Full Committee Discussion
Reed V. Tuckson, M.D.

DR. TUCKSON: So, my colleagues, I think it's time for you to ask the questions, and I think where I'm still struggling and I'm looking for lights to start coming on and hands to start going up here, because you all will make this make sense -- where I'm caught still here, first of all, there's one thing that I think is important that, Judy, I think you were very wise to put a dichotomy out there. I don't think this committee, and I know I'm not interested in regulation for regulation's sake. I am not interested in having more regulations. That doesn't interest me personally, just as a person.

What I think we're just trying to figure out is does there need to be regulation, not should you just have more regulations. But I don't think anybody likes regulations. So the question continues to be, with what FDA does -- Steve, come on up, by the way. You should be up here. There are some laboratories who produce things that are done to the American people, it seems, that do not have to have that thing, that test, go through the FDA process. There are some things that slide past. Again, I'm asking this rhetorically because I'm trying to understand both of your comments.

There is a set of tests that slide past FDA and go into -- and deal with people, human beings. CLIA people say that we evaluate, we're willing to evaluate how good a laboratory it is and you're going to evaluate a specialty and you're going to check to see whether there are bugs running around in the room, and that's important. But it doesn't speak, that I'm hearing, to the same things that Steve does in terms of the test itself. So it seems like what I keep trying to get from you guys is, is there a set of things that slide by both of you? You don't deal with it, and you don't deal with it, and it still goes to my mother or my kid. So there's a second-order issue here as to whether or not that is okay. I'm not dealing with whether that's fine and it doesn't matter because nobody gets hurt and nobody has ever reported anything bad, or it's another order whether or not the poor folks, the lovely laboratory people, who are working night and day for $2.22 and they can't have any more regulation on top of their head -- if they did, they wouldn't produce another test ever again, so leave them alone. That's a different issue.

Is there a set of tests that go to my kids that slide by FDA and/or you guys? That's all I want to know. I just want the answer. I mean, I've been asking this forever. Lord knows, you know. I'm asking my government.

MR. HAMILTON: There are certain things that CLIA does, particularly the analytic validity, are you going to get accurate results. That does not address the clinical validity, should this test be done in the first place, is this really the right test for this kind of thing. It's just going to focus on whether or not a physician ordered the test, then is the test being done accurately.

This came up heavily in the direct-to-consumer testing. There are probably five or six different functions you can look at there, the advertising of the test, the sales, the clinical validity, the analytic validity, the interpretation of results, and the communication of those results to the consumer. Of all of those functions, CLIA itself is just going to deal with one, the analytic validity.

So it's important when you ask that question and we challenge ourselves with regard to the most effective system, it's important that the system be comprehensive, and that means we all have to work together. The FDA has a role in the clinical validity piece for the test kits, but the home brews, I'll let Steve speak to that particular question.

DR. GUTMAN: Well, the answer is yes. Then the corollary answer is maybe it doesn't matter, maybe it matters a lot, maybe sometimes it matters, and maybe FDA is or isn't the right fix, but the answer is yes.

DR. TUCKSON: I'll get off the soapbox now and be just a pure moderator.

I think Debra was first, and then we'll go around.

DR. LEONARD: I kind of like you on your soapbox.

(Laughter.)

DR. LEONARD: Can I answer your question?

DR. TUCKSON: You're up.

DR. LEONARD: Yes, there is a category of tests that doesn't go through 510(k) of FDA that are called laboratory-developed tests, and the CLIA regulations are weak in the evaluation of those. So CLIA has purview, it's my understanding, and correct me if I'm wrong, over tests that are currently being done, but that premarket review of tests, if you will, making sure they're okay before you start doing them, is not necessarily what CLIA does. CAP, in response to SACGT, added a whole list of questions for genetic tests that have to be answered by the inspector. They have to look at validation data. Can that be done effectively? It depends on the quality of the inspector, the education, the training of that particular inspector whether or not they can make an assessment of the validation process that the test went through. But every two years, every test that has been brought online has to be reviewed by the inspector for genetic tests.

So in not deciding to make a genetic test specialty or a genetics specialty, I think there are things that are falling through the cracks, but it's possible that through creating general rules in CLIA that look at test validation for laboratory-developed tests, you could get at this.

Judy, you're shaking your head. Do you look at laboratory-developed tests and the validation data of those?

MS. YOST: Yes, we do.

DR. LEONARD: Because the CAP added regs to their checklist. They have basically paralleled the questions that FDA now uses for its evaluation process, because I was partly involved in the development of those.

MS. YOST: Yes, the CAP does have a specific checklist that asks questions regarding genetic testing. However, CLIA always had a requirement that for every new test, the laboratory has to validate the analytic validity. CLIA does not cover anything regarding clinical validity. That's the distinction that has to be made. But CLIA does always ask is that test accurate, is it precise, what is your reference range for that test, what is the reportable range for that particular laboratory? And if it's a new test, it has to be the sensitivity and the specificity, and we clearly recognize that in some cases our surveyors may not have the expertise to look at that data and to evaluate it.

So we have been talking with both CDC and FDA, who have graciously agreed that if we collect the stuff on site, they will evaluate it to look at it. But it's just did the laboratory get the right

answer, not was that test going to diagnose any kind of disease or malfunction. That's the distinction.

MR. HAMILTON: So you could turn this around and say if we had a genetic testing specialty, could we all go home? Would all the problems be solved? And I don't think so. So we go back to the two parts of the regulations that I think provide overarching authority and responsibility for the laboratory, Title 42 of the Code of Federal Regulations, 493.801(a)(2)(i)(i), each laboratory must establish and maintain the accuracy of its testing procedures. That applies to the home brew tests as well as the test kits. So even though the FDA may not be approving the home brews, the laboratory is still responsible. When it mixes up and produces its home brew, then it's still responsible for the accuracy. Then when we go on to Title 42, 493.1236(c), at least twice annually the laboratory must verify the accuracy of any test that is not subject to proficiency testing. That also applies to the home brews. So all of the quality control requirements in CLIA do apply to the home brews to establish the analytic validity. But again, just to stress, if we're concerned about whether or not the tests are really measuring the thing that you would hope that they're measuring, the clinical validity, that is a different topic.

DR. TUCKSON: This is terrific. We're going to keep this discussion going, and we have three people in the docket.

Chira, Emily, and then Andrea, and I'll look for other hands.

MS. CHIN: I just wanted to restate that you said something about laboratory-developed tests are not being regulated by FDA, but the process of analysis is being regulated by CLIA. So is there any way that the laboratory-developed assay be regulated by somebody?

MR. HAMILTON: Well, if the assay is not producing accurate results, then that falls under the analytic validity area and is subject to CLIA. So when we go back to the responsibility of the laboratory to establish the accuracy of its testing and we find that a laboratory has inaccurate testing, then that's a deficiency under the Laboratory Improvement Amendments.

MR. HAMILTON: But Tom, again, just where we're at here, if I understood your earlier comment, it sounds like, as we keep cutting through this, that there's this general provision that says if it isn't specifically noted, then you have to just have good procedures and processes or else we're going to yell at you, and hopefully somebody is actually checking that, but you have this obligation. Where the problem is, I think you said, is that there is no requirement around the assessment of clinical validity, and that's what you are, I think, also saying. There's no clinical validity. So it's a terrific test, you've got great processes, you're very sharp. By the way, the test isn't clinically valid, and that's what I think they are also saying.

