet was unsafe, could easily be contaminated, and that Keystone no longer would be responsible for the safety and efficacy of the product if it continued to be used by the government. The direct result of this letter was an immediate ban of all high workload jet injectors by the U.S. Department of Defense.

Recently, PATH's endorsement of this ballistic gel model has been removed. However, one of the companies in the room here with us today did independent testing and unlike skin, the ballistic gel model demonstrated little or no ability to absorb fluid, often fractured and artificially produced a fluid rebound, all leading to the erroneous conclusion that splashback was inherent to a jet injector and produced contamination.

So where are we? Recently I was asked by CDC to moderate a panel at the National Immunization Conference in Dallas. The discussion was lively and it certainly centered around everything that we've talked about this
morning--needle sticks and there probably is a technology
that could help the industry immensely at this time.

An individual came up to me and said that he had
spent about 40 years in public health, had been part of the
CDC smallpox elimination program, had been part of the
swine flu epidemic, and during his career he had supervised
or personally administered millions of doses of vaccine
with jet guns, the Ped-O-Jet, and never once did he observe
blood on the nozzle.

At first glance, the WHO stance he talked about--
one needle/one shot--would appear to be an enlightened
policy, one that could have a profound effect on reducing
the spread of blood-borne pathogens in the world. However,
when one leaves the safe havens of Geneva, Atlanta or the
capital city of a developing nation, this enlightened
policy assumes a far more frightening face.

It is my estimate, and this is a direct quote
from him, this well intentioned WHO policy, one needle/one
shot, is very likely responsible for the spread of blood-
borne pathogens to millions--is it 30 million, 50 million,
10 million?--millions of undeserving women and children in
the world.

Continued responsible use of high workload jet
injectors, on the other hand, would have resulted in a
handful, if any, infections.

Until there is clear scientific evidence
indicating jet injectors in the spread of disease, I
believe that these devices are the best alternatives for
all mass immunization programs. Jet injectors are far safer than available needle technologies for both the recipient and the giver of vaccines alike.

Why do we need high workload injectors? They're economic. They're about a penney a shot. They're efficient. A high speed jet injector can do 1,000 people an hour if it has to. They're flexible. They can be used by nonphysicians or nurses, by normal, well trained health employees.

They have no hard currency value. If you bring a program into the Third World and you have 5 million doses and 5 million needles, about 90 percent of the needles don't make it because they're hard currency on the street to be sold.

They're kind to our environment. They have no disposal issues. There's no power required and they have no needle sticks involved with them.

When should you use them? Pandemics, epidemics, national immunization programs, special eradication programs, military readiness and CBW response teams.

What is the future of Am-O-Jet's high workload injectors? We believe in a traditional reusable nozzle, reusable work path. We're continuing the production of that model.

However, we're tired of fighting the battle and we're trying to develop some products, as my colleagues in ANFIM. We're developing a new inexpensive low workload jet injector, something that costs $300 and lasts 30,000 to
50,000 shots, again at a penny apiece. A new disposal nozzle so that there is a pathway that's interrupted. A new autodestruct disposable nozzle because in the developing world, if it's disposable they continue to use it. It needs to autodestruct. And we're also working on, like other people, a self-contained prefilled disposable vaccine capsule. All able to fit the existing injectors in the world and the new injectors.

Over the last 10 years, the following have occurred: the fabrication, development and reinforcement of misinformation, the creation of innuendo and assumption, all connoting jet injectors are unsafe injections, an almost mystical transition of the information from innuendo to scientific fact. The premise that high workload jet injectors are unsafe and easily contaminated has not been proven.

Life is not without risk. I was a military pilot in the 1960s. I went through flight school and two of my classmates were killed in training. That was acceptable. I flew in Asia as a military pilot and a variety of people were killed; that was an acceptable risk again. And more dangerous than all of that, I drove on the beltway this morning to get here and there's an acceptable risk of driving on the beltway.

We do not live in a world where all medical devices or all medical procedures are risk-free. Many have inherent risks, yet they are recommended, accepted and used on a daily basis. Vaccines, by their very nature, have
inherent risks.

There are several questions that we need to ask ourselves. Is there a real risk of disease transmission with jet injection? If there is, how great is that risk? What percentage of those inoculated might have a chance to receive blood-borne pathogens? I'm not saying there is, but if there were, what is it? What would be an acceptable level of risk? Is risk-free, 100 percent chance of no infection, the only alternative?

Why are these questions very important to all of us? Because we live in a world that's changing. If an epidemic were to break out, perhaps something like meningococcal meningitis, where the fatality rate was estimated to be 20 to 25 percent of those infected, tens of thousands of people have to be inoculated quickly. Why options are there other than high workload injectors? What would be an acceptable risk in this case?

If a pandemic were to come out of the Far East, perhaps like bird flu of last year where the fatality rate was estimated at 35 to 40 percent and millions of people--CDC estimated they'd have to do 250 million Americans in approximately 60 days--what options are available other than high workload injectors? What would be an acceptable level of risk at a 35 to 40 percent fatality level?

If a CBW attack were to come to pass with a fatality rate on one of the cocktails that they're talking about--anthrax, smallpox and something else--estimated to be 90 to 95 percent of those infected and millions of
people--11 million people in the city of New York--would have to be inoculated very quickly, perhaps within hours, what options are there other than high workload jet injectors? What would be an acceptable level of risk in this case?

I come to you with two hats. The first is ANFIM. We'd like you to be fair and reasonable to our small manufacturers. I come to you as a manufacturer personally and say there's a great deal of innuendo and misinformation in the world that talks about jet injectors. We are not being treated as fairly as needle companies, which have a variety of issues that go unaddressed. We're being asked to be treated fairly. We're being asked to accept what is a risk and how much is there? And I thank you for your time.

DR. EDMISTON: Thank you, Mr. Harrington.

As always, the script is changing. We deleted one of our speakers, who represents the user side of this industry.

I'd like to call to the podium Deborah Wexler, M.D., the Immunization Action Coalition. Dr. Wexler, please.

[No response.]

DR. EDMISTON: Is Dr. Wexler in the audience?

[No response.]

DR. EDMISTON: So we didn't miss her.

At this time we will take a 10-minute break. Let's come back by 10 after 3.
[Recess.]

DR. EDMISTON: I think we should finish up this afternoon's session.

OPEN PUBLIC HEARING

DR. EDMISTON: At this time I'd like to open the meeting for the open public hearing. Any member of the public may address the panel during this open public period. Please limit your remarks.

