

1 injectors are unsafe and easily contaminated has not been
2 proven.

3 Life is not without risk. I was a military pilot
4 in the 1960s. I went through flight school and two of my
5 classmates were killed in training. That was acceptable. I
6 flew in Asia as a military pilot and a variety of people
7 were killed; that was an acceptable risk again. And more
8 dangerous than all of that, I drove on the beltway this
9 morning to get here and there's an acceptable risk of
10 driving on the beltway.

11 We do not live in a world where all medical
12 devices or all medical procedures are risk-free. Many have
13 inherent risks, yet they are recommended, accepted and used
14 on a daily basis. Vaccines, by their very nature, have
15 inherent risks.

16 There are several questions that we need to ask
17 ourselves. Is there a real risk of disease transmission
18 with jet injection? If there is, how great is that risk?
19 What percentage of those inoculated might have a chance to
20 receive blood-borne pathogens? I'm not saying there is, but
21 if there were, what is it? What would be an acceptable
22 level of risk? Is risk-free, 100 percent chance of no
23 infection, the only alternative?

24 Why are these questions very important to all of
25 us? Because we live in a world that's changing. If an

1 epidemic were to break out, perhaps something like
2 meningococcal meningitis, where the fatality rate was
3 estimated to be 20 to 25 percent of those infected, tens of
4 thousands of people have to be inoculated quickly. Why
5 options are there other than high workload injectors? What
6 would be an acceptable risk in this case?

7 If a pandemic were to come out of the Far East,
8 perhaps like bird flu of last year where the fatality rate
9 was estimated at 35 to 40 percent and millions of
10 people--CDC estimated they'd have to do 250 million
11 Americans in approximately 60 days--what options are
12 available other than high workload injectors? What would be
13 an acceptable level of risk at a 35 to 40 percent fatality
14 level?

15 If a CBW attack were to come to pass with a
16 fatality rate on one of the cocktails that they're talking
17 about--anthrax, smallpox and something else--estimated to be
18 90 to 95 percent of those infected and millions of
19 people--11 million people in the city of New York--would
20 have to be inoculated very quickly, perhaps within hours,
21 what options are there other than high workload jet
22 injectors? What would be an acceptable level of risk in
23 this case?

24 I come to you with two hats. The first is ANFIM.
25 We'd like you to be fair and reasonable to our small

1 manufacturers. I come to you as a manufacturer personally
2 and say there's a great deal of innuendo and misinformation
3 in the world that talks about jet injectors. We are not
4 being treated as fairly as needle companies, which have a
5 variety of issues that go unaddressed. We're being asked to
6 be treated fairly. We're being asked to accept what is a
7 risk and how much is there? And I thank you for your time.

8 DR. EDMISTON: Thank you, Mr. Harrington.

9 As always, the script is changing. We deleted one
10 of our speakers, who represents the user side of this
11 industry.

12 I'd like to call to the podium Deborah Wexler,
13 M.D., the Immunization Action Coalition. Dr. Wexler,
14 please.

15 [No response.]

16 DR. EDMISTON: Is Dr. Wexler in the audience?

17 [No response.]

18 DR. EDMISTON: So we didn't miss her.

19 At this time we will take a 10-minute break.

20 Let's come back by 10 after 3.

21 [Recess.]

22 DR. EDMISTON: I think we should finish up this
23 afternoon's session.

24 OPEN PUBLIC HEARING

25 DR. EDMISTON: At this time I'd like to open the

1 meeting for the open public hearing. Any member of the
2 public may address the panel during this open public period.
3 Please limit your remarks.

4 Also I remind the speaker, if we have any
5 speakers, to approach the microphone, speak clearly into the
6 microphone and identify your affiliation and indicate if and
7 what type of financial interest you may have in this
8 industry.

9 Do we have any speakers? We have two, yes. Dr.
10 Fisher?

11 DR. FISHER: I'm not going to talk about the
12 merits of jet injectors but I would raise the question that
13 if you're going to evaluate--if you consider those factors
14 that I, as an occupational health physician, have to raise,
15 and that is the factor of what is the outcome of a health
16 care worker when you're doing 1,000 an hour, and if it's not
17 properly designed, the potential for musculoskeletal things
18 is great.

19 And the other question I have is around the issue
20 of if there is any spray, if you have certain components,
21 what effect is that going to have, is aerosolization have on
22 the provider? Because it may be a small amount but if
23 you're there all day, then it may be a cumulative dose.

24 So those are factors that should be perhaps
25 accounted for when you're giving approval.

1 DR. EDMISTON: Thank you very much.

2 MS. DUCMAN: Just real briefly, again my name is
3 Kathryn Ducman with Retractable Technologies.

4 I just would like to point out, in contradiction
5 to the previous presentation, not all needle and syringe
6 manufacturers are multi-million dollar corporations. Most
7 of the new technologies that are coming out are comprised of
8 small, innovative businesses out in the marketplace.

9 Some new technologies can make one-shot/one-dose
10 feasible, not to negate the value of jet injections but
11 there are technologies that do have an automated retraction
12 that allows shots to be given safely, efficiently and are
13 absolutely nonreusable in that regard.

14 I think it is a dangerous concept to look at an
15 acceptable level of risk. As Susan Wilburn put so well,
16 with some of the emerging infectious diseases, such as
17 hepatitis C, we weren't even testing those until quite
18 recently. So the idea of a contamination path, there are
19 issues out there that haven't even been delved into and it
20 may be over the next one to two decades before we see the
21 effects of the past, how that has affected health care
22 workers.

23 Thank you very much.

24 DR. EDMISTON: Thank you very much.

25 Do we have any further speakers? Yes, come

1 forward to the microphone.

2 MR. ANTHONY: Thank you. I'm Bud Anthony from the
3 Biologics Consulting Group and I am a clinical consultant
4 for vaccine development.

5 I'd like to ask a question of one of the speakers,
6 if this is an appropriate time.

7 DR. EDMISTON: Yes, it is.

8 MR. ANTHONY: It's for Mr. Austin.

9 Glenn, in connection with Bruce's remarks about
10 using a jet injector with multi capabilities, that is, to
11 deliver multiple vaccines, has it been demonstrated or is it
12 possible to demonstrate that the individual vaccines do or
13 do not mix within the tissues, end up in the same tissue
14 pocket, if you will? Or is it possible to demonstrate that
15 they remain separate or that they may commingle?

16 MR. AUSTIN: I'm not aware of any studies that
17 have been done.

18 MR. ANTHONY: Is it technically possible to answer
19 that question?

20 MR. AUSTIN: Yes.

21 MR. ANTHONY: Thank you.

22 DR. EDMISTON: Do we have any additional questions
23 for the speakers? Dr. Rutala.

24 DR. RUTALA: I had a question for Dr. Weniger.
25 The data that was presented in the MMWR from 1986 where

1 there is the one case of hepatitis B transmission, I was
2 wondering was the jet injector used as directed? That is,
3 was there compliance with the manufacturer's use directions?

4 And then if there was, could it be modified such
5 that the mechanism of transmission could be circumvented or
6 corrected?

