the test results. Tracking clients using these strategies can be expensive and ultimately ineffective. Individuals who learn of their status later in their infection may have poorer health outcomes than those who learn of their status relatively early. Knowledge of infection is also key to clients adopting safer behaviors, thereby reducing the number of partners potentially exposed to HIV.

Rapid testing is essential to enhancing the effectiveness of HIV testing in high-risk communities. Because the majority of individuals tested through these programs are at highest risk for HIV infection, and because tracking positive clients that do not return for their test results can be expensive and ineffective, it is critical that these programs have the ability to inform someone of their HIV infection as quickly as possible.

By allowing the use of rapid tests in outreach settings, these programs will be able to increase the number of individuals aware of their serostatus, and increase the number of HIV-infected persons accessing primary health care and prevention services. Use of rapid testing is also

cost effective, reducing costs spent on tracking clients to provide test results, higher health care costs for clients entering care after their infection has progressed, and costs associated with potentially more people being infected with the virus.

As part of its Strategic Plan, CDC recommends the adoption of rapid testing technologies to enable testing in nontraditional settings, such as street outreach programs, social venues, and public service sites, so that clients do not have to return for their results. Adopting rapid testing for use in providing outreach CTR services is an essential strategy in reaching the CDC goal of increasing the number of HIV-infected individuals aware of their serostatus. The Strategic Plan also notes that providing outreach testing in communities with high HIV prevalence plays an important part in ensuring that all individuals at risk for infection have access to testing, particularly communities of color.

The CDC's Revised Guidelines for HIV Counseling, Testing, and Referral also lay out clear guidelines for incorporating rapid testing technologies into the continuum of CTR services.

The Revised Guidelines discuss approaches to post-test counseling, given that rapid tests provide only preliminary HIV positive results and require confirmation.

In addition, CTR programs already have similar experiences from providing indeterminate results that occur using current testing technology. The Revised Guidelines also note that single session counseling programs to use with rapid testing have been successfully implemented at several test sites and have been readily accepted by clients.

As representatives of the front=line HIV/AIDS programs in each of the 65 jurisdictions directly funded by CDC, NASTAD members recognize the critical role that rapid testing can play in enhancing the effectiveness of CTR programs. NASTAD has long supported the approval of rapid testing and its use in outreach settings.

During the FDA hearing held May 18, 2000, NASTAD went on record with its strong support for expedient FDA approval of rapid tests, emphasizing that data supports the safety and efficacy of rapid testing, as well as its important role in HIV prevention. NASTAD can see no further reason for

delaying the approval of rapid tests or preventing their use in outreach settings by trained personnel.

Counseling, testing, and referral programs supported by health departments serve as the cornerstone of this nation's effort to ensure knowledge of HIV serostatus. Health departments have implemented a continuum of CTR services in both clinical and non-clinical settings, and using a variety of testing technologies, to promote access to HIV testing. Health departments have demonstrated their ability to adapt new testing technologies and still guarantee high quality services.

Given the importance of early knowledge of serostatus, and that outreach CTR programs provide necessary access to individuals at high risk, NASTAD believes it is essential that rapid testing be eligible for a waiver under CLIA to allow administration of rapid tests in non-clinical settings by trained staff other than certified laboratory personnel. NASTAD recommends quick action on both the approval of rapid testing and the granting of a waiver under CLIA.

Thank you.

DR. NELSON: Thank you. Unless there are urgent questions, I'd like to move on. The next person that has a plane or something to catch, Elissa Passiment, representing the American Society for Clinical Laboratory Service. And the committee has your statement, so if you can do it in five minutes or summarize it or something, particularly if there are any different ideas than have been presented already.

MS. PASSIMENT: Good afternoon. As was mentioned, you do have my statement, the statement of the American Society for Clinical Laboratory Science. I am not going to read the entire thing, but rather to highlight a couple of important points.

First of all, ASCLS, which was the American Society of Medical Technology, is actually one of the organizations that founded the whole concept of leveling testing in regulation so that as the technology improved and as technology moved forward, that access to quality testing could be guaranteed, and could be guaranteed without the burden of incredible regulation. However, we, when we advocated for this back in 1988 and 1989, did point out that there will always be a need to

consider the risk of harm to patients when the test results are incorrect, and that's what we need to discuss with most of the infectious disease waived category, and that would include HIV.

Our major concern is that if we had been following the 1995 CDC guidelines, we believe that most of the waived tests that would be approved would be tests that we could live with and we would support. However, with the FDA's change in their guidance documents and how they're going to review the tests for possible waived categorization, we are concerned that the true accuracy and precision of testing is not going to be ensured.

So, therefore, we believe that there is a potential that tests will be waived, and HIV has the possibility of being one of them, that will pose a risk of harm to the patient. That risk of harm has already been described to you, what will happen if a patient is accidently told that they are positive versus negative, so I'm not going to go into that.

We are concerned, however, that that risk of harm not be minimized in an effort to identify those individuals in this country who have HIV. While the public health and the identification of

those individuals is very, very important, the correct identification of those individuals is even more important.

As already stated, we support the advancement of technology when it provides improved patient access to safe and quality testing. We believe that waiving these advancements not only must be done, but there has to be careful assessment of risk of harm.

We believe that the time has come for a more formal, informed, evidence-based public discussion of the risk of harm versus access to testing needs, and that this dialogue should take place with Congress, the various federal agencies, practitioners, manufacturers, and the consumer, to set priorities in a regulatory system for waived categorization of laboratory tests, and we look forward to providing impetus and participating in such a process.

I thank you for the time, and I encourage you to read the remainder of our statement. Thank you.

DR. NELSON: Thank you very much.

The next person, Catherine Ayers from CLMA, and I'm not quite sure what that represents.

Is Catherine Ayers here? No?

Okay, Ron Zabransky from ASM, American Society for Microbiology.

DR. ZABRANSKY: Thank you. Mr. Chairman, members of the committee, the American Society for Microbiology, that is, the ASM, appreciates the opportunity to submit comments to FDA's Blood Products Advisory Committee regarding the issue of waiving HIV tests from certain requirements of CLIA 1988. My name is Ronald Zabransky. I'm a member of the Laboratory Practices Committee of ASM's Public and Scientific Affairs Board.

The ASM is the largest single life science society in the world, with more than 42,000 members representing a broad spectrum of subspecialties, including microbiologists who work in biomedical, clinical, public health, and industrial laboratories. The mission of the ASM is to enhance the science of microbiology to better understand basic life processes and to promote the application of this knowledge for improved health and well-being.

Twenty years ago, AIDS was first recognized. In the intervening period, medical, social, and economic manifestations of this

devastating disease have become well known. In recognition of the increasing worldwide pandemic and the need to reach new populations at risk, specifically women, children, racial and ethnic minorities, and those living in rural and small urban areas, the ASM supports the development and licensing of rapid, sensitive, and specific diagnostic tests for HIV infection. It also supports efforts to review current AIDS strategies to arrest the spread of HIV infection.

However, it must be recognized that erroneous diagnostic test results, that is, false negatives and false positives, will have catastrophic consequences. Infected patients could go undiagnosed and could continue to represent an unrecognized reservoir of infection. Non-infected patients would suffer the emotional trauma associated with the diagnosis of this potentially fatal infection. It could be said that no other laboratory test is weighted more seriously than the one for the diagnosis of HIV at this time.

It is for this reason that ASM opposes the HIV antibody test, waiving it as with CLIA regulation. Granting such a waiver would undermine the purposes of CLIA in providing safe and high

quality lab testing. The intent of CLIA to provide waiver from regulation is only for those tests that feature the most simple and basic of testing mechanisms, not for moderate and high complexity tests such as HIV tests.

HIV tests require QC, proficiency testing, and confirmatory testing to validate results. It is important to point out that even though waived tests are deemed simple to perform, erroneous results are indeed possible and can be devastating. Furthermore, a rapid test producing a result, let's say, in 15 to 20 minutes, has no impact on its complexity categorization.

Our comments here are consistent with the FDA Modernization Act of 1997, which defined waived tests as laboratory examinations and procedures that have been approved by the FDA for home use or, as determined by the Secretary, are simple laboratory examinations and procedures that have an insignificant risk of an erroneous result. And you've seen the other, the subdefinitions.

Although it is conceivable that a simple and accurate test can be developed, it should be noted that currently all positive HIV antibody screening tests performed in clinical laboratories

are repeated in duplicate and confirmed as positive by a more specific test method. Clearly, the accuracy of tests performed by certified medical laboratory personnel still requires appropriate oversight. Furthermore, it must be recognized that an HIV test performed incorrectly cannot be classified as one that poses no unreasonable risk of harm to the patient or to the contacts of the patient.

ASM's concern about the FDA's consideration of HIV tests for waiver is further heightened by the recent studies conducted by the Health Care Financing Administration that Ms. Yost just described. With the lack of quality control and adherence to manufacturer's instructions documented by the HCFA study, there is no guarantee that untrained users of a waived test will seek confirmatory tests to verify positive test results, or even inform the individual tested of the significance of those results, whether they be positive or negative.

Without CLIA-mandated quality control, proficiency testing, and personnel standards, there is no mechanism for assuring that tests are being performed correctly. Tests conducted in

unregulated environments cannot provide patients and health care professionals with the same degree of assurances as those tests conducted in environments subject to quality control, proficiency testing, and the availability of professional counseling. The CLIA waived category does not provide a mechanism to assure any of this.

The alternative approach, such as a limited public health use, would be one avenue that could be considered. This would at least assure access to testing, as well as providing the proper oversight as dictated for non-waived tests.

Prompt diagnosis of HIV and accessibility of testing is critical to the effective treatment of HIV-infected patients. Testing must be safe, valid, reliable, and meaningful for patients and health care providers. Emphasis should be placed on the safety and the accuracy-- and I define accuracy here as comparing to a reference method-- of HIV test results to ensure that the appropriate patient care is provided to tested individuals.

Thank you, and I would be most happy to respond to any questions that the panel may have.

DR. NELSON: Okay. Thanks very much. I would like to, if nobody has burning questions, I

would like to move on.

The next person is Deanna Sykes, California Office of AIDS. Is she here?

Again, if you could be brief, and any repetitive comments that are a repetition of what was already presented, if you could just say "I agree" or something.

DR. SYKES: Well, I've got some slides, but I'm going to skip right over the parts that everybody has already showed, because we've heard a number of things repeatedly. I do have some slides. Okay, we're going to get started.

