Oversight of Genetic Testing Laboratories Through the Clinical Laboratory Improvement Amendments (CLIA)

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We will begin with presentations on the role of the Clinical Laboratory Improvement Amendments, or CLIA regulations. CLIA is administered by the Centers for Medicare and Medicaid Services, CMS, with scientific and technical advice from the Centers for Disease Prevention and Control. We'll begin with Ms. Yost, who, as director of the Division of Laboratories and Acute Care, directs the CLIA program at CMS.

Judith, do you want to join us here at the table? Okay, so you're going to talk from the podium?

MS. YOST: Yes, so I can do my PowerPoint. I have to be in control. (Laughter.)

DR. McCABE: Thank you.

MS. YOST: Okay. Thank you and good morning, everyone. It's a pleasure to be here among this distinguished group. There are some familiar faces and some new faces, so I thank you. I also want to apologize to those of you who already know everything there is to know about CLIA versus those of you who are novices. This is kind of a basic presentation so that at least you can get the general idea of the standards and the approach for CLIA that CMS has taken at this time.

I guess the first and most important message is that genetic testing is already covered under the CLIA regulations as they currently exist. Just as a bit of background, the reason that CLIA came about was because there were a number of cases that were reported of people who had died because of incorrectly read Pap smears due to laboratories that were performing well above a threshold of workload and the inability to recognize positive smears. Also, in the late '80s, early '90s, there was a proliferation of technology, very small mobile technology, that could be placed on a countertop and allowed point-of-care testing to be initiated, particularly in physicians' offices, and there was concern about the quality of that testing as well.

Congress passed the CLIA law in 1988, on Halloween, so it looks like we're approaching an anniversary. CLIA regulates all testing on humans for health purposes using minimum quality standards. That means that any test that is done in any location, whether or not the entity is billing Medicare or not, no matter how many tests or how few tests that entity performs, regardless of where the test is performed. We regulate testing on ambulances, the type of testing that's done on the way to the hospital, to the emergency room; we regulate testing in schools where children perhaps are diabetic and the school nurse does a glucose test. So any type of test, not just your traditional hospital independent laboratory type of testing. Insurance testing is covered as well.

This includes research where the results are returned. So no matter what you call yourself, if you return those results back for use to a patient, to a caregiver, that testing is then covered under the CLIA regulations.

The intent of CLIA is not to put people out of business or to over-burden them with regulation. These are minimum standards. They are not rocket science. They are intended to ensure accurate, reliable, and timely testing.

The regulations to implement CLIA were published in February of 1992. Interestingly enough, it's near my birthday and about two weeks after I was employed by CMS to do this position. So I have a long history, needless to say. There are essentially five quality standards in CLIA. The regulations themselves are based on the complexity of the test that the laboratory performs. So the more complex the test, the more stringent the applicable requirements. Under CLIA, most genetic tests are high complexity because they are, number one, usually not categorized by the FDA, and they usually require a lot of training, they are very technique-dependent, and also require interpretation.

Under CLIA, the laboratory is required to have a certificate, and usually it's one per site. However, there are some exceptions for hospitals and universities. Where there are ancillary testing sites, the entity has the choice to have one or multiple certificates for multiple testing sites. The CLIA program is also unique in that it is entirely user fee funded. We do not get appropriations from Congress to operate the program. So it is our responsibility to utilize the funds that we receive from the laboratories prudently. The fees are pretty straightforward. They are based on the laboratory's test volume annually.

The program is actually a shared responsibility, and that provides us an opportunity to get the best of the best. You get the perspective of each different agency and the expertise of each different agency to hopefully produce the best decisions and requirements. CDC is responsible for the scientific and technical expertise provided to the program. They do a lot of the research. They coordinate the CLIAC or the CLIA advisory committee. The FDA conducts test categorization responsibilities. CMS is responsible for disbursement of funds and also for all the administrative and operational aspects of the program.

Because of the impetus for CLIA being cytology, obviously there are very detailed and specific standards in CLIA for cytology.