We've got Emily, and then Andrea.

DR. WINN-DEEN: So I think we have to accept that this is an imperfect system, because if I asked Andrea or Deb how long does a CAP inspector spend in your laboratory reviewing your validation data on a new test, and I asked Steve Gutman how long does the FDA spend reviewing an IVD submission on a new test and reviewing that data, I'm willing to bet that the FDA spends more time per test and reviews things in more depth than this inspection system can support. So I think what we have to struggle with is some kind of balance between is there a system that works for low-volume tests, for brand new tests, and at what point do we say that a test is so well established that it doesn't make sense anymore to have 200 molecular labs each manufacturing

their own assay, and it makes sense to have six or eight companies manufacturing the assay instead?

But because we're in a field where things are emerging all the time, we don't want to get rid of lab-developed tests, we don't want to get rid of IVDs, but we have to understand that there is a continuum, and there also is some point when those things need to change over. I don't see any way that we're ever going to bring lab-developed tests up to the rigor that a manufacturer-developed test is subjected to.

DR. TUCKSON: So as we go to Andrea, I want to keep in the minds of people to be thinking about, and somebody can start to answer it, is does it matter? Is this much ado about nothing? Maybe that's what we're going to come up to. If you can't ever get at it and it's such a thorny issue, who cares if you don't do it? Is it a big deal? We'll get to that in a moment, but those who know the answer to that should start to help us with that.

DR. FERREIRA-GONZALEZ: I thank all of you for your presentations.

Judy, I was taken by a part of what you said about the proficiency, both of you, Thomas Hamilton and you, about the proficiency testing for cytology that took so many years and taking that as an example. But I look at it a different way. Now when I go to have my Pap smear done, I feel very confident that somebody, if I have a cytotechnologist at this point, that the results will be more accurate or the appropriate result. Before that, results from this proficiency testing, even though it took so many years to come along, we didn't have that confidence. At that same time, now we have addressed issues that we need to go back and continue education in a section of these individuals providing this testing.

So I think we have learned a lot of new things about testing that is being done very broadly that has taken so long to come up with a proficiency testing program. I agree with you that there is a major issue, but it's not because it isn't easy that it shouldn't be done.

The second question that I have, or comment that I have, is that we discussed a lot about processes and quality control, pre-analytical, analytical, but I want to see if you'd mind elaborating a little bit more on specific requirements for individuals performing genetic testing, and specifically inherited disorders. If you are a high-complexity CLIA-certified laboratory director in microbiology or chemistry and so forth, and you decide today to start offering an FDA CLIA product for cystic fibrosis carrier screening, could you do that under CLIA the way it is today, with all the quality control? Is there any specific person and requirements that will assure that the proficiency testing for cystic fibrosis carrier screening will be interpreted by somebody with the adequate training that will assure me of the valid interpretation within a clinical context?

MS. YOST: Currently, the way that CLIA is structured, because there are not specific requirements for genetic testing personnel, the laboratory director obviously has the overall responsibility for hiring the right people to do the job. So that's the part of the process, and in that case, if you're going to add a test where it takes a very specific expertise to do that, then the laboratory director is responsible for either retaining on a contract or hiring individuals who can perform and oversee that particular type of testing and be sure the information that's provided to whomever the authorized person is is accurate and reliable. So there's a responsibility there. There may not be a specific requirement, but there's clearly a responsibility, because we say CLIA personnel requirements are essentially minimal. Even for the type of test you're describing, we're talking about a physician or a Ph.D. with board certification, a number of years of experience, plus specific training. So with all of those three things, you then place in that

individual the responsibility to ensure that they hire the right people to not only do the job but to oversee the job. So if you need a technical supervisor to help with the interpretation of those results, then that laboratory director is responsible for making sure that that does occur.

DR. TUCKSON: Is that good enough? In other words, every doctor that's graduating from school, every professional in the business, you're supposed to do right. Is that enough? Does CMS believe that that's enough?

MS. YOST: I have to say that what we do, we have a very strong practice. Our practice is that if we find quality problems in the laboratory such as this, you have a test and you don't have the appropriate individuals with the appropriate training or experience to be able to perform the testing, guess what we do? We cite the lab director, and that gets their attention. Trust me, it gets their attention, because they know that they are ultimately responsible, and if not, that laboratory can lose its certificate to do testing.

DR. FERREIRA-GONZALEZ: But what is appropriate training? I take a class in undergrad in genetics? I've been going to the genetics clinic? I've learned how to do this? I mean, that's what I'm going to.

MS. YOST: I mean, CLIA is a package deal. You saw that it's a series of checks and balances. You need to do your quality control on a regular basis to make sure that the test results are correct. You also need to have the right people to manage and do the testing. You've got to have an audit system, a record-keeping system to follow the process throughout the entire thing. You need to do the proficiency testing such as Thomas described, whether it's a formal proficiency testing or whether it's the informal. But either one is mandated. You have to do all of those pieces. Plus you have to be able to demonstrate that you're providing accurate and reliable results for all the tests that you're providing, not just your genetic tests, because there are a lot of other tests that are very complicated to perform and interpret, and you've got to be able to provide that information. You have to look not at the narrow scope but at the broader scope of everything a laboratory can do.

Someone said this morning 2,000 tests that a laboratory could possibly do. I put 1,000 up there just as a conservative estimate of how many tests are on the market that a lab might possibly perform. Qwest can tell me. I don't know. What's on your menu? How many tests? It's very expansive. So you have to be responsible for every one of those, and you have to be able to, under those circumstances. So it's not just one thing or another that's going to guarantee you that the system is going to work. It's all those pieces working in concert.

DR. TUCKSON: But now let me just make sure that Dr. Randhawa --

DR. RANDHAWA: Randhawa.

DR. TUCKSON: That's what I said.

(Laughter.)

DR. TUCKSON: I'll just make sure, though, because what you said is important. Can Qwest get a test to the American people, no matter how many zillions they've got on the thing, without going through FDA? They can? They get them out without going through FDA. Thank you very much. So they're in the same deal.

MS. YOST: Can I just add one more comment to what I was saying? It's very important to also put this in context. I'm not saying that every laboratory is perfect because CLIA is here. It's just like Steve said: we have the good, the bad, and the ugly. We truly do. Every once in a while there's a zinger that nobody could have anticipated that we all go and we say, oh my God, what have we been doing all these years, but for the most part we have that bell curve and those labs are doing a good job, as best they can under the circumstances.

DR. TUCKSON: And that continues to come back to the question does anybody have any data for those who aren't doing a good job? Has anything bad ever happened to anybody's kid?

DR. RANDHAWA: Since you called me doctor, now I'll call you Dr. Tuckson.

In the discussion that I've been hearing today, I'm not sure that even if you were in an ideal world of accurately doing laboratory tests when we think it should be done, that is sufficient to improve the public health and outcomes. So I think we're just talking about the first part, and what the downstream consequences of the test are, whether it's a more invasive confirmatory test, whether it's the harms and benefits of the treatment and how we balance that, which is really what improves or has an impact on the public health. So I think it's important for us to get a better handle on doing the tests well, but I haven't heard any discussion about clinical utility or the outcomes of testing, and that hasn't been a part of anything I've heard from either the CMS or FDA. So I'm not sure that even if you were to get everything done perfectly by the labs, that would really solve the problem.

