

Webinar: Final Guidance Documents: “Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use” and “Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use”

Moderator: Irene Aihie

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Coordinator: Good morning and thank you for standing by. Welcome to the FDA webinar. Your lines have been placed on a listen-only mode until the question and answer segment of today’s conference. At that time you may press star 1 to ask a question.

Today’s questions will be taken via phone only. Today’s call is being recorded. If you have any objections please disconnect at this time. I’d now like to turn the call over to your speaker this morning Ms. Irene Aihie. Thank you. You may begin.

Irene Aihie: Thank you. Hello and welcome to today’s FDA webinar. I’m Irene Aihie of CDRH’s Office of Communication and Education. On October 7, 2016 the U.S. Food and Drug Administration published the final guidance document self-monitoring blood glucose test systems for over the counter use and blood glucose monitoring test systems for prescription point of care use.

The purpose of the final guidance document is to improve new blood glucose meters by providing FDA’s recommendation to industry about the types of information to be included in the pre-market submission 510K for these

devices. The focus of today's webinar is to share information and share questions and answer questions about the final guidance document. Today's presenter is Dr. Leslie Landree, Diabetes Team Leader in CDRH Agent Division of Chemistry and Toxicology Devices in the Office of In-Vitro Diagnostics and Radiological Health.

Following the presentation we'll open up the line for your questions related to the topics in the final guidance document only. Courtney Lias, Director for the Division of Chemistry and Toxicology Devices and Ryan Lubert also from OIR will join us to assist with the Q&A portion of our webinar. Now I give you Leslie.

Leslie Landree: Thank you Irene and thank you everybody who's tuned today to listen to this webinar. The purpose of the webinar is to review the two glucose guidance documents that have been recently been finalized. In the presentation I'll provide an overview of the purpose of the glucose guidance document, discuss how these documents differ from what we've typically seen in submissions for these types of devices and highlight the key differences between the final guidance and the draft guidance.

Before I get started I'd just like to review just some of the common acronyms that will be used frequently during this presentation. SMBG is for self-monitoring blood glucose, BGMS, blood glucose monitoring system, OTC, over the counter and POC, point of care.

Blood glucose meters are used by very different and unique intended user populations in a variety of settings. They are used by lay users at home. Also they're used in a variety of healthcare settings such as hospitals, nursing homes, doctor's offices among other settings. As you may know blood

glucose monitoring systems are considered moderate risk and are therefore Class 2 because that require 510K clearance prior to marketing.

During the 510K review we evaluate the performance of the device for its intended use. However this isn't an independent evaluation of the device. Manufacturers are responsible for the demonstration of the performance. Therefore the device information and performance data that we evaluate is generated and provided by the manufacturer. The majority of glucose meter manufacturers have historically sought over the counter clearance which has typically been done to maintain waiver for these devices so that they can be used a variety of waived settings.

In taking this approach what's happened is that the majority of meters on the market today including most of those that have been used in professional healthcare settings including hospitals were designed and validated only for over the counter use. That means that healthcare professional use for this device – for these devices was not evaluated. It's become increasingly clear that these different use settings comprise distinct intended use populations with unique characteristics that should be considered during device design and validation.

We have heard concerns from various stakeholders over the last several years that glucose meters aren't adequately evaluated for the way that they're being used, particularly in hospital settings and they haven't been evaluated for some of the intended use populations that they're commonly used in. It's our intent in writing these guidance documents to address the issue by creating two distinct glucose documents for the different user population and particular use requirements.

These two final guidance documents titled Blood Glucose Monitoring Test System for Prescription Point of Care Use and Self-Monitoring Blood Glucose Test Systems for Over the Counter Use were finalized and issued last month on October 7. The final SMBG guidance only addresses those systems that are intended for self-testing by home users. These systems are for single patient use only.

The BGMS guidance addresses those systems for point of care use that are intended to be used for assisted testing in professional healthcare settings such as hospitals, doctors' offices, long-term care facilities. These systems are intended for multiple patient use. The two guidance documents are meant to be a description of the FDA's current thinking on the information that manufacturers should submit to FDA for future glucose meter submissions.

