In Vitro Diagnostic Product (IVD): Classification
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Moderator: CDR Kim Piermatteo

CDR Kim Piermatteo: Hello and thanks for joining us for today's CDRH Webinar. This is CDR Kim Piermatteo of the United States Public Health Service and I serve as the Education Program Administrator within CDRH. I'll be your moderator for today's webinar.

We are holding this webinar to discuss how in vitro diagnostic products or IVDs are classified by the U.S. FDA. Before I turn it over to our presenter for today, I'd like to provide two administrative reminders. First, please make sure you've joined us through the Zoom app, and not through a web browser to avoid technical issues. And second, the intended audience for this webinar is industry. Trade press reporters are encouraged to consult with the CDRH Trade Press Team at cdrhtradepress@fda.hhs.gov. And members of national media may consult with FDA's Office of Media Affairs at FDAOMA@fda.hhs.gov.

I'd now like to introduce today's presenter, Dr. Brittany Schuck, Deputy Office Director for the Office of Health Technology number seven for in vitro diagnostic devices within the Office of Product Evaluation and Quality within CDRH.

We'll begin with a presentation from Brittany and then address previously emailed questions about today's topic. Thank you all again for joining us, I'll now turn it over to Brittany.

Brittany Schuck: Thanks, Kim and good afternoon, everyone. Thank you for attending our webinar today on in vitro diagnostic product, or IVD, classification.

Today's webinar is intended to explain how to determine the regulatory requirements applicable to a particular IVD. We will provide an overview of how medical devices, including IVDs, are classified by the FDA, walk through how to use FDA's device databases to determine if an IVD is classified and the associated regulatory requirements, and discuss other helpful resources related to medical device classification.

To start, it's important to understand that FDA's regulation of medical devices is risk-based. For example, when the FDA makes a decision about whether a device can be marketed in the U.S., the FDA uses a benefit-risk framework, assessing the risk of the device and whether the benefits outweigh those risks. As another example, when the FDA assesses a corrections and removals report submitted by a manufacturer, FDA assesses the degree of risk to determine its appropriate classification. And as we will discuss today, FDA uses a risk-based approach to the classification of medical devices, including IVDs. This risk-based approach includes evaluating the risk of the device and determining the regulatory controls that are necessary to provide a reasonable assurance of safety and effectiveness.

To put today's information into context, let's first talk about risk, using a non-medical device example – bicycles. There are different types of bicycles, used for different purposes, with different risks based on those uses. The type of bicycle and its use determine the type of protective equipment one would want to have to help mitigate the risks from the use of the bicycle for its intended purpose. On the far left of the screen, we have a bicycle being ridden on a flat, paved surface in a park. If the bicycle doesn't function as intended, the risk of injury is low. Commensurate with the risk, the control, or mitigation for the low risk is a helmet. In the middle, we have a bicycle that is used for mountain biking on rough and

rocky terrain. If the bicycle does not function as intended, the risk of injury is greater than for the first bicycle. The controls, or risk mitigations, for the increased risk include a helmet, gloves, elbow pads, and knee pads. Lastly, on the far right of the screen, we have a motorbike used for high-speed racing where the risk of injury if the bicycle doesn't function as intended is the highest. In this case, there are additional risk mitigations in place, including a full body protective suit. FDA's risk-based classification of IVDs and use of regulatory controls is similar.

As in the case of the bicycles, medical devices, including IVDs, have different intended uses, and different intended uses pose different risks. FDA classifies medical devices based on the risk posed by the device, which is dependent upon the intended use of the device. Each device is assigned to one of three regulatory classes, Class I, Class II or Class III, based on the regulatory controls that are necessary to reasonably assure safety and effectiveness of the medical device. Another way to think about regulatory controls is as mitigations to the risks posed by the medical product, which are dependent on the intended use of the device, as was the case for the amount of protective equipment for the bicycles being dependent on the use and risk of the bicycle. We will walk through the different classes of medical devices and regulatory controls in greater detail in the coming slides.

