LDT Industry Education: Record Keeping and Adverse Event Reporting: Medical Device Reporting, Corrections and Removals and Quality System Complaint Requirements Webinar
October 28, 2024 | 2-3pm *(eastern)*

Transcript

Welcome & Introduction
Susan C. Winckler, RPh, Esq., Reagan-Udall Foundation for the FDA

Susan Winckler (00:01):

Hello everyone and welcome to our session for today. I am Susan Winckler and I serve as the Chief Executive Officer for the Reagan-Udall Foundation for the FDA, and we are so pleased to host this educational webinar on a subset of FDA's expectations for laboratory-developed tests. Today, our speakers will address recordkeeping and adverse event reporting and a whole collection of topics within that, and we are pleased to be working with experts from NDA Partners to provide the content for today's educational session. I have just a few housekeeping announcements and then I will be stepping out of the way so that we can all learn today. We have over 500 people registered for today's webinar, so as they're continuing to join, we thank you for joining us and hope that you will learn from the content presented today. A number of you submitted questions as part of the registration process, and I will be raising as many of those as we can get to in the question and answer session at the conclusion of this webinar.

(01:10):

In fact, we received so many excellent questions that our session may run just a few minutes past the hour, but if you can't stay for the full time, that is all right because we are recording today's meeting and the slides and the discussion will be posted on the Foundation's website later this week. I'll also note that if you have additional questions, feel free to submit those using the Zoom Q and A function.

(01:38):

Let me do a quick recap of the agenda so that we are ready to go. So as we turn to our experts from the in vitro diagnostic and laboratory developed test space, we will hear first from Dr. Alberto Gutierrez. Sorry about that, Dr. Gutierrez, who's going to give us a background in framing for these requirements. Then we'll turn to Dr. Donna Hartzfeld who will address complaints and medical device reporting. Bobbi Druyor-Sanchez will cover corrections, removals and recalls, and Julie Ballard will aspire to synthesize all of this information into some case studies. So that takes us to just two minutes after the hour and we're ready to jump into content. Dr. Gutierrez, would you kick us off with the things that we need to know?

Background
Alberto Gutierrez, PhD, NDA Partners

Dr. Alberto Gutierrez (02:31):

Yes. Thank you, Susan. See if I can get this. Oops. Just a second. Trying to figure out how to work this forward, it's not going forward. Can you? Oops.

Susan Winckler (02:56):

Yep. You know what? Let me take back control and if you just say next slide, we'll run it that way.

Dr. Alberto Gutierrez (03:02):

That would be great. Thank you, Susan. Next slide number six, please. First slide. So over the past 30 years or so, the FDA has maintained that it has jurisdiction over tests that are develop a clinical laboratories for their own use. On May 6th, 2024, the FDA published the final rule that made it clear FDA's jurisdiction. It also made clear what parts of the regulation the FDA will apply and set a timetable for laboratories to comply with the FDA regulations. We're providing a series of webinars meant to help laboratories understand their obligations and to help them understand and comply with FDA regulations. The information provided in this webinar can be found at the FDA webpage on LDTs, as referenced here. Our intent is to try to discuss FDA requirements using terms and concepts that are familiar to the laboratories. Next slide.

(04:15):

On this slide just I have a summary of the phaseout requirements. Although the FDA implicit inclusion of LDTs into the regulations really makes all LDTs regulatory devices. The agency has actually carved out many LDTs that it will not be applying the medical device regulations. A summary of the type of laboratory developed tests which were [inaudible 00:04:51] and that will be enforced and the timing is on this slide. The agency does not plan to enforce device requirements to LDTs that were developed or are similar to LDTs that existed in 1976 when the device amendments were passed. The FDA plans to enforce only the requirements under phase one and phase two and some phase three to LDTs that were being offered before May 6th, 2024. The FDA plans to enforce phase four and phase five requirements to new LDTs offered after May 6th, 2024 or to existing LDTs that have undergone major changes after May 6th, 2024. Next slide please.