DR. TUCKSON: Great. I think I understood what you just said, and that makes sense.

I didn't realize Debra had to go or I would have jumped her in the line. They're trying to run and see if they can catch her.

Other questions from the committee that will help out here, or any questions that are on your mind? Let me just ask the committee, if you don't have questions, do you all feel like you understand any of this so that you're prepared to make some recommendations here?

DR. EVANS: I'm confused about one thing. Is one of the problems that CLIA inspectors don't have the expertise to evaluate the in-house developed tests? Is that a problem?

MS. YOST: It's a problem that has an identifiable solution. We didn't really get to talk about the list of things that we're planning on doing, and one of those is to probably do something creative as far as looking at those tests, because we realize we may not and because most of the labs that we look at are not the type of labs that are going to do this type of sophisticated testing. So we would either create a core of folks who would go around and develop the expertise, train them and get the technical and the investigative training in place, and they could go around and look at all the laboratories in the country rather than the local surveyors, or we could have a contract with someone who already does that and already possesses that expertise and just pay them. So there are a number of ways that we can get at this. I wouldn't take that as an irresolvable problem because it's something that can be addressed, and it's something that we've already been evaluating.

Actually, way back when in 1997, when the recommendations were made from the task force, we knew that we probably would need to look at something because the technology was exploding and we weren't going to be able to keep up with it in-house.

DR. EVANS: Is it related to the lack of a specialty of a genetic testing --

MS. YOST: Nothing at all. No, it is not. No. It's the specific technology. But that, again, is going to happen everyplace, because you'll have microarrays or you'll have other types of technology that will come into place that we can't even anticipate at this point in time, and we'll be in the same position. But don't also forget that those folks that we train, we train them with very detailed, specific investigative skills, how to collect information, how to interview people, what to look at. It doesn't matter what kind of technology they're using. Those folks can find a problem if a problem exists. They know what to ask, they know where to look. They'll have the lab explain the technology if they don't understand it. So that isn't a limitation. It's actually an advantage.

DR. FERREIRA-GONZALEZ: Well, you know, another way to get around this issue of CMS and the subspecialty -- the CDC is here? It is my understanding that the February CLIAC meeting, CLIAC is actually going to look at these specific issues on the genetic specialty. Is that correct?

DR. BRADLEY: I can't speak to that. I'm not involved with CLIAC. I'm sure Judy knows.

DR. FERREIRA-GONZALEZ: If CLIAC actually, which is the advisory to CDC and CMS, is going to look at this specific issue, maybe we can wait for them to see what they recommend with this specific issue.

The other thing that we can do is maybe appoint someone to that group or have somebody from that group come back to this committee and report on what are their recommendations and then see what that group, which are most of them laboratorians, feel about this.

DR. TUCKSON: Would you hold that recommendation for just a minute and resurface it when we get to what we want, if anything, to do as a committee? I think you've raised something that's tangible.

Let me ask, then, Judy, to finish the part where she has some important stuff in terms of what New York is doing. One of the things that I think Judy has emphasized well here that has certainly gotten my attention in this whole discussion, and it came up in the example also with Qwest, is how many of these tests are rolling down the road? So if you put every single test through a pretty serious drill, that might be an almost impossible regulatory burden. So that's important to think about. I'm thinking about it and trying to figure out what that means. New York has done some stuff that gives us a real case scenario for some of this. So can you share with us the New York thing?

MS. YOST: (Inaudible) office. They are the investigative arm of Congress. They were requested to look at direct-to-consumer testing, but also to follow up on the status of the proposed rule at CMS. Just to get back with you, they did identify a number of laboratories that were providing nutrigenomic testing, evaluation of lifestyles. As Thomas indicated earlier, most of the issues surrounding that are not CLIA issues. We do not deal with advertising and marketing and clinical validity and utility of results by a provider, but we are responsible for oversight of laboratories. That's if the test is covered. In this case, some of those nutrigenomic tests, as they're called, evaluate lifestyle. They look at your diet, they look at your nutrition, they look at whether you smoke, they look at how much you sleep, all those kinds of things. Obviously only if it's a health assessment is it covered by CLIA and thereby subject to CLIA requirements.

In this case, these are clearly laboratory-developed tests. Trust me. So in that case we are closely monitoring. I think it's important for you to know the labs that have been identified plus a whole pile of others, because once you find one, they're like little bunnies. They multiply, because they're all associated with one another. They're all in cahoots with one another. That's the only way I can describe it. So you find one, and there's another. One is marketing for the other, one is doing the test, one is interpreting the test. One is in London, one is in Denver, the same lab. It's just incredible. So you just have to un-weave the web constantly to identify these facilities, and we are doing that. We are working very closely with CDC and with FDA on this process.

But let's go on to the New York program, because it's probably the penultimate in oversight of genetic testing, and I have to say that clearly they are overall in New York the most stringent state laboratory standards in the United States. They also have a wonderful infrastructure to share. So it's the difference between the economy in CMS, where we're self-funded, and a laboratory program that has very high fees, very good resources and revenue to support it.

Under this program, there are two types of tests, FDA-approved or cleared, and then everything else, the research only, the investigative use, the in-house developed ASRs and so forth. In those cases, those tests must be approved by the laboratory program before the lab can offer the test. Currently, Steve, you're correct that it's about 12 tests you've approved, genetic tests. So everything else under the sun that's a genetic test has not been approved by the FDA.

Just a typo on this. Actually, they had done up to 450 reviews overall, not just this year. But their review includes both analytic and clinical validity. They also provide the laboratory guidance on the information that they need to provide in order to do this review. But there's an interesting factor here in that all the reference laboratories in the country probably have a site somewhere in the State of New York, because if you understand New York's program, it has tentacles, because any testing on any New York resident, regardless of where it takes place, is covered under the New York State law, and they thereby must submit their tests to the state in order to be approved.

So if you extrapolate that, considering that all the major reference laboratories are there and the major facilities that are there, it is estimated that probably 75 percent of the genetic testing in the United States is already subject to New York State oversight.

The program in New York -- and there's a representative here from the program, so she'll be happy to jump up if I say something off, and she's provided all this information, so I didn't make it up -- but it's broken into two segments. There's cytogenetics, and then all of this information, the clinical information about test selection and interpretation, patient consent, confidentiality, specimen retention, turnaround time, very, very prescriptive, very detailed requirements of all the information that needs to be submitted. In addition, there are requirements for reports to be signed by a cytogeneticist and that there be an interpretation suitable for a non-geneticist, which is just fantastic.

Also, prenatal and preimplantation outcome verification. We're even looking at utility here, and of course the lab is subject to the New York State PT program. The same thing for genetic testing, very similar requirements, as you can see. Again, very detailed QC, clinical and analytic validity, confidentiality and so forth. Now, in this case they have the same thing that CLIA does, essentially, because where there is not PT material available, particularly for rare diseases, then the laboratory is subject to external PT if there's PT available, or the twice per year just as in CLIA.

It's also interesting to note that even though there is a very detailed definition of genetic test under the state law, there are also tests that are disposed through the laboratories, just as in CLIA. There are some tests in microbiology, immunology, chemistry, hematology and pathology. So not everything is all collected into the one area.

That's basically a summary of it, and this affects about 173 facilities. The cytogenetics piece has been in place since 1972, and the genetics piece since 1990.