7 MR. WENIGER: I believe it was used according to
8 direction and all these manufacturers do recommend swabbing
9 of the head after each shot to remove any serum or blood
10 that might be on it.

11 The problem, as I alluded to in my talk, is that
12 there are occasions when health care workers are negligent
13 and they don't remember to do that, and that was the case in
14 Brazil.

15 One of the hypotheses about the Med-E-Jet was that
16 the nozzle actually consists of an internal pin surrounded
17 by a sleeve, leaving basically a potential gap for capillary
18 action to wick fluid from the skin back into the device,
19 which would not necessarily be removed by swab, and that's
20 still a hypothesis.

21 So I guess the issue that you're raising is how
22 can we minimize health care worker negligence or lack of
23 attentiveness to following manufacturers' directions? How
24 can we make such devices so-called failsafe? And I think
25 it's an important question.

1 That's why in putting out contracts for the
2 development of a new generation of devices using disposable
3 cartridges, thinking about the developing world problem, we
4 have encouraged people to figure out ways to make sure that
5 once it's used, it cannot be reused, even intentionally, in
6 places where they might want to save on costs, by having
7 somehow damaged or the piston gets locked into the bottom of
8 the cartridge at the end of the injection or some other way
9 that it can only be used once.

10 DR. RUTALA: I guess just a follow-up. I
11 certainly agree with the comment that there's no such thing
12 as absolute safety, but obviously we always try to minimize
13 risk and minimize disease transmission.

14 Do you believe it is possible to develop a jet
15 injector that would eliminate the risk that was seen in the
16 one case of hepatitis B transmission?

17 MR. WENIGER: Are you referring to a multiple use
18 nozzle--

19 DR. RUTALA: That's correct.

20 DR. WENIGER: Metal nozzle?

21 DR. RUTALA: That's correct.

22 DR. WENIGER: I think it's possible but I think
23 the challenge is to develop a methodology to evaluate that,
24 to convince ourselves of it. I think, and this is my own
25 unofficial personal opinion, that a more promising line of

1 development is to just go the disposable route and figure
2 out some way to make a disposable cartridge work in a high
3 speed gun, and then we have the best of both worlds and we
4 can avoid this uncharted territory we're now in, trying to
5 develop a model to measure extremely small quantities of
6 blood that might theoretically transmit these infections.

7 DR. RUTALA: Thank you.

8 DR. EDMISTON: Mr. Harrington, I believe you had a
9 comment? Come forward, please.

10 MR. HARRINGTON: The term "acceptable risk" is not
11 one that I coined but one that Dr. Margolis, head of the
12 Hepatitis Branch, CDC, coined at a meeting held by Dr.
13 Weniger at CDC and his question was, "Tell me what the risk
14 of transmission is and if I know the mortality rate and my
15 risk is very little for hepatitis transfer, I can deal with
16 treating adult hepatitis but I can save millions of people
17 from dying from the disease."

18 So I'm not suggesting there is a risk of
19 transmission but his concept was what is an acceptable risk
20 if the mortality rate is so much higher?

21 DR. EDMISTON: I think we had one more individual
22 in the back. Please identify yourself.

23 MR. SOLERNO: I'm Larry Solerno. I'm director of
24 operations for Retractable Technologies.

25 I will agree with Mr. Harrington on the point that

1 small business that is doing the innovative work, when
2 they're trying to get their 510(k)s and things passed, is on
3 a very limited budget, that excessive clinical trials or
4 things that make the cost of--we were talking earlier about
5 prototype or devices that were used, if it takes \$10 million
6 to get out of the prototype stage into a process where a
7 company can put a device before they get their 510(k), it's
8 going to help kill the innovative research that the National
9 Institutes of Health and things are putting forward in the
10 process.

11 DR. EDMISTON: Thank you.

12 Are there any further comments or questions?

13 [No response.]

14 OPEN COMMITTEE DISCUSSION/

15 PANEL SUMMARY RECOMMENDATION

16 DR. EDMISTON: I believe at this time we will move
17 into the open committee discussion with recommendations. I
18 should point out that at 4:00 we're going to lose
19 approximately half our panel, so I suggest that we move
20 expeditiously through this.

21 And I would propose that we would combine
22 questions 1 and 2. "In general, what are the key issues
23 that should be considered in the premarket evaluation of jet
24 injectors? And what data should be appropriate to address
25 each of these above issues?"

1 Let me get the ball rolling by suggesting the
2 following. I think it's obvious, whether we're talking
3 about a disposable or reusable device, there's an issue of
4 safety and we have to have some way to evaluate safety, be
5 that bench testing, engineering controls, and I think that's
6 prudent.

7 We also need to ascertain dose accuracy. We also
8 need to ascertain labeling. If the injector comes
9 prefilled, there has to be some indication of labeling on
10 that. Shelf life.

11 And I think as was brought out in the earlier
12 presentation, the issue of ISO standards I think are
13 significant and I would suggest that the FDA be very
14 interested in the development of standards for this industry
15 as it evolves.

16 I think Mr. Harrington's concerns voice one side
17 of the equation but I think what's very important is that as
18 a technology in this area emerges in which children will be
19 able to give themselves injections at school or a variety of
20 individuals who'll be able to give themselves injections in
21 atypical health care environments, there must be some way
22 that we can provide a watchdog area of expertise for these
23 devices.

24 Having said that, I want now to poll my panel
25 members and see what their interests may be and concerns

1 regarding these two questions.

2 Ms. Ryder.

3 MS. RYDER: Well, I guess one of the issues that
4 came to mind as I heard the presentations and the huge
5 numbers of patients who have received injections by this
6 method, and it was also pointed out that we're only
7 beginning to understand some of the emerging communicable
8 diseases, that what type of surveillance has been done on
9 this to determine indeed whether there were any resultant
10 infections or transmissible diseases. In other words, did
11 the infections occur but we just didn't know it? And is
12 anybody actually measuring resultant infections from all of
13 these injections?

14 DR. EDMISTON: Dr. Rutala?

15 DR. RUTALA: I just have a few comments. I
16 thought the presentations were excellent and I really
17 appreciate the information that was provided to us.

18 I have a number of questions or have prepared a
19 number of questions or a number of comments as far as
20 studies not having heard the presentations, but I'm going to
21 comment on a few things, realizing that some of these
22 questions have been answered.

23 When I consider jet injectors, certainly we have
24 to consider efficacy issues and when we consider vaccines,
25 we have to consider things such as seroconversion rates and

1 geometric mean titers. And, of course, that, I think, has
2 been answered.

3 I didn't hear any reference to geometric mean
4 titers and whether jet injectors provide the same geometric
5 mean titers, but everything else that was mentioned
6 regarding the use of that product seemed to be very
7 comparable.

8 As far as drugs, of course, we have to consider
9 pharmacokinetics--half-life, excretion, time to peak level,
10 peak time--and, of course, that needs to be considered by
11 the manufacturers.

12 Side effects, of course. There has to be
13 consideration of the side effects of administration, such as
14 abscessing, bleeding, induration, erythema, superficial
15 papules. And, of course, that can be accomplished and I
16 think it already has been accomplished, according to the
17 presentations, by randomized trials with frequency and type
18 of complications recorded. So I believe that's been
19 addressed.