First, let's take a closer look at the two components that determine device classification, starting with the intended use component, which drives the determination of risk. Or in other words, the risk of a medical device depends on its intended use, including its indications for use. The intended use is the general purpose of the device or its function and includes its indications for use. The indications for use is the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended. There are multiple elements of an IVD intended use, including different elements of the indications for use, all of which are considered in determining its risk and regulatory control necessary to reasonably assure safety and effectiveness of the IVD.

These include, the purpose of the test, for example, is it used to aid in the diagnosis of a disease, predict risk of a condition, monitor severity of disease, etc.? The disease or condition the device is intended to diagnose, monitor or predict risk of. For example, renal disease, cardiovascular disease, cancer, therapeutic response, etc. The test method, including the technology, specimen type, and type of results reported? For example, technologies such as polymerase chain reaction, mass spectrometry, immunoassay, etc., specimen type such as serum, plasma, urine, saliva, etc., and results reported such as quantitative or qualitative results, etc. The patient population the device is appropriate for such as symptomatic patients or asymptomatic individuals, high-risk patients in the intensive care unit, etc. And lastly, the context of use, for example, in a laboratory, at the point of care, at home, etc.

Turning to the risk component, in general, FDA considers there to be three risk categories for medical devices, low, moderate, and high. Although there are exceptions, the classification of a device generally correlates with its risk category with most Class I devices being low risk, most Class II devices being moderate risk and Class III devices being high risk. In general, low risk devices are those that present minimal potential for harm. Moderate risk devices are those that are higher risk than Class I devices but are not high risk. And high risk devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. The risk posed by an IVD is primarily driven based on the consequence of a false, or incorrect, test result. Misinterpretation of the test result, and misuse of IVDs, such as collection devices, can also pose risks that are considered in FDA's classification and regulation.

It's important to know that FDA assesses the intended use and risk of the device to classify it into a generic device type. A generic type is a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to the safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness. Once the FDA has classified a generic type, specific devices that fall under the classification of the generic device type are regulated the same.

For example, as shown on this slide, FDA has classified next generation sequencing based tumor profiling test as a generic device type. Specific next generation sequencing based tumor profiling tests from different manufacturers would generally fall under this classification and be regulated in the same way.

Let's dive a little bit deeper into the three classes of devices. Class I devices are generally low risk and are subject only to general controls, which we will talk about in greater detail in the next slide. Most Class I devices are exempt from premarket notification requirements, or a 510(k). This means that these devices can be marketed in the U.S. without the FDA reviewing information on the device before it is marketed. If a Class I device is not exempt from premarket notification, clearance through a 510(k) submission would be required before the device can be marketed. For example, Class I reserved devices require premarket review through a 510(k). A list of Class I reserved devices can be found at the link on the slide.

In addition, the .9 regulations, which can be found under each part of Title 21 of the Code of Federal Regulations where classification regulations are codified, set forth limitations on premarket notification exemptions, describing circumstances when a premarket notification must still be submitted. For example, limitations to exemptions from 510(k) for clinical chemistry and clinical toxicology devices can be found under 21 CFR 862.9. One such limitation to exemption is in vitro diagnostic devices intended for assessing the risk of cardiovascular disease. We will be showing what a classification regulation looks in a later slide. Class I devices may also be exempt from some general controls. Today, approximately 50% of IVDs listed with FDA are Class I.

Class II devices are generally moderate risk and are subject to general controls and special controls. In general, Class II devices require premarket notification, or a 510(k), in order to be marketed in the U.S. However, some Class II devices are exempt from 510(k) notification. Novel devices that may meet the Class II definition are reviewed through a De Novo classification request. Today, approximately 45% of IVDs listed with FDA are Class II.

Class III devices pose the highest risk. As described earlier, these devices are intended to support or sustain human life, are of substantial importance in preventing impairment of human health, or present a potential, unreasonable risk of illness or injury. Class III devices are subject to general controls and Premarket Approval, or PMA. A PMA is the most stringent type of marketing application, and we will go into greater detail on PMAs in a few slides. Today, approximately 5% of IVDs listed with FDA are Class III.