(05:49):

The timing of the phase out is on this table. We have planned a series of webinars on the major requirements of each of the phase outs, and that's what we'll be providing. Next slide. So we'll start first with this seminar, which addresses the requirements within a year the requirements agency has put on the laboratories that within a year they begin reporting to the FDA adverse events. To be able to do so, laboratories will need to understand medical device reporting requirements, how to perform corrections and removals, and how to handle complaints. That's the topic of this seminar. The second seminar will address labeling requirements and how to register and list your tests with the FDA. The third seminar will discuss what a quality system is and how to build one. There will be special emphasis on design controls. The last seminar, we'll discuss the FDA's expectations for the laboratories [inaudible 00:07:00] analytical and clinical validity for laboratory developed tests. Next slide. For the first seminar, Donna Hartzfeld and Bobbi Sanchez will be presenting. Next slide.

Medical Device Reporting, Corrections and Removals, and Quality System Complaint Requirements

Donna Hartzfeld, PhD, NDA Partners
Bobbi Druyor-Sanchez, MS, NDA Partners

Dr. Donna Hartzfeld (07:21):

Thank you, Alberto. Today we're going to briefly introduce you to the set of FDA medical device regulations that apply to the LDT final rule phase out policy stage one. Specifically we're going to talk about the section of the CFR part 820, regulation 820.198 for complaint files, the CFR part 803 for medical device reporting requirements for adverse events and the 21 CFR part 806 corrections and removal reporting requirements. Next slide please.

(08:04):

FDA's complaint handling requirements focus on identifying test specific problems related to the design or manufacturing of the test, and once the test is on the market. These issues are known as incoming alleged deficiencies. The FDA definition of a complaint is any written electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it has been released for distribution. For an LDT, this would be something like an erroneous test result, a positive or false negative, interactions with other substances or products, degradation of the LDT, labeling issues on a box or carton, errors found in the instructions for use or even promotional materials. The regulation requires that companies intake any issue that someone reports into the company into their established complaint management quality system. After the issue has been documented, recorded, it's reviewed and evaluated to determine whether or not it's a valid complaint.

(09:51):

The regulation requires that each and every complaint is handled in a uniform and timely manner and is established in company procedures. Once a complaint is determined to be valid, the next step is to determine whether or not an investigation is necessary. Next slide, please. The FDA regulation 820.198 for complaint handling is very prescriptive in what is required to be recorded into a complaint file. The minimum information required includes the type or name of the LDT, the date the complaint was received by the company. This is also known as the awareness date and the name, address, and phone number of the person making the complaint. This person is known as the complainant. A description of the complaint, this is typically where you write down the who, the what, the when, the where to describe the product problem in detail and the investigation activities to determine a root cause to the problem.

(11:24):

This section of the complaint file may take a day to complete, a week, a couple of weeks, a couple of months. It just depends on what the noted problem is. The expectation from the regulation, however, is that this section of the complaint file is kept up to date in real time with summary entries recording the activities that's been performed to determine root cause to the problem. If a root cause has been determined, the next step is to establish a corrective and action plan. In this plan are a list of all the different types of actions to correct the problem as well as responsibilities of the departments or even titles or people's names with committed due dates for completion of the actions taken. Sometimes the complainant will require acknowledgement that the company has entered their complaint into their complaint handling system, and if that has been requested, it is attached to the complaint file as well.

(12:42):

A complaint handling program may consist of quality system, standard operating procedures, a software management tool or a manually based form to document all of this information, a filing and archiving record keeping system, as well as monitoring and trending to detect systemic issues that need further escalation. Next slide please. As part of the investigation activities, the company is also required to evaluate the complaint to determine if it's reportable under the regulation CFR part 803 for adverse event reporting. This is a voluntary reporting system and companies use a form known as the 3500A form to record the information and submit it back to the agency. So what is an MDR reportable event? It's an erroneous test result that may have caused or contributed to a death or serious injury, or it's a test that has malfunctioned and that the test or a similar one marketed by the company would be likely to cause or contribute to a death or serious injury if the malfunction were to occur.

(14:16):

Some examples would be design issues of the test, labeling issues, user errors, even if it's been discovered that the test was being used as an off-label use, that's a reportable event. The reports can be found in an FDA mod database for any company that has filed a 3500A form, companies are required to have a system in place to evaluate each complaint to determine reportability. The reason why is because FDA wants to be able to monitor significant adverse events to identify problematic LDTs in the market. Next slide please. So what exactly is a serious injury or illness? FDA has bucketed them into three different types, and you can find this in the 803 regulation. A serious injury or illness can be life-threatening. It can be where the serious injury or illness results in permanent impairment or damage to a body function or structure, or it requires medical or surgical intervention to preclude permanent impairment or damage to a body function or structure.