Also I remind the speaker, if we have any speakers, to approach the microphone, speak clearly into the microphone and identify your affiliation and indicate if and what type of financial interest you may have in this industry.

Do we have any speakers? We have two, yes. Dr. Fisher?

DR. FISHER: I'm not going to talk about the merits of jet injectors but I would raise the question that if you're going to evaluate--if you consider those factors that I, as an occupational health physician, have to raise, and that is the factor of what is the outcome of a health care worker when you're doing 1,000 an hour, and if it's not properly designed, the potential for musculoskeletal things is great.

And the other question I have is around the issue of if there is any spray, if you have certain components, what effect is that going to have, is aerosolization have on the provider? Because it may be a small amount but if you're there all day, then it may be a cumulative dose.
So those are factors that should be perhaps accounted for when you're giving approval.

DR. EDMISTON: Thank you very much.

MS. DUCMAN: Just real briefly, again my name is Kathryn Ducman with Retractable Technologies.

I just would like to point out, in contradiction to the previous presentation, not all needle and syringe manufacturers are multi-million dollar corporations. Most of the new technologies that are coming out are comprised of small, innovative businesses out in the marketplace.

Some new technologies can make one-shot/one-dose feasible, not to negate the value of jet injections but there are technologies that do have an automated retraction that allows shots to be given safely, efficiently and are absolutely nonreusable in that regard.

I think it is a dangerous concept to look at an acceptable level of risk. As Susan Wilburn put so well, with some of the emerging infectious diseases, such as hepatitis C, we weren't even testing those until quite recently. So the idea of a contamination path, there are issues out there that haven't even been delved into and it may be over the next one to two decades before we see the effects of the past, how that has affected health care workers.

Thank you very much.

DR. EDMISTON: Thank you very much.

Do we have any further speakers? Yes, come forward to the microphone.
MR. ANTHONY: Thank you. I'm Bud Anthony from the Biologics Consulting Group and I am a clinical consultant for vaccine development.

I'd like to ask a question of one of the speakers, if this is an appropriate time.

DR. EDMISTON: Yes, it is.

MR. ANTHONY: It's for Mr. Austin.

Glenn, in connection with Bruce's remarks about using a jet injector with multi capabilities, that is, to deliver multiple vaccines, has it been demonstrated or is it possible to demonstrate that the individual vaccines do or do not mix within the tissues, end up in the same tissue pocket, if you will? Or is it possible to demonstrate that they remain separate or that they may commingle?

MR. AUSTIN: I'm not aware of any studies that have been done.

MR. ANTHONY: Is it technically possible to answer that question?

MR. AUSTIN: Yes.

MR. ANTHONY: Thank you.

DR. EDMISTON: Do we have any additional questions for the speakers? Dr. Rutala.

DR. RUTALA: I had a question for Dr. Weniger. The data that was presented in the MMWR from 1986 where there is the one case of hepatitis B transmission, I was wondering was the jet injector used as directed? That is, was there compliance with the manufacturer's use directions?
And then if there was, could it be modified such that the mechanism of transmission could be circumvented or corrected?

MR. WENIGER: I believe it was used according to direction and all these manufacturers do recommend swabbing of the head after each shot to remove any serum or blood that might be on it.

The problem, as I alluded to in my talk, is that there are occasions when health care workers are negligent and they don't remember to do that, and that was the case in Brazil.

One of the hypotheses about the Med-E-Jet was that the nozzle actually consists of an internal pin surrounded by a sleeve, leaving basically a potential gap for capillary action to wick fluid from the skin back into the device, which would not necessarily be removed by swab, and that's still a hypothesis.

So I guess the issue that you're raising is how can we minimize health care worker negligence or lack of attentiveness to following manufacturers' directions? How can we make such devices so-called failsafe? And I think it's an important question.

That's why in putting out contracts for the development of a new generation of devices using disposable cartridges, thinking about the developing world problem, we have encouraged people to figure out ways to make sure that once it's used, it cannot be reused, even intentionally, in places where they might want to save on costs, by having
somewhat damaged or the piston gets locked into the bottom of the cartridge at the end of the injection or some other way that it can only be used once.

DR. RUTALA: I guess just a follow-up. I certainly agree with the comment that there's no such thing as absolute safety, but obviously we always try to minimize risk and minimize disease transmission.

Do you believe it is possible to develop a jet injector that would eliminate the risk that was seen in the one case of hepatitis B transmission?

MR. WENIGER: Are you referring to a multiple use nozzle--

DR. RUTALA: That's correct.

DR. WENIGER: Metal nozzle?

DR. RUTALA: That's correct.

DR. WENIGER: I think it's possible but I think the challenge is to develop a methodology to evaluate that, to convince ourselves of it. I think, and this is my own unofficial personal opinion, that a more promising line of development is to just go the disposable route and figure out some way to make a disposable cartridge work in a high speed gun, and then we have the best of both worlds and we can avoid this uncharted territory we're now in, trying to develop a model to measure extremely small quantities of blood that might theoretically transmit these infections.

DR. RUTALA: Thank you.

DR. EDMISTON: Mr. Harrington, I believe you had a comment? Come forward, please.
MR. HARRINGTON: The term "acceptable risk" is not one that I coined but one that Dr. Margolis, head of the Hepatitis Branch, CDC, coined at a meeting held by Dr. Weniger at CDC and his question was, "Tell me what the risk of transmission is and if I know the mortality rate and my risk is very little for hepatitis transfer, I can deal with treating adult hepatitis but I can save millions of people from dying from the disease."

So I'm not suggesting there is a risk of transmission but his concept was what is an acceptable risk if the mortality rate is so much higher?

DR. EDMISTON: I think we had one more individual in the back. Please identify yourself.

MR. SOLERNO: I'm Larry Solerno. I'm director of operations for Retractable Technologies.

I will agree with Mr. Harrington on the point that small business that is doing the innovative work, when they're trying to get their 510(k)s and things passed, is on a very limited budget, that excessive clinical trials or things that make the cost of--we were talking earlier about prototype or devices that were used, if it takes $10 million to get out of the prototype stage into a process where a company can put a device before they get their 510(k), it's going to help kill the innovative research that the National Institutes of Health and things are putting forward in the process.

DR. EDMISTON: Thank you.