These guidance documents aren't meant to be guidelines or rules for how hospitals, healthcare professionals or patients should use glucose meters. They're not meant to be rules or guidelines for how laboratories should validate glucose meters and they're not meant to apply to those meters that are currently on the market but should be used when making device modifications and preparing future 510(k) submissions for glucose meters.

Many of the aspects of the new guidance documents are similar to what we currently see for these devices so I won't go into many of these details today. However there are some areas of the guidance that are new or different from what we typically see for glucose meters and I've included some of these key differences here in blue.

I'll go into each of these in more detail in the next few slides but briefly they include a different accuracy study design and accuracy goals, a modified way of the analyzing and reporting interference data, a slight modification to the

cleaning and disinfection recommendations that now includes inclusion of the test strip port for cleaning and disinfection robustness, the inclusion of new flex studies and the inclusion of test strip manufacturing lot release criteria in the pre-market submission.

For the most part the finalized document didn't change much from the draft document. However we did make some changes and clarifications based on the comments we received on the draft document. We received many comments expressing concern and confusion regarding the implications of the guidances on the CLIA waiver status of these devices. In response we added clarifications on the intent of the guidances and the implications for CLIA waiver status.

Some of the performance goals have also been modified and the interference testing section was also modified again based on the comments we received on the draft document. We'd like – what I'd like to do now is to discuss the two documents in a bit more detail starting with the BGMS guidance for prescription point of care then I'll discuss the SMBG guidance in less detail giving a higher level overview since there's so much overlap between these two documents.

The intent of the BGMS guidance is to describe the studies that should be tested to demonstrate performance for devices that are intended to be used in a diverse professional healthcare setting on subjects in various states of health. The intended use population for BGMS devices may include patients in all professional healthcare settings, patients in specific healthcare settings such as emergency response vehicles or patients in long-term care facilities or patients in a physician office.

This document doesn't address those systems that are intended for over the counter use, only users at home. These BGMS systems are intended for point of care use and specific professional healthcare settings and should be studied in those specific populations and should be labeled appropriately. Performance studies should account for factors such as various disease states, patient conditions, physiological states and medications that may affect device performance in the intended use population.

For those systems intended for use in many or all professional healthcare settings it may be necessary to identify specific sub-populations in which the BGMS may function differently than in the broader intended use population. These sub-populations and the difference in performance should be identified in labeling. FDA's clearance of 510K submissions for SMBG devices intended for over the counter home use allows for automatic CLIA waiver categorization.

Now as discussed in the previous slides most blood glucose meters on the market today even those that are used for healthcare professionals were previously submitted to FDA with claims for over the counter use by lay users and were therefore giving CLIA waived categorization. Clearance of BGMS systems as prescription use devices intended for point of care use in professional healthcare settings as described in this guidance means that they won't be automatically CLIA waived. However FDA recognizes the importance of having CLIA waived blood glucose meters in point of care professional healthcare settings and intends through the studies described in this guidance to facilitate CLIA waiver for these devices.

The recommendation in the BGMS guidance particularly the recommendations for the accuracy user studies are designed simultaneously to support both clearance and CLIA waiver. For instance the recommended

number of samples and the use of the participants in the study that are representative of the intended CLIA waived users will help to support both clearance and waiver.

Submitting the information described in the guidance as a dual 510K CLIA waiver submission will help to enable BGMS's to be CLIA waived concurrently with the 510K clearance. To go into accuracy in more detail this guidance document describes the accuracy assessment of BGMS systems which will be performed in the hands of the intended users. The studies should represent the actual claims made for the device and should include subjects that accurately represent the intended use population.

A minimum of 350 patient samples per claimed sample type or matrix should be used. Now this is an increase from what we currently see but this means that for each claim such as an arterial, venous or capillary blood claim 350 samples for each type should be submitted though these different sample types can be acquired from the same patient and be used for these different studies.

These samples should span the glucose measuring range for each sample type and be compared to a comparator method. If natural samples with concentrations at the extreme ends of the measuring range aren't obtained during the study then additional samples may be contrived by spiking or glycolysis to obtain an additional 50 samples with high glucose concentrations greater than 300 mg per deciliter and 50 samples with low glucose less than 80 mg per deciliter.