Let's talk about very briefly the complexities under CLIA. As we indicated before, the more complicated the test is to perform, the more stringent the standards. We begin with the waived category. These are tests that basically have no quality standards except to follow the manufacturer's instructions. They are essentially simple tests that should be very accurate, and again where there is no routine oversight, only unless there's a problem or a complaint against the laboratory. These tests include tests done on a glucose meter, urine dip sticks, those types of tests that are very simple, and usually the point-of-care types of testing, cholesterols in the malls, those sorts of things.

Moderate complexity is actually where most tests reside. These are usually automated types of testing, the chemistry profiles, the CBCs, the immunology types of testing. The laboratories that perform these tests have to meet all the quality standards under CLIA and be routinely surveyed.

A subcategory of moderate complexity is provider-performed microscopy. That's kind of a mouthful. These are tests that are done by reading a slide under a microscope, usually by a care provider or a physician during a patient visit. So this category was created specifically for caregivers to allow them to provide instant information about a patient so that they can take appropriate action. They are usually specimens that are labile and don't require a lot of processing. The laboratories that provide those tests must also meet all of the quality standards and have no routine oversight, except again if there is a complaint.

The highest complexity is high complexity. These are typically tests that are more technique

dependent. Oftentimes they are manual tests, like microbiology. They require more training or expertise. Usually there is a result interpretation. These are the most stringent standards, and these laboratories are also routinely inspected.

The quality standards themselves are very straightforward. The first is personnel qualifications and responsibilities. Under CLIA, the laboratory director does have the overall responsibility for quality in the laboratory. There are some additional required positions. For high complexity, where genetic tests usually reside, the laboratory director qualification is an M.D., D.O., or Ph.D. with board certification. Usually the laboratory director, if they choose to, can meet all the other positions if they care to or don't have enough staff.

Under CLIA, there is a unique additional aspect. Besides having the appropriate education, training, and experience, the laboratory director also has responsibility to ensure quality, so that each aspect of the laboratory is also under that qualification. The second quality standard is quality control. This just means that the laboratory needs to do something on a daily basis to check to see that the test is actually working before reporting patient results.

The third is called patient test management, which is really just the laboratory's audit trail, what kind of record-keeping system do they have, what do they have in place to ensure the integrity of the specimens, to ensure that patient specimens are identified correctly, to ensure the confidentiality of patient information throughout the entire testing process, and also protocols for referring tests to other types of laboratories to be performed.

The fourth is proficiency testing. This is really just external quality control. This means that the laboratory receives a specimen from a private organization with a known result in which they test it to see if they can get the correct answer. If the organization -- for example under genetic testing, there is not a lot of proficiency testing available from private organizations. So then the laboratory is obligated to check the accuracy of each test that they perform twice a year in lieu of purchasing from the private organization.

In that case, the laboratory can split specimens, they can compare results from a reference standard, or they can have patient specimens for which they have known answers that they can reconfirm. Or I know a lot of the genetic folks do share specimens where you send samples back and forth between labs. That's perfectly acceptable in this case.

The final one and probably the key aspect of CLIA is quality assurance. It is now called, under the final regulations just recently published, quality assessment. These are the same requirements, just with a more quality system type of terminology. This is really the laboratory's overall plan to assure quality on a regular basis and to communicate with the providers, with the employees of the laboratory, and to resolve problems.

Just as a point of information, CMS recently published final CLIA regulations, actually in January of this year, and these are quality system regulations. So we have taken these standards and basically reorganized them so that they follow the flow of a patient specimen through the laboratory. That way it's very easy for the laboratory to identify which standards and which phase of testing the laboratory needs to meet. We have not made a lot of significant changes, but we feel this has streamlined the requirements to a great extent.

In addition in this final regulation, some of the CLIAC recommendations that were made to the tri-agencies who oversee CLIA were incorporated into this regulation because it was felt that they actually had general applicability and were not just specific to genetic testing, things like ensuring

that the confidentiality of the patient's information and specimen results were carried through the entire testing process, other pre-analytic specimen identification and processing issues, as well as post-analytic test reporting information were also included in this final regulation. So we've already taken steps to incorporate some of those initial CLIAC recommendations, and Dr. Boone is going to tell you a little bit more about what else is being worked on.