DR. TUCKSON: Well, thank you very much.

First of all, I want to really thank Steve, Thomas and Judith for not only their presentations but for putting up with my pain-in-the-neck questions. I really appreciate the way you've handled all of it.

As the committee now tries to think about this as to any next steps that you may decide, or you may just let it lay here, I wish I had never brought this thing up. There are some things that, it seems to me, you take for granted. When it comes to clinical interventions, whether they be diagnostic or therapeutic, one assumes that there is a government that is appropriately looking out for your interests, and you just sort of take that for granted. I do hope that that is the case here, and maybe it is.

I also know that you sure don't want to be piling on needless regulation on the backs of industry that would therefore result in extra health care costs that deny access to the very life-saving diagnostics and therapeutics that you started out with in the first place, and you definitely don't want to pile on a bunch of regulations onto the poor laboratorian in an academic center who barely gets an indirect cost provision from their dean to keep the lights on. So you darn sure don't want to do that.

So somewhere in the middle of all this is a right answer, and I'm trying to make sure that there's sort of an ethical obligation this committee has for having raised it, or our predecessor has for having raised it. Shame on them, except I was on that committee, too. You know, once you raise it, you'd better doggone well deal with it some kind of way, because if at the end of the day it means that people's health could be compromised because of a lack of vigilance, then that's a pretty bad thing to have happen and just decide that it's too complicated or whatever and you just walk away from it. So I really regret ever having asked the question.

So with that, you need to figure out what you want to do and how you want to do it, and you need to determine, I think, first here is there a problem? Is the problem significant? Do you know enough to answer either of those questions? And if you don't know, then what do you want to do, if anything, to find out the answer to is there a problem or if the problem is significant? I look now for wise guidance.

Matthew?

MR. DAYNARD: Is the New York person available?

DR. LILLY: Yes.

MR. DAYNARD: Well, I think you'd be a great place to start to answer Reed's question, namely what has the response been and the effect of the New York law on industry and consumers, to your knowledge?

MS. BERRY: And if I could amend that, too, what is it that prompted New York to act in the first place?

DR. LILLY: I'm Dr. Ann Lilly. I'm the director of policy for the Wadsworth Center, which is the public health lab in the State of New York. I've been responsible for the cytogenetics oversight programs since 1979, and for the implementation of the genetics program in 1990.

What prompted New York State? There's a New York State statute that dates to 1964, predates CLIA in 1967, which requires the State of New York to oversee the practice of laboratory medicine for the testing of all specimens derived from the human body for all purposes. So when cytogenetics, the examination of human chromosomes, became a practice of laboratory medicine, it was an area that required oversight. When biochemical genetic assays for enzymes or PKU or DNA markers for genetic assays became the practice of laboratory medicine, it was required that we establish appropriate good science-based standards for laboratory practice.

The statute requires that all tests performed by a permitted laboratory must be either generally accepted -- by definition, FDA cleared is an in vitro diagnostic device -- and approved by the Department. That means technically we can say no to a test the FDA said yes to. I don't know that we've ever done that. But for any test that is not cleared by the FDA, so as not to limit availability of this general practice of lab-based test development, we had to have some basis by which we would approve those tests that didn't go to the FDA.

Our process for validation review of non-FDA-cleared tests is not unique to genetics. It applies to any laboratory test. It could be clinical chemistry, it could be microbiology, virology. Genetics is only one area. The standards are that the laboratory has to submit adequate data, and for genetics that's usually very small numbers of cases because for most of the tests it's going to be small positive patients, if any. So their validation data and their clinical validity. There must be some known clinical association with the genetic marker.

So, for example, a lab that says they can find SNPs, analytical validity is absolute. They can find every SNP in the human genome, they can print out your CD SNP profile for $1,000; if they cannot establish clinical outcome associated disease state for each SNP, they cannot offer that SNP in New York State.

What's the response been? Consumers are not well informed about how we oversee laboratory tests. Physicians are only slightly better informed. Many of them are told where to order their tests by the insurance that's ordering the services for the patient. So the laboratories themselves, 95 percent or better of all labs are good labs. As I think it was that Steve said, if you don't know that the test you're offering provides good results, what are you doing offering the test? And 95 percent or better, that's going to be the case. If they forgot to submit their validation package, hopefully it's already on the shelf and they can correct the deficiency within a matter of days. If they send us the package, we review it.

We're slow. There are only two technical persons on the staff who actually review all of these submissions. I review all of the cytogenetics, the (inaudible) assays that are ASRs that require individual probe review. All of the genetic testing is reviewed by another individual who is a geneticist. We get behind, and that's the biggest objection from industry. It takes time. They've done the work, and we have to do the reviews.

It's also an educational process. We'd like to streamline it. We'd like to see every application come to us with the table of contents and everything on the same page. That's not the way it happens. But it works.

In the meantime, if a laboratory had a critical clinical need to offer a test for a clinical referral reason, we will issue what we call a non-permitted lab approval for that patient, for that purpose, for that time only, and we tell labs that when they get to 50 requests, we begin to get really unhappy.

Our surveyors do not attempt to review the technical data at the time of survey. They go in and ask the labs what tests you offer. If it's a home brew test, it's not FDA approved, there's no package insert that says it's an IVD, they ask to see the letter of approval from the department of health. If the lab can't produce the letter of approval, then the lab is cited for offering a test without approval, and the deficiency is corrected by submission of the validation data.

There are labs out there offering clinically useless tests that are having dire consequences for fetuses and patients.

DR. TUCKSON: I have been waiting for three hours to hear somebody say that.

(Laughter.)

DR. TUCKSON: Now, first of all, thank God for what you all are doing in New York. Given what Judy Yost told us so clearly about the interconnections between New York and the rest of the country, would a lab have to submit to you and then to other -- I mean, wouldn't this be burdensome for labs to have to jump through your hoop as well as the CLIA hoops and the FDA hoops?

DR. LILLY: New York State is CLIA exempt. For those labs located in New York State, by meeting New York State requirements, they do not have to meet CLIA requirements. For labs outside of New York State, they will get their CLIA certificate from their local state entity. However, to my knowledge, nobody else is reviewing the actual validation data. CAP may be at the time of survey onsite would not discourage that, and they may find things that we don't find. I mean, the more times you look, the more helpful comments, the more constructive criticisms we can offer. Right now, we're not in competition because nobody else is doing it.

DR. TUCKSON: How much money -- oh, I'm sorry. Cynthia has her hand up.

Matthew, by the way, you had the floor. Did you finish your question? And then Cynthia is next.

MR. DAYNARD: Well, I did. Thank you very much. I'm just wondering what do you do about these labs that are offering tests that are hurting people?

DR. LILLY: Well, for New York State, we simply tell them they must cease and desist, and if they continue we can charge them $2,000 a day.

MR. DAYNARD: Are they operating in other states even if --

DR. LILLY: New York State has no jurisdiction in any other state. I'm an attorney as well as a geneticist.

MR. DAYNARD: Right. I'll be in touch.

DR. TUCKSON: We have Cindy, and then Emily.

MS. BERRY: What I think I heard was that there wasn't a particular problem that prompted this. This was a statute that existed a long time ago, wasn't specific to genetics or pharmacogenomics or any of that, and so because of the regulatory scheme in New York State, genetics fell into it, if I'm interpreting it correctly.