I'm basically here just to present California's perspective on this, and in fact I think our perspective is kind of important because we're pretty heavy hit in the HIV/AIDS public health realm. One of the things that we've done to try and deal with the epidemic, of course, is to try and expand into population areas that are at high risk, and we've done that with OraSure. We've been able to go out. We've got 21 mobile vans in our state that go out and access high-risk populations, and currently nearly a quarter of our testing is done in these sites, so this is very impactful for us.

It's interesting, though, that even though we have been able to access these high-risk populations, testing doesn't equal results. And as you have already heard over and over and over again, we are not getting--we are getting a really high no-show rate in these groups. I've got a table to show you.

If you can see this, what you can see is that across every single high-risk group, you've got a much higher no-show rate, failure to return, in the outreach settings than in the regular settings. What this means, of course, is that rapid testing would be hugely beneficial in these sites, and to the extent that it couldn't be applied to these sites, it really has greatly decreased value.

One number I want to point out here, in our outreach settings, over half of the people with a positive test result do not come back and learn their HIV status, which means, we have to assume, that they're walking around assuming that they're negative.

I want to talk a little bit about our experience with rapid testing. When does 20 minutes equal an hour? Our experience with the

SUDS test basically was that, although the test only took about 20 minutes, having to send it to a lab made it take an hour or sometimes more. Because we had to run them one at a time, it was costly and inefficient.

And we found, when we tried to batch the tests so that it was less expensive in terms of technical resources and so on and so forth, that our clients didn't come back. They were a little bit more likely to come back if we said "Come back in two hours" than if we said "Come back in two weeks." It decreased the no-show rate by less than 30 percent. Same day testing is not the same thing as rapid testing.

One of the lessons that we learned is that in order to gain the benefits of rapid testing, it really does have to be rapid. Okay? If it has to go to a lab, if it takes an hour in an outreach setting, we lose these people. They don't come back.

In order to implement it in a widespread fashion, it has to be an efficient and cost effective method. Okay? That means that there can't be personnel requirements that we have to have a lab technician on every single one of our

mobile vans, or with our outreach workers who are walking with backpacks. Okay? This makes the difference between access and not access for this group, in this setting.

It looks like we've got rapid tests that are going to be both rapid and efficient. We don't know yet. We're still collecting data. We're going to hear about it. But whether they're really rapid and efficient in settings of intended use may depend on how they're categorized under CLIA.

Okay, we already know the CLIA waiver stuff. They have to be simple, they have to be accurate. They have to be easy enough to do that we're not going to get bad results. I'm not going to talk about that.

The question really that we've all been trying to address is, should an HIV test, even if it meets those criteria, should it be considered for waiver?

Here are the arguments that I've heard against it. The impact of receiving an HIV test result is of too great consequence for it to be granted waived status. The second argument: Rapid HIV tests can be utilized in moderate complexity.

I'm going to argue against both of those

things, based on the experience that we've had in California. Highest risk populations, highest no-show rates, highest positive no-show rates. We already know that outreach settings are the places we need to have rapid tests. They are also the least feasible for moderate complexity testing.

In fact, our lab people have assured us that if rapid tests are not waived, there will be personnel requirements that will basically prevent us from using them in these settings. You have to understand we're talking about small groups of people going out to access high-risk populations in the middle of the night, at all different times of day. The personnel costs would be enormous if we had to comply with moderate complexity requirements.

How will CLIA categorization impact the delivery of HIV test results? I've heard a couple of folks talk about the fact that we want to make sure that counseling is available. Well, in California, if rapid tests were CLIA waived, the test results would be given by the same people who are giving them now, our trained counselors. Each and every counselor is trained by our Office of AIDS staff.

The differences? Everybody would get their results. Everybody would get result-specific counseling. The 600 people a year in California who test positive and don't come back for their results, they would get hooked up to services. We would contact their partners. They would know their status. They would change their behaviors. And they would get their results sooner.

In sum, I think there are really enormous public health benefits to making this accessible to everybody, to as many people as we can get to. Virtually any personnel requirements are going to limit or even eliminate the accessibility in many of these settings in our state. I would like to see the committee consider at least the CLIA waiver for these tests for those reasons. I think that the other issues can probably be dealt with.

Thank you. Questions? Yes, sir?

DR. HOLLINGER: Just a couple of questions. What effort has been made to find out why the 50 percent who are no-show really never came back? What were the major reasons they didn't come back? And what assurance can you give me that if there was a rapid test, that these patients actually would be part of that 50 percent that

would come for the rapid test?

Many times it's fear of knowing what the answer is. They may not come, they may not be in the group that would come for the rapid test in the first place, whether you gave it to them right away or the fact that they would have to wait. So I'd like to know what effort there has been to find out about that 50 percent.

DR. SYKES: Okay, very good questions. In fact, some of those questions we're hoping to answer with the CD study that we're hoping to do, so I don't have all the answers.

I can tell you that we tried to look and see why those 50 percent who are positive didn't come back in the outreach settings, and it's not because they have a different testing history or because they have different demographics or--you know, they didn't come back, so we couldn't ask them. But we compared all of the data that we have on them, their risk behaviors, their demographics, their testing history, and so on and so forth, and none of those have given us an indication.

My suspicion is that it is the case that people who are doing riskier things, such as drug use and so on and so forth, are also simply less

likely to come back and also more likely to be infected, so it's not the fact of their infection that made them less likely to come back, but of course that's the critical point for us.

As far as whether or not they would test, that's one of the things that we hope to address in a CD study that we hope to do. I think that is probably a fair assumption, that we might lose a few folks that wouldn't come in at all, but in many cases the people who come in to test intend to get their results. They don't come in to test without getting their results. They lose their nerve. Okay?

So if we get to keep them for 15 or 20 minutes and counsel them and talk to them, we stand a much better change of giving them their results. It's certainly possible that some of them will bolt for the door or some of them won't come in at all, but that's--

DR. NELSON: Do you have any data on-- well, one of the issues that's been raised is the adverse consequences of an erroneous result, either a false positive or a false negative, and either of those could happen, but with the SUDS testing or with the populations, you must have had false

positives and false negatives. Do you have any data on what the consequences were? Because any of these tests would have to be--nobody would put somebody on antiretroviral therapy based on a rapid test. You would have to confirm that. Or no sensible person would.

DR. SYKES: Yes, you're exactly right. In fact, in some of the SUDS, there were a couple of studies that were done, and we've talked to some of the Respect Too folks who are working in Long Beach right now. And what they do there, of course, is they give a preliminary positive while they wait for confirmation.

And according to their experience, the folks who get that preliminary positive, first of all, they do come back for confirmation or whatever the other disclosure is. And, secondly, the Respect Too folks say they have been able to predict in most cases, based on the risk category that the person falls into, the predictive value of that result. If this is a person who is not at very high risk, we know that the predictive value of that result is not very high. For folks who fall into fairly high, it's commonsensical in some sense, but borne out by that statistic.

The clients have not had a big problem with that. Most of them have either come in and said, "I'm relieved" or "It was kind of nice to have that time to mentally prepare for what was an actual positive."

DR. NELSON: Brief comment?

DR. CHARACHE: I'd like to ask the same question I asked earlier. If you have the capacity to do the testing in the middle of the night with a high school graduate, do you care whether the test has been waived or is considered moderate complexity? In other words, as long as you meet your goal for accurate, rapid, do you mind if it's not waived?

DR. SYKES: You know, frankly, I don't care what word we use. I really don't care what word we use. If we can get the testing to the people who need it, that's clearly what we're interested in.

DR. CHARACHE: So if it were moderate complexity under the three or so things that were outlined by HCFA a few minutes ago, that would be okay?

DR. SYKES: Well, I actually wanted to address one of the things that you mentioned.

Interestingly, a number of our most effective counselors are not high school graduates. They come from the risk groups that they're accessing, and these are people who have been trained by Office of AIDS. And in fact, another thing that I should mention, most of these folks are using the OraSure, so they're already doing the specimen collection successfully.

And I guess we could get, you know, somebody. We could fire them, or we could get somebody else to do it, but in fact we have--we're doing proficiency testing in terms of their counseling ability and in terms of their specimen collection ability, and the educational requirement itself could be an issue for us. If we have to deal with it, we will, but don't underestimate how much things like that may impact the practicalities of implementing this program.

DR. NELSON: Yes? Go ahead.

MS. KNOWLES: Forget it.

DR. NELSON: Okay. Oh, Paul?

DR. McCURDY: Just one question. Presumably your counselors are trained.

DR. SYKES: Yes, they are. Yes, they are.

DR. McCURDY: Do they receive more or less

training than somebody might receive who does the test? I think the concern, at least mine, is that a waived test can be done virtually by anybody, anywhere, with or without training. And I think the issue or the major issue is training, whether they are adequately trained, and I suspect that you can train somebody to do the test more rapidly and more easily than you can train somebody to do the counseling.

DR. SYKES: I would have to agree. I think the counseling part is very difficult. Every single person who counsels in our testing site is trained by our cadre of trainers from the Office of AIDS, and in fact they would all be trained in--you know, they are also trained in the specimen collection, and if this were available to us, they would of course be trained in the same setting, probably expanded training, on actually doing the test.

So we wouldn't have just anyone in California doing the test, because in fact if we are allowed to do it, it's only the Office of AIDS and its organizations who would be allowed to do it. I don't know, you know, obviously I can't speak for the rest of the country, but I share your

concern about having it available to just anyone.

DR. NELSON: Okay. Thank you.

DR. SYKES: Thank you.

DR. NELSON: The next person is Lee Richardson, CLIAC, whatever that--

MR. RICHARDSON: The Clinical Laboratory Improvement Advisory Committee, CLIAC, advises the Secretary of Health and Human Services on laboratory practice and public health. The members of CLIAC are concerned that tests for HIV infection might be considered for categorization as waived tests. We do not believe that the waived test category is appropriate for HIV tests, for several reasons.

First, the waived category does not provide any mechanism to assure provision of pre-analytic or post-analytic interventions that are essential to meaningful HIV testing. Second, several recent studies have shown that laboratories performing waived testing frequently fail to follow current manufacturer's instructions or required quality control measures.

We do share your concern to make HIV testing more broadly and rapidly available. We urge you to investigate other available avenues,

such as moderately complex testing or certificate for limited public health testing, for expanded access to HIV testing without compromising the quality of the tests or information provided to tested individuals.

Thank you for this opportunity to provide comments. And, Mr. Chairman, I yield back some of my time.

