

1 within multi-center institutions. But I think if specific
2 claims are made--it may be best from the manufacturers'
3 perspective never to make a specific claim but if claims are
4 made, this is going to impact on our presentation or how we
5 view that device.

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

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

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

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

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

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

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

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

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

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

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

22 I think unless someone out there knows something I
23 don't, most of these devices are going to be evaluated, if
24 they're evaluated, in institutions that have health care
25 professionals who are used to using them and they will be

1 the end users. But I think it would be tough to deal with
2 that home care issue, especially the way it's structured
3 currently.

4 Any other comments or questions?

5 MR. DACEY: On that home care issue, despite the
6 fact that it is so terribly difficult and clearly the user,
7 in perhaps most cases, would be a non-health care
8 professional, I too would like to see some effort made, some
9 diligent effort made to examine in a clinical setting, and
10 again I don't have expertise on how to do this, so that
11 there is some feedback statistically on what happens when
12 these things are in the hands of a person at home.
13 Eventually some of them are going to be there.

14 DR. EDMISTON: One of the questions that's going
15 to come up is in terms of education and I think in terms of
16 home care, that's an area where we need to strengthen our
17 education.

18 MR. DACEY: Absolutely.

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

21 MR. DACEY: I certainly can accept that.

22 MS. RYDER: I would just reiterate in terms of
23 your comment then, you're saying that we are going to be
24 able to make the huge assumption that professional workers,
25 if we're able to demonstrate safety and efficacy, that we

1 can assume that it will also be safe for a patient user. I
2 think that's probably a huge leap but also I agree that the
3 ability to be able to study that in a home care environment
4 would be very difficult but it's something that is here and
5 it's something that we're dealing with every day as nurses,
6 and even on the educational basis in talking about educating
7 the health care worker, but they also have to have the
8 ability to educate the patient. And that hasn't been really
9 addressed, either.

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

13 MS. RYDER: That could be a start.

14 DR. EDMISTON: That may be it.

15 MS. RYDER: Through the home care professionals.

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

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

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

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

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

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

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

9 DR. EDMISTON: Yes.

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

12 DR. EDMISTON: Yes.

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

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

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

21 DR. EDMISTON: So devices that are making--

22 DR. RUTALA: Not equivalency. A claim of reducing
23 needle stick injuries.

24 DR. EDMISTON: All devices, if they involve
25 puncture of some type, should be tested on appropriate

1 tissues or simulated tissues.

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

5 DR. RUTALA: That's correct.

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

8 DR. RUTALA: Or the percent reduction.

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

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

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

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

20 [Nods from the panel members.]

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

1 what you're saying?

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

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

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

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

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

1 population?

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

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

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

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

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

24 So you have that component. How can they do that
25 kind of teaching and demonstration if they're not using a

1 safety device? Hopefully the market will come down and
2 we'll be able to have the safety device but that's an issue.

3 When they do their own procedures, what kind of
4 technique? And I must say that I was rather staggered to
5 find out what people are doing in the home. What three
6 years ago would have been done in an ICU, at least in the
7 Bay Area is now being done at home, so that there are very
8 complex procedures that are being done there.

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

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

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

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

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

12 DR. EDMISTON: Thank you, Dr. Fisher.

13 Could I have the speaker in the back, please?
14 Would you please identify yourself, please?

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

22 DR. EDMISTON: Please identify yourself.

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

1 the absence of data.

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

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

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

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

25 Let me see if I can encapsulate this a bit and I

1 want comments from the panel. Would it be appropriate for
2 the panel to recommend to the FDA that efforts be taken
3 under way to investigate the optimal means by which devices
4 such as these can be studied in the home health care
5 environment and to start this as a discussion process with
6 public comment, comment from industry, but not per se make
7 this as a mandate from this panel? Is that appropriate?

8 [Nods from the panel members.]

9 DR. EDMISTON: Does FDA agree with that?

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

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

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

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

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

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

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

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

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

13 DR. EDMISTON: Marcia?

14 MS. RYDER: Could you repeat the question?

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

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

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

1 criteria.

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

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

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

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

15 MR. DACEY: No further comment.

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

22 Yes, Dr. Fisher?

23 DR. FISHER: As flattering and validating of our
24 work are those comments, I think we have to be realistic.
25 We can't even get people to report needle sticks. And I

1 have some suspicions that surveys are not going to--I would
2 be encouraged but I'm not optimistic that we're going to get
3 that kind of data.

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

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

18 So there has to be attention directed to
19 formalized studies and that formalized studies have great
20 specificity. In fact, we submitted a graph and I don't know
21 if it's going to be funded, to NIOSH or not, to have a
22 user-based design pilot study, to come up with a national
23 agenda where we poll people who are interested and develop
24 some criteria for what pilot testing should be, what should
25 be included in pilot testing and, when you give that, to

1 test it with a group of users and with a control group, to
2 see if you can get better data and to have some kind of way
3 that you can quickly get that data, that you don't put a
4 burden onto people who don't even have time for reporting.

5 We did not bring this up but reporting goes from
6 30 percent to 60 percent. No matter what efforts you make,
7 you can't get--the most common one, besides which some
8 people are discouraged because in some hospitals your pay,
9 your merit pay will depend on whether you have a needle
10 stick or not, is "I don't have the time to do that."

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

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

18 As Mr. Ulatowski indicated, there was a lot of
19 work involved in these studies and I think they're a
20 valuable format. I think that in terms of--when would you
21 anticipate that this document would be revised and available
22 for public comment?

23 MR. ULATOWSKI: That's always a good question.
24 Probably sometime in the fall.

25 DR. EDMISTON: Yes, I think it would be very

1 difficult to implement the technology and the research
2 methodology at this stage, to try and address this
3 particular issue.

4 DR. FISHER: I was giving that as a perspective--

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

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

13 [Nods from the panel members.]