And on January 31, 2024, FDA announced its intention to initiate the reclassification process for most IVDs that are currently Class III into Class II. The majority of these tests are infectious disease and companion diagnostic IVDs. We therefore anticipate that there will be even fewer Class III IVDs going

forward. The reclassification process will include opportunities for public comment and FDA aims to complete the entire process before November 2027.

In addition, FDA intends to continue taking a risk-based approach in the initial classification of IVDs to determine the appropriate level of regulatory control and whether a new IVD may be classified into Class II through De Novo classification rather than being Class III and subject to the PMA pathway. Based on our experience, we believe that special controls could be developed that, along with general controls, could provide a reasonable assurance of safety and effectiveness for most future companion diagnostic and infectious disease IVDs, such that they could be regulated as Class II devices.

Now, let's dive deeper into regulatory controls and the different premarket review pathways.

General Controls are the baseline requirements for medical devices under the Federal Food, Drug, and Cosmetic Act and apply to all medical devices, regardless of class. In other words, general controls apply to Class I, Class II, and Class III devices. Some devices may be exempt from certain general controls and such exemptions will be stated in the device specific classification regulation.

The table on this slide provides some examples of general controls and the regulations describing those controls. For example, labeling requirements under 21 CFR Part 801 and IVD specific labeling requirements under 21 CFR Part 809, which help ensure appropriate information is provided to users; medical device reporting requirements under 21 CFR Part 803 that require reporting to FDA of device-related serious injuries, deaths, and malfunctions that would be likely to cause or contribute to a death or serious injury if the malfunction were to reoccur; establishment registration and device listing under 21 CFR Part 807 that require companies to register and identify their devices with FDA; and quality system requirements under 21 CFR Part 820 that help ensure devices consistently meet applicable requirements and specifications to assure that they are safe and effective. Additional information, including additional examples of general controls and the statute and regulations you should refer to for those controls, are described on FDA's website that is linked on this slide.

Special controls are regulatory requirements for Class II devices, and they are usually specific to a device classification. The special controls that are assigned to a specific device type are listed under the device type specific regulation in the Code of Federal Regulations. The table on this slide provides some examples of special controls. Special controls can include among others, performance standards or specific performance characteristics an IVD must meet, special labeling requirements, specific postmarket surveillance requirements, and specific requirements for design validation requirements and specific premarket data requirements. Additional information on special controls can be found on the FDA website linked on this slide.

Turning to the different premarket review pathways, there are two pathways to bring to market a device that is similar to a device that has already been classified or reviewed as a PMA by the FDA. Either a 510(k) premarket notification or a PMA. Devices that require a 510(k) premarket notification are generally moderate risk, Class II devices. As mentioned earlier, Class I reserved devices also require premarket review through a 510(k). In addition, the .9 regulations set forth limitations on premarket exemptions, describing circumstances when a premarket notification must still be submitted for certain devices.

In a 510(k), the device manufacturer demonstrates that their device is as safe and effective, or substantially equivalent to, a legally marketed, also known as a predicate, device. It's important to know that substantial equivalence does not mean the new and predicate devices need to be identical. In fact, the standard for substantial equivalence includes demonstrating that the new device compared to the predicate device has the same intended use and the same technological characteristics or has different technological characteristics that do not raise different questions of safety and effectiveness. Importantly, a new device with an indications for use that is different from its predicate can be found to be substantially equivalent if the different indications for use are within the same intended use.

During its premarket review of a 510(k) for IVDs, FDA reviews information supporting the analytical validity, clinical validity, and safety of the IVD.

A premarket approval application, or PMA, is for Class III, or the highest risk devices. In a PMA, a manufacturer demonstrates that there is a reasonable assurance of safety and effectiveness. During its premarket review of a PMA for an IVD, FDA reviews the same information it would in a 510(k) as well as manufacturing information.

General information on these pathways, including relevant guidance documents and CDRH Learn webinars, can be found on our website at the links included on the slides.