Are there any further comments or questions?
OPEN COMMITTEE DISCUSSION/

PANEL SUMMARY RECOMMENDATION

DR. EDMISTON: I believe at this time we will move into the open committee discussion with recommendations. I should point out that at 4:00 we're going to lose approximately half our panel, so I suggest that we move expeditiously through this.

And I would propose that we would combine questions 1 and 2. "In general, what are the key issues that should be considered in the premarket evaluation of jet injectors? And what data should be appropriate to address each of these above issues?"

Let me get the ball rolling by suggesting the following. I think it's obvious, whether we're talking about a disposable or reusable device, there's an issue of safety and we have to have some way to evaluate safety, be that bench testing, engineering controls, and I think that's prudent.

We also need to ascertain dose accuracy. We also need to ascertain labeling. If the injector comes prefilled, there has to be some indication of labeling on that. Shelf life.

And I think as was brought out in the earlier presentation, the issue of ISO standards I think are significant and I would suggest that the FDA be very interested in the development of standards for this industry as it evolves.
I think Mr. Harrington's concerns voice one side of the equation but I think what's very important is that as a technology in this area emerges in which children will be able to give themselves injections at school or a variety of individuals who'll be able to give themselves injections in atypical health care environments, there must be some way that we can provide a watchdog area of expertise for these devices.

Having said that, I want now to poll my panel members and see what their interests may be and concerns regarding these two questions.

Ms. Ryder.

MS. RYDER: Well, I guess one of the issues that came to mind as I heard the presentations and the huge numbers of patients who have received injections by this method, and it was also pointed out that we're only beginning to understand some of the emerging communicable diseases, that what type of surveillance has been done on this to determine indeed whether there were any resultant infections or transmissible diseases. In other words, did the infections occur but we just didn't know it? And is anybody actually measuring resultant infections from all of these injections?

DR. EDMISTON: Dr. Rutala?

DR. RUTALA: I just have a few comments. I thought the presentations were excellent and I really appreciate the information that was provided to us.

I have a number of questions or have prepared a
number of questions or a number of comments as far as studies not having heard the presentations, but I'm going to comment on a few things, realizing that some of these questions have been answered.

When I consider jet injectors, certainly we have to consider efficacy issues and when we consider vaccines, we have to consider things such as seroconversion rates and geometric mean titers. And, of course, that, I think, has been answered.

I didn't hear any reference to geometric mean titers and whether jet injectors provide the same geometric mean titers, but everything else that was mentioned regarding the use of that product seemed to be very comparable.

As far as drugs, of course, we have to consider pharmokinetics--half-life, excretion, time to peak level, peak time--and, of course, that needs to be considered by the manufacturers.

Side effects, of course. There has to be consideration of the side effects of administration, such as abscessing, bleeding, induration, erythema, superficial papules. And, of course, that can be accomplished and I think it already has been accomplished, according to the presentations, by randomized trials with frequency and type of complications recorded. So I believe that's been addressed.

Of course, nosocomial infection risk is very important in risk of disease transmission. That has been
addressed. It appears that there is at least one case of evidence of transmission.

Of course, as was mentioned by Marcia, there's always a concern if there's not an active surveillance system or if there's not some in vitro studies that demonstrate the absence of transmission, what the true prevalence of transmission or the real incidence of transmission is.

As far as delivery amount, our chair has already mentioned the delivery amount. Contamination has been mentioned. Those studies can be done both in vitro and in vivo.

Contraindications. Of course we have to evaluate the efficacy and safety in groups most at risk for failure or injury.

Those are some of the issues that immediately come to mind.

DR. EDMISTON: Mr. Palomares?

MR. PALOMARES: I just want to remind the panel that this product has already been classified as a Class II device, such that it's supposed to be regulated by general controls, as well as some performance standards if they're established.

So we have to really look at the safety and effectiveness of this product, as well as the risks and benefits that the products do provide here. There's a lot of data here, some of them established, some of them not so. We have to look through that carefully.
DR. EDMISTON: As a potential use, Mr. Dacey?

MR. DACEY: I'm going to offer what I would call a very generalized overview, speaking as a consumer. That is I want to go back to the definition of the word "medicine." As I understand it and have been using it, medicine is a science-based remedy.

Ultimately, every consumer, every patient, despite all the hype and all the stuff that goes on in the marketplace, must at some level place its trust and faith in the science and not in the most effective marketing strategy and salesmanship.

So as a consumer, I have to trust each of you as scientists to do what is not only best but what is right because I don't know, as a consumer. I'm not that much of a scientist.

DR. EDMISTON: Mr. Ulatowski?

MR. ULATOWSKI: Could I defer comment until I hear from the other side?

DR. EDMISTON: Dr. Fowler?

DR. Fowler: I think the presenters were most interesting and enlightening and there are a number of questions certainly brought to mind.

I wonder if one way to consider some of these issues might be to divide to some degree, although I realize there's a lot of overlap but to divide the projected use and the type of product--to divide our thinking by the type of use or product.

For instance, we've heard very little about the
insulin injector that an individual subject or patient might use, and perhaps many of the concerns for that product are not at all the concerns that we're hearing much more about as far as the general vaccination uses.

And then a third section, which would seem to me to perhaps be the most important one for further thought would be the use of these types of products for medications to replace individual needle injection in a hospital setting or in a facility setting or in a doctor's office or dental office setting, to replace the use of needles and thereby to help reduce the risk of needle stick injury.

And so in looking at that issue, as Dr. Rutala mentioned a bit, I think there are a number of issues about drug stability and where the dose is delivered. With a vaccination maybe it's great to have a little more in the skin so the Langerhans cells can get to it and enhance your reactivity, but with some other medication that you don't want there, that might be a drawback. And I think that seems to me to be an area where this type of product might have great promise but has certain concerns that are not present in either of the other two areas.

DR. EDMISTON: Mr. Ulatowski?

MR. ULATOWSKI: Very quickly, I think I've heard pieces of what FDA came here to find out in terms of how to approach the evaluation of these products and I've seen a couple of overheads from Bruce and others on an approach.

I guess our concern, as I said originally, primarily is in terms of the clinical data. Whenever you
say clinical data it kind of scares half the population of manufacturers.

We want to be very careful in when we're looking for data above and beyond the engineering types of bench tests. What's the clinical question? You've heard that from Larry Kessler this morning. What's the clinical question that we need to ask and get data on to answer, that we don't otherwise have information on from the published literature, from documented experience?

Von talked about valid scientific evidence. What is out there in terms of valid scientific evidence to support the safety and performance of jet injectors and the powder injectors and others, for delivery of the products for which they are labeled, intended for use?