20 Of course, nosocomial infection risk is very
21 important in risk of disease transmission. That has been
22 addressed. It appears that there is at least one case of
23 evidence of transmission.

24 Of course, as was mentioned by Marcia, there's
25 always a concern if there's not an active surveillance

1 system or if there's not some in vitro studies that
2 demonstrate the absence of transmission, what the true
3 prevalence of transmission or the real incidence of
4 transmission is.

5 As far as delivery amount, our chair has already
6 mentioned the delivery amount. Contamination has been
7 mentioned. Those studies can be done both in vitro and in
8 vivo.

9 Contraindications. Of course we have to evaluate
10 the efficacy and safety in groups most at risk for failure
11 or injury.

12 Those are some of the issues that immediately come
13 to mind.

14 DR. EDMISTON: Mr. Palomares?

15 MR. PALOMARES: I just want to remind the panel
16 that this product has already been classified as a Class II
17 device, such that it's supposed to be regulated by general
18 controls, as well as some performance standards if they're
19 established.

20 So we have to really look at the safety and
21 effectiveness of this product, as well as the risks and
22 benefits that the products do provide here. There's a lot
23 of data here, some of them established, some of them not so.
24 We have to look through that carefully.

25 DR. EDMISTON: As a potential use, Mr. Dacey?

1 MR. DACEY: I'm going to offer what I would call a
2 very generalized overview, speaking as a consumer. That is
3 I want to go back to the definition of the word "medicine."
4 As I understand it and have been using it, medicine is a
5 science-based remedy.

6 Ultimately, every consumer, every patient, despite
7 all the hype and all the stuff that goes on in the
8 marketplace, must at some level place its trust and faith in
9 the science and not in the most effective marketing strategy
10 and salesmanship.

11 So as a consumer, I have to trust each of you as
12 scientists to do what is not only best but what is right
13 because I don't know, as a consumer. I'm not that much of a
14 scientist.

15 DR. EDMISTON: Mr. Ulatowski?

16 MR. ULATOWSKI: Could I defer comment until I hear
17 from the other side?

18 DR. EDMISTON: Dr. Fowler?

19 DR. FOWLER: I think the presenters were most
20 interesting and enlightening and there are a number of
21 questions certainly brought to mind.

22 I wonder if one way to consider some of these
23 issues might be to divide to some degree, although I realize
24 there's a lot of overlap but to divide the projected use and
25 the type of product--to divide our thinking by the type of

1 use or product.

2 For instance, we've heard very little about the
3 insulin injector that an individual subject or patient might
4 use, and perhaps many of the concerns for that product are
5 not at all the concerns that we're hearing much more about
6 as far as the general vaccination uses.

7 And then a third section, which would seem to me
8 to perhaps be the most important one for further thought
9 would be the use of these types of products for medications
10 to replace individual needle injection in a hospital setting
11 or in a facility setting or in a doctor's office or dental
12 office setting, to replace the use of needles and thereby to
13 help reduce the risk of needle stick injury.

14 And so in looking at that issue, as Dr. Rutala
15 mentioned a bit, I think there are a number of issues about
16 drug stability and where the dose is delivered. With a
17 vaccination maybe it's great to have a little more in the
18 skin so the Langerhans cells can get to it and enhance your
19 reactivity, but with some other medication that you don't
20 want there, that might be a drawback. And I think that
21 seems to me to be an area where this type of product might
22 have great promise but has certain concerns that are not
23 present in either of the other two areas.

24 DR. EDMISTON: Mr. Ulatowski?

25 MR. ULATOWSKI: Very quickly, I think I've heard

1 pieces of what FDA came here to find out in terms of how to
2 approach the evaluation of these products and I've seen a
3 couple of overheads from Bruce and others on an approach.

4 I guess our concern, as I said originally,
5 primarily is in terms of the clinical data. Whenever you
6 say clinical data it kind of scares half the population of
7 manufacturers.

8 We want to be very careful in when we're looking
9 for data above and beyond the engineering types of bench
10 tests. What's the clinical question? You're heard that
11 from Larry Kessler this morning. What's the clinical
12 question that we need to ask and get data on to answer, that
13 we don't otherwise have information on from the published
14 literature, from documented experience?

15 Von talked about valid scientific evidence. What
16 is out there in terms of valid scientific evidence to
17 support the safety and performance of jet injectors and the
18 powder injectors and others, for delivery of the products
19 for which they are labeled, intended for use?

20 And it's a time right now, as we develop this
21 guidance, to look at what we have in hand in terms of valid
22 scientific evidence and to say to ourselves, these claims
23 are acceptable because the data is there and it is as
24 follows, for certain antibiotics, for certain drugs, for
25 certain vaccines. But to permit a broad indication for use,

1 for delivery of drugs or vaccines, I think that's an area
2 that we have to be very careful about and be data-driven.

3 So it's a time to look at the data. We're
4 primarily concerned with clinical information now that we're
5 looking at. And I heard from Dr. Rutala about the
6 information in terms of drug and vaccine information, taking
7 that into account, in terms of the Class II nature of the
8 product, which allows us a lot of flexibility for these
9 kinds of products in terms of how we approach these devices,
10 and about dividing up these products. Not every type of
11 product necessarily needs the same amount of data. And, of
12 course, being data-driven.

13 DR. EDMISTON: I think we can clear this up fairly
14 quickly. If you look at the first two questions, I think
15 the issue of safety relative to the engineering, there has
16 to be some engineering controls built into these devices,
17 especially these new innovative devices which can be used by
18 a variety of end users, both adults and children. And I
19 suspect these devices will also find their way probably in
20 the Third World at some time in the future, as the costs
21 come down.

22 That kind of testing is relatively easy. Also
23 validating dosing. The science is well established in terms
24 of the unit volume that's delivered and the pharmacokinetics
25 has been well developed in other studies.

1 What you're really talking about is the third
2 question, and that question is, "If and when clinical data
3 are appropriate, what are the panel's general
4 recommendations regarding the form and content of the
5 studies?" Am I correct?

6 MR. ULATOWSKI: I think that's the biggest point
7 of concern of the industry.

8 DR. EDMISTON: So, in essence, we've answered
9 questions 1 and 2 and we're now going to move to question 3.

10 MR. ULATOWSKI: Taking stock of what we've heard
11 today in total, I think a lot of points have been covered.

12 DR. EDMISTON: I think for questions 1 and 2, what
13 the panel may want to consider as a recommendation, and I'll
14 poll the panel, is that there should be an effort on the
15 part of industry to provide engineering controls documenting
16 the safety of these devices, and that type of documentation
17 can be derived from bench data, from laboratory data.

18 MR. PALOMARES: I'll concur with that.

19 DR. EDMISTON: We're in agreement with that?

20 Now let me ask you one more question as the FDA
21 liaison here. The drug side of it, how closely do you work
22 with your colleagues on the drug side of it to validate that
23 that dose going in there is the appropriate dose for that
24 injector?