DR. LILLY: There was a terrible problem in the early 1960s when, if you sent the same specimen to two different chemistry labs, you got two different answers. The hypothesis was that there's the same potential problem in every area of clinical laboratory medicine if you don't put appropriate oversight in place.

MS. BERRY: So what I'm wondering, then, is that maybe there are things that New York does that could be done at the federal level with some tweaking or whatever, but I'm not totally convinced that genetics is unique, that whatever these problems are could apply to many tests and many labs. So I'm struggling a little bit with why is it we need to focus on a genetics component to CLIA or whatever, because it seems to me there are other things that could fall through the cracks.

DR. TUCKSON: Well, given that you're going there, in your opinion and with your experience, and we appreciate you stepping up and helping us here, is there a special need? We wrestled with this question of genetic exceptionalism, and it's on our menu of activities for all the things we're supposed to be doing. Is there a special need for genetic exceptionalism here, or is this just diagnostic laboratory medicine?

DR. LILLY: I'm a geneticist, but I have a personal bias. I believe this is good for all of laboratory medicine, and the success of the New York State program is because it does not treat genetics differently. It makes no exceptions for genetics, but it simply holds it to the same standards.

DR. TUCKSON: Emily, and then Andrea.

DR. WINN-DEEN: I had a question regarding FDA-cleared tests. Once they're cleared, is there any incentive for New York State licensed labs to switch over to a cleared assay, other than the fact that they don't have to prepare a dossier for you?

DR. LILLY: It is of concern, I believe, to some of the vendors of IVDs, that if they go to the trouble of producing an IVD and getting FDA clearance -- this is true in genetics; I can't speak to other areas -- that a lab will use an FDA-cleared IVD as their gold standard against which they will validate their in-house developed assay perhaps because the in-house assay is cheaper. So, yes, there would still be an incentive for a lab to do a home brew, home-developed assay if they thought it was cheaper than the IVD cleared.

DR. WINN-DEEN: But the state doesn't have any mandate that says that in order for a test to be available at this level, you have to --

DR. LILLY: No, but it is probable that if there's an IVD-cleared assay, that is the standard against which we're going to expect the lab to validate, and that may put them at a high standard that they won't be able to meet.

DR. WINN-DEEN: And I had a quick question for Judy. I actually was sort of distressed to look at the CAP molecular surveillance panel and to see that they're just genomic DNAs and they're really not full process controls. Is there any plan to work with CAP to develop full process controls for genetics?

MS. YOST: Not specifically, no.

DR. FERREIRA-GONZALEZ: What do you mean by that?

DR. WINN-DEEN: Well, it doesn't go through the isolation purification part like a clinical sample would. It just comes as a purified genomic DNA.

DR. FERREIRA-GONZALEZ: For the proficiency testing?

DR. WINN-DEEN: Yes, for the proficiency tests.

DR. FERREIRA-GONZALEZ: There are major issues of how you manufacture and have a license --

DR. WINN-DEEN: Yes, I understand that. I just didn't know how it met CLIA's requirements.

MS. YOST: Actually, because they're not required. That PT is not approved by CMS. The only PT we look at when we approve proficiency testing providers are for the 83 analytes that I mentioned that are in the regulation. Everything else is voluntary for the laboratories to perform, or in the case of certain accrediting organizations where they require every analyte to have formal PT. One of the difficulties, again, is the fact of the shortness of materials. There are not materials available that are easily transportable, or in the case of a rare disease it's just that there are so few materials that it's impossible to create PT the way we're used to seeing traditional PT. So there are limitations to what can be done with that, and I think that's part of the process.

DR. FERREIRA-GONZALEZ: And that's the problem you have with cytology, too?

MS. YOST: Yes, it was only one. It was one of the problems we had, that there were not enough slides available.

DR. FERREIRA-GONZALEZ: There are significant efforts through the CDC to develop controls and materials that could be used for genetic testing for a significant amount of different things.

MS. YOST: Yes, there are.

DR. FERREIRA-GONZALEZ: So maybe that could be a venue for different professions for materials that could be used to have the enforcement. I strongly believe that there's got to be some enforcement for PT for the laboratory.

MS. YOST: You're absolutely right, and there have been major efforts by CDC in that area, both in PT and QC, for genetic tests, and we have been working with the CDC to support those efforts, because I think we're paying for most of them anyway under CLIA. But it's important to know that in addition to working with them, we hope to develop educational materials for genetic testing laboratories that would encourage the use of those types of materials then. So we would

get at it from that direction. We really didn't go through my list in detail, but that's one of the things that we had talked about doing.

DR. FERREIRA-GONZALEZ: A question for the New York -- the New York lady, I'm going to call you. You mentioned that when you have FDA-cleared IVD products, that when the laboratory brings them online, you don't have to submit for your review before these laboratories start using them.

Now, if you use an ASR, you're still doing a laboratory-developed assay, and then you have to submit for the review by the New York State Health Department. Is that correct?

DR. LILLY: I'm sorry. I didn't hear the second part.

DR. FERREIRA-GONZALEZ: When you use an ASR --

DR. LILLY: ASRs, yes. When you use an ASR as a component of an in-house developed assay -- and we greatly appreciate the FDA's recent clarification that when you buy a single component, you're buying an ASR. So when you put them together -- you know, your control probe and your target probe and you're making up an assay -- then, yes, all in-house developed assays using ASRs require departmental approval, whether it's genetics or microbiology.

DR. FERREIRA-GONZALEZ: I think at the core of some of these issues that we come back and forth, certainly to genetic testing, is just that within CLIA there is no need to show clinical validity of the testing that we bring it. This is not just for genetic testing. It's for all laboratories. So we've tried to fit a 9 foot into a size 6 shoe.

(Laughter.)

DR. FERREIRA-GONZALEZ: You know, this is at the core. Who does the oversight at New York State or sending it to the other agencies? You know, the problem is that the current CLIA regulation does not include demonstration of clinical validity.

The CAP Molecular Biology Checklist has a significant amount of questions now put into that program to deal with this issue. It's three days. Like last month, they came and inspected us and spent three days in our laboratory looking specific about data. It's a different issue, and again, these are your peers looking at what you're bringing online.

But at the core, it will be that issue that there's not in CLIA a specific regulation for the clinical validity of the test.

DR. TUCKSON: And I think that we all get that what that means, as you described, Dr. Lilly, is that there could be or there are in some cases people who are purchasing a test, people are paying for it, that may not work. It may not tell you any information that would be useful or it could be that a clinician is using that information to make a diagnosis that leads to a therapeutic intervention that may not be appropriate. That's where the importance of the question mark arises, if I understand the discussion.

DR. RANDHAWA: This is a question for my CMS colleagues for my clarification. Is the reason New York State is exempt from CLIA is because they already had a program equal to CLIA?

And the second part of that question. This is a hypothetical, sort of a dangerous question to answer. Suppose another state comes up with a program similar to New York State. Would it also become potentially exempt from CLIA if it wanted to?

MS. YOST: States have to apply in order to become exempt and then we do an excruciating review of their standards to ensure that they actually are at least equivalent. They could be more stringent, as obviously these are, but they must be at least equivalent to CLIA.