(15:50):

Next slide, please. What is a malfunction? This type of adverse event applies to scenarios where LDTs have not performed as intended and fails to meet its performance specifications as outlined in the procedures. The performance specifications include all claims being made in the labeling. This is a critical area because current LDTs are more high-tech and involve complex instrumentation and software to generate results or clinical interpretations. Malfunctions may also include user errors or labeling errors. However, not every malfunction is reportable. The malfunction has to be likely to cause or contribute to the death or serious injury of a malfunction to recur. Next slide please.

(17:04):

The regulation has put in a time requirement for companies to report their adverse events to the agency. The death or serious injuries or malfunctions have to be reported within 30 calendar days of becoming aware of an event. The key word here is becoming aware. Once the problem has been communicated out to the company, that's the first day of becoming aware, and from there you have 30 calendar days to fill out the 3500A form and it submitted into the agency. The regulation does not grant extensions for holidays or vacations or business shutdowns. You have to hit that 30-day mark, otherwise, it may cause issues for the company. There is one exception to where if an adverse event is discovered to pose a serious risk of harm to the greater public. The company has five working days to report it to the agency.

(18:27):

Becoming aware of the adverse event is by many types of different communication pathways. It can be verbal or written, including social media, journal articles, telephone calls to the company, either by a user, physician, health professional. They can be received in by emails, faxes, texts, even through a salesperson possibly having a conversation with a health professional. Any type of communication counts as receiving an alleged deficiency. Oftentimes, companies will set up an 800 number or a

dedicated email address for companies to report that information into the company's complaint handling department. Laboratories do have the option to request from the FDA to report on malfunctions on a quarterly basis through summary reports. A special request has to be made and it can or cannot be granted, it's on a case by case basis. Next slide please.

(19:47):

This slide shows a link where you can reach the 3500A form, which is accompanied by a very detailed attachment appendix that lists the instructions on how to complete the form. There's also a FDA presentation that facilitates understanding that as well. The company needs to set up an electronic submissions gateway portal in order to submit MDRs electronically. They are no longer accepting manual forms through FedEx or email or anything of that nature, and so in conclusion, the company needs to set up complaint handling systems as well as MDR adverse event reporting systems in order to comply with the stage one phase out rollout. Next Bobbi will be talking about corrections and product recalls.

Bobbi Druyor-Sanchez (20:55):

Thank you, Donna. Appreciate your help. According to 21 CFR part 806, there are definitions such as corrections and removals. A correction is repair, modification, et cetera, where the product is not physically removed to execute some changes, whereas the physically removing the device is part of the removal, where it goes to another location for repair, modification, adjustments, relabeling, et cetera. Next slide please. Under 21 CFR part 806, corrections or removal process should be organized in the following way. First, you identify the problem followed by investigating the problem to determine what caused the issue including its scope. The third one is determining the actions needed to fix the problem, excuse me, and finally determine if the issue is reportable to the FDA. We'll be providing some case studies in the following of the webinar towards the end and Julie will be providing some examples to help understand each aspect. Next slide.

(22:18):

What is a recall? A recall is a method of removing and correcting product that are in violation of laws of the FDA. Recalls are typically voluntary and their whole goal is to protect the public from risk or injury or gross deception of otherwise being defective. 21 CFR part seven is the voluntary guidance for the companies to help understand how to execute a recall and there's rare instances where the FDA determines there's a risk to health and they may decide through 21 CFR part 810 if they won't actually execute this on the behalf of the company if they felt that the company did not execute it voluntarily and then they will ask them to execute it themselves. Next slide.

(23:11):

FDA recalls are classified into class one, class two, class three. Class one is the most severe and is a reasonable probability that the use of the test will cause serious adverse health consequences. Class two is the more moderate, whereas the test may cause temporary or medical reversible adverse events and class three is not likely to cause any adverse events consequences. These will be important to distinguish when you're executing a recall process. Next slide. How to notify the FDA. Class one and two recalls must be reported to the FDA. They must be reported within 10 days and here's some various links to execute a recall based on the state of where you live. Our next speaker is going to be Julie Ballard who will reviewing some case studies to help you understand some of the information that's been provided in this webinar. Next slide.