For the CLIA survey process, I think folks always have a lot of anxiety about what are they going to do, here come the feds. The surveys themselves are required to be biennial, and they are announced to be sure that the appropriate people are there and the laboratory has an opportunity to get their records in order. So we feel that it's more important that we announce and schedule the survey, particularly in smaller laboratories where there are very few people available.

The routine surveys include only the laboratories that perform moderate and high complexity testing. Others are for complaints or to gather information. The laboratory actually has a choice under CLIA whether they can have an inspection by the state agency who is contracted by CMS to do the inspection -- these are medical technologists with extensive laboratory experience -- or by approved accrediting organizations that have been approved by CMS as having equivalent standards to CLIA. An example is CAP, the Joint Commission, the American Association of Blood Banks, the American Osteopathic Association, and so forth.

CMS uses an educational approach for CLIA, feeling that it's more important that the laboratory does the right thing. So we have always used an educational approach with an outcome orientation, outcome in this case being test results. Since we often don't have a patient there, the outcome is whether the test result is accurate and a quality assurance focus.

We have data. We have been doing this for a while. We have 11 years of data, and we have indications that starting in 1993 when we first began visiting laboratories with CLIA, approximately 35 percent of the laboratories had quality issues. At this point in time, we are happy to say that about 5 percent of the laboratories we visit have quality issues. We feel that part of the improvement is that, yes, they were afraid of us, but we also feel that by providing insight to the laboratory to give them resources and ideas about correcting problems has helped improve their performance as well.

Just some general information for compliance for genetic testing. Labs need to enroll in the program. That's the first step. The application is located on the website that's included on my slides, so you can download it very easily and send it in, whatever means you have. You need to meet the five major quality standards that I just talked about. But there is flexibility permitted to the laboratory in how and when the laboratory meets the standards. We realize that for a new laboratory, that may be an overwhelming task, so we give the laboratory an opportunity to meet the requirements incrementally.

The priority obviously depends on the quality impact. That's how we do this program. Everything that impacts the quality of the laboratory testing is the priority. There are no penalties at this point in time for non-enrollment. However, if you are doing testing and you know you are, you need to enroll because if we find out that you're not enrolled, then we can obviously take some action. So only after notification and refusal to comply would we take some action.

Again, I think it's most important that CMS is willing to provide technical assistance to any lab coming into CLIA.

Some survey facts. The first survey is always information sharing so that we can kind of get to

know you, you can kind of get to know us and what the requirements are about. The survey process again looks at outcomes or results, again the problems that we are looking for. If you didn't dot your i or cross your t, we're not going to be overly concerned, or you missed this temperature on this particular day of the week, it is not a problem. However, if you have serious problems where you are not evaluating the quality of your tests, then we are going to be citing deficiencies.

However, again, we offer customized guidance to help the laboratory fix the problems. We will set priorities based on that laboratory's operation. It's really important. We basically look at every laboratory as a unique operation. They're not one size fits all by any means, and our experience has certainly taught us that. Again, we will suggest resources and time frames for which the laboratory can correct their problems, and where there are small problems that we see, we'll provide verbal recommendations rather than citing them on a deficiency report. Most of all, the lab is given credit for what they do right so that they have a starting point.

The survey process itself is pretty straightforward. We come into the laboratory and schedule what we call an entrance interview. We meet with the laboratory director and key folks to talk to them about who we are, what we're going to do that day, about how long it's going to take, and what they should expect. Then we're going to tour the lab, and a lot of this occurs concurrently. It's not like a step by step sort of thing. We tour the lab, and that's including the storage areas, the collection areas, all the areas in the laboratory where testing is performed.