Novel devices, or in other words, any device that is of a type that has not been classified or previously reviewed through a PMA by FDA, are automatically Class III. Novel devices that are high risk would be reviewed through the PMA pathway that was just discussed. Novel devices that are moderate or low risk are eligible for classification through what is called a De Novo classification request, which we generally refer to as just a De Novo. A De Novo is a marketing submission for devices that are of a type that are automatically Class III by virtue of not having been previously classified or approved through a PMA and for which there is no legally marketed device on which to base a review of substantial equivalence, but which would be appropriately classified as Class I or Class II.

During its review of a De Novo for an IVD, FDA reviews information supporting analytical validity, clinical validity, and safety and determines the level of regulatory control needed for that device and devices of its type. If granted, the De Novo submission establishes the new device type along with its classification, as Class I or Class II, the necessary controls, and product code. Exemptions, including exemptions from premarket notification, are determined at the time of the classification. If the new device type is Class II and not exempt from premarket notification, subsequent devices of the same type are subject to 510(k) premarket review and the device reviewed under the De Novo can serve as a predicate for subsequent devices of the same type.

Additional resources on the De Novo classification request program, including relevant guidance documents and CDRH Learn webinars, can be found on our website at the links included on the slides.

Now that we have provided an overview of the device classes and associated premarket review pathways, let's discuss how an IVD manufacturer would determine the classification, controls, and regulatory requirements for a particular IVD. We recommend first assessing whether the IVD is of a type already classified or approved through a PMA by searching the product classification database. Querying the product classification database will search all medical devices.

If your IVD is of a type that falls within an existing classification regulation or is of a type that has been approved through a PMA, the database will identify the Class of the device, whether the device type is exempt from premarket notification or subject to either premarket notification or premarket approval requirements, and the classification number if applicable.

As we will show in examples in the coming slides, the product classification database generally will include a link to the classification regulation for Class I and Class II devices. You can use the link to find the full description of the device type, applicable controls, and exemptions in Title 21 of the Code of Regulations. If there is a classification regulation listed but it is not linked to the CFR, you can search the De Novo Database, using the product code indicated in the product classification database for the device type, to find a full description of the device type, applicable controls, and exemptions.

Most Class III devices do not have a classification regulation. If your device is of a type that has been classified as Class III through review of an approved PMA, the database will indicate that a PMA submission is required for that device type. We will walk you through an example a little bit later.

You may also want to search our review pathway specific databases, which can be found at the link at the bottom of this slide and through the direct links for each database included in the resources section at the end of this slide deck.

You can search the 510(k), De Novo, and PMA databases using the product codes listed in the product classification database or by key word searches, to help identify IVDs that have similar intended uses to yours and the pathway under which they have been authorized. While we aren't going to go into detail on searching these databases today, we do intend to host a future webinar to provide additional information on FDA premarket review of IVDs.

If the IVD is not of a type that is already classified or approved through a PMA, the manufacturer of the IVD should first assess the risk of the IVD. If the manufacturer believes the risk is high, it likely requires a PMA. If the manufacturer believes the IVD is low or moderate risk, it may be eligible for De Novo classification request. Additional information on the De Novo classification request process can be found on our De Novo classification request website linked on slide 12 and at the end of this presentation.

Once the manufacturer has assessed the risk of the IVD and determined the premarket review pathway for their IVD, they should proceed with submitting the appropriate submission based on their assessment of risk. If manufacturers have questions, FDA is here to help and can provide feedback through what is called a 513(g) request or Pre-Submission request, which we will discuss in greater detail a bit later.

Before we dive into the examples, we want to provide a bit more information on the product classification database and the CFR. First, as we will demonstrate in the coming examples, the product classification database provides the classification, premarket review information such as the Office and Division responsible for premarket review of the device type and the submission type, product code as well as other regulatory information for all device types. Within this database you can search by key word or words. You can also select Advanced Search if you have more specific criteria you wish to search by. It's important that you use exact spelling when searching the product classification database.

Classification regulations are codified in Title 21 of the Code of Federal Regulations. You can search Title 21 of the CFR using the link in the first box on this slide. Classification regulations for existing IVDs can be found in Parts 862, 864, and 866 of Title 21. We have included screenshots of example Class I and Class II classification regulations on this slide. The classification regulation for a device includes the generic device name, the description or identification of the device type, and the classification of the device, which includes a description of the controls that device type is subject to. Exemptions from premarket notification or other controls will be expressly stated in the classification regulation for the device type.