Another difference from the studies that we currently see is the recommendation in the guidance that the test strips used in these studies have undergone typical shipping and handling conditions prior to use in the study. If the intended use population of the device includes neonates then a separate

neonatal study should be performed to support this use. Neonatal blood is known to differ from adult blood and it can often have higher hematocrit levels and lower blood glucose concentrations compared to adult blood.

Because of these differences, because these differences may have a direct impact on performance of blood glucose monitoring a neonatal accuracy studies should be performed to validate any neonatal claim, neonatal samples are defined as samples from subjects less than 28 days old and for this study the accuracy of 100 to 150 fresh neonatal capillary blood samples should be assessed by comparing meter results to the results from a comparator method.

Before going into the accuracy goals described in this guidance for the BGMS system, I'll briefly touch on the 2013 version of ISO 1519000. FDA doesn't recognize this standard and the glucose guidance document tried to address some of the issues that FDA believes are important for these devices that aren't addressed in the standard by differentiating over the counter versus point of care healthcare use. These guidance documents addressed the different user populations for these devices and they're not just focused on over the counter use.

In doing so the guidance has addressed different use and design requirements important for the different use settings that aren't addressed in the standard as well as assessing the performance in the hands of the different intended users. We've also addressed the need for the improved performance in the hypoglycemic range in the guidance document. Though not identical to the study described in the ISO standard. The FDA documents described studies that are designed to be compatible with ISO so that studies performed according to the guidance document will also satisfy ISO.

The accuracy goals that are described in the BGMS guidance for point of care use have changed slightly since the draft guidance have been loosened based on comments we received on the draft. The draft stated that 99% of meter results should be within 10% of the comparator method for glucose concentrations greater than 70 and plus or minus 7 mg per deciliter for glucose concentrations less than 70 and that 100% of value should be within 20%.

This final guidance now states that 95% of the meter results should be within 12% for glucose concentrations greater than 75 or within 12 mg per deciliter for concentrations less than 75 and that 98% instead of 100 of the meter results should be within 15% or 15 mg per deciliter of the comparator method. In cases where data points fall outside of these accuracy goals on the previous slide a clinical justification should be provided in the pre-market submissions for each of these data points along with a description of any other proposed mitigations.

And as described in the draft the study should be accompanied by a description of the study setting including the size, type and location of the site should be provided in the pre-market submission along with a justification for how the study conditions represent the intended use condition. The patient demographic should be described including the age, disease state and any medications the study subject may be on along with the description of the shipping and handling conditions of the test strips prior to using the study.

The pre-market submission should also include an evaluation of the effect of potentially interfering exogenous and endogenous substances on the device. This study should include common conditions such as lipemia, varying hematocrit levels as well as common medications. There are certain substances that we know from experience interfere with current meter

technologies such as acetaminophen, uric acid, xylose, etc. However in addition to testing the common interfering substances we recommend that manufacturers conduct a risk analysis to assess commonly used drugs in the intended used population.

This analysis should take into account device technology, the intended use population, the intended use setting. Any relevant potential interference should be included in the testing. The study design for these studies isn't really all that different from what we see now but there are a few differences. Similar to what we see now it's recommended that a comparison be made between a test sample that contains the potential interferent measured on the candidate meter and the result of control sample containing a solvent or vehicle, also measured on the candidate device.

The analysis and presentation of the results does differ from how we typically see these studies analyzed. The glucose documents described presenting the results as relative bias and present percent bias with 95% confidence intervals. Now this is instead of using the more typical non-interfering criteria. Depending on the bias, the interference and the concentration of the interference, language may be added to the labeling to explain the expected device performance in the presence of each interference.

It's well known that hematocrit levels can significantly affect blood glucose meter readings with a significant positive meter bias at low hematocrit and a significant negative bias at higher hematocrit concentrations. Due to this known interference a separate hematocrit study should be performed with these devices as is currently done. The blood sample to use should span – reasonably span the glucose measuring range and hematocrit range.