14 DR. EDMISTON: Okay.

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

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

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

22 MR. ULATOWSKI: Well, we showed a couple of slides
23 of elements of the guidance document in terms of the bench
24 testing, biocompatibility, preclinical, clinical, simulated
25 and clinical.

1 The panel, though, is primarily
2 concerned--typically any panel that we bring here is
3 concerned with the clinical aspects of guidance documents
4 and not the engineering aspects so much.

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

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

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

25 MS. RYDER: A question for you. Are the current

1 items in this document in compliance with AMMI and ISO
2 standards today?

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

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

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

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

22 DR. EDMISTON: Mr. Palomares?

23 MR. PALOMARES: To the degree of testing, whether
24 it's bench, simulated clinicals or clinicals, I agree and
25 disagree with the panel to a certain extent and I'll work

1 with the panel here. However, one thing as a manufacturer
2 that we see is we want to be working off the same playing
3 ground. What I mean is on microbial challenges--

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

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

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

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

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

1 Dr. Rutala?

2 DR. RUTALA: No questions.

3 DR. EDMISTON: So with the evaluation criteria in
4 place, we feel comfortable with the evaluation criteria,
5 with the caveat that the panel recommends that the FDA look
6 at the development of standardized testing protocols,
7 specifically in microbial challenge protocols, in comparing
8 these devices. Inclusion.

9 Is the panel in agreement with this?

10 [Nods from the panel members.]

11 DR. EDMISTON: Thank you.

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

17 Dr. Rutala?

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

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

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

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

8 DR. RUTALA: A range of expected reduction.

9 DR. EDMISTON: A range of expected reduction.

10 DR. RUTALA: Compared to standard devices.

11 DR. EDMISTON: Compared to standard devices.

12 DR. RUTALA: That's correct. Again we're talking
13 about the device that has a claim of efficacy.

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

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

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

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

23 MR. ULATOWSKI: He needs to identify himself.

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

25 DR. EDMISTON: We understand what our obligations

1 are in terms of training our employees, whether they're
2 full, part-time or contract employees, as they come into our
3 institution, especially in terms of blood-borne pathogens.

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

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

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

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

23 Does that sound reasonable, Mr. Palomares?

24 MR. PALOMARES: It does sound reasonable.

25 Unfortunately, the perspective from industry is that your

1 directional insert that comes in with your case of product
2 usually ends up on the floor of central supply. It doesn't
3 get to--

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

8 MR. PALOMARES: No, it's not.

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

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

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

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

24 DR. RUTALA: The only other comment that I would
25 make is that this question seems to go beyond just the

1 efficacy issue and I was wondering if we should consider
2 other issues, such as intended uses, unapproved uses,
3 training required for use and disabilities which preclude
4 use, such as a sight-impaired person to use the device, or
5 potential dangers with using the device.

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

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

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

15 DR. EDMISTON: Okay. I think in terms of--well,
16 within an institution in terms of visually impaired
17 individuals, I suspect the greater onus is placed upon the
18 institution.

19 Marcia, how do you feel, in terms of the education
20 of that person?

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

24 I believe, if I'm not mistaken and we can
25 certainly address this, that many of the things that Dr.

1 Rutala detailed are already part of requirements of
2 labeling. Is that not true?

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

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

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

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

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

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

23 And when you put that in perspective with the
24 clinical situation, a very volatile and uncontrollable
25 setting, to label something as nonreusable might be

1 physically impossible. And how will the FDA regulations
2 back-track and look at that issue in regard to standard
3 products as it does to safety products?

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

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

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

11 DR. EDMISTON: Right.

12 MR. ULATOWSKI: We do have a policy forthcoming.

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

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

25 MS. DUCMAN: Thank you.

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

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

14 Is the FDA in agreement with that?

15 MR. ULATOWSKI: [Nods.]

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

20 "Currently sponsors submitting applications for
21 needleless access devices-- intravenous systems that do not
22 require the use of a needle--are asked to demonstrate that
23 their device is substantially equivalent by providing
24 nonclinical bench data to demonstrate that their device does
25 not increase the risk of microbial contamination of the

1 fluid pathway, validation of the cleaning method, and
2 instructions for use. What additional type of information
3 should be considered for our premarket review?"

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

8 [Nods from the panel members.]

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

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

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

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

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

25 And I think in terms of the message, that's part

1 of another question.

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

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

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

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

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

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

23 MR. PALOMARES: I think it already occurs. I
24 don't think it needs to be part of the regulatory process
25 simply because in order for a facility to take on this,

1 they're asking the manufacturer to provide this information.
2 They're asking to train us, demonstrate how this product is
3 used, give us some support.

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

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

9 MR. PALOMARES: That is correct.

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

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

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

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

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

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

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

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

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

25 My book shelf is crowded with instructional

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

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

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

20 DR. EDMISTON: Dr. Rutala?

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

25 First, the issue of training, user training. I

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

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

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

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

22 So the two points that I would like to bring up
23 are the issue of considering minimal criteria, and I don't
24 know that we decide what they are--we've addressed a few of
25 them but minimal criteria for user training of these

1 needleless devices or protective sharps.

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

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

12 I think in terms of your comments that the FDA's
13 position should be that the information, the insert
14 information provided by industry should describe the
15 intended use of the device in which it should be
16 appropriately used and also should address, as you've
17 indicated, the competency, the potential competency of those
18 individuals who are using the device.

19 Now in terms of how this information can get
20 across, I think there is some area of debate--whether it's
21 part of an in-service by your colleagues in the industry or
22 is there some formal mechanism by which the FDA puts
23 together a series of educational tapes and then provides
24 those to the end user?

25 I don't know if that format needs to be completely

1 worked out but it sounds to me, from listening to Dr.
2 Joseph, she is addressing this particular area in terms of
3 education. Is that correct?

4 DR. JOSEPH: That's correct.

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

10 DR. JOSEPH: We have certainly heard it.

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

18 So the time that nurses have to spend in educating
19 patients becomes less and less and less. And now we're
20 suggesting that--I'm suggesting that we be careful on where
21 we put that responsibility.