Case Studies
Julie Ballard, NDA Partners

Julie Ballard (24:23):

Thank you, Bobbi. So now that Bobbi and Donna have given us a nice intro and we understand some of the basics of the MDR corrections and removal and recall requirements, what we'll do is walk through some typical lab scenarios following this table so that you can better understand how to apply these in your lab. Please keep in mind that this is meant to be a general broad overview to give you an idea of how to apply it, but whether you actually have to report to the FDA will depend on your specific tests and situation. Next slide please.

(25:10):

So our case study number one involves a lab personnel error, where the ordering physician calls the lab because the patient's test result was not consistent with the other clinical information. Since the ordering physician called the lab and alleged a potential deficiency with the performance of a test, this is considered a complaint and the lab must now follow their complaint handling procedure that Donna talked about, where you must record this as a complaint, evaluate it to determine if it's a valid complaint and if it is initiate an investigation. In this case, what the lab found was that there were two specimens, one from patient A and one from patient B where they were swapped by laboratory personnel during testing. As a result, patient A received patient B's result and patient B received patient A's result.

(26:05):

Is this a reportable event? If the erroneous test result may have caused or contributed to a death or serious injury, then it is reportable. An example of this is if the test had been a cancer diagnostic test and patient A who should have received a negative result received patient B's positive result and received unnecessary treatment or for patient B who should have received treatment and did not receive treatment or received delayed treatment, that is considered serious and could have contributed to the serious injury or death.

(26:48):

It's also reportable if the error was caused by a malfunction. For example, if the test did not have procedures in place to ensure that specimens did not get mixed up or if there were procedures in place but for whatever reason perhaps didn't work, and that's what caused the mix-up. Now, if the erroneous test results did not cause or contribute to a death or serious injury, an example of this is let's say a low-risk vitamin D test or a test where the results did not have a clinical impact. So let's say with a cholesterol test, let's say both patients received results that were less than 200, which is a typical reference range and it didn't impact any clinical decision-making and it did not cause or contribute to any serious death or injury, then you don't have to report it.

(27:50):

Is a correction or removal required? Since incorrect results did go out, a correction is required to correct the wrong results and the test results must be recalled and replaced with the correct value. The recalls, as Bobbi mentioned, fall into three classes. Class one is the most serious, so if this test had been the cancer diagnostic test which could have caused or contributed to a death or serious injury, then it'd be reported as a class one. If it caused something that could be reversible or temporary, then it'd be class two, both class one and class two are reportable. An example of a class two recall would be, let's use our vitamin D test example where let's say one of the patients whose actual result was in the normal range perhaps received a result that indicated that they were deficient. What could have happened was that

their doctor may have told them start taking vitamin D supplements. Since taking D supplements generally is low risk and does not cause any harm. That's an example of where the recall would fall into class one.

(29:14):

Next slide please. All right, our case study number two is related to specimen collection error. Once again, our order clinician calls the lab indicating that the patient's test result is not consistent with their data. Is this a complaint? Since they are an issue with the performance of the test, it is a complaint and once again, the lab has to follow their complaint handling procedures. In the investigation, it turns out that two of the specimens, one from patient A and one from patient B, were swapped by phlebotomy personnel during the specimen collection at the blood draw site that is unaffiliated with the testing lab. As a result, patient A and patient B received each other's result. Is this a reportable event? Again, yes if the incorrect test result may have caused or contributed to a death or serious injury and no if it did not cause or contribute to a death or serious injury. In this case, since the issue occurred before the specimen was even in the lab and had nothing to do with the LDT, the malfunction does not apply in this case.

(30:34):

Is correction or removal required and is a recall required? In both cases, they do not have to be reported to the FDA. Now, the lab does have to correct the incorrect result for clear purposes to ensure that the patient gets the correct result, but they do not have to report it to the FDA. Next slide please. Case study number three involves a reagent issue where test results were reported. Our clinician calls the lab again because patient test results are not consistent with information, other clinical information, is this a complaint? Once again, this is since it is alleging a deficiency with the performance of the test and the lab must follow its complaint handling procedure.