Please understand that we're talking about opposites here. This is the continuum of laboratory oversight. This is one end of the spectrum and we are the other. CLIA was put in place as minimum standards for laboratory quality with certain caveats, again, that the lab director has that overall responsibility and that should pick up where it needs to in the event that they can, and the laboratory has a choice about who's going to inspect them under CLIA. They have the choice of either the state department of health, who use the CLIA standards, or an approved accrediting organization, many of whom also have more stringent standards than CLIA, because it just is equivalent. It doesn't say identical.

That's the way the program was developed. It was developed also that it would essentially dovetail into FDA because they didn't want duplication of effort. CLIA would look at is the answer right, and FDA would decide if it was a useful test. So it makes sense if you put all the pieces together.

DR. TUCKSON: All right. So here we are, 15 minutes left.

Dr. Ann Lilly, you are just terrific, and I just can't thank you enough.

DR. FERREIRA-GONZALEZ: Can I add one monkey to the wrench?

DR. TUCKSON: Well, first of all, what you get to do is, you get to add one monkey to the thing, but what you also get to do is to start to formulate the beginning of a consensus of what, if anything, we want to do. You need to do two things.

DR. FERREIRA-GONZALEZ: I'm not sure about the second one, let me tell you that.

(Laughter.)

DR. FERREIRA-GONZALEZ: As I commented this morning, I'm a member of the IRB for VCU. As a member of the IRB, we review a lot of protocols that actually are clinical trial protocols where some of the clinical trial protocols propose to do, for example, pharmacogenetic testing on individuals to be placed in a specific arm of a clinical trial, and then certain drugs are given to that patient.

But I was talking to and asked my IRB members and said who is doing the testing for these clinical trials? And somebody looked at me and said what does that matter?

I started bringing the issue of research testing that is being used to make decisions on how a patient is treated in clinical trials, and my understanding is this is under CLIA purview, but it seems to me there is some disconnect between what actually IRBs in different areas of the country are knowledgeable about these specific issue.

So one of the concerns I have is also the research laboratories. How are they regulated for these private tests?

DR. TUCKSON: All right. Let me try this.

Thank you, by the way.

Let me give you an option to shoot at because I'm looking for somebody smarter than me to say it or figure it out. What I'm thinking is is that we say to the Secretary in a letter that we've had a chance to discuss this, learn a lot about it, and that we have certain principles that we have come to understand.

Principle number 1 is that the public should be protected or there should be oversight. Not even protect. That's negative. The public should expect that there is appropriate oversight in place for the diagnostic and therapeutic interventions that they receive.

Number 2, that this transcends genetics but because our focus, our mission, is on genetics, we recognize that genetics fits into the larger continuum of clinical care, and that we come at this from the point of view of specifically looking at genetics.

Number 3, that we as a principle understand that inappropriate regulations do no good and we have a report that's already out around our concern about access to genetic technology that could be compromised by unnecessary, burdensome rules and regulations that are not helpful. We put that as a principle as well so we clearly get on record as not looking to be a bunch of irresponsible nuts running around talking about regulate everybody and everything.

Number 4, that we've heard good testimony from his -- in this case, because he's a man -- own agencies that leave this committee with some questions as to the adequacy of oversight of genetic testing.

And that finally, because of the potential implications of a lack of adequate oversight on the health of the public, that it would behoove him to bring his people together -- FDA, CDC, CMS -- and they should report to him and give him an answer as to whether or not there is a significant problem and what the remedies might be to be able to address it, and hand him the transcripts of our testimony, a synopsis of all that we've gone through, and simply say, you know, this is on you. I mean, this is what you get paid to do and all these smart people in government get paid to do, and the FDA, that's all they exist for, and CLIA, that's all they exist for, and the CDC, in part that's what they exist for. Figure it out.

I just put that out there for you all to shoot at.

MS. BERRY: Hasn't that already been done to an extent? I mean, Thomas, you went through kind of the laundry list, the thought process or the approach that you take when you analyze is there a problem, and if so, is the proposed solution necessary to correct that problem? You know, the whole thing that you outlined for us. I mean, was that done just at CMS? Was that done with input from FDA and others? I'm wondering if we've already done what Reed has kind of outlined.

MR. HAMILTON: Well, again, we weren't looking at the entirety of genetic testing in that. We were looking at the question of a proposed reg that would establish a genetic testing specialty. So

it was a narrow focus within CMS. We obviously discussed it with CDC and the FDA, but our clearance process was within CMS.

DR. TUCKSON: Kevin?

DR. FITZGERALD: I'm just wondering if we could be more specific in the letter to try to give the Secretary a bit more concrete focus and mention that in this process which you mention, with these principles that you mention, one of the things that came up that Andrea also mentioned is this fact that there is a difference between a plan like New York's and what is currently federal regulation, and it focuses around clinical utility.

So the question is to say not that the federal has to be the same as New York, but, as we heard, New York is at one end of the spectrum. Should we move more in that direction and, if so, then how and to what extent? So I'd say you could break it down into fairly specific sorts of issues.

DR. TUCKSON: Joe?

DR. TELFAIR: Yes, I would agree with both you and Kevin, but also take into account, I think, what has been said. Mine is real simple, hopefully. I think it seems like the issue is broader and it's bigger than just our committee as a whole, and it seems like what we can do in terms of the strongest thing we can do is to hear what is the bigger issue of clarity, and then determine based on, well, even what was just presented, and also I think because there's a committee coming up, to say this is our piece to the bigger solution and that's the most we can do, okay? That would be a thought.

DR. TUCKSON: Thank you.

DR. FERREIRA-GONZALEZ: What we heard earlier from CMS is that genetic testing is currently regulated under CLIA. Our thinking is a specialty will produce more strong or more defined criteria for this testing, but I think maybe letting CLIAC come out with their recommendation, specifically if there is a need to increase oversight of genetic testing by the creation of a subspecialty or specialty within CLIA might not be a bad idea, and just wait for that group to look at this and report back to us before we make our final recommendation.

DR. TUCKSON: When are they meeting?

DR. FERREIRA-GONZALEZ: February.

DR. FITZGERALD: Andrea, one quick question, though. In that process, will even the issue of clinical utility ever come up? Because it wouldn't normally, right, even with a new specialty?

MS. YOST: My guess is it will.

DR. FITZGERALD: Your guess is it will come up. So this would be a first.

MS. YOST: No.

DR. FITZGERALD: You have clinical utility for other --

MS. YOST: It's been coming up in that venue also.

DR. FITZGERALD: Oh, I see.

DR. FERREIRA-GONZALEZ: So this might tip it over the edge?

DR. TUCKSON: Andrea, first of all, the committee needs do it with the consensus, and I think we've got to keep raising consensus.

My concern -- and I think, first of all, we've gotten extremely frank, well-meaning, and good testimony from Steve, Thomas, and Judith, and clearly they are honorable people serving the public's interest -- at the end of the day, the natural tendency, inevitably, for people in government agencies has to be to tell us that things are moving along and doing fine. I think we need to put it on the Secretary and ask him, in the quiet of his own deliberations, whether or not this is going as it should, because I think there are things that can be explored in private that can't be explored as well in public. That's just a bias.

DR. FERREIRA-GONZALEZ: Well, that committee will report to the Secretary.

MS. BERRY: I just think whatever we send to the Secretary should more clearly define what the problem is because we're hearing that 75 percent of the labs are regulated by New York State. We also know that health plans to a large extent tell doctors which labs to use so that something is reimbursed and kits are regulated by FDA. Is that correct? So if some consumer just on his own gets something -- so he or she is protected to a certain extent.