DR. NELSON: Thank you very much. That was terrific. Questions or comments? No? Thank you.

Richard George from OraSure?

DR. GEORGE: Most of the comments I was going to make have been already made, so I will make mine very brief, and I will dispense with the slides. I won't need those.

I just want to say that this is almost like deja vu from the days when we were talking about approving home testing. I hear the same concerns, the same fears from this group that I heard those days, none of which really materialized.

I want to say that there is a tremendous need out there for rapid tests. Since 1996, OraSure Technologies, then called Epitope, has been

promoting oral fluid testing, oral fluid testing being a way to take testing to people who don't come in necessarily to conventional testing sites, or who might resist testing when blood drawing is required.

Since its introduction, the need for a noninvasive device that can be used in any setting has been proven by a steady increase in its acceptance by public health agencies. In 2001 we anticipate more than 800,000 devices will be used by various public health and community based organizations to test people at risk for HIV infections. This is a 45 to 50 percent increase in the use of OraSure over the year 2000.

The major disadvantage of OraSure testing is that it still requires that samples be sent to the laboratory. Results are not available sometimes for as long as one to two weeks. A person must return to the counseling and testing site to learn the results. Many people choose not to return.

Rapid testing is a logical next step to OraSure testing. We anticipate that, if given waived status, these rapid tests can be performed in practically any setting by appropriately trained

personnel. OraSure Technologies believes, and has based their market estimates on the use of OraQuick in outreach programs, doctors' offices, and testing and counseling centers. We also believe that OraQuick will potentially replace OraSure testing in many of these settings. Use of rapid tests clearly will allow more people to learn their HIV status.

And just in closing, I would like to point out that if new innovations such as rapid testing, such as OraQuick, are discouraged, then companies such as OraSure will never consider delivering to the public health and to the U.S. market other needed tests for infectious diseases such as HCV, HBV, and things like syphilis.

So, again, I think that a lot of the things said here have a lot of validity, but I also think that we have to really understand that we're not talking about delivering inaccurate testing that will be used in isolation. There will still be confirmatory testing. These things have been studied very carefully, and will continue to be studied very carefully by the CDC and by the companies. So I urge you to consider a way to deliver these tests in a way that they can be used

for the populations most in need.

Thank you.

DR. NELSON: Yes, David?

DR. SCHMIDT: Is OraQuick presently used in other countries?

DR. GEORGE: OraQuick right now is being used in a number of other countries, mostly in African countries. We have done a number of studies that have been presented at various meetings. It has not yet been published in the peer reviewed literature.

We did a study in Thailand where we looked at 1,000 high-risk subjects, with extraordinarily good results. It's being used by the CDC in a number of studies in the United States and in Africa. It's being used by Johns Hopkins University for a large study in pregnant women in India. So many, many thousands of OraQuicks have been used in studies by very prestigious organizations in the past two years.

DR. MITCHELL: You mentioned previously that you were comparing this to the home HIV testing. Now, my understanding is that a home HIV test, that you have to send in the sample in order to get the results. Is that--

DR. GEORGE: Well, I was comparing the comments to what--

DR. MITCHELL: I'm sorry. Is that correct?

DR. GEORGE: No, I'm not comparing rapid testing to home testing. I was comparing a lot of the concerns that I hear expressed to those concerns that I heard expressed about the dire consequences of approving home testing.

DR. MITCHELL: Thank you.

DR. NELSON: The next is Rob Christenson for American Association for--Paul?

DR. McCURDY: I have one question. We heard earlier today that somebody was using a glucose testing apparatus of some sort and inserting the strips upside down. Clearly they weren't following the manufacturer's instructions.

DR. NELSON: Well, maybe they were having an insulin--

[Laughter.]

DR. McCURDY: Who knows? But one of the criteria, I presume, or one of the more important criteria is to design something so it's very difficult, if not impossible, to use it wrong. And my question is, how is yours designed from that

standpoint?

DR. GEORGE: One thing I think that should go without saying, but I'll say it anyway, is that you can't believe how rigorous the criteria is that FDA applies to approving any test, rapid tests being no exception.

The ability to perform the test, how well we study the instructions, how well we can prove that people who are the intended users of our tests perform those tests, all of those things we have to validate and provide that validation to the Food and Drug Administration before we can get approval. The instructions are gone over with a fine tooth comb.

We are very much studying whether or not people can follow the instructions for performing an OraQuick test correctly and get the right results. That's a big part of our clinical trials.

DR. McCURDY: There's a difference, however, between personnel who have a background and training, which is what laboratory staff have, versus somebody who may have no background and very limited training, other than perhaps attempting to read the instructions. A waived test is something that presumably could be used by anybody, and I

guess the problem is, how much training is necessary to use the test correctly.

DR. GEORGE: I will give you a good example that I think will partially, at least, answer your question. OraSure samples are being collected by the same type of people that we are proposing to perform the OraQuick test. These people are required by the Food and Drug Administration to be trained individuals.

More than 30 million OraQuick tests have already been performed worldwide. It has been shown time and time again that these people can collect the samples correctly. Performing the OraQuick test is only marginally more complex than collecting an OraSure sample. So I think the answer is, these people can be trained.

DR. HOLLINGER: Just a clarification. Is the OraQuick, it has been approved for home use, is that correct?

DR. GEORGE: It is not. It has not been approved for home use anywhere, and we are not seeking approval for home use.

DR. STRONCEK: This may be a dumb question, but I know the waived tests, anyone can perform the test, but can anyone buy the equipment

and do the test if it's waived, like a glucose meter? You know, anybody with diabetes can buy one and do their blood sugars at home. If this is a non-waived test, can any store or any establishment buy one of these apparatus and offer the tests, for whatever reason?

DR. NELSON: Sure, yes, if they've got enough money. Yes?

DR. MACIK: There are other tests that are waived tests. For example, the home PT monitor, you have to have a prescription to get the instrument and to get the reagents. So you have to have a doctor's prescription to get--

DR. STRONCEK: What--

DR. MACIK: Home prothrombin times.

DR. STRONCEK: Oh, okay.

DR. MACIK: You have to have a prescription to get the reagents, to get the monitor, so it's still under control. It's not like you walk into a store and can buy it.

DR. CHARACHE: Just addressing that point, we have been told at CLIAC that the criteria for the waived test can be much more liberal than the criteria for a moderate complexity test. Similarly, the home use test has even more liberal

criteria of sensitivity and specificity than a waived test. So if it's home use, it's automatically waived, but the reverse is not the case.

DR. NELSON: Next speaker is Rob Christenson, American Association for Clinical Chemistry. Again, if you could--

DR. CHRISTENSON: I'll cut the statement down a lot. Hi. My name is Rob Christenson. I'm a professor of pathology at the University of Medicine School of Medicine, and director of clinical chemistry, tox, and rapid responses at the University Hospital in Baltimore, and today I'm representing the American Association for Clinical Chemistry, which actually is comprised of 10,000 professional laboratory directors and scientists working in hospitals, independent laboratories, and also in the diagnostics industry worldwide.

In recent years, technological advances have allowed manufacturers to develop new and simpler laboratory testing devices which make it easier for individuals with less testing training to accurately perform tests that previously could only be conducted in sophisticated laboratories. This technology-driven trend is clearly likely to

accelerate in the future.

Also clearly there are great benefits to simple waived tests, such as the potential for diagnosing and treating the patient earlier and reducing overall health care costs. However, as we move forward into this dynamic and fast-growing area, it's important to remember that no device is foolproof, and that errors can and in fact do occur.

Although AACC generally supports placing simple and highly accurate devices in the waiver category, we believe it is important that the FDA recognize that some tests, if inaccurate, present a greater risk of harm to the patient and the public than others. AACC believes that these tests should receive a higher level of scrutiny than the waiver category currently provides.

It is our view that the HIV test is such a test because an inaccurate result, either a false positive or a false negative, could have devastating results for the patient, his or her family, and potentially society. AACC also believes that it is critical that all positive HIV tests be subject to confirmation.

Although AACC believes that manufacturers

can develop highly accurate HIV tests, we have serious reservations about permitting tests with significant patient and public health implications, such as HIV testing, in laboratories that are not subject to periodic inspection, either private or public; are not required to have trained health care personnel perform the tests; and are not required to participate in proficiency testing to evaluate the accuracy of their testing.

Ironically, the only substantive requirement placed on waiver facilities, that they follow manufacturer's instructions, is not being followed. According to the recent HCFA study that we heard about earlier, nearly one-half of all waiver facilities that were reviewed failed to perform or appropriately follow the manufacturer's instructions. We're concerned that these findings, which indicate possible QC problems in these facilities, might result in mistakes that could harm the patient and the public.

And, finally, the AACC recommends that the FDA, in conjunction with its partner agencies, manufacturers and laboratories, develop a list of tests and/or diseases such as HIV that should not be waiver at this time because of significant risk

of harm to the patient and the general public. As part of this process, the agencies may wish to consult the appropriate congressional leaders, such as the authors of the statute, regarding which criteria, risk of harm or ease of use, should take precedence in making waiver determinations.

On behalf of AACC, I want to thank you very much for your attention and the opportunity to comment on this critically important health care issue.

DR. NELSON: Thank you. Does anybody have questions?

The next is Robert Neri, CLMA: Leadership in Clinical Systems Management. Is he here? Robert Neri? No?

And the final one is Vince Stanci. Is he here? He didn't identify--no? Okay, so we're done. Does anybody else want to make any comments that haven't already been made? Yes? Okay. Could you identify yourself? I don't have you listed. Sorry.

MR. JENNY: I do have slides. I have slides. Richard Jenny.

Yes. I am Deputy Director of the Division of Lab Quality Certification in the New York State

Department of Health Wadsworth Center. We conducted an investigation of waived testing that was very similar to HCFA's, and in fact our observations and conclusions were also very similar, if not identical, and Judy has done a wonderful job in summarizing those findings, so I won't belabor the point.

J-E-N-N-Y. Actually, I'm filling in for Dr. Lorraine Clarke, who is Division Director.

There is an important observation I'd like to share with you. It's on slide number eight in the presentation, if you can find that. But while we're looking, we refer to Certificate of Waiver test sites in New York as limited test sites. These are sites that provide testing at the point of care, limiting their testing to the use of waived devices and PPMP. Yes, I did share the presentation with the committee, so it is on your table.