(31:22):

And in the investigation it turns out that a reagent that had passed QC testing and was subsequently used during patient testing was found to be contaminated, causing quantitative test results that were incorrectly higher for all specimens tested with that reagent. Is this a reportable event? Once again, yes if that test result may have caused or contributed to a death or serious injury or if this error was caused by a malfunction. For example, if the lab did not have any procedures to prevent or detect contamination, or if they did and that process failed. Is a correction or removal required? Yes, a correction is required to rectify this and possibly any other specimens that may have been tested with this reagent and were affected, and removal of the contaminated reagent is required. Is the recall required? Yes. The original test report for the erroneous test result and any other specimens that may have been affected are recalled and should be replaced with a corrected test report with a correct test result. Next slide please.

(32:37):

Case study number four also related to a reagent issue. This time though test results were not reported. So lab personnel using a new lot of controls report that the positive and negative controls for a quantitative test repeatedly fails. No patient test results were reported. Another acceptable lot of controls was subsequently used for patient testing and patient test results were reported using the acceptable controls. Is this a complaint? No, it's not a complaint. Since the test using the failed lot of controls were never reported. They were not distributed and there were no communications alleging deficiencies with this device. The lab does have to do an investigation as far as, and any troubleshooting experiments to understand why the controls were contaminated and why it kept failing, but it doesn't have to do the formal complaint investigation since there was no complaint involved. Also, this is not a

reportable event and a correction or removal and a recall are not required since the tests used in the failed lot was never distributed, meaning test results were never reported. Next slide please.

(34:01):

Case study number five involves a limbs issue where a test result was reported. Again, our ordering clinician calls the lab reporting that the patient's test result is not consistent with the patient's other clinical information. This a complaint? Yes, it is. Since they're alleging a deficiency with the performance of the test and with the lab looking at this issue, they found that the test was performed correctly. However, due to a new software bug that entered their commercial off-the-shelf validated LIMS system, the incorrect test result was reported. Is this a reportable event? Yes. Again, if the erroneous test result may have caused or contributed to a death or serious injury, and it is not required, if it did not cause or contribute to a death or serious injury. Since the LIMS is not part of the LDT malfunction here does not apply.

(35:03):

Is a correction or removal required? The lab does have to correct the result for clear purposes and quality purposes to ensure that the patient gets the correct result, but it does not have to report it to the FDA as a correction since the error was a result of the LIMS system, which is not part of the LDT or device. This applies also for recall. Next slide please. Case study number six, involving a complaint around turnaround time. A patient calls the lab and states that he has not received his test result and the test turnaround time is too long. Is this the complaint? Yes. Since they are alleging a deficiency with the quality of the test.

(35:53):

The complaint handling team as they're looking into this, sees that the patient submitted their specimen, that the lab received the specimen five days ago and all the labeling for the LDT for the device states that the turnaround time for the test is 10 days. So while this issue is not a valid complaint and a full complaint investigation is not required, this still must be recorded. This since there was no erroneous test result that may have caused or contributed to a death or serious injury, and it is not a test malfunction, this is not a reportable event. The LDT is being performed as stated in its labeling and instructions for use. So it's not a reportable event, a correction or removal is not required and a recall is not required. Next slide please.

(37:01):

And for our last case study, we have a complaint to a salesperson. So an office assistant mentions to a lab's salesperson on October 1st that several patients have stated that they don't like having to give four tubes of blood for the test because taking that much blood makes them feel faint. The salesperson relays this information to the lab's complaint handling department on October 15th. Is this a complaint? Yes. This is an oral communication that alleges a deficiency with the safety of the test, a complaint that goes to anyone who's part of the manufacturer. So it's all employees, not just lab personnel of the LDT becomes if they become aware of any complaint, it must be treated as such. Is an investigation required? So the lab does need to look into this, but a formal complaint investigation in this case is not required since the lab's LDT was developed and validated using four tubes of blood, all the specimen collection requirements and precautions for the tests are stated in its labeling and instructions for use.

(38:15):

Is this a reportable event? No, this is not, since it doesn't involve an erroneous test result that may have caused or contributed to a death or serious injury and it's not a malfunction. I do want to note and reiterate something that Donna talked about earlier. If this had been a reportable event, there are deadlines to pay attention to. The deadline in this case, since the complaint was made on October 1st,

the deadline to report to the FDA would be October 30th, 30 days of first becoming of the complaint, not November 5th, 30 days after the salesperson told the lab's complaint handling department.