And it's a time right now, as we develop this guidance, to look at what we have in hand in terms of valid scientific evidence and to say to ourselves, these claims are acceptable because the data is there and it is as follows, for certain antibiotics, for certain drugs, for certain vaccines. But to permit a broad indication for use, for delivery of drugs or vaccines, I think that's an area that we have to be very careful about and be data-driven.

So it's a time to look at the data. We're primarily concerned with clinical information now that we're looking at. And I heard from Dr. Rutala about the information in terms of drug and vaccine information, taking that into account, in terms of the Class II nature
of the product, which allows us a lot of flexibility for these kinds of products in terms of how we approach these devices, and about dividing up these products. Not every type of product necessarily needs the same amount of data. And, of course, being data-driven.

DR. EDMISTON: I think we can clear this up fairly quickly. If you look at the first two questions, I think the issue of safety relative to the engineering, there has to be some engineering controls built into these devices, especially these new innovative devices which can be used by a variety of end users, both adults and children. And I suspect these devices will also find their way probably in the Third World at some time in the future, as the costs come down.

That kind of testing is relatively easy. Also validating dosing. The science is well established in terms of the unit volume that's delivered and the pharmacokinetics has been well developed in other studies. What you're really talking about is the third question, and that question is, "If and when clinical data are appropriate, what are the panel's general recommendations regarding the form and content of the studies?" Am I correct?

MR. ULATOWSKI: I think that's the biggest point of concern of the industry.

DR. EDMISTON: So, in essence, we've answered questions 1 and 2 and we're now going to move to question 3.
MR. ULATOWSKI: Taking stock of what we've heard today in total, I think a lot of points have been covered.

DR. EDMISTON: I think for questions 1 and 2, what the panel may want to consider as a recommendation, and I'll poll the panel, is that there should be an effort on the part of industry to provide engineering controls documenting the safety of these devices, and that type of documentation can be derived from bench data, from laboratory data.

MR. PALOMARES: I'll concur with that.

DR. EDMISTON: We're in agreement with that?

Now let me ask you one more question as the FDA liaison here. The drug side of it, how closely do you work with your colleagues on the drug side of it to validate that that dose going in there is the appropriate dose for that injector?

MR. ULATOWSKI: Well, there's the rub. We have an historical context here in terms of jet injectors that we want to provide--be fair to the manufacturers in regard to what's been permitted in the past but let's all get firmly footed in the data and then move on from that point as to what we need from now on in regard to additional claims for additional drugs, for example.

DR. EDMISTON: So as new drugs come to the market and as they're delivered by this type of technology, will that evaluated separately?

MR. ULATOWSKI: That's evaluated in harmony with our drug evaluation center. If we see a drug product that
has not been in the labeling before, we'll send that for a consult review to our drug evaluation group.

DR. EDMISTON: That's not really a 510--

MR. ULATOWSKI: Yes, it may still be.

DR. EDMISTON: It still may be a 510(k)?

MR. ULATOWSKI: Mm-hmm. Comparing one jet injector to another is difficult sometimes. One does not know whether the performance characteristics will end up providing equivalent doses to the desired site. There's insufficient data showing ranges of parameters that are acceptable for various types of drugs. So it's a case by case basis sometimes that we ask our questions.

DR. EDMISTON: Let me ask Dr. Weniger of the CDC to go to the podium. I'd like to ask him a question relative to vaccines. When you've looked at various devices, this issue of dose accuracy between devices, what is your interpretation based on your experience?

MR. WENIGER: Well, I'm not privy to any dose accuracy studies that may have been submitted for devices already on the market. I haven't collected all the 510(k)s and maybe I can do that some day.

I guess my sense is that it would be reasonable to request device manufacturers to provide that information but I guess my recommendation would be that we not try to be too rigid about it because clearly when needles and syringes are used and the nurse is measuring the 1.0 ml dose or the half cc dose, there's probably 5 to 10 percent variation right then and there. So I think we ought to
have some flexibility around the nominal dose in that regard.

If I can just comment a little bit about the Catch-22, I think that we have in this situation where the drug manufacturers and the vaccine manufacturers don't have an incentive to do the additional clinical studies of their products with jet injectors because it's such a tiny market.

On the other hand, the device manufacturers, this cottage industry, cannot afford to do the studies on each and every possible drug that might go into them, and they are held back by the lack of market demand for these devices because until the manufacturers are going to prefill the drugs or the vaccines into cartridges to eliminate that filling step, they're very inconvenient for the end users. So there's this chicken-egg phenomenon. Neither the chicken exists nor the egg exists and it's hard to get them started. That's why we're trying to promote prefilling, to help overcome that.

But the challenge will be, and I think this is where public health agencies can help and universities can help and NIH grantees can help, to develop clinical data on the use of a jet injector with vaccines A, B, C and D and new vaccines that are coming along, like for example hemophilus. There to date has never been a study of hemophilus vaccine administered with a jet gun.

If we can provide that kind of data, perhaps not under an I&D but at least get it into the literature, maybe
this will help a manufacturer of a device to say this has been shown to be effective with this type of a gun.

Did that answer your question? I'm not sure I completely answered it.

DR. EDMISTON: I don't believe there is an answer.

Do any of the panel members have any questions for Dr. Weniger?

[No response.]

DR. EDMISTON: I think at a minimum, we should have some assurance that there is sufficient dose available in these devices, so there has to be some labeling criteria as to when the dose was put it, what's the shelf life of that. And I suspect that's already in place to some extent, isn't it?

DR. WENIGER: Well, I think we're sort of talking about two quite separate issues. One is the issue of jet injectors as simply delivery devices, like needles and syringes. And the other is if we can convince manufacturers to prefll into cartridges to go into jet guns, then we have to deal with all the potency and stability and compatibility with the plastic questions and the shelf life in that, and I think that’s quite reasonable and that burden ought to be on the vaccine manufacturer who proposes to put them in and we need to create enough incentives to encourage the manufacturers to do that.

DR. EDMISTON: Do you anticipate that will occur in the foreseeable future?
DR. WENIGER: Well, like I say, until we can develop enough demand for needle-free devices, guns that physicians and hospitals can buy, I don't see the manufacturers seeing a large enough market to justify doing the studies on the several hundred patients that might be necessary to develop the serologic assays or the bioavailability studies.

DR. EDMISTON: So from your perspective the real issue here is the safety and engineering designs of these devices.