22 DR. EDMISTON: I think this whole issue of home
23 health care is really a black box that's not going to be
24 clearly defined by this criteria document, but I think we
25 need to be thinking about it in the work that Dr. Joseph and

1 Dr. Fisher and others in the audience are alluding to needs
2 to be considered, especially in future revisions of this
3 documentation.

4 Is the FDA in agreement with our comments?

5 MR. ULATOWSKI: [Nods.]

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

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

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

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

20 Let me panel the panel.

21 MS. RYDER: No added comments.

22 DR. EDMISTON: Dr. Rutala?

23 DR. RUTALA: [Nods.].

24 DR. EDMISTON: Mr. Palomares?

25 MR. PALOMARES: [Nods.]

1 DR. EDMISTON: Mr. Dacey?

2 MR. DACEY: I agree.

3 DR. EDMISTON: Terrific. That was painless.

4 Yes? We have a guest.

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

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

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

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

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

1 studies.

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

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

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

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

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

22 Are there any final comments from our panel
23 members?

24 [No response.]

25 DR. EDMISTON: If not, I'd like to ask the FDA if

1 we have addressed the questions sufficiently.

2 MR. ULATOWSKI: [Nods.]

3 DR. EDMISTON: If so, I will now close this part
4 of the meeting so that we can break for lunch. We will
5 reconvene at 1:30. Thank you very much.

6 [Whereupon, at 12:30 p.m., the meeting adjourned
7 for lunch, to reconvene at 1:30 p.m. the same day.]

A F T E R N O O N S E S S I O N

[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

1 reintroduce themselves, starting with my colleague on the
2 right.

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

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

9 MR. PALOMARES: I'm Salvadore Palomares. I'm
10 industry representative. I'm the manager of regulatory
11 affairs for ICU Medical.

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

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

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

19 This is a great entrance.

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

24 MS. O'LONE: Okay, and now we'll have Tim
25 Ulatowski, the division director for Dental, Infection

1 Control and General Hospital and Personal Use Device
2 Division provide an overview on the topic for this
3 afternoon's session.

4 FDA PRESENTATION

5 MR. ULATOWSKI: Thanks again, Martha, and welcome
6 back to the panel for the afternoon session.

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

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

22 This being a drug and biologics delivery device,
23 we are not alone in this Center in the evaluation of these
24 products, typically. When the need arises, we will obtain
25 the opinions of our drug or biologics centers on drug or

1 biologic aspects with the injectors. And in fact, some of
2 the products that may be touched upon today are, in fact,
3 primarily regulated by our Center for Drugs and Center for
4 Biologics, those injectors that may be prefilled with a
5 biologic or a drug when it's sold to an end user.

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

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

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

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

23 And that's really the challenge in front of us.
24 As a center, we have to deal with both ends of the spectrum
25 in the device area. One of the critical areas that we have

1 to deal with with this technology is when clinical data are
2 needed and providing some criteria along those lines, of
3 when more than just bench or engineering information is
4 necessary.

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

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

14 CAPT. NAKAYAMA: Thank you, Tim.

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

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

24 [Laughter.]

25 CAPT. NAKAYAMA: A jet injector is a preamendment

1 device that's an alternative means to administer a drug or
2 biologic. Jet injectors can be labeled for the specific
3 administration of specific compounds, such as insulin, or
4 for general purpose use, such as IM injections of
5 vaccinations. Jet injectors are designed for personal use
6 or multi-patient use.

7 The prevalence of jet injector use may increase
8 due, in part, to increased public health awareness of needle
9 stick injuries, sharp disposal, reuse of single use needles,
10 and the possible cost-effectiveness of mass immunization
11 programs.

12 Two things jumped out at me over the weekend that
13 I just want to interject here. Malaria infects 275 million
14 people a year. TB deaths account for 1.5 million deaths a
15 year. Treatment of these epidemics may be most effective,
16 cost-effective, using jet injectors rather than a
17 traditional needle and syringe.

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

24 Part 21 CFR 880.5430, nonelectrically powered
25 fluid injector--the jet injector that we're talking

1 about--is a device used by health care providers to give a
2 hypodermic injection by means of a high velocity jet fluid.
3 This fluid penetrates the surface of the skin and delivers a
4 fluid to the body.

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

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

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

23 The second is for multiple patient use, where the
24 device is used by a health care provider, generally for
25 public health initiatives like immunization programs, and

1 can be categorized into three types: low, medium and high
2 workload devices. High, medium and low workload devices are
3 terminologies recognized as developed through various
4 CDC-sponsored conferences on jet injector devices.

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

10 The mechanism of action of a jet injector is the
11 acceleration of a drug or biologic using spring or
12 compressed gasses to high velocity that will deposit the
13 drug or biologic into the tissue without any part of the
14 device penetrating the tissue. Jet injectors use nozzles
15 instead of needles and may have a single nozzle to inject a
16 single injectate in a single stream or an admixture in a
17 single stream.

18 Multiple nozzle designs, on the other hand, can
19 inject a single injectate or admixture through several
20 streams or simultaneously inject several different
21 injectates in one action.

22 There are several important review issues in the
23 evaluation of a jet injector for safety and effectiveness.
24 The first is the identification of an appropriate legally
25 marketed device to which a jet injector device can be

1 compared. The CFR definition of a jet injector is--I'll
2 repeat it again--a device that injects fluids to the body
3 through the skin. We have used an elastic interpretation of
4 "substantial equivalence" to include injectors that inject
5 solids--powders and particles--not only through the skin but
6 in some cases to the skin.

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

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

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

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

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

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

20 Then there's the issue of mutually conforming
21 labeling. Is the device labeling consistent with the drug
22 and biologic labeling, and vice versa? Are there possible
23 conflicts that could arise from the use of the device with
24 the drug or the biologic? Most drugs and biologics are
25 labeled with the route of administration, such as

1 subcutaneous, intramuscular IV. The method of
2 administration is generally not specified.