Now, let's look at some specific examples. For our first example, we will use a Class I IVD. In this example, we will be looking at the classification for a laboratory-based enzymatic lactic acid test used to aid in the diagnosis of lactic acidosis. Here we have searched the product classification database for lactic acid. You can see that by using this search term, two product classifications appear, both of which have been classified as Class I.

Since the test in this example is laboratory-based and not for over-the-counter use, we are going to select the first entry, by clicking the device link. A product classification window will appear that contains the relevant classification information.

The product classification page lists the device name, product code, KHP in this example, submission type, 510(k) exempt in this example, and regulation number. Clicking the regulation number hyperlink will bring you to Title 21 Code of Federal Regulations where the classification regulation is codified. In this example, you will see that the device type, which is a lactic acid test system used in the diagnosis and treatment of lactic acidosis is Class I, subject to general controls, and exempt from 510(k). Lactic acid tests for other intended uses would not fall under this regulation. The product classification page also includes the device class and additional regulatory information.

Our next examples are Class II IVDs. In these examples, we will be looking at the classifications of different newborn screening tests.

By typing newborn screening into the product classification database, a list of device types appear. While all IVD device types that appear in this search have been previously classified as Class II, there are different IVD device types that have been classified. As discussed earlier, each device type has its own special controls that have been determined based on the intended use and risk of the device type. In this example, we are first going to select the first product in the list, which is for newborn screening test systems for amino acids, free carnitine, and acyclcarnitines using tandem mass spectrometry.

As with the previous example, selecting the name of the device type will lead to the product classification page for that device type. This page shows that newborn screening test systems for amino acids, free carnitine, and acylcarnitines using tandem mass spectrometry are subject to 510(k).

By selecting the regulation number, the codified regulatory information for this device type will appear. This shows that this IVD device type is subject to special controls, in addition to general controls.

As described in the classification regulation, this IVD type's special control is a special controls document. Special controls documents named in classification regulations can be found by searching Class II special controls documents on FDA's website. Manufacturers of these device types must address the specific risks to health identified in that document.

Choosing a different device type in the list, a severe combined immunodeficiency disorder newborn screening test system, navigating to the product classification page and then to the regulation classification, you will see that this IVD device type is subject to 510(k) and special controls that are described in the classification regulation itself. Most special controls are described within the classification regulation itself although for older device types, the special control may be a special controls document as shown for newborn screening test systems for amino acids, free carnitine, and acyclcarnitines using tandem mass spectrometry.

Choosing another different IVD device type in the list of newborn screening tests, this time a muscular dystrophy newborn screen test system, leads to a product classification page where the regulation number is not a clickable link. In these cases, the regulation has not yet been codified in the CFR. To find information on the classification regulation for these device types, you will need to navigate to and search the De Novo classification database, using the product code. In this example, the classification database shows the product code for muscular dystrophy newborn screening test systems is QUE. When you search this product code in the De Novo database, it returns results for DEN200044. By clicking either the device name or De Novo submission number, you are directed to the De Novo information page which includes the reclassification order.

The reclassification order, obtained by clicking the link, includes the classification information, including the regulation name and regulatory class. The reclassification order also includes the classification description for the new generic device type and special controls, if any. In this case, the classification identification and description is for the new generic device type, a spinal muscular atrophy newborn screening test system, and the special controls are described in the linked reclassification order.

Our last example is a Class III IVD. In this example, we will be looking at the classification for total prostate specific antigen, or PSA, tests used to aid in the detection of prostate cancer. In this example, using key words total prostate specific antigen to search the product classification database as shown on the left side of the screen returns a single result as shown on the right side of the screen. The product classification record shows that this device type is Class III, requiring premarket approval.