The meter results should be compared to a comparator method by comparing each meter replicate to the average of the comparator value. The bias for sample with glucose concentrations greater than 75 should be less than 5% on average with no individual value greater than 10%. For samples with glucose less than 75 the absolute bias should be provided along with 95% confidence intervals and a clinical justification.

The guidance states that for point of care BGMS systems a minimum hematocrit range of 10 to 65% should be validated and claimed. This is based on the very broad hematocrit range that could realistically be presented in the intended use population for this type of device. If the device is intended to be used in patients with a broad range of blood oxygen levels then a study should be conducted to demonstrate a range of blood oxygen levels that the device can be used with.

The oxygen study may be supplemented with blood oxygen levels of patients used in the method of comparison, user evaluation. If blood oxygen levels don't affect the performance of a particular device then a comprehensive justification should be provided supported by analysis of blood oxygen levels on the device performance in the method comparison user evaluation study.

As I'm sure most of you listening are aware, that in 2010 FDA modified the way we review all blood glucose monitoring systems to ensure that validated cleaning and disinfection instructions are provided to users. This was in response to concerns that had been raised regarding blood borne pathogen transmission linked to the shared use of blood glucose meters when appropriate infection control measures haven't been followed.

This guidance document describes validation studies that aren't much different from what manufacturers are currently doing. One difference that I'd

like to highlight is the expectation that meters be designed such that all external materials can be cleaned and disinfected. This includes the test strip port, other ports and any seams on the meter, etc. the validation studies in the two guidance documents are almost the same, differing mainly in the number of cleaning and disinfection cycles that represent the amount of cleaning and disinfection that the needle will be exposed to in the use life.

Therefore a meter used in multiple times in a day on multiple patients in a professional healthcare setting will need to be robust to many more cleaning disinfection cycles as compared to a single patient over the counter meter. The validated cleaning and disinfection instructions should be included in the device labeling. The BGMS guidance also includes a description of flex studies that should be performed, some of which are new from what we currently see.

These studies are designed to demonstrate that the BGMS design is robust and that all known sources of error are effectively controlled. The test system design should incorporate fail safe mechanism whenever it's technically feasible. Examples of failsafe mechanisms are the use of lock out functions to ensure that the test system provides no result or an error rather than displaying an incorrect result in cases where for example test conditions are inappropriate.

Other failsafe mechanisms are those measures that are put in place to prevent operator error such as inserting the wrong test strip. Manufacturers should conduct a comprehensive risk analysis that identifies all potential sources and error including test system failures and operator errors, identifying control measures to reduce the risks of these sources of error and then when appropriate flex studies should be performed to validate effectiveness of the control measures.

This guidance document includes several examples of such flex studies and some of them are listed here so highlighting – just a couple, test strip stability should be established by assessing test strip performance throughout the claimed shelf life and condition. The effects of temperature and humidity during device use should also be assessed.

The use of used test strips or insufficient blood sample volume should also be assessed. Included in the guidance that is new from what we currently see is a request that the description of the test strip manufacturing lot release criteria be provided in the pre-market submission. Lot release criteria is criteria used by the manufacturer to assess and release into market manufactured lots or batches of test strips.

This has been included in the document to try to help prevent less accurate test strips from being released onto the market. Test strip lot release criteria should be sufficient to ensure consistent quality of test strips. They should be designed to ensure that release lots conform to the label device performance in the hands of the intended users. These criteria should be more stringent than the criteria used to evaluate total error in the performance studies and these criteria should assure statistical confidence for a full lot.

Manufacturers should provide a description of the lot release criteria and a summary of the sampling scheme and acceptance criteria in the pre-market submission. Now I'll discuss the SMBG guidance briefly to highlight some of these differences.

This guidance is meant to address only those blood glucose monitoring systems intended for lay users at home. This encompasses individuals with wide ranges of age, dexterity, vision and training received on performing the

testing and other factors that can be critical in the patient's ability to accurately use the device and interpret test results.