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

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

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

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

21 The jet injector can involve multiple tissue
22 dosing versus single target tissue from needle and syringes.
23 Various dose forms can be administered through a jet
24 injector. The needle and syringe will inject a liquid.

25 There are also multiple fluid paths and multiple

1 drugs that can be administered in a single jet injection.

2 The concomitant dose is a single drug and fluid path.

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

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

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

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

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

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

1 And this is what they're not.

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

4 DR. EDMISTON: Thank you.

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

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

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

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

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

1 infections.

2 In addition to transmitting blood-borne diseases,
3 needles also pose obstacles to immunization, which is one of
4 the most cost-effective interventions to prevent disease.
5 Just a decade ago in this country, to fully vaccinate a
6 child in accordance with the recommended immunization
7 schedule required only eight injections. Today is requires
8 a minimum of 14 injections, and this number will increase to
9 16 injections next January when the oral polio vaccine is
10 entirely replaced by the injected polio vaccine.

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

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

24 Jet injectors are devices to administer drugs by
25 shooting through the skin a fine stream of liquid under high

1 pressure through a small orifice. The first commercial
2 needle-free injector in the United States was the Hypospray
3 shown here, developed in the late 1940s, and this first
4 model was developed primarily to reduce needle phobia among
5 diabetic children.

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

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

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

25 Unlike the previous devices shown, this J-Tip is

1 unusual as a completely disposable single use only device.
2 The user loads the drug through the orifice, through this
3 protective cap into the chamber, and pressurized gas stored
4 here drives the drug into the tissue.

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

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

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

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

1 regulations.

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

7 Another example of a prefilled needle-free
8 cartridge for use in a reasonable device was brought to an
9 advanced stage of development with several published
10 clinical trials by Pasteur Merieux Connaught. This Imule
11 cartridge is about the same size and shape as a standard
12 unit dose vaccine vial.

13 Now almost all the previous devices I showed you
14 have the disadvantage of requiring the health worker or end
15 user to fill them by manually transferring the vaccine or
16 drug from another container. This is inconvenient, takes
17 time, and often expends a needle and syringe or some other
18 transfer container.

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

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

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

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

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

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

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

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

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

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

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

1 in antigen-processing cells.

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

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

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

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

19 Tissue deposition tends to be diffuse, in a
20 generally conical shape with the apex at the skin. The drug
21 tends to follow the path of least resistance, often glancing
22 off muscle fascia, especially if the angle of penetration is
23 not perpendicular.

24 Where the drug ends up depends on a variety of
25 factors, as listed here, related to the device or to the

1 operator or to the patient. In actual reality, it's hard to
2 predict precisely where a dose is going to end up.

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

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

19 This is an x-ray of a living human biceps,
20 comparing simultaneous intramuscular injection between a
21 needle, which is the upper contrast injection, and the
22 Hypospray injector, the lower contrast one, and you can see
23 how the contrast appears to spread along the muscle fibers,
24 with perhaps the Hypospray dose spreading a bit faster. And
25 by 45 minutes later, most of both injections have diffused

1 away.

2 This is more recent magnetic resonance imaging of
3 simultaneous subcutaneous injections in a living human
4 thigh. The needle dose in the upper left position of these
5 four shots is the needle dose and the jet injector dose is
6 the one in the central right.

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

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

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

24 Now the great variation in where jet injector
25 doses end up is revealed in this product brochure and the

1 next slide I'll show you for the Biojector 2000. Bioject
2 varies the syringe size and thus the orifice size as a means
3 of achieving different depths of penetration. Based on
4 magnetic resonance imaging this data was obtained and it
5 found that almost one-third of the number 3 syringe here,
6 only 29 percent of the injections went into muscle or
7 actually got into muscle, even though they were intended for
8 subcutaneous use.

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

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

21 Let us now return to the issue of the safety of
22 multiple use nozzle jet injectors. In the mid-1980s one
23 Med-E-Jet device, as I mentioned earlier, was documented to
24 cause a hepatitis B outbreak in California. Several dozen
25 confirmed cases were identified who had received multiple

1 hormone injections in one weight loss clinic. There was no
2 evidence of problems in other branches of this chain of
3 clinics using similar devices for similar injections. As
4 part of the investigation, CDC did laboratory testing of the
5 Med-E-Jet.

6 The Ped-O-Jet device, another device I showed you,
7 was also tested as a control and most of the results were
8 reported in this 1990 Archives of Internal Medicine article.

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

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

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

24 After intentional contamination of the nozzles of
25 the two devices, the Ped-O-Jet and the Med-E-Jet, in both

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

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

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

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

22 Given chimp studies indicating that carrier blood
23 may contain 100 million chimpanzee infectious doses per
24 milliliter, this calculates to a theoretical single
25 infectious dose of 10 picoliters of blood, and this is an

1 extremely small volume that challenges detection
2 methodologies.

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

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

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

24 This is a photograph from our injections of
25 anesthetized pigs in Florida. After various control

1 specimens are collected, including mock injections in the
2 first boxes of this injection grid, 100 real injections of
3 phosphate-buffered saline are given in each series.

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

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

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

25 If 100 consecutive specimens are clean, what would

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

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

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

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

23 Now in 1976, upwards of 75 million Americans were
24 vaccinated with these devices in a short space of time in
25 order to protect them from the swine flu. But now with

1 these devices in limbo, we lack any alternatives means to
2 quickly vaccinate large numbers of persons with limited
3 manpower.

4 And it is not a question of whether the deadly
5 1918 swine influenza pandemic will recur but really a
6 question of when it will recur. The recent H5N1 fatal
7 influenza cases in Hong Kong were perhaps a warning of this
8 vulnerability.

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

16 That might be a burdensome obstacle and would be
17 inconsistent with how new needles and syringes are licensed,
18 perhaps.