If you were to broaden your search to just prostate specific antigen, not specific to total PSA, the product classification database would return five results since there are multiple prostate specific antigen device types, three of which are Class III and two of which are Class II. We will show how looking at the product classification information for each generic device type would lead to the same conclusion as the first more specific search. That total PSA tests used to aid in the detection of prostate cancer are Class III devices requiring a PMA.

First, the product classification return with the more specific search is listed as the second device type in these results and indicates that total prostate specific antigen tests for detection of prostate cancer are identified as Class III. Clicking the link to this device type would take you to the same product classification page as the first more specific search. In addition, looking at the other two Class III device types, the device descriptions reveal that those device types are complex and free PSA, not total PSA.

Clicking the links for the two Class II device types and then the links to the classification regulations for those devices, as was shown in an earlier example, would reveal that the Class II generic device types have intended uses that are not for aiding in the diagnosis of prostate cancer.

For example, IVDs under 21 CFR 866.6010, tumor-associated antigen immunological test systems, including PSA test systems, are intended to aid in monitoring patients for disease progress, response to therapy or for the detection of recurrent residual disease. In other words, PSA IVDs under this regulation are intended for use in managing patients already diagnosed with prostate cancer, not for use in aiding in the detection of prostate cancer. In addition, PSA IVDs under 21 CFR 866.6040 are gene expression profiling-based test systems, not test systems that measure total PSA. As described earlier, the intended use and risk of the device determines the appropriate classification. Taken together, the conclusion using less specific search terms is the same as if the more specific search term was used.

If after searching the FDA databases, you have questions or want formal feedback from the FDA on the classification and regulatory requirements for a specific device, there are two mechanisms for you to ask those questions and seek FDA feedback, and we are of course here to help.

The first way is via a 513(g) device classification information request. This is a mechanism for manufacturers to formally request information specifically on the classification and regulatory requirements for a specific product. Additional information on how to submit a 513(g) request can be found at the link in the green box on this slide.

The second is a Pre-Submission request. Pre-Submissions are a type of Q-Submission, where manufacturers can pose specific questions to FDA and request written feedback and a meeting with FDA to discuss their feedback on the specific questions posed. These questions may include requests for feedback on regulatory pathway for a specific product as well as questions related to other topics, such as analytical and clinical validation studies. Additional information on our Pre-Submission Program can be found in our Q-Submission Program guidance linked on this page.

That's the end of today's webinar on IVD classification. We hope today's webinar has been helpful in providing an overview of IVD classification and how to find information on IVD classifications using our medical product databases.

Our next webinar related to FDA's final rule on LDTs will be August 222nd, 2024 from 1-2:30 PM Eastern Time and will address medical device reporting requirements, corrections and removals reporting requirements, and quality system complaint records requirements. Please keep your eye out for additional details on the website linked on this slide and submit questions in advance to the email address shown on the slide. We hope you will join us for the August and future webinars!

The following slides include resources and references mentioned during today's webinar.

Thank you again for joining today's webinar.

CDR Kim Piermatteo: Thank you Brittany for that presentation. At this time, we will now transition to address some of your previously submitted questions related to today's topic. For this segment, I'll read a question aloud and then Brittany will provide a response. As a reminder, we will not be taking live questions during today's webinar, therefore, please refrain from raising your hand in Zoom.

So Brittany, let's get started. Our first question is, does FDA classify laboratory developed tests as test systems, including instrumentation, sample preparation and pre-analytical processing, or does classification of LDTs only pertain to the parts that the laboratory develops or modifies on its own?

Brittany Schuck: Thank you Kim. FDA classifies IVDs manufactured by laboratories, including laboratory developed tests, in the same way it does other IVD test systems.

Test systems are a set of components, such as reagents, instruments, and other articles, that function together to produce a test result. Test systems include components and are accompanied by instructions for use for sample preparation and pre-analytical processing. Classification of the test system is based on the intended use and risk of the test system.

The most efficient method for an IVD manufacturer to determine the classification of a device type that has already been classified by FDA is by searching the product classification database as shown in the webinar today. And this product classification database is included on the resources and references page of the webinar slide deck. Searching FDA's 510(k), PMA, and De Novo databases may also be helpful in understanding what specific IVDs fall within a given device type and how such IVDs are regulated.