Now, approximately one-third of the limited test sites in New York are in fact affiliated with a permit laboratory, so these limited test sites have access to expertise in the clinical laboratory, and in fact often do seek guidance and consultation in their lab practices.

And the slide is intended to compare the compliance with accepted standards of lab practice among affiliated sites and the freestanding or nonaffiliated sites. And we may not be able to find the presentation.

In essence, to summarize that slide, on survey we asked or we determined whether laboratories--yes, very good. We asked whether or we evaluated whether the laboratory followed manufacturer instructions for quality control, whether the laboratory documented its quality control, and whether it had policies and procedures in place when in fact there was a need for corrective action.

And among those limited test sites that are affiliated with a permanent laboratory, about 3 percent of them were cited for not following manufacturer instructions for quality control, compared to a noncompliance rate of 46 percent among those laboratories performing glucose not affiliated with test sites. Thirty percent of the laboratories not affiliated with a permanent laboratory did not record their quality control, and 57 percent did not have policies and procedures in place for corrective action. And that pattern

holds for virtually all analytes that we reviewed.

And again, this is a follow-up to some of Judy's comments, comparing affiliated with nonaffiliated laboratories. We surveyed 278, and again, about a third are affiliated. Twenty-two percent of the nonaffiliated laboratories had no documentation of training. Eighty-one percent placed devices into use without verifying their performance. Twenty-four percent did not have a current SOP, compared with 5 percent of the limited test sites that had access to consultation and guidance.

The point to be made in comparing affiliated with nonaffiliated, ostensibly these sites are exactly the same. They are staffed by personnel with similar professional credentials, performing the same test, but it makes a difference having access to parties that in fact can provide proper consultation.

So, last slide, please, our conclusions. Compliance with accepted standards of lab practice, our observation is, lacking documented lab proficiency or documentation of competency, there is no assurance that the delivery of lab services poses no unreasonable--that should be unreasonable-

-risk of harm. As noted by HCFA, personnel do in fact welcome education and training opportunities. There needs to be developed an appropriate and effective regulatory and outreach program, outreach training opportunities for staff who otherwise don't have access to such training.

Manufacturers need to assume greater responsibility for training certification of analysts. That's a common statement made by these test sites as we visit them, that they are somewhat disappointed with manufacturer support and would look to much more training and education on the part of manufacturers. And we certainly would support such manufacturer involvement, to the point of perhaps certifying the competency of analysts using their devices.

The New York State Department of Health urges the FDA to approve, as quickly as possible, a rapid HIV test, and in its deliberations on access to those technologies, that it consider the capabilities of test sites to deliver reliable laboratory services. Thank you.

QUESTIONS FOR THE COMMITTEE AND VOTES

DR. NELSON: Yes?

DR. SCHMIDT: This very last point you

made is, I guess, the first time we've heard this. And I guess the question is, if the educator is the detail man, it doesn't work very well. He gets paid by how many he sells. And I guess there is no way of enforcing a situation where a company has to make sure that the users of a product are adequately trained, so I guess we're just stuck with that. Is that correct?

MR. JENNY: I don't know if that's entirely true. The drug testing industry, SAMSHA, which is developing rules for workplace drug testing, they are now considering the use of on-site devices for drug testing, and in their rules they are requiring certification of analysts, possibly by manufacturers. In fact, it's stated in the rule that it be provided by the manufacturer.

DR. NELSON: Comment?

DR. GEORGE: Just to answer your question, OraSure, as a condition of approval, we have to train the laboratory, we have to require the laboratory to demonstrate proficiency by sending a panel of specimens that they have to analyze, correctly identify, and return to us, and successfully complete that before we are permitted to make the first shipment to that laboratory.

DR. CHARACHE: That's obviously exemplary, but I wonder if all manufacturers of rapid tests could be counted on to do the same thing?

DR. GEORGE: If FDA requires it, they can be.

DR. NELSON: All right. Are there any other people that want to comment? Hopefully not.

Is Elliot here? Yes. Let's then go back, let's have some discussion, but let's have discussion around the questions, and there are three questions. First of all, I'll read them, and you all have them.

Considering the known benefits and risks of rapid HIV testing, should FDA consider the possibility of removing all CLIA quality assurance oversight for such tests, i.e., waive simple and accurate HIV testing from CLIA, under its proposed criteria?

Now, that seems to me to be a yes or no question, maybe yes, no, or maybe, but I hope we'll vote on yes or no.

The second question is, if not, what are the criteria that should be applied in making waiver decisions for these tests?

That's not a yes or no question, and I

would propose that we, depending on the outcome of the first question, that we change the order in which these questions are considered, considering second what is now the third question:

If rapid tests are not waived, and that is, if the committee votes not to waive, is it appropriate to pursue other approaches under CLIA, e.g., limited public health use, to promote wider access to rapid HIV testing?

And then maybe we can discuss the other options, if there are, you know, what other options there are as a third issue. Is that reasonable?

DR. COWAN: Well, something that we would like to get a sense from the committee on is the sorts of studies that should be done to consider these tests for waiver. What sort of data are you looking for?

DR. NELSON: So you want to go to one, two, three instead of--

DR. COWAN: One, two, three I think would be a better, more logical way to go.

DR. NELSON: Okay. Let's have a discussion, then, by the committee on the first question. Yes?

DR. SIMON: I was going to start, by way

of clarification, it seems to me we've heard a lot from the professional societies in terms of the disadvantages of waiver as a technique or a methodology to use, and a lot of data to support that that can lead to inaccuracy and incorrect test results, but yet we have the obvious public health urgency of trying to make these available. So it kind of directs us to the number three option, it seems to me. I wonder if--

DR. NELSON: That's what I thought.

DR. SIMON: And I suspect other people are thinking. Can you expand a little bit about what you could do--

DR. NELSON: Yes. What is the public health option? You know, what is the FDA thinking, or what are our options as a public health test? Could you clarify that?

DR. COWAN: Sure. Well, let me back up for just one second. The point of number one, I think, was just to get to whether we should include rapid HIV tests in the context of the draft guidance that CDRH is coming up with, since they have some deadlines that they want to meet to put out this guidance. And we would like to know whether rapid HIV tests should stand apart from

that guidance or should be included as a general test under that guidance. That's really our reasoning, I think, behind number one.

To get to Dr. Simon's question, I guess, limited public health use, where we're coming from there is the CLIA definition of limited public health use. In other words, at the present time, for the data--since we don't have data, to have these tests classified as moderately complex and then have them used--yet expand access for those tests using the limited public health use option or the other couple of options that Judy Yost had mentioned before.

Is there something more that I can expand about?

DR. SIMON: Those are the options, what she mentioned, like the van?

DR. COWAN: The van, right, the temporary site, the mobile van sort of thing.

DR. SIMON: So people would have to have demonstrated--they would have to meet the requirements for moderately complex?

DR. COWAN: Correct. What we're talking about here is waived versus moderately complex.

DR. SIMON: So if we do say yes to number

one, does that mean that you would move to waive these tests based on the urgency?

DR. COWAN: That would probably be the case, that there really would not be any--there wouldn't be an exception for rapid HIV tests under the guidance, and the criteria that are established for waiver under the guidance would apply to rapid HIV tests as they would to any test that would be considered for waiver.

DR. SIMON: But if we say no--I mean, I'm trying to just clarify--if we vote "yes" on number one, that means the test would be waived?

DR. COWAN: No, no, no. That means that a test could be waived, if it met the criteria for waiver.

DR. SIMON: So it would still have to meet the criteria. But if we say no to number one, then it would not need to meet the criteria?

DR. COWAN: No. If you say no to number one, that means the rapid HIV test would be pulled out and would have specific other criteria that would have to be applied to it for consideration for waiver, which gets us to number two.

DR. SIMON: Okay, now I see. Okay.

DR. NELSON: The way number one is worded,

it's rather tenuous, "consider the possibility." I mean, I suspect FDA is already considering the possibility and, you know, with--

DR. SIMON: So if we remove it, then we need to give you other criteria to consider for how to make it available?

DR. COWAN: Yes.

DR. NELSON: So even if we vote "yes" on number one, we still have to answer number two, because that is the points to consider in this possibility? Is that--

DR. COWAN: Dr. Epstein wanted to make a comment.

DR. NELSON: I don't understand the way this works.

DR. EPSTEIN: Maybe I can explain what we're trying to say here. There isn't an option whether to categorize tests or consider requests for waiver. That's what the act provides.

What's at issue here is, what should be the criteria for waiver? Now, CDRH, part of FDA, is coming forward with a guidance which has been shared with you and publicly for comment, which has set a certain standard for the waiver determination. We have the opportunity here to say

that that guidance doesn't apply to the HIV rapid tests, or we could say it doesn't apply to HIV tests in general.

We would then have to provide a separate guidance that said exactly what did apply to HIV tests, since it's not optional to categorize them and consider waiver requests. That, we must do. The only issue, when we say "should we consider," is should we consider the criteria as put forward in the draft guidance? That's the issue.

Does that help anybody?

DR. NELSON: No.

DR. EPSTEIN: I see a lot of puzzled faces.

DR. NELSON: I guess the sticking issue, really, is that the adverse consequences of an erroneous test are not insignificant as applied to HIV.

DR. EPSTEIN: Well, that's right. Well, again, I think it's for the committee to decide which concerns are pertinent, but the issue is whether having the removal of the quality assurance and quality control standard and proficiency monitoring required for a moderate complexity test is compatible with how we think testing can be

properly performed.

Additionally, as has been pointed out, under the waived scenario the threshold for being allowed to offer the test is fairly minimal. You register with HCFA, you pay your fee biennially, and you say that you're going to comply with manufacturer's instructions. On the other hand, you're not inspected and you're not subject to proficiency controls.

So that's point one, and although we think that may open the door to inaccuracy, the countervailing argument would be, "Well, the trials have shown that, you know, untrained users get accurate results, that it's not in fact less accurate than in professional hands, you know, under further controls."

But then there's this whole other dimension, which is the notion that it's also being offered in a setting where we haven't made any stipulations about pre-test counseling, post-test counseling, training of the operator as a counselor. Okay? And simply none of that applies. And so it's one step removed from more typical medical settings in which a test result gets provided. So we're saying that's another impact of

waiver, and it's under the umbrella of what do we mean by risk.

DR. KOERPER: Jay, if we say no to number one and then we start saying what are the criteria, this would then result in development of a different set, a different category for this one particular test.

DR. EPSTEIN: That's correct. We would then have to come up with a guidance document that said exactly what criteria we would be applying to an HIV rapid test.