SMBG systems should be designed to be robust and reliable to accommodate actual use by people affected by diabetes such as more varied storage and handling conditions as compared to devices used in professional settings. This document is not meant to address those systems that are used for point of care use. As in the BGMS guidance this document recommends that accuracy of the system be demonstrated in the hands of the intended user which in this case is lay users. This should be done under conditions reflective of expected use.

The recommendation is to use a minimum of 350 patient samples obtained and tested by the lay users when they're given only the device and the device labeling with no training, coaching or prompting. Three hundred fifty samples should be obtained per sample type such as for finger stick, palm or thigh. These samples should span the glucose measuring range for each claimed sample type and meter results should be compared to the comparator method.

At least 10% of the participants in the study should have no experience with SMBG. Now these subjects can be non-diabetics. Test strips used in the study should've undergone typical shipping and handling conditions prior to the study. We recognize that the user study may not provide the sufficient evaluation of the device performance of extreme upper and lower ends of the measuring range. Therefore if natural patient samples aren't obtained at the extreme ends of the measuring range, then additional samples may be contrived by spiking or glycolysis to obtain an additional 50 samples with high glucose concentration greater than 250 mg per deciliter and 50 samples with low glucose concentrations less than 80 mg per deciliter.

The accuracy goals outlined in the SMBG guidance haven't changed from the draft. They stated that 95% of SMBG results in the accuracy study should be within 15% of the comparator method across the entire claimed measuring range of the device and that 99% of the SMBG results should be within 20% of the comparator method.

If there are outliers that don't meet the accuracy goal in the previous slide they should be specifically addressed by manufacturers in the pre-market submission with a justification for why the errors occurred and a description of the potential for that error to affect user safety when extrapolated to the end intended use setting that's when millions of test strips are used.

We understand that some SMBG devices may not be able to reliably measure glucose at very low concentrations and meet this accuracy goal. However we've heard from the clinical community that it could be acceptable for lay users to narrow the claimed measuring range based on the accuracy results so that readings as low as 20 mg per deciliter aren't reported for a particular device. However the measuring range for this intended use population shouldn't be any more narrow than 50 to 400 mg per deciliter.

The interference testing described in this document is the same study design as outlined in the BGMS guidance with the testing of common endogenous substances that may interfere with the technology and that would likely be present in the user population. As with the BGMS document the meter results from the test sample are compared to those of a control sample and the relative bias and percent bias with 95% confidence intervals are provided instead of the non-interference criteria.

As with the BGMS document the effect of hematocrit on device performance should also be evaluated. However here a claimed hematocrit range of 20 to

60 is considered ideal as the intended user population may reasonably be expected to have hematocrit values between 20 and 60%. This document also lists a minimum claim range that should be known narrower than 30 to 55% hematocrit. And in this SMBG document the goal is to have a bias of less than 8% on average for the study for glucose concentrations greater than 75 with no individual value having greater than 15% relative to the comparator.

Similar the infection control studies are very similar in this document as described in the BGMS document. The validation studies are based on expected use and the use life of the device. Therefore the single patient use devices will typically have fewer validation cycles for the robust in the study to support the device use life.

As with the BGMS guidance the over the counter meter should be designed so that all external materials can be cleaned and disinfected and this includes the test strip port. The validated cleaning and disinfection instruction should be included in the labeling and language that is easily understood by home users. The SMBG guidance recommends similar flex studies that are described in the BGM guidance and also recommends that the test strip manufacturing lot release criteria be provided for the over the counter systems.

For SMBG devices the following warning should be included prominently on the outer box label and packaged insert for SMBG systems. This warning emphasizes that the system isn't intended for use in healthcare or assisted use settings such as hospitals, physician offices or long-term care facilities since it's not been cleared for these uses and the use on multiple patients could lead to the transmission of blood borne pathogens such as hepatitis B.

Currently consumers have no way to distinguish meters based on performance before they purchase them. The lay users along with their healthcare

professionals have the ability to choose the SMBG that's right for them and it's important to clearly describe the accuracy of the device in a way that's easy for them to understand. It's also important for this information to be located in a prominent way in the product labeling so that lay users can understand the performance prior to purchase and also when they're learning to use the device.