An IVD may be of a type that has not already been classified by FDA and, therefore, would not be in the product classification database. As a reminder, device types that have not been classified by FDA previously, and that were not on the market prior to the enactment of the Medical Device Amendments on May 28, 1976, are automatically Class III unless they are reclassified by the FDA. If an IVD has not been classified, manufacturers should assess the risk of their IVD and submit the appropriate premarket submission based on the assessed risk. If the manufacturer believes their IVD is high risk, a PMA is likely required. If the manufacturer believes their IVD is low or moderate risk, the IVD may be eligible for De Novo classification. The De Novo process provides a pathway to Class I or Class II classification for medical devices for which general controls or general and special controls provide a reasonable assurance of safety and effectiveness, but for which there is no legally marketed predicate device.

CDR Kim Piermatteo: Thanks Brittany. Ok so for our next question, that is, some classification regulations include sample matrices and/or technology types. If an IVD test system's intended use matches the description in the regulation but uses a sample matrix and/or technology that is different from those specified in the classification regulation, could it be classified in accordance with the identified regulation?

Brittany Schuck: In general, yes. However, where differences in specimen type or technology between a subject IVD test system and those specified in a classification regulation raise different questions of safety and effectiveness, the classification regulation describing use for a specific specimen type or technology would not be appropriate for a different specimen type or technology. If manufacturers have questions regarding the classification of a specific test, they can submit a Pre-Submission or 513(g) request to request specific feedback from us.

CDR Kim Piermatteo: Great, thanks again. Ok Brittany so for our next question that is, how does FDA classify an LDT test system that includes instruments or reagents labeled for research use only by another manufacturer and how do laboratories list such IVDs with FDA?

Brittany Schuck: Thanks Kim. As discussed previously, FDA classifies LDTs the same way it does other IVD test systems. If a laboratory chooses to use one or more components labeled for research use only, or RUO, by another manufacturer in its IVD offered as an LDT, then the laboratory is responsible for qualifying such components in its IVD and appropriately listing their IVD test system with FDA. As long as the laboratory has implemented a quality system that meets the quality system requirements, as applicable, and is able to appropriately manage the quality of these components under that quality system, then the components may be incorporated as part of an IVD offered as an LDT. The RUO-labeled components will be reviewed in the premarket submission for the IVD offered as an LDT, as applicable.

CDR Kim Piermatteo: Great. Thanks again Brittany. So for our next question that is, are Laboratory Information Management Systems or LIMSs incorporated in the classifications of IVD test systems?

Brittany Schuck: In general, LIMS are not included as part of IVD test systems. Rather, LIMS are generally regulated under their own classification regulation. Please refer to 21 CFR 862.2100, product code JQP. And in general LIMS are Class I, exempt from 510(k) subject to the limitations to exemption under 21 CFR 862.9. In addition, to better understand FDA's regulatory approach for Device Software Functions, please see Section V of FDA's Guidance document, Policy for Device Software Functions and Mobile Medical Applications.

CDR Kim Piermatteo: Great. So for our next question, that question is, how does a laboratory manufacturer determine which type of premarket submission is required, if any? What type of premarket submission is required for a test that is not classified?

Brittany Schuck: Thanks Kim. We recommend laboratories start by searching the product classification database to see if the device type has already been classified by FDA. If the IVD is of a type that has already been classified by FDA, the database includes the device Class, so Class I, II or III, the type of submission required, if any, and if applicable, the classification regulation number. If the IVD is not of a type listed in the classification database, the manufacturer should assess the risk of your IVD to determine the premarket submission type that is most likely appropriate based on the assessed risk.

If the manufacturer believes the IVD is high risk, a PMA is likely required. And as a reminder, only about 5% of IVDs currently listed with FDA require a PMA. A moderate or low risk device may be eligible for De Novo classification. If after searching FDA’s medical device databases and assessing the risk of an IVD, manufacturers have questions regarding the classification of the IVD, they can seek feedback from FDA via a Pre-Submission or 513(g) request.