(38:58):

If the reportable event poses a serious risk or harm to public health, it must be reported within five working days. So this is really, I want to really emphasize the importance of making sure that folks understand when it comes to complaints, it doesn't involve just the lab. This is where it's important to have a robust complaint handling process where all employees are trained on it and you may want to include within that policy and procedure that all employees must, once they become aware of a complaint, notify the company's complaint handling department within 24 hours so they have sufficient time to report it to the FDA. In this example of correction, a removal is not required and a recall is not required since the LDT is being performed as stated in its labeling and instructions for use. Next slide. And that concludes the case studies. Thank you.

Question and Answer

Susan C. Winckler, RPh, Esq., Reagan-Udall Foundation for the FDA
Alberto Gutierrez, PhD, NDA Partners
Bobbi Druyor-Sanchez, MS, NDA Partners
Julie Ballard, NDA Partners

Susan Winckler (40:04):

So I have to say, Julie, Bobbi, Alberto, and Donna, thank you for walking us through those core requirements. And then Julie in particular, it's helpful to have that rubric of thinking through is this a complaint and walking through that analysis. I'm thrilled we have time for some of the questions that were submitted beforehand. So let me see if I can give voice to some of those and have our experts weigh in on the question here. So this first one I'll note, it's asking how FDA does something, and obviously none of us on this call speak for the agency, but perhaps we can think through some of the components here. But the question relates to assessing a company's compliance. So how might you expect the FDA to assess a company's compliance or a laboratory, their compliance with the record keeping and adverse event reporting through an inspection or some other component? Who might want to, Alberto, do you want to take that one?

Dr. Alberto Gutierrez (41:27):

I'll take that one. So typically most of the quality system requirements are assessed by the agency in inspections. So record handling, complaint handling, all that part is usually looked at by the inspector. When they go and inspect, they will actually pull the files and go through them. Now, there is some component of this that the agency will look at if you have a class three device in which you're filing a PMA. For PMAs, which are high-risk devices, the agency requires companies to send a lot of the quality system files to the agency and they will look at some of that, but it will also be followed by an inspection. So in general, for most, 99% of the time the agency is looking at the complaint files only in inspection and once in a while, in some cases it will be done pre-market.

Susan Winckler (42:42):

Got it. So these are things that you want to have obviously in order and available and then should expect that there would be some review of that in an inspectional environment?

Dr. Alberto Gutierrez (42:55):

Yes, it is actually one of the things that the agency typically looks into the complaint handling.

Susan Winckler (43:00):

Okay. And I would assume for a couple of disparate reasons, to say just what are you hearing and what of the company are hearing and how do you track that and do your investigation and assess the severity?

Dr. Alberto Gutierrez (43:19):

That's correct. And also, yes, for all those reasons. By going through the complaints, they usually get to the issues. They get to see whether a company is doing corrections appropriately. It just follows through their whole quality system.

Susan Winckler (43:37):

Great, great. So that's helpful just as thinking through then the work that the laboratory is doing and then how it might be reviewed. So this is another one, recognizing that none of us are speaking for the agency, but is this a space where you would expect the agency to provide checklists or fact sheets or other downloadable resources for labs to use to ensure compliance?

Dr. Alberto Gutierrez (44:07):

So the agency is providing, if you go to the website, they're providing guidances. They're providing, for example, the forms with which you report or you do corrections and usually fairly detailed guidance as to how you fill those in. They don't usually provide checklists in the form, like the laboratories are used to seeing, in part because the quality system regulations are fairly general. They're meant to cover small one-man shops, small laboratories, large laboratories, large manufacturers, and exactly what they do differs quite a bit and what they need to do differs quite a bit. So the agency itself doesn't provide checklists per se.

Susan Winckler (44:58):

Yep, that makes sense. So it's more about the broad structure and then each organization thinks through how they would apply that. It strikes me though that a checklist would be a great thing for an organization to have to make sure that they are meeting those requirements. Does that make some sense?

Dr. Alberto Gutierrez (45:20):

It does make some sense. I mean, for example, regulatory consultants typically have such things for themselves just to make sure that they're heading on all the different parts of the quality system, when they're working through what a company is doing. So yes, you will find that there are people who have such checklists and typically you can get those from people in the field.