19 Obviously if they're sold for diabetes there ought
20 to be clinical data on their use with insulin. If they're
21 sold for vaccines I could understand the need for perhaps
22 some representative, a live vaccine or an inactivated
23 vaccine, as markers for all the many possible vaccines.

24 Instead however, recognizing the public health
25 advantages of needle-free injection, the clinical data on

1 efficacy and safety for specific vaccines delivered by jet
2 injector might properly be a part of the license application
3 for the biological because currently the manufacturers
4 really only provide data on vaccines delivered with needles.

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

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

22 And finally, let's ask if it would not be
23 reasonable in determining the safety and efficacy of common
24 vaccines that were prefilled into such cartridges to use
25 relatively small clinical studies for reatrogenicity and

1 serologic response with jet injectors. And then bridge from
2 those studies to perhaps the large field trials that may
3 have been conducted in the past with needle and syringe and
4 show comparable rates of immune response.

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

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

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

25 PRESENTATION BY INDUSTRY

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

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

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

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

22 Also, we've done at PATH about 11 years worth of
23 functional and safety testing that might be of interest.

24 Are there areas that are of particular interest to
25 the panel?

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

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

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

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

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

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

25 We also have a special interest in eliminating

1 unwanted reuse, and this is, as Bruce said, a very common
2 problem in developing countries.

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

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

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

22 If it's normal to the fascia and there's a shallow
23 subcutaneous overlying tissue, it will typically penetrate
24 the muscle fascia. If it's deep subcutaneous tissue, you
25 get a wide dispersion in the fatty tissue. And, of course,

1 the needle is going to deliver at the tip of the needle
2 primarily.

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

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

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

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

1 States.

2 They did establish this working group and time
3 line. It has representation from ANFIM, which Bob
4 Harrington will talk about in a minute. And they are
5 addressing sort of the typical starting point of
6 standards--the physical dimensional characteristics, safety
7 and quality.

8 I don't think they're yet addressing all of the
9 aspects that are unique to jet injection, although I hear
10 there's been some follow-up discussions about the effect on
11 the drug in terms of the sheer and the high pressure
12 exposure.

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

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

25 The nozzle can be either multi-use, durable or

1 disposable.

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

6 I would add that some jet injectors are being
7 designed now with autodisposable features so that the nozzle
8 or cartridge cannot be reused. This is of particular
9 interest, as I said, in developing countries but maybe also
10 here.

11 Hybrid devices have some reusable portion of the
12 fluid path but also have some disposable portion and this is
13 to add a margin of safety, and I'll talk a little bit more
14 about that in a minute and show you some cut-away views.

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

23 There are considerations about the fluid path, as
24 well, particularly if you're considering contamination. How
25 much of the fluid path is reused? How much is exposed to

1 potential blood being wicked back up into the system after
2 exposure to the nozzle face? And is the dose adjustable or
3 fixed?

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

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

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

23 In fact, the Med-E-Jet Corporation has just now
24 changed their instructions and has sent out copies to all
25 their customers and to us, trying to find a safer way to use

1 that device that was implicated in the weight loss clinic
2 hepatitis B outbreak. There is a distinction there and
3 that's something for the panel to consider.

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

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

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

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

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

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

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

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

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

23 So there's another picture of that. The items you
24 see in red are now additional device components that become
25 incorporated, depending. These are all variants within

1 reusable nozzles and there's many different subflavors of
2 this that are either in development or in commercial
3 devices.

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

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

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

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

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

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

12 There's also partial cartridges with a separate
13 nozzle face and if that nozzle face were to be reused,
14 obviously that's a potential carrier for contamination.

15 User interface issues are very important.
16 Particularly in our constituency with low literacy users,
17 the device must be easy to learn to use and learn to use
18 properly.

19 I think one of the most important things is
20 assuring compliance through good design. And if we're
21 talking about disposable cartridges, this new family of jet
22 injectors, we want to watch out that we're not introducing
23 another means of contamination through handling.

24 This is one design actually that I was involved in
25 that if you were to reload the cartridge with bloody gloves,

1 you'd want to have an overcap over this, as an example.
2 That's hands-on.

3 Getting back to the autodisposable features, just
4 like with the syringes, there's active versus passive.
5 Obviously whenever possible, passive is the preferred.

6 And then there's some kind of interaction with the
7 device. The device has to participate with the cartridge
8 usually in order to result in a disabled cartridge.

9 There are other standards that probably at some
10 point will need to be discussed about disposal, reuse. Is
11 it sterilizable or disinfectable, as most of the current
12 campaign injectors are? What are the methods used? How
13 often is it done? Are there cold liquid disinfectants
14 allowed?

15 And then what is the wear life over multiple uses,
16 including exposure to things like steam sterilization and
17 liquid disinfectants?

18 Again there's the difference between a prefilled
19 unit dose, which does become a package, versus filling on
20 site, which then has to be compatible with some sort of
21 intermediate filling mechanism.

22 I'm just going to show you a couple of quick
23 pictures. We've done developmental tests for about 11
24 years. They're not meant to develop standards. They're not
25 guaranteeing performance. However, they give you a little

1 bit of insight into the sort of dynamics that are going on
2 when a jet injection is given.

3 The three tests that I'll talk about are a
4 combination of target photography test, force test and
5 penetration test.

6 Target test is very simple. We're shooting
7 through a thin piece of plastic and looking at the resulting
8 hole. It does tend to correlate, at least in our limited
9 human and porcine studies, to the trauma of the entry
10 puncture hole and it does very strongly correlate to the
11 jetstream quality.

12 Again reviewing this picture, you can see these
13 would make quite large targets and we double up and do this
14 photography test because a substream like this is too weak
15 to penetrate the target and that would result rather than in
16 a rough trauma at the entry or puncture wound, it would
17 result in undelivered injectate.