25 MR. ULATOWSKI: Well, there's the rub. We have an

1 historical context here in terms of jet injectors that we
2 want to provide--be fair to the manufacturers in regard to
3 what's been permitted in the past but let's all get firmly
4 footed in the data and then move on from that point as to
5 what we need from now on in regard to additional claims for
6 additional drugs, for example.

7 DR. EDMISTON: So as new drugs come to the market
8 and as they're delivered by this type of technology, will
9 that evaluated separately?

10 MR. ULATOWSKI: That's evaluated in harmony with
11 our drug evaluation center. If we see a drug product that
12 has not been in the labeling before, we'll send that for a
13 consult review to our drug evaluation group.

14 DR. EDMISTON: That's not really a 510--

15 MR. ULATOWSKI: Yes, it may still be.

16 DR. EDMISTON: It still may be a 510(k)?

17 MR. ULATOWSKI: Mm-hmm. Comparing one jet
18 injector to another is difficult sometimes. One does not
19 know whether the performance characteristics will end up
20 providing equivalent doses to the desired site. There's
21 insufficient data showing ranges of parameters that are
22 acceptable for various types of drugs. So it's a case by
23 case basis sometimes that we ask our questions.

24 DR. EDMISTON: Let me ask Dr. Weniger of the CDC
25 to go to the podium. I'd like to ask him a question

1 relative to vaccines. When you've looked at various
2 devices, this issue of dose accuracy between devices, what
3 is your interpretation based on your experience?

4 MR. WENIGER: Well, I'm not privy to any dose
5 accuracy studies that may have been submitted for devices
6 already on the market. I haven't collected all the 510(k)s
7 and maybe I can do that some day.

8 I guess my sense is that it would be reasonable to
9 request device manufacturers to provide that information but
10 I guess my recommendation would be that we not try to be too
11 rigid about it because clearly when needles and syringes are
12 used and the nurse is measuring the 1.0 ml dose or the half
13 cc dose, there's probably 5 to 10 percent variation right
14 then and there. So I think we ought to have some
15 flexibility around the nominal dose in that regard.

16 If I can just comment a little bit about the
17 Catch-22, I think that we have in this situation where the
18 drug manufacturers and the vaccine manufacturers don't have
19 an incentive to do the additional clinical studies of their
20 products with jet injectors because it's such a tiny market.

21 On the other hand, the device manufacturers, this
22 cottage industry, cannot afford to do the studies on each
23 and every possible drug that might go into them, and they
24 are held back by the lack of market demand for these devices
25 because until the manufacturers are going to prefill the

1 drugs or the vaccines into cartridges to eliminate that
2 filling step, they're very inconvenient for the end users.
3 So there's this chicken-egg phenomenon. Neither the chicken
4 exists nor the egg exists and it's hard to get them started.
5 That's why we're trying to promote prefilling, to help
6 overcome that.

7 But the challenge will be, and I think this is
8 where public health agencies can help and universities can
9 help and NIH grantees can help, to develop clinical data on
10 the use of a jet injector with vaccines A, B, C and D and
11 new vaccines that are coming along, like for example
12 hemophilus. There to date has never been a study of
13 hemophilus vaccine administered with a jet gun.

14 If we can provide that kind of data, perhaps not
15 under an I&D but at least get it into the literature, maybe
16 this will help a manufacturer of a device to say this has
17 been shown to be effective with this type of a gun.

18 Did that answer your question? I'm not sure I
19 completely answered it.

20 DR. EDMISTON: I don't believe there is an answer.

21 Do any of the panel members have any questions for
22 Dr. Weniger?

23 [No response.]

24 DR. EDMISTON: I think at a minimum, we should
25 have some assurance that there is sufficient dose available

1 in these devices, so there has to be some labeling criteria
2 as to when the dose was put it, what's the shelf life of
3 that. And I suspect that's already in place to some extent,
4 isn't it?

5 DR. WENIGER: Well, I think we're sort of talking
6 about two quite separate issues. One is the issue of jet
7 injectors as simply delivery devices, like needles and
8 syringes. And the other is if we can convince manufacturers
9 to prefill into cartridges to go into jet guns, then we have
10 to deal with all the potency and stability and compatibility
11 with the plastic questions and the shelf life in that, and I
12 think that's quite reasonable and that burden ought to be on
13 the vaccine manufacturer who proposes to put them in and we
14 need to create enough incentives to encourage the
15 manufacturers to do that.

16 DR. EDMISTON: Do you anticipate that will occur
17 in the foreseeable future?

18 DR. WENIGER: Well, like I say, until we can
19 develop enough demand for needle-free devices, guns that
20 physicians and hospitals can buy, I don't see the
21 manufacturers seeing a large enough market to justify doing
22 the studies on the several hundred patients that might be
23 necessary to develop the serologic assays or the
24 bioavailability studies.

25 DR. EDMISTON: So from your perspective the real

1 issue here is the safety and engineering designs of these
2 devices.

3 DR. WENIGER: No, actually I think that's a side
4 issue relevant primarily to the multiple use nozzle devices.
5 I think the existing devices that have disposable
6 cartridges, I don't see any inherent problems with them.
7 They've passed 510(k)s and they get their insulin in and
8 they get a number of other devices in and the side effects,
9 although slightly increased, are not unreasonable.

10 DR. EDMISTON: So you don't think it would really
11 be necessary for them to provide documentation, or at least
12 bench documentation, on the efficacy or the engineering
13 characteristics of their--

14 DR. WENIGER: No, I think any device, whether a
15 disposable cartridge or a multiple use cartridge, ought to
16 demonstrate that it gets into the tissue that it states it
17 goes into, whether it's subcutaneous or not, and to provide
18 either human studies with radioisotopes and nuclear magnetic
19 resonance imaging, which is not invasive and doesn't expose
20 you to x-rays--those techniques are there--to do cadaver
21 studies or animal studies to show that it gets in where it
22 states it gets in.

23 The challenge, though, is that if someone wants to
24 use an IM vaccine in a device that only a third of the time
25 or less delivers IM, we now have an off-label--well, not an

1 off-label but sort of a conflict situation. There may be
2 clinical data that says you can use a jet gun for this
3 product, even though it doesn't get into the nominal
4 compartment that's stated in the manufacturer's label for
5 that vaccine, but it works. So there's little incentive to
6 get the manufacturers to do some additional studies to show
7 that jet injection subcutaneously will work just as well as
8 needle and syringe IM.

9 DR. EDMISTON: Well, that issue really is a
10 prevalent issue in health care, especially in
11 anti-infectives and other types of biologics, the off-label
12 use. You'll never be able to address that per se.

13 DR. WENIGER: But I guess what I'm hearing from
14 the manufacturers is they want to bring today, 1999, not
15 1995, to the FDA an application or a 510(k) for a device and
16 they can show it gets subcutaneously but then they want to
17 be able to market it for the following six vaccines or maybe
18 vaccines in general and I'm hearing the requirement for
19 proof.