DR. KOERPER: But that criteria could include the on-site presence of counselors who would spend time counseling the individual before and after they got the test results, or--

DR. EPSTEIN: Well, yes. I mean, it would need to somehow be within the four corners of the act, and there might be a lot of head-scratching. But yes, conceivably, if it's the committee's feeling that the risk of inaccurate results provided in the outreach setting is so great that there should be stipulations about counselor training for operators, I mean, we can consider that. But we would have a whole new task, which is to consider criteria, and they would have to be

legally within our authority, and we would have to work on that.

DR. NELSON: John?

DR. BOYLE: Two of the things we know about task performance, which is part of the whole testing issue, is that it tends to be different in natural settings than it does in experimental settings, so it will behave differently in the bath house than it did in the lab. And in either setting, it tends to change over time, and as likely to degrade or improve, particularly as you lose your instructions, you think you're so proficient you don't have to do them anymore.

So the key issue in keeping uniformity is some kind of monitoring, and as I understand it, if we vote for waiver, we give up all forms of monitoring. If we vote for public health use, there may be monitoring because the public health department feels obligated to, but it is not required to under the act. And what I'm not clear on is whether or not monitoring is a criteria that is used in some other way to make these things available, but still to keep that criteria.

DR. NELSON: Yes?

DR. MACIK: I guess I have a real problem

here, because if we look at what laboratories do, laboratories now as it stands, if the test goes to a laboratory, the laboratory has no interaction with the patient. You know, you send this HIV test off to a laboratory and they send the answer back to the doctor or clinician who ordered the test, and they don't have any counseling now. There's nothing about the test that is being ordered now that is in any way linked to counseling, you know.

So yes, it is a better test. I believe that what you do in a laboratory, that the current laboratory standard tests are better than the rapid test. I mean, 99.9 percent specificity is better than 98 percent. But I think we're taking a leap of faith, thinking that the better test is also associated with better care of the patient when it may not be. If you don't, as many of the results have shown us, you're not getting the results of that test into the hands of somebody who is going to adequately counsel the patient.

And if you have a rapid test that's available, and perhaps we can come up with some way of saying that in order to do this rapid test, you have to also provide counseling, maybe limit it to organizations who could do that, maybe that would

be helpful. It would be helpful if we did that right now with our current test, because I know many physicians, family medicine, may send an HIV test and get the result back, but what counseling that patient gets is highly variable. One, do they ever get their answer? And, two, do they ever get any counseling?

So I think, you know, really we're spending a lot of time talking about counseling which is what needs to be done, but I don't think the current test does that at all. So now we're requiring a--you know, talking on waiver, saying the waiver then has to be associated with counseling, as if that's something that's already happening, but it's not.

So I think there's a lot of issues here at hand, that we are putting a stronger requirement on a waived test for the counseling or association with a patient than we are with the current laboratory test. And so, you know, there are a lot of issues here that I don't think are necessarily being approached.

DR. KOERPER: Can I just comment very quickly?

DR. NELSON: Yes.

DR. KOERPER: I don't know what the law is in other states, but in California the law is that, (a) you have to get permission to do the test. Before you get that permission, you have to do counseling, and you also sign that you will provide post-test counseling as well. I mean, it's the law.

DR. MACIK: But the laboratory doesn't have anything to do with that. The clinician does.

DR. NELSON: Well, the lab can't do the test unless--

DR. MACIK: Unless the clinician orders it and sends it to them, and the clinician--

DR. NELSON: And assures the patient has been counseled. Otherwise, the lab won't do the test. At least most places I think this is true.

Go ahead.

DR. CHARACHE: Two things. I want to speak to Question 1, when we get to it, but--

DR. NELSON: We're there right now.

DR. CHARACHE: We're there. Okay. I'm going to speak then with both my hats on. I'm an ID consult, and I'm also a laboratory QC person.

I think we've got to separate very sharply two issues. One is whether a test should be waived

or not, and the other is the need for a rapid, on-site, accurate test. So I think we should just not talk anymore about the need for a rapid on-site test. I think we all can perceive the public health and medical needs for that to happen.

Not all tests should have to be done in a laboratory, off-site, with the turnaround time associated with it. Perhaps all confirmatory tests require that, but certainly not the screening tests which are sufficiently accurate to be used for screening in such sites.

So if we can get away from that issue and just talk about now the issue of whether the test should be waived or moderate complexity, or in some cases high complexity if you're doing PCR or whatever, there are four issues, three we have talked about, and one I would add, that made CLIAC--and also they established two meetings ago a working group to work on just the waived testing issue, which four members of the parent committee were on, and I was one of the people on that committee, reported back to CLIAC. And CLIAC came out strongly in favor of making waived tests moderately complex tests with structures, and you have heard three of them outlined, that make it

feasible to have them done where they're needed, where the patients may be.

Now, the four that I will just comment on, one is the problem with the current guidelines proposed by the FDA. They are extremely permissive. We talked about the issue of the definition of accuracy. We heard from Judy Yost that 32 percent of the waived tests that were surveyed in the eight states did not do quality control the way the manufacturers required that it be done.

The FDA's new guidelines does not require any QC be done. It recommends it, but it doesn't have to be done. Whereas if it were moderately complex, they would have to do the QC that the manufacturer recommends. So there is a lot of permissiveness in the new FDA guidelines that headed us away from the waived tests on that category.

The second issue is the issue of off-label use. Now, we've heard that we don't have to worry about that in terms of the blood supply in the use of these, because the FDA does surveillance of the laboratories that provide blood. There is no surveillance for the waived testing that would be

used elsewhere. We know that the urgency we've been hearing about is for high prevalence populations.

We've heard that there are 96,000 laboratories already registered for doing only waived testing, 46,000 of which don't follow manufacturer's directions or have QC problems, either because they don't have the directions or because they misuse them, and I think that number added up to 64 percent of 96,000.

We know that if a test has been licensed for use as a screening procedure in those waived tests, it may be used off-label for a definitive answer. The best example of this is the screening for Group A Strep. It's required that you follow all negatives with a culture because of the sensitivity of the test, but they're not followed with a culture in a very high percentage of the labs. So it can be used off-label, and there is no follow-up by the FDA for off-label use.

We can't predict. These tests will not only be used in high prevalence populations, but in physicians' offices, or perhaps for women about to deliver, which may be a low-risk population, so they know whether the mom gets AZT or whatever when

the fetus is born. So it's the off-label use that I think is a very major question. And then I think this issue of the false positives and the definition of what a high risk is becomes very important.

The fourth and final thing which I would point out is the precedent that would be set. If the definition of risk to the patient, risk of harm if the test is erroneous, is defined only as an analytical risk--can I see if that line is there or not there? Or is that color pink or just a very dark shade of white, or whatever you want to call it? And that precedent is that if you don't define risk of harm as risk to the patient of harm from a false positive or an erroneous result, then we get into trouble with other tests which are very simple to do but have a high medical or social or emotional risk attached to them, such as genetic testing.

CLIAC has recommended and is leaning towards emphasizing that things like definition of genetic tests which involve whole kindreds should not be waived because of the risk of harm, which is not the risk of getting the test wrong as you do it, but the total risk of the entire procedure,

pre-analytical and post-analytical as well. So that is, I think, what was behind CLIA's very strong stand on advising that the other alternatives to test availability and rapid turnaround time of information be pursued, rather than the waived testing strategy.

DR. NELSON: Yes?

DR. FITZPATRICK: One quick thing. The problem that we heard with OraSure is not that it's not waived, but that it has to go back to the lab to be done. In my former life I was the head of a lab in a hospital, and there were a number of ancillary labs that were doing waived tests, and the problem of bringing them under control in a hospital setting is enormous enough.

Yet doing 92,000 of them throughout the country that are certificate-waived, as HCFA has professed to do, is an awesome task. And if 48 percent of them are already not doing what they should, it's phenomenal to me that in their presentation they said, "The number of waived laboratories continues to increase, as do the number of waived tests." Okay? It's a process that seems to be out of control, and it sounds like CLIA is trying to put it under control.

So if we add to that by suggesting that HIV be waived, just in the face of what to me is-- there is a definite need for the rapid availability of test results to the population that needs them. The agencies that are asking for that are responsible agencies who want to help and counsel those individuals, but I believe under what HCFA presented to us there is a means for them to deliver rapid results to those people under moderate complexity.

So that would allow us to meet a moderate solution here while CLIA works out how we deal with this waived test problem. And that is that there is a way to provide rapid results to the individuals for the 20 minutes that they wait, even though there might be a high school degree problem, but we don't know the extent of that problem, with the person administering the test.

So I think the counseling issue and those things are things that kind of cloud the issue. To me the issue is, should we add to this burden of waived tests, or should we say that you need to provide them rapidly under the methods that HCFA is allowing, so that we can have rapid response to this problem with AIDS? And it appears to me that

we can probably do that.

DR. NELSON: I have a question for the FDA. One is the issue raised by Deanna from California, and that is, her conclusion was that if the test were not waived, it would require added personnel and added costs that would preclude its being available in settings where it is needed to up the 50 percent of people who get tested and don't get the results, or who don't ever get tested, because they need to--you know, their blood or they need to go to some particular site, and it can't be done on-site.

Does FDA see a way that, in the absence of a waiver, that this personnel and cost problem can be solved? Or is Deanna correct in her assumption that unless we do a waived test, that the costs will not--that the cost of doing the test where it's needed can't be done?

DR. COWAN: I'm not sure it's really an FDA question, but--

DR. NELSON: Well, the reason I'm asking the FDA is because the FDA would, if it's not waived, would enforce what rules there are.

DR. MITCHELL: I'd like to address that question, if you don't mind.

DR. NELSON: Oh, fine. Sure.

DR. MITCHELL: And I'd like to do it in the capacity, for four years I was the Deputy Director of the Kansas City Health Department, and for seven years I was the Director of the Hartford Health Department, which serves a 70 percent black and Latino population. Also, I've worked in free clinics and done a lot of counseling and testing myself. I also was in charge of QA/QC for laboratories, not only in the health departments but in also a number of the other clinics, and particularly including gay clinics and those targeted at black and Latino populations, and ran a couple of STD clinics.

I think that the moderate complexity with the limited public health use does have a lot of benefit in this case. I think that it's very, very workable. I think the local health departments know, first of all, the importance of getting the counseling and testing done and getting the rapid response immediately, and they have a sense of who can do it locally, you know, which agencies have the capability of performing the test. Also, you know, there are state laws, and even if there weren't state laws, I think that health departments

would require the counseling and testing, both the pre-test and the post-test counseling.