Susan Winckler (45:53):

That makes sense. And then those people could help you adapt it so that it matches what your organization does with what the broader requirements are?

Dr. Alberto Gutierrez (46:03):

That's correct.

Susan Winckler (46:06):

Okay. All right. So let's do a little bit back to enforcement expectations. How might you think that the enforcement expectations in this space, in complaint handling and medical device reporting, would connect to the unique assay or test method identification? So the unique identifier, should we be thinking about UDIs right now or is that a little further down the road?

Dr. Alberto Gutierrez (46:40):

You should be, but the agency hasn't quite defined how they're going to do that. For now, for event reporting, you actually do not need to have a UDI. By the time you register a list that is the first two, you will have to deal with UDI, and the agency has said in the preamble that they will be putting out information as to how to do that. So right now to be able to meet the requirements for the next year and a half, really, you do not have to deal with UDI.

Susan Winckler (47:20):

Okay. All right. So that'll be a yes, but not right now?

Dr. Alberto Gutierrez (47:26):

Right.

Susan Winckler (47:27):

It's coming. Okay. Then this might be, now I've got a set of questions that probably relate a little within the case study or thinking through something that happens. So if a consumer reports to the lab, and actually this ties Julie to a case study that you provided, but let's explore it a little bit more. Let's say that a consumer reports to the lab, a false positive or a false negative. Should that be considered a product complaint?

Julie Ballard (48:12):

Yes, it is. It is a complaint because they're alleging a deficiency with the performance of the test.

Susan Winckler (48:17):

And then they'd walk through that rubric of, yes, it's a complaint, and then walk through what that means?

Julie Ballard (48:27):

Correct. So the lab's complaint handling department would follow the procedures to record the issues, all the information related to it, determine if it's a valid complaint or not, and if it is doing an investigation. In the investigation, if it turns out that an erroneous test result that could have caused or contributed to serious injury or harm, that is a reportable event. If it didn't cause harm or a serious event, but there was a malfunction with the LDT, that is also a reportable event.

Dr. Alberto Gutierrez (49:11):

So this is an area that is difficult for in vitro diagnostics in general, not just LDTs. And that is no test is perfect. You are going to have a false results that are within the performance characteristics of the test. So being able to determine that the false result that you got is an expected false result because it is within the performance characteristics is important. That requires that the laboratories have some

tracking and trending, because at some point, if they're getting more false results than they expect, then it is a malfunction. But that's not always easy to tell. So this is a challenge and issue for in vitro diagnostics in general, not just for LDTs.

Susan Winckler (50:06):

Super helpful. And that I think ties to, we had a question where someone was asking about the intersection between a malfunction and a reportable event, and I think Alberto, you were just explaining that they're related but not always equivalent.

Dr. Alberto Gutierrez (50:27):

That's correct. So if you report a false result, even if it is within your performance characteristics, that leads to a serious event, that's reportable. Once you do the investigations, you may say, well, it actually fits within the characteristics of the test and is not a malfunction, and you may not have to do a recall on all the other part, but it is originally reportable.

Susan Winckler (50:57):

Yep. Okay. Great. Super helpful. Then this is kind of a broader conceptual, but I think important as we're thinking about that complaint investigation. How might a lab distinguish between an adverse event from treatment and an adverse event from their test? You're just all anxious to answer that one, right? Go ahead, Alberto.

Dr. Alberto Gutierrez (51:28):

The first part of it is somewhat irrelevant. If there was an adverse event that is reportable, it is reportable, it is then on investigation that the lab would get to determine whether, and it's not always easy to find out, but they can make a determination as to whether, again, it could be that it is really unexpected or that it is an adverse events that is seen on the treatment and it is on the treatment, or it could be that it is the result of an erroneous result, and that's what the lab has to determine.

Susan Winckler (52:14):

Got it. So that piece that their investigation process would lead them through aspiring to answer that question?

Dr. Alberto Gutierrez (52:23):

That's correct.

Susan Winckler (52:27):

And it's quite possible it would be challenging and you may not be able to completely do it, but you have to investigate it?