20 Now we have some information in the literature
21 that they can use smallpox vaccine, they can use measles
22 vaccine, they can use a variety of vaccines, but what about
23 the practitioner who wants to use it for a vaccine that
24 doesn't have that data yet, like hemophilus influenza, for
25 example? How can they label this device, well, you can use

1 it for some vaccines but not all? Do you want them to
2 specify--

3 MR. ULATOWSKI: And that's a problem. It's the
4 mutually conforming labeling, we call it as bureaucrats,
5 making sure the vaccine is labeled to be delivered by that
6 particular method of delivery.

7 It's an issue that's in front of our Biologics
8 Center right now, as far as how they're going to approach
9 this issue with jet injectors. But I certainly would want
10 to rely upon what we've already cleared and permitted in the
11 past to continue, but to be watchful for additional uses
12 until some data comes forward, more data comes forward that
13 says everything is very similar in terms of delivery aspects
14 from one method to another, and I don't think that data is
15 there. It's probably going to be a product by product,
16 vaccine by vaccine issue in many cases.

17 We have a representative from Biologics here who's
18 going to consider what's been said today and you've already
19 heard from Norm Baylor at a couple of conferences where his
20 concerns have been voiced in regard to this.

21 We've had examples, for example, a device coming
22 forward that delivers a dose but doesn't match a dose of any
23 drug in the PDR. So you ask, "Well, what drug exactly do
24 you intend on delivering by this injector?" It turns out to
25 be something like a product looking for a use, which isn't

1 good thinking. You're trying to provide a product that's
2 going to deliver a therapeutic or prophylactic, in terms of
3 drugs, dose to the patient.

4 There have been many other cases where it's not
5 been very well thought out exactly what the product is and
6 what it's intended to deliver and we're seeing that more and
7 more, I think, in my division.

8 DR. EDMISTON: Well, let me try this again, and I
9 need my panel's help on this, that in devices that present
10 themselves to the FDA, if those devices are deemed
11 significantly the same or similar to devices on the market--

12 MR. ULATOWSKI: We're looking at a grandfathered
13 situation for many products still.

14 DR. EDMISTON: It's the FDA's call as to whether
15 or not additional data is required.

16 MR. ULATOWSKI: That's correct.

17 DR. EDMISTON: However, devices which represent
18 new technology, innovative technology, I think those
19 devices--

20 MR. ULATOWSKI: Additional data.

21 DR. EDMISTON: Additional data, bench data,
22 engineering data, that would be appropriate. Adding to that
23 the intended use of the device in terms of the serum, the
24 vaccination, anti-infective, whatever is going to be
25 delivered, can that be documented? Can the manufacturer

1 document that the effective therapeutic dose is delivered by
2 that device?

3 MR. ULATOWSKI: By those parameters?

4 DR. EDMISTON: Right.

5 MR. ULATOWSKI: By the specifications. Maybe not
6 even that device necessarily.

7 DR. EDMISTON: Does to panel agree with that?

8 [Nods from panel members.]

9 DR. EDMISTON: Now let's get to the area of the
10 clinical. I'd like to refer to the slide that Dr. Weniger
11 presented on the regulatory issues for jet injectors, which
12 I think is a very nice slide because it summarizes some of
13 the issues that we're looking at.

14 For instance, needle-free injectors as empty drug
15 delivery devices. Do you require clinical data on all drugs
16 or only representative ones which the end user might
17 administer? And I want you to help me with this as I go
18 through it.

19 Your tactile recommendation there is probably no,
20 and can you tell me why?

21 DR. WENIGER: No, actually that probably refers to
22 the more extreme proposition, which was to require you to
23 have clinical data prepared by the device manufacturer for
24 every possible drug that a physician might put into that
25 device, and obviously the answer is no.

1 I think there may be some reasonable balance in
2 terms of selecting, and I use the example for a new jet
3 injector that comes along that doesn't have a predicate, to
4 ask for some clinical data on a representative live vaccine,
5 representative inactivated vaccine, perhaps one that has a
6 good serologic correlate so you can get an answer with 100
7 patients or 200 patients and not have to do a field trial of
8 10,000 patients. I think that might be a reasonable
9 balance, to ask for that for a new device.

10 DR. EDMISTON: Then you state to require animal
11 and clinical data demonstrating compartments for doses
12 deposited. We discussed that already. Is the appropriate
13 drug being delivered in the appropriate area? Or
14 demonstrate equivalence to proven devices. You said maybe.

15 I think the FDA is well positioned to make that
16 decision in terms of equivalent devices because though I've
17 looked at devices similar to that in the past, in terms of
18 whether or not that drug is being delivered into that
19 department, that is a key issue and my concern is again what
20 is the dose that's in there and is all that dose getting to
21 the site of action?

22 Now that could be onerous because we know
23 pharmacokinetic studies are very costly. I don't think this
24 committee has to recommend any number, but I think there has
25 to be some basic clinical studies conducted, especially on

1 those products, as you mentioned, the new vaccines that have
2 not been tested in these devices before.

3 What are the comments from the panel? Marcia?

4 MS. RYDER: I would concur.

5 DR. RUTALA: I agree.

6 MR. PALOMARES: Usually I've seen where you're
7 talking about dose deliveries; it usually falls on the onus
8 of the pharmaceutical manufacturer, not on the medical
9 device. There are some drugs that you have to look at and
10 determine is it compatible with this product, but not
11 determine if I use vaccine A, does it get into the
12 appropriate dosage.

13 DR. EDMISTON: I think the issue would be if you
14 used a cartridge but that device only delivered half the
15 dose, that would be a concern, correct?

16 DR. WENIGER: Yes, and I think obviously there
17 ought to be data in the licensure of that product that
18 states that when the nominal dose is a half cc it delivers a
19 half cc plus or minus some reasonable variation. So that
20 would be solved in terms of the required animal or human
21 data to demonstrate that in the license phase, but that's
22 really separate from efficacy of the drug or the vaccine
23 achieving its intended use.

24 MR. PALOMARES: Well, maybe Mr. Ulatowski can help
25 us here. When you have prepackaged combination on

1 device-drugs, does it usually go through CDER or ERH?

2 MR. ULATOWSKI: As I mentioned up front, if it's a
3 prepackaged, prefilled vial, it's evaluated by our biologics
4 or drug component, rather than by devices. We'll evaluate a
5 jet injector that's applied without a drug product or
6 biologic product, as sold.

7 DR. EDMISTON: See, dose accuracy will have impact
8 on efficacy, so there has to be some way, at least on the
9 front end, for the user to be confident that he's getting an
10 accurate level of that dose, at a minimum. It may or may
11 not be efficacious, depending on what he's delivering, but
12 you want to be assured that you're getting that basic dose.
13 Under those circumstances I think the FDA would want to have
14 clinical data.

15 MR. ULATOWSKI: Yes, I think maybe our biologics
16 rep, if they're here, would want to comment. I think she
17 does want to comment.

18 DR. CHANDLER: I'm Donna Chandler. I'm here from
19 the Center for Biologics Office of Vaccines. I'm deputy
20 director of the Division of Vaccines and Related Products
21 Applications.

22 I think part of this has to do with the grey area
23 and the case by case sorts of language that we always run up
24 against with biologics.