DR. WENIGER: No, actually I think that's a side issue relevant primarily to the multiple use nozzle devices. I think the existing devices that have disposable cartridges, I don't see any inherent problems with them. They've passed 510(k)s and they get their insulin in and they get a number of other devices in and the side effects, although slightly increased, are not unreasonable.

DR. EDMISTON: So you don't think it would really be necessary for them to provide documentation, or at least bench documentation, on the efficacy or the engineering characteristics of their--

DR. WENIGER: No, I think any device, whether a disposable cartridge or a multiple use cartridge, ought to demonstrate that it gets into the tissue that it states it goes into, whether it's subcutaneous or not, and to provide either human studies with radioisotopes and nuclear magnetic resonance imaging, which is not invasive and doesn't expose you to x-rays--those techniques are there--
to do cadaver studies or animal studies to show that it gets in where it states it gets in.

The challenge, though, is that if someone wants to use an IM vaccine in a device that only a third of the time or less delivers IM, we now have an off-label—well, not an off-label but sort of a conflict situation. There may be clinical data that says you can use a jet gun for this product, even though it doesn't get into the nominal compartment that's stated in the manufacturer's label for that vaccine, but it works. So there's little incentive to get the manufacturers to do some additional studies to show that jet injection subcutaneously will work just as well as needle and syringe IM.

DR. EDMISTON: Well, that issue really is a prevalent issue in health care, especially in anti-infectives and other types of biologics, the off-label use. You'll never be able to address that per se.

DR. WENIGER: But I guess what I'm hearing from the manufacturers is they want to bring today, 1999, not 1995, to the FDA an application or a 510(k) for a device and they can show it gets subcutaneously but then they want to be able to market it for the following six vaccines or maybe vaccines in general and I'm hearing the requirement for proof.

Now we have some information in the literature that they can use smallpox vaccine, they can use measles vaccine, they can use a variety of vaccines, but what about the practitioner who wants to use it for a vaccine that
doesn't have that data yet, like hemophilus influenza, for example? How can they label this device, well, you can use it for some vaccines but not all? Do you want them to specify--

MR. ULATOWSKI: And that's a problem. It's the mutually conforming labeling, we call it as bureaucrats, making sure the vaccine is labeled to be delivered by that particular method of delivery.

It's an issue that's in front of our Biologics Center right now, as far as how they're going to approach this issue with jet injectors. But I certainly would want to rely upon what we've already cleared and permitted in the past to continue, but to be watchful for additional uses until some data comes forward, more data comes forward that says everything is very similar in terms of delivery aspects from one method to another, and I don't think that data is there. It's probably going to be a product by product, vaccine by vaccine issue in many cases.

We have a representative from Biologics here who's going to consider what's been said today and you've already heard from Norm Baylor at a couple of conferences where his concerns have been voiced in regard to this.

We've had examples, for example, a device coming forward that delivers a dose but doesn't match a dose of any drug in the PDR. So you ask, "Well, what drug exactly do you intend on delivering by this injector?" It turns out to be something like a product looking for a use, which isn't good thinking. You're trying to provide a product
that's going to deliver a therapeutic or prophylactic, in terms of drugs, dose to the patient.

There have been many other cases where it's not been very well thought out exactly what the product is and what it's intended to deliver and we're seeing that more and more, I think, in my division.

DR. EDMISTON: Well, let me try this again, and I need my panel's help on this, that in devices that present themselves to the FDA, if those devices are deemed significantly the same or similar to devices on the market--

MR. ULATOWSKI: We're looking at a grandfathered situation for many products still.

DR. EDMISTON: It's the FDA's call as to whether or not additional data is required.

MR. ULATOWSKI: That's correct.

DR. EDMISTON: However, devices which represent new technology, innovative technology, I think those devices--

MR. ULATOWSKI: Additional data.

DR. EDMISTON: Additional data, bench data, engineering data, that would be appropriate. Adding to that the intended use of the device in terms of the serum, the vaccination, anti-infective, whatever is going to be delivered, can that be documented? Can the manufacturer document that the effective therapeutic dose is delivered by that device?

MR. ULATOWSKI: By those parameters?
DR. EDMISTON: Right.

MR. Ulatowski: By the specifications. Maybe not even that device necessarily.

DR. EDMISTON: Does to panel agree with that? [Nods from panel members.]

DR. EDMISTON: Now let's get to the area of the clinical. I'd like to refer to the slide that Dr. Weniger presented on the regulatory issues for jet injectors, which I think is a very nice slide because it summarizes some of the issues that we're looking at.

For instance, needle-free injectors as empty drug delivery devices. Do you require clinical data on all drugs or only representative ones which the end user might administer? And I want you to help me with this as I go through it.

Your tactile recommendation there is probably no, and can you tell me why?

DR. WENIGER: No, actually that probably refers to the more extreme proposition, which was to require you to have clinical data prepared by the device manufacturer for every possible drug that a physician might put into that device, and obviously the answer is no.

I think there may be some reasonable balance in terms of selecting, and I use the example for a new jet injector that comes along that doesn't have a predicate, to ask for some clinical data on a representative live vaccine, representative inactivated vaccine, perhaps one that has a good serologic correlate so you can get an
answer with 100 patients or 200 patients and not have to do a field trial of 10,000 patients. I think that might be a reasonable balance, to ask for that for a new device.

DR. EDMISTON: Then you state to require animal and clinical data demonstrating compartments for doses deposited. We discussed that already. Is the appropriate drug being delivered in the appropriate area? Or demonstrate equivalence to proven devices. You said maybe.

I think the FDA is well positioned to make that decision in terms of equivalent devices because though I've looked at devices similar to that in the past, in terms of whether or not that drug is being delivered into that department, that is a key issue and my concern is again what is the dose that's in there and is all that dose getting to the site of action?

Now that could be onerous because we know pharmacokinetic studies are very costly. I don't think this committee has to recommend any number, but I think there has to be some basic clinical studies conducted, especially on those products, as you mentioned, the new vaccines that have not been tested in these devices before.

What are the comments from the panel? Marcia?

MS. RYDER: I would concur.

DR. RUTALA: I agree.

MR. PALOMARES: Usually I've seen where you're talking about dose deliveries; it usually falls on the onus of the pharmaceutical manufacturer, not on the medical device. There are some drugs that you have to look at and
determine is it compatible with this product, but not
determine if I use vaccine A, does it get into the
appropriate dosage.

   DR. EDMISTON: I think the issue would be if you
used a cartridge but that device only delivered half the
dose, that would be a concern, correct?