18 We also test the force. These nice neat bell
19 curves are not an exact representation of what's happening
20 because the test mechanism has some mass and it smooths out
21 and slows down the bell curves. However, as a comparative
22 test, there's some value.

23 Mostly I wanted to show you this to show you how
24 wide a range efficacious injectors cover, more than a factor
25 of 2 in terms of peak force and length. This is all half-cc

1 shots. This is all the same volume.

2 We use a foam model that was developed originally
3 for training people to insert Norplant capsules as a test
4 for penetration. This shows the sort of thing we would
5 observe with human subject tests--a very small amount of
6 residual fluid, a few drops, and this actually depicts a
7 running liquid down the arm. And this is the range that you
8 would see with human subjects, as well.

9 We tried to develop a gel penetration test. It's
10 become part of the nomenclature or discussions among the
11 industry. We're now recommending that this not be pursued
12 until someone finds a gel that actually simulates human
13 tissue better. This is something we worked on for nearly 10
14 years and have now abandoned.

15 I think that's my time, unless you'd like me to
16 discuss the safety tests. I think I should stop.

17 DR. EDMISTON: I think we're going to move along.

18 Do the panel members have any questions at all for
19 Mr. Austin?

20 [No response.]

21 DR. EDMISTON: Thank you very much.

22 Our next speaker is Mr. Bob Harrington, who is
23 here to represent the Association of Needle Free Injector
24 Manufacturers.

25 MR. HARRINGTON: Good afternoon to the panel. I

1 think I'm the last speaker so if you want to run early, you
2 can run, and if I keep you too late, boo at me or something.

3 I would like to thank Von and Dr. Weniger and
4 Glenn for talking about jet injection and giving you some
5 background. Unfortunately, they used probably most of my
6 material so I'll be quite quick through my slides and I will
7 eliminate some that I already have prepared.

8 My first presentation today is about ANFIM, the
9 Association of Needle Free Injection Manufacturers. The
10 second presentation is about the Ped-O-Jet, since I was
11 president of Vernitron and currently owner and president of
12 American Jet Injector, and I'll talk a little bit about the
13 truth and the myth of high workload injector contamination.

14 ANFIM was an association that was created to
15 promote an understanding and advancement of needle-free
16 injection technology through the world, to develop common
17 standards that facilitate invention and progress within the
18 field of jet injection--needle-free injection, I should say.

19 We want to represent industry as a unified group
20 when dealing with regulators like yourselves,
21 standard-setters, government agencies and other
22 organizations and the general public. We're trying to
23 disseminate information to the common benefit of all
24 members.

25 We want to act as liaison between PHRMA and IFPMA

1 or the pharmaceutical equivalents of our organization.

2 There are four classes within our organization:
3 needle-free manufacturers, needle-free developers and
4 related industry members, such as pharmaceuticals or vaccine
5 manufacturers, and then observers from the public health
6 community.

7 We have five board members that are actually
8 voting and two nonvoting board members: myself, Linda
9 D'Antonio and Valerie D'Antonio from DCI, John Lloyd, who is
10 head of the Program for Expanded Immunization at WHO, and
11 Ralph Bitdinger from Becton Dickinson.

12 We have two liaisons to the board, one from Center
13 for Disease Control, Dr. Weniger, and the other is Pat
14 Cricenti from FDA Center for Devices and Radiological
15 Health.

16 I'm here to talk a little bit today as an industry
17 about regulatory fairness. According to Congress, a vibrant
18 and growing small business sector is critical to creating
19 jobs in a dynamic economy. Small businesses, however, bear
20 a disproportionate share of regulatory costs and burdens.

21 According to reputable sources, there are about 12
22 billion vaccine injections in the world each year on an
23 annual basis. The needle industry is made up of
24 multinational million dollar if not billion dollar
25 corporations with tens of thousands of employees. Unsaid,

1 however, is they have significant dollars available for PR
2 and lobbying efforts.

3 The needle-free industry, on the other hand, is
4 made up of small businesses with less than \$10 million in
5 sales and less than 50 employees. So we need to have some
6 regulatory fairness here as a small business.

7 Why is ANFIM here? Because we want to deserve a
8 federal regulatory enforcement process that is reasonable
9 and predictable. We want a common sense to problem-solving
10 and a strong voice in the federal regulatory process.

11 Congress has mandated that small businesses should
12 have this by passing Public Law 104 to 121 or known as
13 SBREFA, the Small Business Regulatory Enforcement Fairness
14 Act. This act makes certain that small business have a
15 voice that will be heard by the FDA or other federal
16 agencies as they go through the rule-making process. It
17 gives small business expanded opportunities to challenge a
18 federal agency's final regulatory decision.

19 The bill makes the Small Business Administration,
20 the SBA, responsible for giving us the tools to do that.
21 According to Congress, these boards will shoulder much of
22 the responsibility for making regulatory fairness a more
23 integral part of government.

24 There are six aspects of this regulation and I
25 will not read them to you. I'll just paraphrase the top.

1 It's regulatory compliance simplification. It should be
2 comprehensive; it should be in plain English.

3 Equal access to justice. If we go to court and
4 challenge an agency that has made regulations that we think
5 are unfair, we are able to have court and attorney fees
6 returned to us.

7 There's a congressional review process. Congress
8 is authorized to review each major rule promulgated by any
9 agency before it becomes regulation.

10 There's enforcement reform. Within one year of a
11 new regulation, the FDA shall establish a policy for
12 reduction and, in some circumstances, the waiver of civil
13 penalties for violations by small businesses.

14 There's an advocacy review panel. There's an
15 oversight of regulatory enforcement. All of these things
16 are part of the law and we're just asking please that they
17 take effect on regulations within the needle-free industry
18 because we are a cottage industry.

19 Under judicial review and a new act, the RFA,
20 Regulatory Flexibility Act, we have an opportunity to seek
21 review of federal agencies' compliance with the law through
22 the SBA if you fail to meet the required analysis and
23 disclosure obligations. We can ask the chief counsel to
24 file a friend-of-the-court brief on our behalf, appealing
25 any ruling or violation of RFA by a federal agency.