25 I think when we approve vaccines, for the most

1 part we're looking at approving essentially up through the
2 packaging. That's part of the labeling and would be part of
3 the licensure application. For example, we would look for
4 stability studies showing that the vaccine is compatible
5 with the labeling, with the packaging. And normally we'd be
6 thinking in terms of referring to our device colleagues for
7 the device that was going to actually deliver that
8 particular product.

9 Now when we start to think about a jet injector,
10 we're starting to get across issues that are going to be
11 important to both of the centers.

12 I happened to be looking through some labeling
13 recently for something else and came across the fact that
14 certain multi-dose vials are approved for use with jet
15 injectors but when you start to talk about cartridges that
16 are going to be used with a jet injector prefilled, we would
17 expect data, probably clinical data, to show that any change
18 in delivery system would give--you'd still assure the safety
19 and efficacy.

20 For a vaccine we're primarily looking at
21 immunogenicity. And oftentimes when there's changes such as
22 in a regimen or a route of administration, we would look for
23 clinical studies, head to head, the proposed change versus
24 the standard of care or what is already approved.

25 DR. EDMISTON: Because of the intimacy of your

1 interest and this panel's interest, would you feel that it
2 would be appropriate that the recommendation is that the
3 dose accuracy and efficacy be linked, especially for new
4 vaccines?

5 DR. CHANDLER: Well, by efficacy we probably
6 wouldn't expect a large scale field trial. I mean that
7 would be overkill. But we use oftentimes immunogenicity as
8 a surrogate in many, many cases for vaccines, and that's not
9 the equivalent of a study. I mean clearly you have to have
10 immunogenicity studies or immunogenicity assays well in
11 place and potency assays for the approval of a product.

12 So immunogenicity, clinical immunogenicity data
13 and potency, either in vitro or animal studies, would be
14 appropriate. Does that answer your question?

15 DR. EDMISTON: But you feel that the issue of dose
16 accuracy is extremely important for these devices?

17 DR. CHANDLER: Well, probably not so much--I mean
18 it's not going to be quite as important for vaccines. It's
19 going to be much more important for drugs, I would think,
20 because your response to a vaccine is going to be--it's
21 going to be somewhat variable. The immune response to a
22 vaccine is oftentimes much more variable than, say, the
23 pharmacokinetic response to a drug.

24 DR. EDMISTON: So you differentiate between one of
25 these devices being used to vaccinate someone against measles,

1 as opposed to one of these devices being used to deliver a
2 dose of insulin to a diabetic?

3 DR. CHANDLER: Yeah, I would think so. But again
4 it's a matter of data.

5 Well, let me go back. I think that we would
6 generally expect to have at least stability data and maybe
7 even some clinical data for the use of prefilled syringes,
8 and I think that's about as close as we get to what you all
9 are talking about now.

10 DR. EDMISTON: Is the onus, though, on the
11 manufacturer of the jet injector at that point for prefilled
12 syringes or vials?

13 DR. CHANDLER: No, that's part of the vaccine's
14 license. In other words, when we approve the vaccine we
15 approve the final package. Again that's why I say this jet
16 injector is getting into a grey area. I think it's going to
17 require cooperation and collaboration between the two
18 centers and probably between the two manufacturers.

19 DR. EDMISTON: So what I'm hearing, what we know
20 currently about vaccination is that the dose accuracy is
21 less of a concern than it would be for other biologic agents
22 if we go into anti-infectives, liposomal compounds or other
23 biologics of that type.

24 DR. CHANDLER: Right, but that might well be
25 balanced by or counterbalanced by the concern for the site

1 of delivery, for muscular versus subcutaneous or
2 intradermal.

3 DR. EDMISTON: So the FDA should have wide
4 latitude then, in terms of evaluating what type of clinical
5 data they would need relative to whether it's a new
6 technology and a new application of that technology--the
7 delivery of anti-infectives or delivery of other biological
8 entities like insulin.

9 DR. CHANDLER: Right. I would think that a
10 question could be we have experience with a vaccine, for
11 example, the hemophilus vaccine, that's been given--an
12 approved vaccine given by a specific regimen using approved
13 devices.

14 And if we would be involved, and this is just sort
15 of a personal viewpoint and not having had a chance to be
16 involved in previous discussions but I would think that if
17 somebody came to us and said, "We now have a cartridge that
18 we would like to evaluate that we would like to have
19 approved and we'd like to add that to our labeling for a
20 hemophilus vaccine," we would like to see data to show that
21 that hemophilus vaccine delivered by that cartridge and jet
22 injector system is--that that vaccine is as equivalently
23 immunogenic as the needle and syringe method.

24 DR. EDMISTON: Thank you.

25 MR. PALOMARES: But who is the onus on again?

1 Excuse me but who's the onus on? Is it going to be on the
2 pharmaceutical or biologics or is it on the device
3 manufacturer?

4 DR. CHANDLER: Well, that's going to have to be
5 worked out between the manufacturers, I think. And then
6 probably it's going to need further discussion.

7 DR. EDMISTON: I can see where there is a lot of
8 data available on immunizations with these devices and there
9 is virtually nothing available on other biologics in terms
10 of both the pharmacology and possibly even the efficacy, but
11 it's indelibly linked to whether or not the correct amount
12 of the drug is being delivered to the patient.

13 So I think it's going to be on a case by case
14 basis as to whether or not the device is being used for an
15 old application or is it being used for a new application.

16 Dr. Weniger?

17 DR. WENIGER: Yes, just to follow up on that
18 point, I think clearly this issue is more important with
19 nonvaccine pharmaceuticals because the immune response has
20 so many factors that affect it and it's usually either
21 protected or not protected and there's a fair amount of
22 overkill. There's probably more antigen in most vaccines
23 than a patient needs to be protected.

24 But I would ask what is the current requirement
25 for dose accuracy for a manufacturer of a simple needle and

1 syringe? Do they have to provide data that 100 nurses
2 measuring up a half cc dose accurately deliver that dose and
3 a variation above and below that dose?

4 Because if you don't require that for needle and
5 syringe manufacturers--it seems you ought to apply the same
6 requirement for jet injectors. If there's a plus or minus 5
7 percent on the nominal dose that's read in the indicator, if
8 that's applied for one, it should be applied for the other
9 because my guess is there's a lot of dose variation, high
10 dose variations with needles and syringes.

11 DR. EDMISTON: The only problem is you can see the
12 dose in a syringe.

13 DR. WENIGER: Well, I think most of jet guns--

14 DR. EDMISTON: Can you see it in the jet injector?

15 DR. WENIGER: In the ones that have disposable
16 cartridges, the goal and I think the ideal is that you can
17 always see the dose in there. And if it's prefilled at the
18 factory, it's--

19 DR. EDMISTON: So you can determine whether or not
20 the entire dose was delivered.

21 DR. WENIGER: Yes, you should be able to see that
22 it reaches the right marker on the--if it's a syringe and I
23 have a sample, I can show you afterwards. If it's a
24 cartridge, the end user who fills it usually has the
25 gradations to mark the amount, such as a syringe. Then at

1 the end of an injection you can see that the plunger has
2 gone all the way down.