   DR. WENIGER: Yes, and I think obviously there
ought to be data in the licensure of that product that
states that when the nominal dose is a half cc it delivers
a half cc plus or minus some reasonable variation. So that
would be solved in terms of the required animal or human
data to demonstrate that in the license phase, but that's
really separate from efficacy of the drug or the vaccine
achieving its intended use.

   MR. PALOMARES: Well, maybe Mr. Ulatowski can
help us here. When you have prepackaged combination on
device-drugs, does it usually go through CDER or ERH?

   MR. ULATOWSKI: As I mentioned up front, if it's
a prepackaged, prefilled vial, it's evaluated by our
biologics or drug component, rather than by devices. We'll
evaluate a jet injector that's applied without a drug
product or biologic product, as sold.

   DR. EDMISTON: See, dose accuracy will have
impact on efficacy, so there has to be some way, at least
on the front end, for the user to be confident that he's
getting an accurate level of that dose, at a minimum. It
may or may not be efficacious, depending on what he's
delivering, but you want to be assured that you're getting
that basic dose. Under those circumstances I think the FDA would want to have clinical data.

MR. ULATOWSKI: Yes, I think maybe our biologics rep, if they're here, would want to comment. I think she does want to comment.

DR. CHANDLER: I'm Donna Chandler. I'm here from the Center for Biologics Office of Vaccines. I'm deputy director of the Division of Vaccines and Related Products Applications.

I think part of this has to do with the grey area and the case by case sorts of language that we always run up against with biologics.

I think when we approve vaccines, for the most part we're looking at approving essentially up through the packaging. That's part of the labeling and would be part of the licensure application. For example, we would look for stability studies showing that the vaccine is compatible with the labeling, with the packaging. And normally we'd be thinking in terms of referring to our device colleagues for the device that was going to actually deliver that particular product.

Now when we start to think about a jet injector, we're starting to get across issues that are going to be important to both of the centers.

I happened to be looking through some labeling recently for something else and came across the fact that certain multi-dose vials are approved for use with jet injectors but when you start to talk about cartridges that
are going to be used with a jet injector prefilled, we would expect data, probably clinical data, to show that any change in delivery system would give—-you'd still assure the safety and efficacy.

For a vaccine we're primarily looking at immunogenicity. And oftentimes when there's changes such as in a regimen or a route of administration, we would look for clinical studies, head to head, the proposed change versus the standard of care or what is already approved.

DR. EDMISTON: Because of the intimacy of your interest and this panel's interest, would you feel that it would be appropriate that the recommendation is that the dose accuracy and efficacy be linked, especially for new vaccines?

DR. CHANDLER: Well, by efficacy we probably wouldn't expect a large scale field trial. I mean that would be overkill. But we use oftentimes immunogenicity as a surrogate in many, many cases for vaccines, and that's not the equivalent of a study. I mean clearly you have to have immunogenicity studies or immunogenicity assays well in place and potency assays for the approval of a product.

So immunogenicity, clinical immunogenicity data and potency, either in vitro or animal studies, would be appropriate. Does that answer your question?

DR. EDMISTON: But you feel that the issue of dose accuracy is extremely important for these devices?

DR. CHANDLER: Well, probably not so much--I mean it's not going to be quite as important for vaccines. It's
going to be much more important for drugs, I would think, because your response to a vaccine is going to be--it's going to be somewhat variable. The immune response to a vaccine is oftentimes much more variable than, say, the pharmacokinetic response to a drug.

**DR. EDMISTON:** So you differentiate between one of these devices being used to vaccine someone against measles, as opposed to one of these devices being used to deliver a dose of insulin to a diabetic?

**DR. CHANDLER:** Yeah, I would think so. But again it's a matter of data.

Well, let me go back. I think that we would generally expect to have at least stability data and maybe even some clinical data for the use of prefilled syringes, and I think that's about as close as we get to what you all are talking about now.

**DR. EDMISTON:** Is the onus, though, on the manufacturer of the jet injector at that point for prefilled syringes or vials?

**DR. CHANDLER:** No, that's part of the vaccine's license. In other words, when we approve the vaccine we approve the final package. Again that's why I say this jet injector is getting into a grey area. I think it's going to require cooperation and collaboration between the two centers and probably between the two manufacturers.

**DR. EDMISTON:** So what I'm hearing, what we know currently about vaccination is that the dose accuracy is less of a concern than it would be for other biologic
agents if we go into anti-infectives, liposomal compounds or other biologics of that type.

DR. CHANDLER: Right, but that might well be balanced by or counterbalanced by the concern for the site of delivery, for muscular versus subcutaneous or intradermal.

DR. EDMISTON: So the FDA should have wide latitude then, in terms of evaluating what type of clinical data they would need relative to whether it's a new technology and a new application of that technology—the delivery of anti-infectives or delivery of other biological entities like insulin.

DR. CHANDLER: Right. I would think that a question could be we have experience with a vaccine, for example, the hemophilus vaccine, that's been given—an approved vaccine given by a specific regimen using approved devices.

And if we would be involved, and this is just sort of a personal viewpoint and not having had a chance to be involved in previous discussions but I would think that if somebody came to us and said, "We now have a cartridge that we would like to evaluate that we would like to have approved and we'd like to add that to our labeling for a hemophilus vaccine," we would like to see data to show that that hemophilus vaccine delivered by that cartridge and jet injector system is—that that vaccine is as equivalently immunogenic as the needle and syringe method.

DR. EDMISTON: Thank you.
MR. PALOMARES: But who is the onus on again? Excuse me but who's the onus on? Is it going to be on the pharmaceutical or biologics or is it on the device manufacturer?

DR. CHANDLER: Well, that's going to have to be worked out between the manufacturers, I think. And then probably it's going to need further discussion.

DR. EDMISTON: I can see where there is a lot of data available on immunizations with these devices and there is virtually nothing available on other biologics in terms of both the pharmacology and possibly even the efficacy, but it's indelibly linked to whether or not the correct amount of the drug is being delivered to the patient.

So I think it's going to be on a case by case basis as to whether or not the device is being used for an old application or is it being used for a new application.

Dr. Weniger?

DR. WENIGER: Yes, just to follow up on that point, I think clearly this issue is more important with nonvaccine pharmaceuticals because the immune response has so many factors that affect it and it's usually either protected or not protected and there's a fair amount of overkill. There's probably more antigen in most vaccines than a patient needs to be protected.