Dr. Alberto Gutierrez (52:33):

That's correct. Usually, if you can tell that it was an erroneous result, then it is on the test because the patient had a treatment that was not relevant to them. But if the test was actually a correct result that the treatment still led to an adverse event, then it's on the treatment side.

Susan Winckler (52:58):

Okay. Then this relates, somebody's thinking about there are already other requirements that they have to complete. Maybe it's a New York State requirement or CAP requirements. Do any of those fulfill the record-keeping and adverse event reporting requirements from FDA? Or how should labs be thinking about the requirements they may have at a state level versus the emerging FDA requirements?

Dr. Alberto Gutierrez (53:30):

So clearly they can leverage some of those record-keeping processes that they have, but they don't meet the entire requirements that the agency has because they say nothing about adverse event reporting or correction and removals. So even though those records can be leveraged and they're going to have to be melded to a certain extent, they don't actually meet the full requirements that the agency has.

Susan Winckler (54:07):

Okay. So it will probably be helpful, but then the FDA agency requirements are likely more comprehensive?

Dr. Alberto Gutierrez (54:20):

That's correct.

Bobbi Druyor-Sanchez (54:20):

When they do their auditing internally, what they want to do is actually evaluate it for both instances to make sure that even when they make changes to the FDA requirements, that they're not then making modifications that now not allow them to have, say, the New York requirements. So what they should do is perhaps start with what they already have, add the FDA, but also cross-reference and make sure that they're compliant with both aspects.

Susan Winckler (54:53):

Bobbi, I'm so glad you chimed in with that, because then otherwise you might assume that you can just do the FDA piece and it would cover the other requirements, but you're pointing out that there may be some distinctions or some nuance between the FDA requirement and the state-level requirement or some other.

Bobbi Druyor-Sanchez (55:17):

Yeah. Especially for stage one or phase one, depending on how you want to call it. You really want to make sure that you're aligned with all the applicable regulations and standards that are specific for your lab.

Susan Winckler (55:32):

Right. Well, and that's a good reminder too, this is evolving, and so as it's implemented, are you growing into those requirements or growing into compliance with those requirements? I think we have time for one additional question, but it's a little different than what we've been talking about, but I think it relates to a case study. So let me ask it and then I'll provide some context for another piece. But here's our last content question. What if a lab finds an error in reported results, so it's not a complaint coming in, but they find something that is wrong? Does that become a reportable activity, even though there isn't a complaint to trigger it?

Dr. Alberto Gutierrez (56:30):

Do you want to take that Bobbi, or should I?

Bobbi Druyor-Sanchez (56:32):

I was going to have Donna actually. Go ahead. Alberto.

Dr. Alberto Gutierrez (56:38):

So many companies have internal processes, even though they're not really complaints but fall under the complaint handling. So they will feed and it could be an internal complaint or somebody who found it internally. They may not call it a complaint, but again, it's also the result. They found that there's an issue, they need to deal with it through, and it's easiest to deal through the complaint handling and do your investigation, figure out whether you need to do a recall, all that, just feed it into the same system.

Susan Winckler (57:20):

Yep. Okay.

Bobbi Druyor-Sanchez (57:23):

It's just another avenue of what you're dealing with, and you also have to include your internal quality management system processes, whether it's CLIA, FDA, or for some, ISO 13485. You need to utilize the quality system that you have in place, do the analysis, then look at the FDA guidances to determine if it's applicable, and if it is, use those specific CFR guidances for the processes to execute.

Susan Winckler (57:53):

Okay. So certainly it starts the yes, document, look into it, and then follow the reporting requirements. Excellent. That takes us to two minutes to the hour, and so I'll just note one of the other questions. It was expressed interest in broader parts of a quality management system, which yes, that's why there are subsequent webinars, and our conversation today was focused on much here in looking at the adverse event reporting and investigating and seeing what it is that needs to go to the agency and how to evaluate that.

(58:36):

Allow me to say thank you to our experts who joined us today, Donna, Bobbi, Julie and Alberto, really helpful baseline understanding and education, and then the illustration through the case studies was helpful as well. I love to do these because I learned so much from each of you. I'll note that the meeting recording slides and a transcript will be made available on our website, reaganudall.org later this week, and we will allow you all to return to the rest of your day. I hope that you found the content that we shared of interest and helpful in your efforts as you explore implementing these requirements. Take care and have a great day.