3 Now, of course, some of it might leak out on the
4 skin in some cases, so that can occur.

5 DR. EDMISTON: So it's a very difficult issue to
6 thrash out. From the perspective of the manufacturer, one
7 could say the efficacy isn't really in my ballpark. The
8 efficacy is in the ballpark of the pharmaceutical company.

9 MR. ULATOWSKI: Well, we have cleared a lot of
10 products that say a lot of things about drugs and vaccines
11 and before we go any further down that path we want to make
12 sure that we're clearing products appropriately with their
13 intended use labels and not extrapolating or extending
14 ourselves beyond the data.

15 DR. EDMISTON: But you said that. This is the
16 second or third time you've said that, so I think this is a
17 key that you're trying to get me to pick up on. It always
18 takes at least three times. The device--

19 MR. ULATOWSKI: I had a bat here. I was trying to
20 get your attention.

21 DR. EDMISTON: The device's intended use should be
22 clearly defined.

23 MR. ULATOWSKI: Yes.

24 DR. EDMISTON: Clearly defined. So a
25 recommendation from this panel would be that the intent of

1 the device, its use, clinical use, is clearly defined.

2 Now the issue of where there is a concern for
3 clinical studies, I think it was very well demonstrated that
4 there are other ways of getting around clinical studies.

5 But again the issue is I'm not sure that's the purview of
6 the manufacturer. More the requirement of the
7 pharmaceutical company.

8 Am I off-base on this or do you think--

9 MR. ULATOWSKI: Well, if the jet injector
10 manufacturer wants to list a specific drug, then he or she
11 is in a bind by having to provide the data showing it's
12 efficacious with that drug. If there's no data, then there
13 can be no claim, and that data can come from historical
14 information, experience of use, that valid scientific
15 evidence I spoke of.

16 DR. EDMISTON: So there will have to be minimal
17 efforts on their part.

18 MR. ULATOWSKI: Yes.

19 DR. EDMISTON: To demonstrate some type of
20 efficacy.

21 MR. ULATOWSKI: And I think we might even
22 construct some sort of labeling that would be acceptable for
23 jet injectors based upon the historical information now
24 available.

25 DR. EDMISTON: And it's unlikely that we're going

1 to need the types of studies involved in randomized
2 double-blinded type studies with these devices.

3 MR. ULATOWSKI: Well, I would hope they would be
4 incorporated into evaluations of drugs when the drugs are
5 being studied.

6 DR. EDMISTON: Yes. So it makes a rather
7 simplistic evaluation.

8 Any comments from the panel?

9 [No response.]

10 DR. EDMISTON: Now you're taking notes back there
11 so you can tell me if I'm misspeaking on this, but I think
12 in terms of the first and second questions, we felt that in
13 devices that are similar to devices that have been approved
14 by the FDA in the past, that the FDA has wide latitude to
15 determine whether or not there's a similar or dissimilarity
16 between these devices.

17 If these devices, as a result of being new and
18 emerging technologies, and there's very little historical
19 data available, then the FDA is probably within its right to
20 request bench engineering-type data to demonstrate the
21 safety of these devices.

22 In terms of the clinical trial, it would be
23 important for the manufacturer to document what these
24 devices are going to be used for. And if they do that, then
25 there is some level of onus to determine whether or not

1 there is an efficacy for the utilization of this device.

2 I think it's unclear how that efficacy is going to
3 be determined but I believe it gives wide latitude to the
4 agency, plus in consultation with the manufacturers, to come
5 to some consensus on this.

6 Would that be an appropriate interpretation?

7 MR. ULATOWSKI: I think that's fine, yes.

8 DR. EDMISTON: Dr. Weniger, would you concur with
9 that?

10 DR. WENIGER: Yes.

11 DR. EDMISTON: Are there any other questions by
12 panel members?

13 [No response.]

14 DR. EDMISTON: Members of the audience? Yes.

15 MS. RYDER: Were you finished with number 3, as
16 well?

17 DR. EDMISTON: I thought I was. Go ahead and jump
18 in there.

19 MS. RYDER: I just was questioning whether we
20 addressed the issue of transmission of infectious diseases
21 among devices, how they would demonstrate that.

22 DR. EDMISTON: Let me defer to Dr. Weniger on
23 this. Can you jump in here and give us a little bit of
24 help?

25 DR. WENIGER: Well, I was looking at the guidance

1 document for the morning discussion that talked about how
2 many sharps engineered devices need to be tested without a
3 failure of either a needle stick or a failure of the device
4 that might have resulted in needle stick, and they came up
5 with a guidance of 500 and they showed the statistics for
6 the confidence limits around 100, 500 and 1,000 and so
7 forth.

8 Having some kind of guidance like that to help us
9 in doing these studies with the pigs and the cows I think
10 would be helpful. It'll tell us what the ground rules are
11 for this effort and if zero shots out of 500 is reasonable,
12 zero out of 1,000, I think that might be realistic.

13 Beyond 1,000 it becomes a bit burdensome, so it
14 would be nice to have some feedback that if you shoot in
15 some model that you believe can detect the lowest infectious
16 dose, what number would satisfy you that you'd let your
17 daughter or son have an injection with one of these devices.

18 DR. EDMISTON: Now we're talking about a
19 preclinical model, correct?

20 DR. WENIGER: Yes, this is animal studies.
21 Actually the Brazilians have actually done a human one in
22 which they injected infected carriers of hepatitis B and
23 then put the subsequent injections into vials and then
24 sterilized the device before the next subject in that study,
25 so there was no danger of cross-contamination, but the

1 results are not yet in on that. But that's a very
2 difficult--

3 DR. EDMISTON: Now what you'd propose, for
4 instance, if there were 500 consecutive injections, at that
5 point the device is taken apart or at that point the device
6 is evaluated to determine if there's any contamination?

7 DR. WENIGER: What I would say is you'd give an
8 injection to the animal and then the next injection would go
9 into a vial and you would search for quantities of blood
10 from that animal and if you find any quantities above your
11 cut-off, you would say that was a potential contamination
12 event. And the question is how many of those
13 pairs--animal-vial, animal-vial--would be needed in which
14 you resulted in no episodes of a contamination event that
15 would satisfy the regulatory review. That's the difficult
16 question.

17 What is the magic denominator? Zero out of 500 or
18 zero out of 1,000 or zero out of 100 or zero out of 10,000?
19 I don't want to put a number before I'd like to hear what
20 number people might think would be reasonable.

21 DR. EDMISTON: Fortunately, I don't think we have
22 to determine that. I think there's probably enough
23 statistical knowledge at the FDA to figure that out,
24 correct?

25 MR. ULATOWSKI: Yeah, I would just quickly premise

1 the thought, though, that what comes up front is a design
2 process to minimize the potential. Like the one product
3 that was implicated with some problems, you could test that
4 till you're blue in the face; you're still going to have a
5 problem because of the fundamental design flaw with the
6 product.

7 So assuming you've done all the right stuff up
8 front in design controls, then the tests are confirmatory.
9 Otherwise, I mean there's the premise here that you can't
10 test quality until product. You're designing quality and
11 then confirming and validating that at the tail end.