So I want to hone in on what is the actual problem? What is it that's the problem? Who's unprotected? What are the gaps? And I'm not certain I have a good understanding of what that is.

DR. LILLY: Can I just make one technical point? Seventy-five percent of the testing is regulated by New York State. That's because the very large commercial labs are all regulated by New York, and the reality is the majority of tests are still done by those large labs, not 75 percent of the labs.

DR. TUCKSON: And, by the way, you may want to, Cindy, again, in this section in the briefing book on page 8, there is a set of one, two, three, four identified gaps which are part of it.

So the challenge we have, based on what Cindy has said -- and I was sort of expecting that that's where we also are here -- is that there are still, despite the information we've gotten, some unclarities in the basic database in the background.

So let me just ask you your preference here, Cindy, based on what you said. You could postpone writing a letter to the Secretary and try to discover some more of these things and make it more clear what you want to write in terms of the problem and the issue. We could come back at it in the next meeting. You know, work on this in the interim between the meeting and then finalize it at the next meeting, or you could just simply say we've had all this stuff, we're uncertain, and we urge you to take a look at it. So it's really a matter of sequencing as to how you think you may want to proceed.

MS. BERRY: I mean, I've read the briefing book. I just, from today's discussion, don't know precisely are all of these problems real problems? What is the scope of these problems? Is there agreement, universal agreement? Are there others that were not mentioned here? I don't have any objection to, if people know what that is -- and this is not my expertise, so there are others

here who deal with this on a daily basis who would be able to articulate much better than I what the problems are. If there are truly concrete issues and problems and gaps, I just think we should identify it in a letter, and I don't object to doing a letter right away if we're able to put our arms around the nature of the problem immediately. If not, then I would suggest that we postpone the letter until we can get that nailed down.

DR. TUCKSON: Other points of view as we try to determine what your wishes are in this regard?

DR. FITZGERALD: Just a quick question, and again, if you would help maybe clarify this a little, and perhaps we can look at it this way. Rather than listing, perhaps, all the specific problems there might be, my question would be is there an approach or solution that would pretty much address all that list of problems; i.e., clinical utility?

DR. LILLY: I don't think there's one solution, but I think there are many options. One is greater use of the FDA option. One is changing CLIA's authority for all testing to include clinical validity, heaven forbid. One is something specific for genetics. I mean, there isn't one solution.

DR. FITZGERALD: No, I'm not saying there's -- maybe I didn't phrase that properly. What I'm asking is there's a whole list of things that may be wrong. Is there a solution? Not one solution. Is there a solution? Or maybe there are several different solutions, all of which, as you mentioned, could address the list of problems.

It's the list of problems I'm trying to get at. Do we need to list all the problems or are there a set of solutions that would pretty much take care of all the problems, whether it's one in the set or many?

DR. LILLY: I don't have the list of what you've identified as the problems.

DR. FITZGERALD: Okay.

MR. DANNENFELSER: I guess I would want to know how rigorous it is to determine the accuracy of the test, and then what is told in terms of to the patients how accurate the tests are in terms of is there a percentage of accuracy and how certain can we be and how accurate that assessment is.

DR. LILLY: Accuracy of a test has a very specific scientific definition. It's not hard to establish accuracy. That is, if you have a specimen that has the target, how often do you find the target or how often do you get a negative answer when you should have gotten positive and positive when you should have gotten negative.

I don't think that's the accuracy you mean. I think you mean the predictive value in the particular clinical circumstance of that patient. That is much more difficult.

DR. TUCKSON: Marty, is that what you mean?

DR. LILLY: So in a laboratory, I can tell you that cytogenetics laboratories, their accuracy rate is 99.9 percent. One out of 1,000 cases would get the wrong answer, right? That doesn't mean much to a patient where the predictive value depends on why the test was ordered by that physician in that circumstance. I, the laboratory, can't tell you that without knowing exactly the clinical reasons the physician ordered the test.

MR. DANNENFELSER: Can you do studies after the fact to determine if the --

DR. LILLY: In New York State, we ask laboratories to confirm prenatal and preimplantation genetic diagnosis results for all pregnancies. That's the only way that lab can do quality assurance on outcomes, but that doesn't give them predictive value, again, in the clinical circumstance. It gives them test accuracy.

MR. DANNENFELSER: Well, here's a hypothetical. A number of pregnant women are told the child has Down's syndrome, they give birth, and then there's a determination how many of those were actually accurate. If 40 percent of the children did not actually have Down's syndrome, can you then conclude that perhaps that test is 40 percent inaccurate or does that give you reason to think it might be?

DR. LILLY: No, it wouldn't give you analytical accuracy. That wouldn't be how you'd establish analytical accuracy. That's how you would establish predictive value. They're two different measures.

DR. TUCKSON: By the way, Steve, would just remind us again of this postmarketing surveillance that we're getting at here? Again, who handles that again? Just so we have the right information.

DR. GUTMAN: Well, I can't speak for New York State. At the FDA, there obviously is an entire program. Actually, it's being reenergized. There was a report out I think last week about the new contours of that program.

We in Devices are sort of responding to the issues in Drugs, which is that not New York State, not CMS, not FDA looking at a premarket package can predict the future when you extrapolate it to the huge universe of use. So it's always sort of an estimate, and the reason you want to track tests is to see the truth.

DR. TUCKSON: All right. Thank you.

So we're back to decisions, and the decision is standing between you standing in the lobby being picked up to go to dinner. By the way, at 7 o'clock, you're supposed to be in the lobby, and if you're late, God help you, because you won't eat for free.

MS. CARR: It's not --

DR. TUCKSON: It's not even free anyway.

(Laughter.)

DR. TUCKSON: You won't enjoy each other's company. That's it.

So you have two choices here. Cynthia has -- oh, great, Phyllis. Save us.

DR. FROSST: I'm sorry. Never get between a committee and it's dinner, but I do have a third option that's somewhere between a letter to the Secretary saying there's an issue that he needs to get his smart people working together on and between doing what sounds a bit more like a short report really highlighting the issues that are at stake here, and that would be to write a letter, but including an illustrative example that highlights a gap that an individual could fall into. It seems

to me that that might be a way of getting a busy person to notice that there's a real personal element here that he can make an effect in.

DR. TUCKSON: That's actually a very cogent recommendation, and if the committee were to adopt that, you would have to have a few people who would volunteer to sort of put that together, and then we would float that by the full committee in time to send that forward.

So what you've done, Phyllis, because obviously you're an active listener, you have summarized the three options better than the chairperson ever could.

So, committee, which of those three options that have been laid out do you enjoy first? So which of those seem to make sense?

Phyllis, start with the first one. Raise your hands for those that like 1, 2, and 3. What's the first one again? You did great.

DR. FROSST: The first one is suggesting that the Secretary get his wise heads together and try to address the problem that we superficially highlight.

DR. TUCKSON: Good. Then the second one was?

DR. FROSST: Similar to Option 1, but to include sort of a case study, and example, if you will, highlighting an example that would demonstrate the gap that we've discussed today. A gap that we've discussed today.

DR. TUCKSON: That was the third one.

DR. FROSST: No, that was --

DR. TUCKSON: Here they go again. Just so we've got them. See, I'm active listener, too.