There is also the issue of follow-up, and I think that, you know, if there is not a requirement--you know, the laboratories, if it's available, if it's a waiver test, you can't really require that there be follow-up to any kind of screening. And I think that the limited public health use would allow the health departments to make sure that there is a required follow-up, you know, recognize it as a screening test and make sure that there's a follow-up, and also make sure that people come back. You know, as the evidence has shown, when people get the information that they're likely to be positive on a test, they are much, much more likely to return or likely to follow up, and particularly in the black and Latino community.

The issue about the high school degree and requirements of high school education, I think that that could be an issue but it's probably not going to be a significant issue. Most of our, you know, our experience is, most of our outreach workers were high school educated. I personally didn't feel that that was necessary, but it seemed to

work. The outreach education and testing seemed to work with the requirement. We were able to find people, high school educated, who had the skills in order to get out into the community and have a rapport with the people in the community. So, I mean, although I prefer that a high school degree not be required, I think that it's workable. It's a workable portion of what is being asked for.

DR. NELSON: Thank you. Are we ready to vote on this, or is there more comments? Yes, Mary?

DR. CHAMBERLAND: A couple of things. One is, I guess that is one of the big concerns I have, is that if we were to vote--do we have enough data or information to make a definitive decision about Question No. 1? Because the limited public health access requires the test to be categorized as moderate complexity, and I'm not sure that I've heard whether we know, if that can be evaluated, what would it take to--would it be feasible, would it be practical, for a health department, under limited public health access, to use that, to get the test available in the community?

Oftentimes we raise this question that the person from the California Health Department

raised, concerns about having a moderate complexity test, to have it categorized as moderate complexity, and the personnel issue. And Ms. Yost from HCFA was shaking her head negatively, meaning no, that's not quite right. So I wanted a little clarification on that.

But, I mean, I would be concerned if we vote "no", that if we say that these tests are not waiverable under any circumstances, that if we fall back on the limited public health access option, do we really know with confidence right now that that is implementable, you know, to have a moderately complex test implementable? You know, I totally agree with Ms. Charache's comments that really what we want, it doesn't matter what we call it, but we want a test available at the point of access, where we can get results delivered in a very quick period of time. So that's one point.

Another is the point that you make, that the FDA has made, is that we consider the known benefits of rapid HIV testing under the proposed criteria. And I guess I'm a little concerned because the proposed criteria are really only draft proposed criteria, and in all probability, given some of the comments we have heard, as things

usually evolve, this guidance may indeed change and in its final form may differ, perhaps significantly, from its draft. So we're being asked to vote on something that is actually somewhat a moving target, and we don't know at this point what the final outcome is going to be.

And then, finally, I wondered--you know, Dr. Onorato spoke that there are a number of studies underway at CDC, and could potentially provide some data that would be helpful in trying to assess this question. So I guess my concern is that if we vote, you know, a vote in some sense may be premature, in that we don't have enough information or data at this point. And if we say these tests are not waiverable, it really would more or less shut a door. Now, FDA is always free to not take our advice, etcetera, and whatever, but I guess it's my concern.

DR. COWAN: If I could just make a comment about that, I am not sure that voting "no" for number one is actually shutting a door. It would be shutting a door on considering waiver for these tests under the draft FDA guidance. There would still be the opportunity for considering these tests for waiver, but applying other criteria,

special criteria, to the rapid HIV tests to allow them to be considered to waiver.

DR. CHAMBERLAND: What Jay Epstein talked about, developing a separate guidance?

DR. COWAN: Yes, right.

DR. NELSON: That's Question No. 2, right?

DR. COWAN: Right, so I just wanted to make sure we understood that we're not saying, by voting "no" on number one, we're not saying we can never waive a rapid HIV test. Rather, it's saying what makes a rapid HIV test special? What criteria should we apply to rapid HIV tests that aren't necessarily applied to all other tests that are covered under the draft FDA guidance?

Although your point about this being a work in progress is correct, all the comments have been received, and I don't know what those comments are at this point and how much the document will change. But you're right, we do have to take that into account.

DR. SIMON: But is my understanding correct, you need this committee to vote today because if you're going to pull these tests out of that document, you need to know that now?

DR. COWAN: That is correct.

DR. SIMON: Right, and if we vote "yes" on number one, we're basically applying the same criteria for waiving these tests as are applied to glucose or whatever.

DR. COWAN: Exactly.

DR. SIMON: If we vote "no" then somebody has got to come up with different criteria.

DR. COWAN: Which is number two, and that's what we're asking for.

DR. NELSON: Yes, Paul?

DR. McCURDY: It seems to me that we are in pretty much general agreement about the need for quality control and proficiency testing. It also seems to me that if the test is waived, there is limited if any managerial control over what's going on in the quality control.

Taking a quick look at the guidelines, the draft guidance, there is some discussion in there about quality, the need for quality control, also the need for a fail-safe, essentially no result if you didn't do the test right. I'm not sure there is anything very wrong with the guidance, even as applied to this, except that I don't think that what I know so far about these rapid tests would survive under the guidance. And I think that

unless you can impose, on a waived test, a requirement for proficiency testing and quality assurance, then I think it doesn't fit the criteria, those tests don't fit that criteria.

DR. NELSON: Pat?

DR. CHARACHE: The reason I said there was no requirement for quality control is because the word "should" is used, and when CLIA asked to use the word "must" for all the requirements for quality control, that's not in there. And anytime you say that this should be done, it means that it doesn't have to be, and a detail person can say, "Oh, well, that costs you more money and you really don't have to do that."

DR. COWAN: I can actually comment on that. This gets into something that's very tricky. The word "must" makes it a legal requirement, and this is only a guidance. In a guidance we need to use words like "should," where by using "must" we're turning it into a regulation, which is a very different sort of a thing. So that may explain why that language was used. I understand your concern, but we do have some legal guidelines that we have to follow.

DR. NELSON: Did you want to say

something?

DR. HOLLINGER: Yes. There are many layers here, obviously, these questions, and I would sort of agree with what Paul has said also about there needs to be an oversight on a test like this. I'm still not--I still don't have any data or I haven't seen any data which really tells me that the people who are not showing up initially would be the ones who would be detected with a rapid test, that they are going to be the ones that are going to come in. I don't know that for a fact, and I don't think I've seen any data that would suggest that.

The second thing is that once you get a test result, we talk about counseling, but what are you going to counsel? The counseling here is that you've got a positive, let's say--you want to know if they've got a negative test, but you can say you've got a positive test, and then the answer is, you've got to follow that up. How are they going to do that? You've got insurance problems here, you've got cost of test to do that.

Are they going to leave? If these are the people that weren't showing up, would be the ones who would not show up initially for those tests

that were done in the regular laboratory, will they now, with the tests that are to follow, show up for the results of those tests when they come back? I mean, there's a lot of it.

But if we assume that we're going to do a rapid test, and I think rapid tests are very good for these things, then I think it needs to have oversight to make sure that the tests are done properly, like any test should be.

DR. NELSON: I think that every possible comment has been made at this point. Let's vote on number one, since you want to vote: "Considering the known benefits and risks of rapid HIV testing, should FDA consider the possibility of removing all CLIA quality assurance oversight for such tests, that is, waive simple and accurate HIV testing from CLIA, under its proposed criteria?" Underline "under its proposed criteria," which includes no monitoring.

All of those voting yes?

[A show of hands.]

DR. NELSON: All of those voting no?

[A show of hands.]

DR. NELSON: Abstentions?

[A show of hands.]

DR. NELSON: The consumer?

MS. KNOWLES: No.

DR. NELSON: Industry?

DR. SIMON: Well, I don't know if I misunderstood. I'm voting yes because my understanding is that voting yes means you would apply the same criteria to these HIV tests as you would to any other test, is what I thought people--

DR. NELSON: No. No, it said removing all CLIA quality assurance--

DR. SIMON: You would consider whether to waive the test based on the same criteria you would for glucose, hemoglobin, or whatever. That's what the "yes" vote means, I think. Am I not correct on that?

DR. COWAN: Should I clarify that?

DR. NELSON: Yes, please do.

DR. COWAN: I think Dr. Simon is correct. What we're asking is, should a rapid HIV test be considered the same as any other test for waiver?

DR. NELSON: I don't know whether I voted for Bush, Gore, or--

[Laughter.]

DR. SIMON: That means that the same standards for quality assurance, etcetera, would be

applied to these tests as to other tests. I think most of the people--

DR. COWAN: Or lack thereof. They're really both the same thing, when it comes right down to it. Should rapid HIV tests be considered the same as any other tests, or is there something special about a rapid HIV test for which we should consider other criteria for waiver?

DR. SIMON: So you would apply the same criteria for waiver that you would to other tests, if you vote yes?

DR. COWAN: Same as a glucose test, same as a hemoglobin test, yes.

DR. SIMON: And if you vote no, you would come up with special criteria for HIV tests?

DR. COWAN: Correct.

DR. SMALLWOOD: Results of voting on Question 1: There were no "yes" votes; 15 "no" votes; 2 abstentions. The consumer rep agreed with the "no" vote. The industry rep agreed with the "yes" vote.

DR. NELSON: So now that the majority were "yes" votes--

SEVERAL VOICES: "No" votes.

DR. NELSON: --"no" votes, rather--what

special criteria would you like to propose that--and I think one criteria was that there be some oversight that is not now required for a dipstick or something like that, a urine dipstick or a glucose test. And without specifying necessarily what that can be, I think we could give the FDA that advice, because the details I think are difficult to enumerate.

DR. COWAN: I should point out--I'll defer to the CLIA people. Correct me if I'm wrong. There are specific regulations that we have to follow for waiver, and oversight isn't one of them. Is that correct?

DR. CHARACHE: That's correct.

DR. SIMON: See, that's why I think the committee misunderstood when you voted the way you did.

DR. NELSON: I'm sure we did.

DR. SIMON: If what you say is, then you'd want it moderately complex. You wouldn't want them to waive it, you'd want it--

SEVERAL VOICES: That's right.

DR. SIMON: --you'd want them to follow the current criteria.

SEVERAL VOICES: No.

DR. FITZPATRICK: Under the current criteria, they could put this under it. There's nothing to preclude them, from the way this test is done, under the current criteria, to waive it. It would meet the specificity--

DR. SIMON: It would meet the requirements for waiver.