12 DR. EDMISTON: Keeping in mind also there's at
13 this point no standard methodology for defining
14 contamination per se, other than the study that was
15 presented and showed how contamination was determined, but
16 there's no standard methodologies available within the
17 industry.

18 DR. WENIGER: And we have to remember that these
19 models have not been corroborated or validated with some
20 kind of a gold standard. And I think the point that Ms.
21 Ryder made about the fact that maybe our surveillance
22 systems over the last 40 years have not been sensitive
23 enough to pick up those rare transmissions that might have
24 occurred. Then once again we have to balance this desire to
25 reduce risk to a bare minimum with the existing risk that we

1 know half the injections in the world today are unsafe and
2 causing literally millions of cases of hepatitis B from
3 needles and syringes.

4 So we need to have a level playing field between
5 these new devices and the classic needle and syringe.

6 MS. RYDER: I think I just wanted to feel
7 comfortable that there was some issues addressed in terms of
8 an obvious design flaw that was picked up in the past, that
9 that would have some level of control in the future.

10 DR. EDMISTON: There's probably two ways of
11 looking at this. One is to do what we did in the morning
12 session and look at a postmarketing surveillance of these
13 devices, pick it up on the back end. Or recommend that the
14 FDA investigate the possibility of developing standardized
15 methodology to determine contamination within these devices.

16 I think probably doing postmarketing surveillance
17 will allow you to pick it up on the back end. However, what
18 is the level of risk you're willing to accept?

19 So I would recommend the following, that the FDA
20 look at potential models for looking at cross-contamination
21 of these devices, at the same type develop the mentality for
22 doing postmarketing surveillance on these devices once
23 they're out there and being used by the public.

24 Would that be a reasonable recommendation?

25 [Nods from panel members.]

1 MR. ULATOWSKI: Noted.

2 DR. EDMISTON: Does that address any more
3 concerns? Oh, yes.

4 MR. HARRINGTON: There is one caveat from
5 industry. You've heard this morning that one of the things
6 on needle stick devices was following manufacturers'
7 directions, an explicit training program. What we're asked
8 for in the jet injection business and in the testing
9 protocols is a worst-case scenario: we do nothing, we allow
10 it to contaminate and we ask how clean you are.

11 So the question deserves to be answered: are you
12 going to follow the manufacturer's directions or is it
13 always a worst-case scenario?

14 DR. WENIGER: I think he's implying that the
15 health worker doesn't swab the nozzle, for example.

16 DR. EDMISTON: Right.

17 MR. HARRINGTON: No, I'm implying that in the test
18 to prove safety and efficacy, are we going to follow the
19 manufacturer's directions? Are we going to try to keep a
20 clean product between patients? Or do we automatically
21 assume that it has to be nothing on it? We need to know
22 what that is, one way or the other.

23 Certainly there is a demonstrated improvement on
24 sterility and cleaning when CDC swabbed the nozzles.

25 So if a manufacturer says you need to do this and

1 such to my product between patients, if you don't do that,
2 we're responsible for it being dirty, or is the test going
3 to be implied that it's always going to be dirty? We need
4 to have an answer to that question, is my response.

5 DR. EDMISTON: Well, the recommendations that the
6 manufacturer would make for the device I assume would be
7 prudent and appropriate for those devices.

8 MR. HARRINGTON: But they have not been followed
9 in all the tests in the world to date.

10 MR. PALOMARES: Yeah, but the data that you're
11 generating would have to follow your protocol. Why wouldn't
12 you promote your product and why wouldn't you study your
13 product unless it's following your method?

14 MR. HARRINGTON: I absolutely agree. My point is
15 that WHO is ignoring those and testing it to a different
16 level than the manufacturer--

17 DR. EDMISTON: Well, we can't deal with WHO issues
18 in this meeting. We can only deal with what would be
19 appropriate for the FDA.

20 MR. ULATOWSKI: Well, I'd have to say that yeah,
21 you follow labeling but the labeling has to reflect actual
22 use conditions, real life conditions. And if you're
23 disregarding some common event or occurrence or some aspect
24 of the environment, then the labeling is not quite correct,
25 either.

1 MR. PALOMARES: But then you should put that in
2 your warnings.

3 DR. EDMISTON: See, your device, for the most
4 part, the devices that you've been talking about, for the
5 most part, that device is going to be used by health care
6 workers with some minimal level of training.

7 MR. HARRINGTON: Not necessarily. It was used by
8 the Army for 35 years and it was always wiped. Never had an
9 issue. Good tracking system. And there's nothing recorded
10 in the world that says that it wasn't wiped. It's in a
11 study that was presented using a method that isn't approved,
12 it was not wiped and it said oh, we can contaminate 31 out
13 of 100.

14 MR. ULATOWSKI: You want to come up to the mike?
15 Because that's not getting transcribed.

16 DR. EDMISTON: Do you want to do that again?

17 MR. HARRINGTON: Sure. What I'm saying to you is
18 we believe that there are situations--the U.S. military for
19 35 years used the product appropriately. There was never an
20 indicated transmission of hepatitis. Certainly they follow
21 cases of hepatitis in the U.S. military.

22 Here is a situation where a test was made, it was
23 used with a method that was not approved, a new experimental
24 assay, and it was used intentionally dirty. I don't know if
25 that's fair.

1 DR. EDMISTON: I think it's going to be very
2 difficult to answer these questions. I believe that what we
3 need to really look at is both the postmarketing
4 surveillance and then also look at potential models for the
5 future evaluation of these devices.

6 I think what you're saying is absolutely true but
7 at the same time, this technology is emerging and we need to
8 keep abreast of how this technology may actually be
9 responsible for transmitting infections in the future, like
10 hepatitis C. We just don't have those answers.

11 So I suspect--I'll ask my committee members
12 here--that the FDA consider looking at appropriate test
13 methodologies for looking at possible cross-contamination of
14 these devices with multiple use and that the FDA also
15 consider a postmarketing surveillance program to track these
16 devices once they leave the manufacturer in the hands of
17 both the health care worker and other health care
18 professionals.

19 Now having said that, I realize that many of these
20 devices will not be in the hands of health care
21 professionals. They're going to be in the hands of high
22 school kids and others. But that's the worst-case scenario
23 and we can't do anything about that.

24 Does the FDA have any other questions?

25 MR. ULATOWSKI: No.

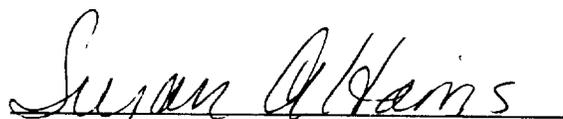
1 DR. EDMISTON: That said, I would like to wrap up
2 this meeting and thank you all for your presentations and
3 your time and activities and this meeting is adjourned.

4 [Whereupon, at 4:14 p.m., the meeting was
5 adjourned.]

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C E R T I F I C A T E

I, **SUSAN A. HARRIS**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.

A handwritten signature in cursive script, reading "Susan A. Harris", is written over a horizontal line.

SUSAN A. HARRIS