But I would ask what is the current requirement for dose accuracy for a manufacturer of a simple needle and syringe? Do they have to provide data that 100 nurses
measuring up a half cc dose accurately deliver that dose and a variation above and below that dose?

Because if you don't require that for needle and syringe manufacturers--it seems you ought to apply the same requirement for jet injectors. If there's a plus or minus 5 percent on the nominal dose that's read in the indicator, if that's applied for one, it should be applied for the other because my guess is there's a lot of dose variation, high dose variations with needles and syringes.

DR. EDMISTON: The only problem is you can see the dose in a syringe.

DR. WENIGER: Well, I think most of jet guns--

DR. EDMISTON: Can you see it in the jet injector?

DR. WENIGER: In the ones that have disposable cartridges, the goal and I think the ideal is that you can always see the dose in there. And if it's prefilled at the factory, it's--

DR. EDMISTON: So you can determine whether or not the entire dose was delivered.

DR. WENIGER: Yes, you should be able to see that it reaches the right marker on the--if it's a syringe and I have a sample, I can show you afterwards. If it's a cartridge, the end user who fills it usually has the gradations to mark the amount, such as a syringe. Then at the end of an injection you can see that the plunger has gone all the way down.

Now, of course, some of it might leak out on the
DR. EDMISTON: So it's a very difficult issue to thrash out. From the perspective of the manufacturer, one could say the efficacy isn't really in my ballpark. The efficacy is in the ballpark of the pharmaceutical company.

MR. ULATOWSKI: Well, we have cleared a lot of products that say a lot of things about drugs and vaccines and before we go any further down that path we want to make sure that we're clearing products appropriately with their intended use labels and not extrapolating or extending ourselves beyond the data.

DR. EDMISTON: But you said that. This is the second or third time you've said that, so I think this is a key that you're trying to get me to pick up on. It always takes at least three times. The device--

MR. ULATOWSKI: I had a bat here. I was trying to get your attention.

DR. EDMISTON: The device's intended use should be clearly defined.

MR. ULATOWSKI: Yes.

DR. EDMISTON: Clearly defined. So a recommendation from this panel would be that the intent of the device, its use, clinical use, is clearly defined.

Now the issue of where there is a concern for clinical studies, I think it was very well demonstrated that there are other ways of getting around clinical studies. But again the issue is I'm not sure that's the purview of the manufacturer. More the requirement of the
Am I off-base on this or do you think--

MR. ULATOWSKI: Well, if the jet injector manufacturer wants to list a specific drug, then he or she is in a bind by having to provide the data showing it's efficacious with that drug. If there's no data, then there can be no claim, and that data can come from historical information, experience of use, that valid scientific evidence I spoke of.

DR. EDMISTON: So there will have to be minimal efforts on their part.

MR. ULATOWSKI: Yes.

DR. EDMISTON: To demonstrate some type of efficacy.

MR. ULATOWSKI: And I think we might even construct some sort of labeling that would be acceptable for jet injectors based upon the historical information now available.

DR. EDMISTON: And it's unlikely that we're going to need the types of studies involved in randomized double-blinded type studies with these devices.

MR. ULATOWSKI: Well, I would hope they would be incorporated into evaluations of drugs when the drugs are being studied.

DR. EDMISTON: Yes. So it makes a rather simplistic evaluation.

Any comments from the panel?

[No response.]
DR. EDMISTON: Now you're taking notes back there so you can tell me if I'm misspeaking on this, but I think in terms of the first and second questions, we felt that in devices that are similar to devices that have been approved by the FDA in the past, that the FDA has wide latitude to determine whether or not there's a similar or dissimilarity between these devices.

If these devices, as a result of being new and emerging technologies, and there's very little historical data available, then the FDA is probably within its right to request bench engineering-type data to demonstrate the safety of these devices.

In terms of the clinical trial, it would be important for the manufacturer to document what these devices are going to be used for. And if they do that, then there is some level of onus to determine whether or not there is an efficacy for the utilization of this device.

I think it's unclear how that efficacy is going to be determined but I believe it gives wide latitude to the agency, plus in consultation with the manufacturers, to come to some consensus on this.

Would that be an appropriate interpretation?

MR. ULATOWSKI: I think that's fine, yes.

DR. EDMISTON: Dr. Weniger, would you concur with that?

DR. WENIGER: Yes.

DR. EDMISTON: Are there any other questions by
panel members?

[No response.]

DR. EDMISTON: Members of the audience? Yes.

MS. RYDER: Were you finished with number 3, as well?

DR. EDMISTON: I thought I was. Go ahead and jump in there.

MS. RYDER: I just was questioning whether we addressed the issue of transmission of infectious diseases among devices, how they would demonstrate that.

DR. EDMISTON: Let me defer to Dr. Weniger on this. Can you jump in here and give us a little bit of help?

DR. WENIGER: Well, I was looking at the guidance document for the morning discussion that talked about how many sharps engineered devices need to be tested without a failure of either a needle stick or a failure of the device that might have resulted in needle stick, and they came up with a guidance of 500 and they showed the statistics for the confidence limits around 100, 500 and 1,000 and so forth.

Having some kind of guidance like that to help us in doing these studies with the pigs and the cows I think would be helpful. It'll tell us what the ground rules are for this effort and if zero shots out of 500 is reasonable, zero out of 1,000, I think that might be realistic.

Beyond 1,000 it becomes a bit burdensome, so it would be nice to have some feedback that if you shoot in
some model that you believe can detect the lowest infectious dose, what number would satisfy you that you'd let your daughter or son have an injection with one of these devices.

DR. EDMISTON: Now we're talking about a preclinical model, correct?

DR. WENIGER: Yes, this is animal studies. Actually the Brazilians have actually done a human one in which they injected infected carriers of hepatitis B and then put the subsequent injections into vials and then sterilized the device before the next subject in that study, so there was no danger of cross-contamination, but the results are not yet in on that. But that's a very difficult--

DR. EDMISTON: Now what you'd propose, for instance, if there were 500 consecutive injections, at that point the device is taken apart or at that point the device is evaluated to determine if there's any contamination?

DR. WENIGER: What I would say is you'd give an injection to the animal and then the next injection would go into a vial and you would search for quantities of blood from that animal and if you find any quantities above your cut-off, you would say that was a potential contamination event. And the question is how many of those pairs--animal-vial, animal-vial--would be needed in which you resulted in no episodes of a contamination event that would satisfy the regulatory review. That's the difficult question.
What is the magic denominator? Zero out of 500 or zero out of 1,000 or zero out of 100 or zero out of 10,000? I don't want to put a number before I'd like to hear what number people might think would be reasonable.