DR. FITZPATRICK: It looks like it would, yes.

DR. MITCHELL: Mr. Chairman, yes, I agree that by the way we voted, you know, previously they could have put it under any of the classifications, depending on each individual test. But I believe that it is important that it be considered a moderately--what is it?--a moderately complex test, and that we have the limited public health use, because first of all this--I mean, in some of the other tests, many of the other tests are not screening test. Many of the other tests are monitoring tests, and to me those are very different. Monitoring tests are very different from a screening test.

So that as a screening test, and particularly a screening test with such importance, where the results are so important, I think that

the moderately complex with the limited public health use is the appropriate requirements.

DR. STUVER: Yes, I mean, I think that that's what I was hearing, that people were feeling more that there should be oversight, and so it kicks it into the other category of being regulated as moderately complex. And so in some ways then Question 2 becomes irrelevant, if we're not thinking that it should be waived, or the special criteria in fact would make it moderately complex.

DR. NELSON: I think the second question says that if it doesn't meet the current criteria for waiver, are there other criteria that we could apply to this test, that would allow it to meet a waiver criteria? Is that--

DR. COWAN: Yes. If I could offer some suggestions for things to consider, and that would be, what types of studies would you like to see performed to give you a comfort level with a rapid HIV test that would allow you to waive it? Also, what is it that makes a rapid HIV test special, that would--what sort of concerns do you have about rapid HIV tests that would not allow it to qualify as an ordinary test, for want of a better term, under the draft guidance

DR. CHARACHE: I think there are two issues that pertain to the process of waiver, as among other things in the document. One of the most important is the definition of risk of harm. One of the things that CLIAC, for example, was very concerned about was the waiver of the tumor marker for bladder cancer. The test was easy to perform, but obviously the risk of harm to the patient, if you looked at the post-analytical part, was there.

So that if harm is defined too narrowly, then perhaps HIV would never be able to be waived because of the pre-analytic counseling that is required now in many states, and because of the post-analytical, not the analytical part, which is the easy part. So it's the definition and how the FDA applies the issue of risk of harm that's triggering the concern here for oversight and quality control and proficiency testing, being sure it's accurate.

I think the other piece that would require monitoring or review of the labs that are doing it, is the question of using this as a definitive test rather than as a screening test, which is its intent.

DR. BOYLE: It might move things along if-

-there has been a sense that the committee thinks that there should be oversight, meaning oversight of training and quality control of this particular test. If we say that it does, then it takes away the issue of other criteria or other studies, because it definitely moves it out, as I understand, from the waiver category. So if we took a vote on whether or not we think that oversight is necessary for this particular screening test, then that would definitely move us on to the third question.

DR. NELSON: Okay.

DR. SCHMIDT: I think you were right in asking for the last question next, because after that we're into a lot of hypotheticals. If you do this, you do this, you do this. We can't give one or even a set of criteria with the background of knowledge we have. That's the FDA's responsibility to bring those forward to us.

DR. COWAN: At the same time, I'd like to remind the committee that we really don't have data to consider in terms of the performance of this test, of these types of tests, in the hands of lay versus professional users and that sort of thing.

DR. SCHMIDT: If there are no data, we

certainly shouldn't be making decisions here.

DR. COWAN: Right, which is the reason for the second question, what types of information do we need to come to a decision like that, which will help CDC to perform the correct studies?

DR. NELSON: Well, I think we need a clinical trial of this test, the benefits, how many, as Blaine has talked about, how many people, what proportion of the people that need to be identified and counseled and gotten into therapy, etcetera? How effective is this? And then what, if any, are the adverse consequences of erroneous, and somebody who gets a false positive and never comes back?

And I assume that that's part of the CDC study, so I would say that we would like to see the results of the CDC study. Is that fair?

DR. CHARACHE: I'd also like to see the results of the educational program that HCFA is going to do to ensure that the laboratories on their own do quality control and follow manufacturer's directions.

DR. FITZPATRICK: This is a problem that goes beyond an HIV test. I mean, HCFA can do a program this year, and because of the personnel

that staff these offices and organizations, turnover is a tremendous problem. So you can do an education this year, you come back 18 months from now and you have all new personnel and you have to start all over again.

So, I mean, if you were to ask me what criteria should be done, I think you should use the home use criteria and have two categories, moderately complex and home use, and waivers should be done away with. And what we should address, to make life easier for those organizations that need the rapid results, is it possible, could they demonstrate through training and competency, for a moderately complex test, that a non-high school graduate is competent to address and administer the test? And if that were possible, to waive the high school requirement and demonstrate through training and competency assessment that the user is competent, then can they use the test?

DR. MACIK: Part of the reason I abstained from voting is, I don't have enough data on this whole issue to really say anything. But one of the questions that gets back, something that Mary made think about was, you know, the states have certain criteria. You have to have them sign up to take

the test. You have to give counseling.

What does it matter whether the test you're using is a moderate complexity that goes to a laboratory? If the test you're doing is a waived test that you're doing there, the state law would apply if you're doing a test, wouldn't it?

You know, I mean, the laboratories don't do the counseling. The laboratories don't order the test. They don't, you know, pick the people who need a test. All they do is do the test very well, to give you a result, but they don't do anything as far as following up counseling with the patient.

So if it's a waived test, I mean, the state still would require you report it if it's positive. If you're going to--you know, you could put perhaps some stipulation on this test that it is a screening test, therefore it has to be confirmed with, you know, the confirmation test. I don't know why that wouldn't be available in this type of test, and still have something that's available to people, that can be done by a non-high school trained.

And I actually like the idea of the fact that--you know, we tend to put things into such

tight categories. Make it home test or moderate. You know, come up some different ways to address the issue.

DR. KOERPER: The laboratories in California are, their license is on the line if they run an HIV test without the signed consent form.

DR. MACIK: But like they're not going to get the test unless the clinician orders it.

DR. KOERPER: No, no. But my point is, if there's no oversight over these waived tests because there's no oversight, they could be doing tests on anybody. Nobody's coming in there and saying, "Where is your consent form?"

MS. KNOWLES: Right, without the consent.

DR. KOERPER: Now, I would love to hear, are you getting consent forms for all these tests that you're doing?

DR. SYKES: We get signed consent forms in confidential tests, but in anonymous tests we get verbal consent, so the lab doesn't have any evidence of consent whatsoever. So the possibility of cheating, so to speak, already exists.

DR. SMALLWOOD: Please use the microphone.

DR. SYKES. Okay. Just to repeat what I

just said, we get signed consent forms in confidential testing. In anonymous sites, we get oral consent, and the only witness to that is the counselor who is in the room, so the labs right now are running tests on the verbal assurance of the counselor that consent was given. So I don't think that, you know, having a waived test would change that.

DR. NELSON: No, it's still a consent, but with this waived--if there was a waiver, consent would not be necessary.

DR. KOERPER: I'm curious how that would apply to the law in California.

DR. CHAMBERLAND: Is that true?

DR. KOERPER: I mean, people would still have to technically obtain consent before they ran this test.

DR. NELSON: I guess that's true. If it didn't go to a lab, this person would still have to get consent. Although I don't know how that would be monitored.

DR. KOERPER: Well, that's my point. There's no way to monitor the type of consent, of pre-test counseling and consent that was obtained.

DR. NELSON: Let's--

DR. CHAMBERLAND: Ken, can I ask Ida Onorato to address some of this that has come up about the issues surrounding consent? I think we need some clarification.

DR. ONORATO: I just, what I want to clarify is that the process of obtaining consent and doing pre- and post-test counseling for HIV tests has nothing to do with what kind of a test it is or the categorization of the test. That process is based on recommendations developed by CDC and the Public Health Service, and they have been since 1985, and are published by CDC as PHS/CDC guidelines; as is the process of requiring confirmatory testing, is also a CDC/PHS guideline or recommendation as to how HIV testing should be done. It really has nothing to do with whether the test is done by a rapid test, an EIA, Western Blot, an OraSure collection device, or anything else.

So informed consent is required for all HIV testing in the U.S., according to CDC guidelines, and in addition I think all states have some statement of regulation or laws about this. Now there may, in addition, be something written in the package inserts about this, but in fact those all refer to, as I understand it, CDC

recommendations. And Elliot, maybe you can talk to what--I mean, you or Jay can talk about that.

DR. EPSTEIN: Well, I agree with what you have said about consent, but with respect to counseling, in the case of the home sample collection test system and in the case of the OraSure oral fluid collection system, FDA took the point of view that counseling was part of the test; that we could not regard the test as safe and effective for its intended use without regarding the counseling as an integral part. In other words, we looked at the test as actually a test system.

And so I think that we potentially could look at the HIV rapid test the same way, and say that because the counseling is part of the test, it raises it to moderate complexity because of the issues that have been raised about risk related to adequacy or lack of adequacy of counseling. Now, I'm not saying we necessarily want to go that route, but I think the precedent of regarding the counseling as integral to the test already exists.

DR. ONORATO: But then let me ask you, who monitors that? How is there any connection between getting back the results of this test and the

counseling? Because the counselors who do these, this counseling, actually have nothing to do with the laboratory.

DR. EPSTEIN: Well, yes, that's right. In the case of the OraSure, we actually did specify a relationship between the laboratory and the counseling individual. In other words, it's not the lab that does the counseling, but the provider of the service was responsible for the counseling. And we have taken that exact same point of view with respect to the home sample collection system, which is, you know, blood spots.

So it's true that in the standard medical environment there's no relationship between the laboratory and the counselor, but the presumption is that the counselor is part of the medical setting where the test was provided. In other words, how it got ordered and how the results get provided is within the medical setting.

The whole issue here, as I understand it, is that the CLIA act deals with categorization based on the complexity of the test, but the issue that it has presented to us is that under waiver, waived laboratories can offer the test and there's very little restriction on what they might be. I

mean, it can be, you know, it can be storefronts in malls, it can be individuals who have registered and, you know, pay their biennial fee, and there's no oversight.

So, you know, the problem is that we sort of are under two different rubrics, trying to get to where we want to get to. We have, you know, the CLIA statute which deals with categorization based on test complexity, and then we have the implication of waiver which deals with permissive settings, and they are really not linked ideas, which is the thing that you have pointed out and that Gail Macik has pointed out.