The first one was you send a letter to the Secretary saying get your smart people together and figure this out. Number 2 is you do something that's essentially a report where we put together and really go through some of the things that were implied by Cindy's very good recommendation. The third is you send the letter soon, but you indicate in there an example of somebody falling through the cracks because you want to illustrate what's going on.

DR. FERREIRA-GONZALEZ: Let me throw a monkey.

DR. TUCKSON: Go ahead.

DR. FERREIRA-GONZALEZ: I have a fourth one, to wait until CLIAC reports in the specific issue of the genetic specialty and see what the Clinical Laboratory Improvement Advisory Committee has to say on this.

DR. TUCKSON: Right. Now, you're assuming on that fourth one of waiting for the CLIA folks to meet, that whatever they come up with is actually the solution to the problem or are you just saying it would help inform your situation?

Okay. So we're going to do it in reverse order. All those -- I'm not good at counting.

DR. FROSST: One point of clarification. A sense of when input from the CLIAC would be forthcoming?

DR. FERREIRA-GONZALEZ: February.

DR. TUCKSON: February. Good for you. That's the right question to ask.

DR. McGRATH: We could also include in either of those three options a statement about the CLIAC meeting that he then could follow up on that himself with his wise heads.

DR. TUCKSON: So we would build that into an assumption for whatever --

DR. EVANS: And one could also take one of the other three after the CLIAC recommendations, right?

DR. TUCKSON: One could do that as well. God, I love you all.

DR. FERREIRA-GONZALEZ: Do you have enough monkeys there?

(Laughter.)

DR. TUCKSON: This is a sense of the committee, including the ex officios, because you've all worked hard and you deserve the right to vote. So we're going to ask you with a sense of the committee -- you raise your hand -- Number 1, that we don't do diddly-squat until February after the CLIA folk meet. So how many of you all like that idea?

(Show of hands.)

DR. TUCKSON: So we've got one, two, three, four, five. I love this.

The next one is you're going to send a letter to the Secretary today and say get your smart people together and figure it out, knowing that the CLIA people are meeting in February and yadda, yadda, yadda. Who wants that one?

(No response.)

DR. TUCKSON: All right. That's out.

(Show of hand.)

DR. PAREKH: I'll be the lone hat.

DR. TUCKSON: Good for you, man. The courage of your convictions.

The next one is --

DR. TELFAIR: Letter plus scenario.

DR. TUCKSON: Letter plus scenario. Right. So letter plus scenario. Who's for that?

(Show of hands.)

DR. TUCKSON: Two. Three. One, two, three, four, five. Oh, don't give me a tie.

(Laughter.)

DR. PAREKH: You know, Reed, you really should count my vote also for the letter plus the example because the key here is the letter, and maybe I shouldn't vote because --

DR. TUCKSON: Six to five.

DR. PAREKH: But yes, I would count my vote there.

DR. TUCKSON: So he's with the last one.

DR. TELFAIR: No, the point of voting is, you know, pick one.

PARTICIPANT: You can't vote for more than one.

MS. AU: Mine is wait for CLIAC, but start working on the letter with examples, so you can get it out quickly.

DR. TUCKSON: Okay, this is fine. This is great. We're almost done.

You've got two choices. It's all down to two.

MS. AU: (Inaudible.)

DR. TUCKSON: Which one is that?

MS. AU: Wait for CLIAC --

DR. TUCKSON: Wait for CLIAC --

MS. AU: Wait for CLIAC while working on the letter with examples, so you can get out right away. Hurricane preparedness.

DR. TUCKSON: So here we have a compromise. Are people excited by that? Those that did not vote for wait for CLIAC, would be happy to jump on the bandwagon of wait for CLIAC and start writing the report? That sort of makes everybody happy? Who's upset with that?

DR. McLEAN: I'm just wondering if getting the letter out now might help influence the CLIAC meeting, and that's why I'm wondering if getting the letter out now might be a good thing.

DR. TUCKSON: We've got two hands up, but we've got an interesting point of view here, which is nice. This is simple. We can do this.

So do you send out the letter now, therefore juicing up attention around the CLIAC deal?

DR. PAREKH: My very humble advice, you all have identified clearly a very important issue, and a potential gap. In whatever form you all feel comfortable, get a letter out. Get a letter out. Whatever in addition you do, that's wonderful, but don't lose the momentum and don't wait for the perfect thing. Get a letter out and let work continue.

DR. McLEAN: And is there anything that CLIAC may give us that may materially alter what we want to say? We'll get a curveball? I don't know.

DR. TUCKSON: So we're going to revote. Let me phrase the consensus options. Number 1, get a letter out, get it to the Secretary so they can start working it. In your letter, allude to the fact that CLIAC is going to be meeting in February, among other things that are relevant for the Secretary's staff to review.

Option 2 is wait until CLIAC meets in February and simultaneous to that continue to gather information and fact find and so forth, such that by the time you come back after the February CLIAC thing, you've got some work done.

Now, we're going to now show hands again. Option 1, I want to see what you feel for sending a letter to the Secretary now that tells him there's an area of concern and, among other things in that letter, noting CLIAC's meeting in February.

How many want to do that strategy?

(Show of hands.)

DR. TUCKSON: And we've got one, two, three, four, five, six, seven, eight.

The alternative, how many for wait until CLIAC meets and simultaneously begin to do some fact finding?

(Show of hands.)

DR. TUCKSON: And we've got one, two, three, four, five, six. So it's 8 to 6.

Let me ask the outliers, would you be terribly unhappy with doing it the other way? Are you violently opposed?

MS. BERRY: I would be opposed if we're just going to send a letter that just skates on the issue and really doesn't clearly identify the specific problems. Not only identify the problems, but how are genetic technologies different from all complex tests?

DR. TUCKSON: Got it.

MS. BERRY: And I feel we need to really nail that down, and if we can, then I don't object to sending a letter, but I'm not sure we're there yet.

DR. TUCKSON: Good. Well, how about we'll do this then? Joseph, are you in that ballpark?

DR. TELFAIR: I'm in this ballpark because I think I agree you need to have as clear and as strong evidence and information.

DR. TUCKSON: All right. What I would like is volunteers for the letter-writing effort who would put something together and would work not as a permanent subcommittee, but just as a single issue, non-bureaucratic subcommittee to put something together which we'll circulate to our colleagues with the expectation that we will have sent this letter to the Secretary on or before January 1.

So are there some people who would like to help to try to draft such a letter with the Cindy Berry modification? Who would like to help out on that, other than me?

DR. FERREIRA-GONZALEZ: I can't take the lead, but I can review whatever you write.

DR. TUCKSON: So we've got Andrea with that. Scott is in on that. Cindy's on it. Cindy writes well.

PARTICIPANT: I'll be part of the review.

DR. TUCKSON: You'll be part of the review. We've got Phyllis, and did Ann leave? Ann's gone? I think we might want to consult with Ann. We'll certainly consult with FDA and CMS on that as well. So we've got a committee.

Let me just tell you, first of all, again, Judy, Thomas, Steven, we owe you a debt, especially for putting up with the irritable Reed Tuckson. You are terrific.

Committee, good work. We are in the lobby at 7 o'clock, and feel good about the fact that you guys can reach consensus on such complex issues. The hotel lobby, 7 o'clock.

(Whereupon, at 6:31 p.m., the meeting was recessed, to reconvene at 8:30 a.m. on Tuesday, November 14, 2006.)