1 My basic message under the ANFIM message is
2 simple. The children of the world need needle-free
3 injection products. The entire world and the environment we
4 live in need needle-free injection products.

5 We, the citizens of the developed world, have an
6 obligation to the less fortunate inhabitants of the
7 developing world. We cannot continue to pollute,
8 contaminate and infect the developing world by a policy
9 which recommends disposable needles, all the time knowing
10 that they routinely are reused dirty or are improperly
11 disposed of.

12 ANFIM and the FDA perhaps have two choices. The
13 FDA can either allow this technology and our industry to
14 grow, prosper and flourish by providing reasonable
15 direction, guidance and support or create a burdensome
16 bureaucracy that unnecessarily overregulates needle-free
17 products, with the end result of potentially forcing all of
18 my member companies out of business.

19 Three questions deserve answering in this process.
20 Are new regulations economically justified? Are the safety
21 issues associated with needle-free products real or
22 perceived? Do needle-free products really require
23 regulations? If we have the answer to those three
24 questions, I think we have a significant step forward.

25 We must remember that in hundreds of millions of

1 injections by jet injectors, there has only been one
2 documented case of a contamination in the entire world, yet
3 as the result of reused, dirty or improperly disposed of
4 needles there have been millions of unsuspecting and
5 undeserving children throughout the world that have been
6 needlessly infected with hepatitis or HIV.

7 Okay, that ends my ANFIM presentation and I will
8 change hats here and become an entrepreneur and a
9 businessman and a member of the industry community.

10 As I said, my name is Bob Harrington. I'm
11 president and CEO of American Jet Injector. It's an
12 entrepreneurial company that began in 1995. Prior to
13 forming Am-O-Jet I was president and CEO of Vernitron
14 Medical Products. Vernitron, together with Walter Reed Army
15 Hospital, developed and patented the most widely used high
16 workload jet injector device in the world, known as the
17 Ped-O-Jet.

18 Today Am-O-Jet, a company that I formed,
19 manufactures under FDA 510 approval two high workload jet
20 injectors. One is a foot-powered and one is an
21 electric-powered.

22 A brief history of the Ped-O-Jet. Researched and
23 developed from mid-1950s to 1965. Released for military
24 field use circa 1965.

25 There are prior immunization programs of note. My

1 numbers are conservative by nature in the terms of what they
2 really did.

3 The US DOD, from 1965 to 1980, did 35 years of
4 continuous service, to include the Vietnam and the Gulf War
5 build-up, on 20 to 40 million military personnel, which each
6 were injected on multiple times.

7 CDC, WHO and U.S. AID sponsored the smallpox
8 eradication program, 50 to 100 million people around the
9 world.

10 Swine flu in 1976, according to Dr. Weniger, did
11 75 million injections. Conservatively, I was 20 to 50.

12 The Brazilian African meningitis program in
13 1988-1998 did 80 million injections in 60 days. The
14 Brazilian measles eradication program did somewhere between
15 60 and 80 million in 60 days.

16 Numerous CDC, U.S. AID, WHO--name is
17 all--sponsored routine vaccination and/or emergency epidemic
18 immunization programs over the last 30 years--100 to 500
19 million injections.

20 Conservatively there are more than a half a
21 billion, roughly, shots in the world, all without a reported
22 contamination.

23 We've talked about the CDC MMWR article in 1986.
24 Thirty-one cases were confirmed with the Med-E-Jet.
25 Unreported in the CDC MMWR article was that the other

1 injector tested, the Ped-O-Jet, the leading injector in the
2 world, in all cases tested negative for any traces of
3 hepatitis. And if you go to the article you can see it on
4 page 375, line 21.

5 What has happened as a result of that one
6 contamination is the axiom that says that all injectors are
7 unsafe. Since there has been one reported contamination of
8 a jet injector, it is theoretically possible to contaminate
9 all jet injectors.

10 As a result of the MMWR article and the Med-E-Jet
11 contamination, the Journal of the AMA, Newsweek and Middle
12 East Health all reported this contamination, saying that
13 prior to it, jet injection had been considered a safe method
14 of inoculation.

15 WHO and their policy--Dr. Henderson came out with
16 a policy that said we are strongly recommending that jet
17 injectors should not be used if alternative methods are
18 available. He further explained that in the past, jet
19 injectors were always used for mass immunization programs
20 when large numbers of people needed to have quick
21 inoculation.

22 Ironically, he added in the same press release,
23 "For such emergencies, however, we are still saying that jet
24 injectors should continue to be used."

25 "All jet injectors should be used only as a last

1 resort for mass immunization epidemics until studies under
2 way at Centers for Disease Control show whether a design of
3 a jet injector needs modification." Very quickly, after
4 eight or ten or 12 years since that time, the policy remains
5 in effect today with very, very minor modifications.

6 The problem is that CDC had no opportunity or no
7 plan to go further with any hepatitis evaluations. They
8 were very content with the fact that the leading jet
9 injector was not and could not be contaminated in their
10 previously run hepatitis positive chimpanzee experiments.

11 The myth continues in 1996 when WHO and Public
12 Health Laboratory in Kings College do a study. They tried
13 to simulate the infection of hepatitis in calves in a
14 scenario.

15 The first information coming out of the study said
16 all but one injector was shown to be easily contaminated
17 when evaluated. They developed a new optically read ELISA
18 assay, 10 to the minus 9, designed to simulate hepatitis.

19 The net result of this PHL testing was issued in a
20 work in progress report 1998 was to reaffirm the theory that
21 high workload jet injectors, those with reusable fluid paths
22 and reusable nozzles, were easily contaminated and therefore
23 not acceptable.