But FDA potentially can link them, if we regard some of the ancillary aspects of testing as linked to the test. And I'm only saying that we at least have that precedent for the oral fluid collection system and for the home blood spot collection system, and those two cases are spanning both a home use product and one which is not home use, which has to be provided by a trained operator that is ultimately under some oversight by the manufacturer. Because the manufacturer was obligated, as Richard George said, by FDA to assure that they don't sell it to anyone who doesn't take

responsibility for the training of the operator, including proficiency testing of the operator.

So there are these different models, and I'm just trying to clarify that whereas I agree that the issue of counseling and what happens in the setting where it occurs is not itself linked to a complexity determination, FDA does have the ability to regard parts of that larger environment as integral to the test. And I think, without a lot of depth of consideration, that that in and of itself would kick tests up to moderate complexity if we say that's part of the test.

DR. MACIK: I guess I still don't understand, because by linking it to the test, you're now putting, where the laboratory is required to follow the rules of CLIA, but you have linked it to a clinician or a counselor to that patient to follow the rule, who has really--over whom CLIA has no authority, over the clinician. But now you're saying for the laboratory test to be done, you're going to link a counseling component to it that requires a second professional counselor, to the laboratory's ability to perform a test. So I'm having some problems how you are getting that clinician into the idea of performing

a test.

DR. EPSTEIN: Well, I didn't say clinician.

DR. MACIK: Or professional or counselor. In their laboratory--

DR. EPSTEIN: --a trained counselor.

DR. MACIK: Okay, so I guess counselor isn't going to come from the laboratory, counselor is going to come from somebody who is clinically involved with that patient or involved with that--

DR. NELSON: yes, but the lab, to do the specimen, can require whoever submits the specimen to have the patient and the counselor sign a certification that they've done this, and that is as I understand the way the system works now.

DR. MACIK: Yes, but then you'd have to have some ability to--what if the counselor says, "I'm not going to sign that piece of paper"? Then the lab says, "I'm not going to do the test"?

DR. KOERPER: That's exactly right.

DR. NELSON: That's exactly right.

DR. KOERPER: The lab cannot do the test if they don't have that signed piece of paper. That's how they are linked.

DR. NELSON: That's it.

DR. KOERPER: The lab must have that piece of paper before it will run the test, before it can legally run the test.

MS. KNOWLES: And this has been happening since 1985, when FDA first approved these tests to begin with, the original test.

DR. CHARACHE: I think what we're also getting back to is the definition of a test, because CLIA does say you divide tests on the basis of complexity, but it defines a test as having three parts. The analytical part is only one part of the complexity. The other is the pre-analytical, which includes consent as well as other things, and the post-analytical. So I think what we're hearing is that the FDA is now paying attention to all three components of the test, as opposed to just the analytical component.

Also, CLIA says that each laboratory, moderate complexity and high complexity, has to have a clinical consultant available. That person doesn't have to be on board, and it can be the person who directs the lab, but they have to be able to refer patients or clinicians to a clinician who can talk to them about the test.

DR. NELSON: Has the discussion adequately

dealt with your Question 2? We've discussed a lot of criteria. Or do you want something more specific or more--

DR. COWAN: I have a feeling that I'll be shot if I say that I want any more. If you'd like to go on to number three--

DR. NELSON: Yes, I would.

DR. COWAN: --you are the chairman, you have that prerogative.

DR. NELSON: Okay. Let's deal with number three, and I'm not sure that's clear. But if rapid HIV tests are not waived, is it appropriate to pursue other approaches under CLIA, e.g., limited public health use, to promote wider access to rapid testing?

Is there any comment on this? Yes?

DR. CHAMBERLAND: I just have a question for HCFA. How often has the limited public health access route been used, and can you give us an idea for what kinds of tests?

MS. YOST: I don't have any specific data, but I know that a lot of people have availed themselves of it. I don't have that data with me. But definitely a lot of state laboratories have availed themselves of that, because we've worked

with them to do that.

DR. NELSON: Yes? From CDC?

DR. HEARN: Our data is a little bit old, but we actually do have data. Early on in the CLIA program we took a look at that. At that time there were 2,500 certificates covering 14,000 laboratories. I don't know if that is close to the same number today, but that was about in '95, but that's what the picture was at that time.

MS. YOST: We definitely have a lot using the temporary testing site and the mobile laboratories, as well. I think the whole AABB uses the temporary testing site.

DR. NELSON: Okay. Before we vote on this, there was a submission by Dr. Gibson from the Council of State and Territorial Epidemiologists, and I won't read it because you have been given it, but I will read one sentence.

"CDC is in the process of studying the issues related to the availability of rapid tests. We ask that any decision on the CLIA waiver status of HIV rapid tests be deferred until data bearing on these issues is available." And so that's for the record, and I guess kind of that's what we've done.

Okay, let's vote on Question 3. How many would answer "yes" to Question 3, which is up on the board?

[A show of hands.]

DR. HOLLINGER: We'll vote on anything.

DR. NELSON: What?

DR. HOLLINGER: We'll vote on anything.

DR. NELSON: How many "no" votes?

Abstentions?

DR. NELSON: Consumer?

MS. KNOWLES: Yes.

DR. SIMON: Yes.

DR. SMALLWOOD: The results of voting on Question No. 3: There were 15 "yes" votes. There were no "no" votes and no abstentions. And both the consumer and industry representatives agreed with the "yes" votes.

Just for the record, I wanted you to know that there are 17 individuals eligible to vote on this question, and apparently there are two that were missing when we took a vote just now.

DR. NELSON: Right. Okay. It wasn't that close, anyway. We're now at 4:15, in case you wanted to know. The next item, and I think we do need to discuss this, is revision of the uniform

donor history questionnaire, and the first speaker is Alan Williams, who is with the FDA.

SEVERAL VOICES: Can we take a break?

DR. NELSON: Yes. Why don't we stand up for a few minutes, but not too long. Could we be back in like 5 or 10 minutes, maybe 10 minutes?

[Recess.]

DR. NELSON: I apologize for all the people who waited for this part, but please, this is very important. Actually we were talking about testing all day, but the questionnaire has preceded and is probably more efficient in many ways than all the testing that's being done.

REVISION OF UNIFORM DONOR HISTORY QUESTIONNAIRE

DR. WILLIAMS: Thanks very much. I am Alan Williams, with the Division of Blood Applications in the Office of Blood since the end of January. I was going to cover some background as well as provide introduction, but much of the background is covered in the review paper that was shared with the committee, so I will show one slide for context and then proceed with the introduction.

Our group of presenters are into streamlining, so they're going to do that with the informational presentation, and then we will

present a set of questions which I will introduce here. We very much would like to get key comments by the committee here, if possible. We'd like to take more minor comments which can be submitted direct to FDA within the next couple of weeks. But we would particularly like to avoid any discussions that might constitute wordsmithing of individual questions, because that takes a lot of time and there are probably some good reasons for not trying to do it this afternoon.

So, my one context slide. Most of the day has been discussions of lab activities, and actually we frequently get the question, why should we in fact qualify donors when we have lab testing that really is so elegant and so good at reducing post-transfusion infection risk? And I would just like to review four elements as to why donor qualification by a screening process is important.

First of all and most importantly, to maximize blood safety, to reduce the threat from known agents for which laboratory screening tests exist. As you all know, there are window periods, there are other reasons for false negative testing, and it provides an extra layer of safety to not having that donation collected at all and subjected

to laboratory testing.

Second element there, there are unknown threats with no laboratory screening test in place, and in some cases, certainly from history you can think of examples, but in the future should we have an agent for which we need to provide a margin of safety and no test exists, we owe it to ourselves to understand the question process, to have the highest level of predictive accuracy that we can in identifying donors at risk.

Secondly, we should have an accurate process to minimize donor loss due to inappropriate deferral. These are wasted blood donors if they are excluded from donation for no good reason and they are in fact safe.

Thirdly, we need to minimize the negative operational impact. This can include burdens placed on the donors themselves, on the blood centers, and things like submission of post-donation information, which in effect means that a donor does not respond appropriately to a question that is placed to them at the time of the blood donation, but come back later with information and might have to stimulate recalls and other procedures that are quite inefficient and

unnecessary if the questioning was done optimally.

And then, fourthly, one that doesn't really get a lot of attention, but why collect a unit of blood and have the staff exposed to it through the collection and testing process if you don't need to? It's wise to minimize staff exposure to infectious diseases.

Please jump to slide 9. Now, the Uniform Donor History Task Force which you'll be hearing about today is a multi-institutional task force established at the encouragement of the Food and Drug Administration, and in fact FDA has had liaison participants, Judy Ciaraldi, Robin Biswas, and John Lee. I was a member of the task force before joining FDA, and now I am also a liaison.

The goals will be reviewed by Dr. Fridey, but primarily it's with the aim of streamlining and improving the overall questionnaire to make it more efficient, not only to make it so it can be done more quickly and more efficient, but in doing so, probably it's best to focus on the most important questions so that you get better predictive value out of those questions.

The speakers today are Dr. Joy Fridey, who is the chairperson of the Uniform Donor History

Task Force. She'll be giving an update on the task force progress; and, secondly, Dr. Sharon Orton, who is with the American Red Cross Holland Laboratory and has conducted now numerous focus groups to assess donor comprehension of the screening questions, including one published paper.

Now, the questions that we would like you to think about in the course of these presentations and jot some notes, particularly some of the key items that you'd like to express, first of all, is the task force using the best overall approach in revising the donor screening instrument with respect to the donor comprehension studies that have been conducted and are being planned? Secondly, identification of questions that are proposed for elimination from the questionnaire, either elimination overall or movement to the information sheet. And I've just said the third one, transfer some question content to the information materials.

Question 2: Are the following elements of the redesigned questionnaire instrument appropriate? First, the use of capture questions to identify individuals who are candidates for more in-depth questions, and travel would be a very good

example of where this might work. Secondly, is there a need, and what would be best process to ensure on-site reading and understanding of the questionnaire by donors? C, use of separate medication and medical condition lists that can be expanded at local medical director discretion. And, finally, provision of a user manual for the donor screening process, in effect, a product insert for the screening process.

Final question has to do with suggestions as to how the FDA should look at the task force product, once the final product is available. Looking for suggestions about what criteria and end points should FDA use to review the content of the task force questionnaire; the format of the questionnaire, both the structure of the questions as well as the secondary structure of the questionnaire overall; the studies of attention and comprehension that have been conducted. And, fourthly, probably the most difficult aspect of the whole issue, how should we and how should we look at the estimated impact of changes in the donor screening questionnaire with respect to blood safety? We're talking about validation of the questions against the ultimate impact on blood