We will look at some testing to see whether or not folks are actually following the procedures that the laboratory has for that particular test. We would interview personnel performing testing and in different types of positions, doing different types of testing in the lab. We are going to look at QC. We're going to look at instrument maintenance. We're going to look at other data and information in the laboratory. But the key is not to sit in a closet and read the procedure manual. The key is to see what the lab is actually doing to perform quality testing.

Again, we're assessing outcomes, and we're going to determine whether or not the laboratory is in compliance with CLIA. When we're all said and done, we're going to ask the director to come back and the folks involved in the laboratory and talk to them about what we saw, what we found, what we think is good or not, and it also provides a last opportunity for the laboratory to provide additional data or information to the surveyor based on any findings that they may have had. Then the laboratory will receive subsequently a report of the findings for which they will need to develop a plan of correction, and that's just not saying, oh, I'll fix it later. We need to have specifics: "I'm going to take these particular actions, and here's the invoice for this quality control material I'm going to buy, and here's the records that show you that I'm actually doing it now." So that's the kind of evidence we need to show that the problem has been corrected.

CLIA state surveyors. I think it's very important that you know that they are medical technologists. In fact, we just recently concluded some training for our final regulations for them, and I was looking at the amount of experience. We have folks who have 20 and 15 and 10 years of experience in the laboratory prior to coming to be inspectors. So they're not bureaucrats. These are laboratorians, so they're people that you can speak to who are professional and knowledgeable about CLIA and laboratory practices, and especially quality assurance.

They're going to look at the lab's overall ability to provide accurate results. So if we can see from our initial reviews that the laboratory is providing good quality, we are not going to increase the depth of the review. Once we start to see problems, however, we're going to dig and dig and dig and dig until we can find the source of the problem. The root cause is what we're looking for.

We don't want to fix the symptoms. We want to fix the cause of the problem.

The inspectors do receive periodic training by CMS, and where there is new technology or technical science that we are not familiar with, we will engage experts to assist. We have guaranteed on multiple occasions to this committee and others that we will provide very specific detailed training with any CLIA genetic testing regulations and use experts that are nationally recognized.

However, it's important that you know that these folks are intelligent folks. They can still come into a genetic testing laboratory and even though they may not be familiar with the precise technology, there's a lot of stuff they can look at to determine whether or not that lab is doing a pretty good job. They obviously need to look at the laboratory director's qualifications, determine whether that director is meeting his or her responsibilities. They can look at QC data to see whether the QC is in or whether it's out and whether they've taken appropriate action to fix it.

Instrument maintenance, reagents, supplies, analytical test validation information, PT data, PT performance, interview testing personnel, look at testing to see whether procedures are being followed, look at specimen integrity and so forth. They are going to look at what kind of plan the laboratory has in place to assure accurate and reliable testing and whether, again, the lab is resolving its problems, communicating appropriately with its patients and clients, and then assist the laboratory to meet CLIA requirements.

We've had some experience already with genetic testing research laboratories, and we have found in most cases much of what that laboratory has done to verify that a brand new test works and the results are correct will facilitate meeting CLIA. So it's not like you have a separate process that has to be met. Existing documentation in the laboratory and data that the laboratory may have already produced are very useful in this case. Again, organizational materials that are available are also acceptable, things like job descriptions. So you don't have to rewrite responsibilities if you've already got job descriptions. If you have a safety plan in place, that's fine. All we need to see is that it's available and that it's being followed.

So I can tell you for sure, and they're still alive and breathing, that there are genetic testing research laboratories that have CLIA certificates.

Again, CMS considers every laboratory unique. But just as a point of information, if you needed a priority order, I've provided you one where personnel is most important. You need to get a director in place who can pull that place together. Quality control we think is the next most important piece that the laboratory needs to meet. Proficiency testing is next, and finally quality assurance, because we found that people can't do QA if they don't know what QC is, because QA is basically taking all the CLIA requirements, putting them in a box and wrapping them in a bow with the quality assurance, because that's your overarching standard. So that's basically the sequence that we suggest that you might follow.

I thank you very much for you time, and Joe is going to segue into where we're going from here.

DR. McCABE: Thank you very much.