24 All the time, however, WHO continues to recommend
25 an enlightened policy of one needle/one shot, utilizing

1 disposable needles and/or an autodestruct needle, knowing
2 full well that they are used dirty in 70-90 percent of the
3 developing world, that the developing world simply can't
4 afford autodestruct syringes and that the resulting sharps
5 from either type are improperly disposed of and routinely
6 left unprotected on the street or in a dump to easily infect
7 unsuspecting men, women and children.

8 The facts of this whole scenario say that the
9 contamination study has not been replicated at an
10 independent laboratory; nor has it been subject to any peer
11 review.

12 In an ongoing CDC public-funded SBIR phase 1
13 research project that Dr. Weniger talked about, my company,
14 Am-O-Jet, the University of Florida, Kings College and an
15 independent U.S. laboratory, we think that the findings of
16 this WHO study are seriously flawed. I'm not as tactful as
17 the public health community because I'm paying the bills on
18 this one and I do not see the replication of the data.

19 Of importance and for the record for the FDA when
20 we start looking at these studies that people begin to make
21 up and say, "This should be the standard," it is not one of
22 the three approved tests for FDA for hepatitis. The test
23 method may not be scientifically valid. And there is no
24 indication that this test method will be acceptable to the
25 FDA for any future device submission.

1 The myth continues. In a steering committee on
2 jet injection in Geneva, Glenn Austin from PATH gave a
3 report on its ballistic gel testing, replicating skin and
4 depth penetration in contamination with ballistic gels. It
5 described an experimental process and its report said that
6 the Ped-o-Jet could be easily contaminated as a result of
7 back pressure or splashback when fired into ballistic gel.

8 Subsequently, WHO issued a report and this report
9 was used by Keystone Industries, the purchaser of the
10 Ped-O-Jet assets and trademarks out of a bankruptcy sale in
11 1995, as the basis to write a letter to the Department of
12 Defense informing them that the product Ped-O-Jet was
13 unsafe, could easily be contaminated, and that Keystone no
14 longer would be responsible for the safety and efficacy of
15 the product if it continued to be used by the government.
16 The direct result of this letter was an immediate ban of all
17 high workload jet injectors by the U.S. Department of
18 Defense.

19 Recently, PATH's endorsement of this ballistic gel
20 model has been removed. However, one of the companies in
21 the room here with us today did independent testing and
22 unlike skin, the ballistic gel model demonstrated little or
23 no ability to absorb fluid, often fractured and artificially
24 produced a fluid rebound, all leading to the erroneous
25 conclusion that splashback was inherent to a jet injector

1 and produced contamination.

2 So where are we? Recently I was asked by CDC to
3 moderate a panel at the National Immunization Conference in
4 Dallas. The discussion was lively and it certainly centered
5 around everything that we've talked about this
6 morning--needle sticks and there probably is a technology
7 that could help the industry immensely at this time.

8 An individual came up to me and said that he had
9 spent about 40 years in public health, had been part of the
10 CDC smallpox elimination program, had been part of the swine
11 flu epidemic, and during his career he had supervised or
12 personally administered millions of doses of vaccine with
13 jet guns, the Ped-O-Jet, and never once did he observe blood
14 on the nozzle.

15 At first glance, the WHO stance he talked
16 about--one needle/one shot--would appear to be an
17 enlightened policy, one that could have a profound effect on
18 reducing the spread of blood-borne pathogens in the world.
19 However, when one leaves the safe havens of Geneva, Atlanta
20 or the capital city of a developing nation, this enlightened
21 policy assumes a far more frightening face.

22 It is my estimate, and this is a direct quote from
23 him, this well intentioned WHO policy, one needle/one shot,
24 is very likely responsible for the spread of blood-borne
25 pathogens to millions--is it 30 million, 50 million, 10

1 million?--millions of undeserving women and children in the
2 world.

3 Continued responsible use of high workload jet
4 injectors, on the other hand, would have resulted in a
5 handful, if any, infections.

6 Until there is clear scientific evidence
7 indicating jet injectors in the spread of disease, I believe
8 that these devices are the best alternatives for all mass
9 immunization programs. Jet injectors are far safer than
10 available needle technologies for both the recipient and the
11 giver of vaccines alike.

12 Why do we need high workload injectors? They're
13 economic. They're about a penny a shot. They're
14 efficient. A high speed jet injector can do 1,000 people an
15 hour if it has to. They're flexible. They can be used by
16 nonphysicians or nurses, by normal, well trained health
17 employees.

18 They have no hard currency value. If you bring a
19 program into the Third World and you have 5 million doses
20 and 5 million needles, about 90 percent of the needles don't
21 make it because they're hard currency on the street to be
22 sold.

23 They're kind to our environment. They have no
24 disposal issues. There's no power required and they have no
25 needle sticks involved with them.

1 When should you use them? Pandemics, epidemics,
2 national immunization programs, special eradication
3 programs, military readiness and CBW response teams.

4 What is the future of Am-O-Jet's high workload
5 injectors? We believe in a traditional reusable nozzle,
6 reusable work path. We're continuing the production of that
7 model.

8 However, we're tired of fighting the battle and
9 we're trying to develop some products, as my colleagues in
10 ANFIM. We're developing a new inexpensive low workload jet
11 injector, something that costs \$300 and lasts 30,000 to
12 50,000 shots, again at a penny apiece. A new disposal
13 nozzle so that there is a pathway that's interrupted. A new
14 autodestruct disposable nozzle because in the developing
15 world, if it's disposable they continue to use it. It needs
16 to autodestruct. And we're also working on, like other
17 people, a self-contained prefilled disposable vaccine
18 capsule. All able to fit the existing injectors in the
19 world and the new injectors.

20 Over the last 10 years, the following have
21 occurred: the fabrication, development and reinforcement of
22 misinformation, the creation of innuendo and assumption, all
23 connoting jet injectors are unsafe injections, an almost
24 mystical transition of the information from innuendo to
25 scientific fact. The premise that high workload jet