CDR Kim Piermatteo: Thanks Brittany. Ok our next question, I think the next couple of ones are a little bit more general, but this question is, what does FDA mean by low risk?

Brittany Schuck: Thanks Kim. As described in this webinar, low risk devices are those that pose minimal potential for harm. Although there are exceptions, the classification of a device generally correlates with its risk category with most Class I devices being low risk.

CDR Kim Piermatteo: Thanks Brittany for that clarification. Also more general, what is a FDA product code?

Brittany Schuck: Yes, a product code identifies the generic category of a device for FDA. A classification regulation may have multiple product codes associated with it. In this case, classification product codes help to delineate technology and indication subgroups within a regulation. However, a product code is only associated with one classification regulation or no regulation at all. In the latter case, they serve to categorize unclassified or Class III, PMA devices. Classification product codes are assigned and maintained by the Agency.

For non-510(k) exempt devices, the submitter of the premarket submission identifies a product code they believe to be appropriate for their device. The proposed product code is reviewed by FDA staff for accuracy during the premarket review. If the proposed product code is incorrect, or a more appropriate product code should be used, the FDA reviewer will change the product code and notify the submitter.

The reviewer will assign a classification product code based on the regulation or the device intended use, indications for use or technology. The most common method of assignment is to use an existing product code from the product classification database. A device will be assigned an existing classification product code when it has the same intended use, indications for use, and relies on technology that does not raise new safety and effectiveness questions. In other words, if the device is determined to be substantially equivalent to the predicate device, it will typically be assigned the predicate device's product code. However, if the proposed device differs significantly from the predicate device with respect to technology, intended use or indications for use or is found not substantially equivalent or NSE, a new product code should be assigned.

In some cases, product code definitions may be updated to accommodate a new technology. Additionally, new product codes may be created for tracking purposes for a specific technology or device area. For additional information on product codes, please refer to FDA guidance on Medical Device Classification Product Codes.

CDR Kim Piermatteo: Great, thanks again Brittany. So we have one more question for today. And that question is clarification as well, so the question is, what is the process for reclassification?

Brittany Schuck: Thanks Kim for that question. The original classification of a device can be changed through reclassification, for which multiple processes exist in the federal Food, Drug & Cosmetic Act. In general, the FDA follows a process for reclassification that includes issuing a proposed order, convening a classification panel as appropriate, receiving and considering public comment, and issuing a final order. Back to you Kim.

CDR Kim Piermatteo: Great, thanks again Brittany. That will wrap up our previously submitted questions for today. I'd like to thank everyone who submitted questions in advance of today's webinar, as well as to Brittany and her team for developing responses to these questions and presenting them today.

I'll now turn it back over to Brittany for her final remarks on today's topic.

Brittany Schuck: Thanks Kim. And thank you all again for joining us today. We hope this webinar has been helpful to gain a better understanding of IVD classification and how to use FDA's product classification database to determine the classification and applicable regulatory requirements for a particular IVD. We look forward to future webinars and hope you will be able to join us for those. Thank you all.

CDR Kim Piermatteo: Thanks again Brittany for those final remarks.

A few closing remarks from me, for your information, printable slides of today's presentation are currently available on the CDRH events webpage for this webinar, as well as on CDRH Learn at the link provided on this slide. Sorry, I will advance this, my apologies. As well as on this slide under CDRH Learn, under the section In Vitro Diagnostics. A recording of today's webinar and a transcript will be posted to the webinar webpage and CDRH Learn in the next few weeks. And then a screen shot, like I said, of where you can find that is on this slide.

If you have additional questions about today's webinar, feel free to reach out to us in DICE at DICE@fda.hhs.gov.

And lastly, as Brittany mentioned, our next IVD related webinar will be held on August 22nd from 1-2:30 PM eastern time. And the topic for this webinar will be, IVD MDR Requirements, Correction and Removal Reporting Requirements, and Quality System Complaint Requirements. You will be able to find information on how to attend this webinar and submit questions in advance of this webinar and any of our upcoming webinars on our CDRH Events page and the link to this page is provided on the bottom of this slide.

So thank you all again for joining us. This concludes today's CDRH Webinar.

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