DR. EDMISTON: Fortunately, I don't think we have to determine that. I think there's probably enough statistical knowledge at the FDA to figure that out, correct?

MR. ULATOWSKI: Yeah, I would just quickly premise the thought, though, that what comes up front is a design process to minimize the potential. Like the one product that was implicated with some problems, you could test that till you're blue in the face; you're still going to have a problem because of the fundamental design flaw with the product.

So assuming you've done all the right stuff up front in design controls, then the tests are confirmatory. Otherwise, I mean there's the premise here that you can't test quality until product. You're designing quality and then confirming and validating that at the tail end.

DR. EDMISTON: Keeping in mind also there's at this point no standard methodology for defining contamination per se, other than the study that was presented and showed how contamination was determined, but there's no standard methodologies available within the industry.

DR. WENIGER: And we have to remember that these models have not been corroborated or validated with some
kind of a gold standard. And I think the point that Ms. Ryder made about the fact that maybe our surveillance systems over the last 40 years have not been sensitive enough to pick up those rare transmissions that might have occurred. Then once again we have to balance this desire to reduce risk to a bare minimum with the existing risk that we know half the injections in the world today are unsafe and causing literally millions of cases of hepatitis B from needles and syringes.

So we need to have a level playing field between these new devices and the classic needle and syringe.

MS. RYDER: I think I just wanted to feel comfortable that there was some issues addressed in terms of an obvious design flaw that was picked up in the past, that that would have some level of control in the future.

DR. EDMISTON: There's probably two ways of looking at this. One is to do what we did in the morning session and look at a postmarketing surveillance of these devices, pick it up on the back end. Or recommend that the FDA investigate the possibility of developing standardized methodology to determine contamination within these devices.

I think probably doing postmarketing surveillance will allow you to pick it up on the back end. However, what is the level of risk you're willing to accept?

So I would recommend the following, that the FDA look at potential models for looking at cross-contamination of these devices, at the same type develop the mentality
for doing postmarketing surveillance on these devices once
they're out there and being used by the public.

Would that be a reasonable recommendation?

[Nods from panel members.]

MR. ULATOWSKI: Noted.

DR. EDMISTON: Does that address any more
concerns? Oh, yes.

MR. HARRINGTON: There is one caveat from
industry. You've heard this morning that one of the things
on needle stick devices was following manufacturers'
directions, an explicit training program. What we're asked
for in the jet injection business and in the testing
protocols is a worst-case scenario: we do nothing, we
allow it to contaminate and we ask how clean you are.

So the question deserves to be answered: are you
going to follow the manufacturer's directions or is it
always a worst-case scenario?

DR. WENIGER: I think he's implying that the
health worker doesn't swab the nozzle, for example.

DR. EDMISTON: Right.

MR. HARRINGTON: No, I'm implying that in the
test to prove safety and efficacy, are we going to follow
the manufacturer's directions? Are we going to try to keep
a clean product between patients? Or do we automatically
assume that it has to be nothing on it? We need to know
what that is, one way or the other.

Certainly there is a demonstrated improvement on
sterility and cleaning when CDC swabbed the nozzles.
So if a manufacturer says you need to do this and such to my product between patients, if you don't do that, we're responsible for it being dirty, or is the test going to be implied that it's always going to be dirty? We need to have an answer to that question, is my response.

DR. EDMISTON: Well, the recommendations that the manufacturer would make for the device I assume would be prudent and appropriate for those devices.

MR. HARRINGTON: But they have not been followed in all the tests in the world to date.

MR. PALOMARES: Yeah, but the data that you're generating would have to follow your protocol. Why wouldn't you promote your product and why wouldn't you study your product unless it's following your method?

MR. HARRINGTON: I absolutely agree. My point is that WHO is ignoring those and testing it to a different level than the manufacturer--

DR. EDMISTON: Well, we can't deal with WHO issues in this meeting. We can only deal with what would be appropriate for the FDA.

MR. ULATOWSKI: Well, I'd have to say that yeah, you follow labeling but the labeling has to reflect actual use conditions, real life conditions. And if you're disregarding some common event or occurrence or some aspect of the environment, then the labeling is not quite correct, either.

MR. PALOMARES: But then you should put that in your warnings.
DR. EDMISTON: See, your device, for the most part, the devices that you've been talking about, for the most part, that device is going to be used by health care workers with some minimal level of training.

MR. HARRINGTON: Not necessarily. It was used by the Army for 35 years and it was always wiped. Never had an issue. Good tracking system. And there's nothing recorded in the world that says that it wasn't wiped. It's in a study that was presented using a method that isn't approved, it was not wiped and it said oh, we can contaminate 31 out of 100.

MR. ULATOWSKI: You want to come up to the mike? Because that's not getting transcribed.

DR. EDMISTON: Do you want to do that again?

MR. HARRINGTON: Sure. What I'm saying to you is we believe that there are situations--the U.S. military for 35 years used the product appropriately. There was never an indicated transmission of hepatitis. Certainly they follow cases of hepatitis in the U.S. military.

Here is a situation where a test was made, it was used with a method that was not approved, a new experimental assay, and it was used intentionally dirty. I don't know if that's fair.

DR. EDMISTON: I think it's going to be very difficult to answer these questions. I believe that what we need to really look at is both the postmarketing surveillance and then also look at potential models for the future evaluation of these devices.
I think what you're saying is absolutely true but at the same time, this technology is emerging and we need to keep abreast of how this technology may actually be responsible for transmitting infections in the future, like hepatitis C. We just don't have those answers.

So I suspect—I'll ask my committee members here—that the FDA consider looking at appropriate test methodologies for looking at possible cross-contamination of these devices with multiple use and that the FDA also consider a postmarketing surveillance program to track these devices once they leave the manufacturer in the hands of both the health care worker and other health care professionals.

Now having said that, I realize that many of these devices will not be in the hands of health care professionals. They're going to be in the hands of high school kids and others. But that's the worst-case scenario and we can't do anything about that.

Does the FDA have any other questions?

MR. ULATOWSKI: No.

DR. EDMISTON: That said, I would like to wrap up this meeting and thank you all for your presentations and your time and activities and this meeting is adjourned.

[Whereupon, at 4:14 p.m., the meeting was adjourned.]