Therefore the SMBG guidance recommends that accuracy information be placed prominently on the outer box label and in the test strip package insert. The guidance recommends that the data be presented in easily understandable tabular as well as graphical format. The tabular example provided in the guidance is similar to the accuracy table currently used for these devices with the percentage of meter results displayed within different accuracy bins such as 5, 10, 15% with the comparator method.

This is the example of the tabular format that's included in the guidance. Here the numbers represent the number of meter results that were within the level of accuracy shown relative to laboratory comparator methods. Now these are only examples and we continue to encourage manufacturers to discuss alternate ideas with us. Now that the guidances have finalized we're working with manufacturers on phasing in the recommendation with the goal of phasing them in over the next several months. We recognize that the development of the current devices were performed prior to the release of the guidance.

So we would encourage manufacturers to contact us with questions and concerns with implementation. We have been contacted my manufacturers that are in situations where they have completed their studies and are prepared to submit their submissions when the guidance was published. If you're in a similar situation or have other questions or concerns we encourage you to

contact us. We also recognize that certain recommendations may be easier to implement such as the labeling recommendations as opposed to other aspects of the documents. And that concludes my slides and we'll be taking any questions you have now.

Coordinator: Thank you. At this time if you do have any questions or comments you may press star 1. Please unmute your phone and state your first and last name when prompted. Again that's star 1 if you do have any questions. One moment please. (David Phipps) you may go ahead.

(David Phipps): Good morning. I just have a question that may be a little bit off subject. Life scan who as you know makes OneTouch meters is telling people from their customer service end that FDA allows a 30% difference between differing brands of monitors and a 20% difference between your actual blood work. I have a patient who recently – they had a Walgreens TrueTouch meter that was made by Nipro and those were discontinued. He had some strips left. His insurance company recommended that the preferred was a OneTouch mini so he got that and started noticing that he's testing 100 on the TrueTouch and he's 130, 140 on the Ultra Mini.

So when we called him and asked him about it he was told this and they – I argued with him about it, said I never heard that and his doctor never heard of that. He provided them with the last two weeks of values on both of the meters and they agreed that he was running above 30%. I think he was running around 33, 34% so he sent him a new meter which basically has the same results.

He talked to his doctor. If he got 90 on his new meter he's actually testing around 65, 68 on his TrueTouch and wondering why he was feeling dizzy. Question I have is if that's actually a standard we use these meters in the

hospital that makes it un-useable for a sliding scale. If you've got one value versus another and actually this patient had come back and told me that his values were actually closer with the TrueTouch to his lab work that was drawn in the doctor's office than the OneTouch was but of course OneTouch like all the rest of them claims that theirs is the most accurate on the market.

Is this going to be – number one, are those values true as far as how much the FDA allows currently and is this something that's going to be corrected by the 95% that should be within 12%?

Leslie Landree: Hello, yes. This is Leslie. Thank you very much for that question. We understand exactly what you're saying but the criteria that we have, we don't compare meter to meter. We don't have any sort of acceptable difference for that – you're correct. The goal for these guidances really are to improve the consistency and quality for glucose meters in the different intended use populations.

(David Phipps): Sure. The other concern I have is he's not on insulin but (unintelligible) on insulin he'd be giving himself more insulin based on these higher values and I think the public at large is – certainly as a healthcare professional I've always been given to believe that as long as you're using their strips and the proper technique that your accuracy should be basically the same from one meter to another. I had no idea that there was that much of a swing that was loud. Is that true though, is it 3% difference that they say is allowed by the FDA currently? Is that accurate?

Leslie Landree: No. We don't have any such 30% criteria and I hear some concerns from you based on the results that you've seen. As always if you have any concerns you're always – we always encourage you to submit a MedWatch report if you have any problems with any devices.

(David Phipps): Okay. That was my next question, was who goes back and talks to them for making these kinds of claims? Don't mean to drag you into this basically saying the FDA says we're allowed to be this far – we're allowed to have this much of a difference between two different brands of meters.

Leslie Landree: True. We review all those reports and try to address them appropriately.

(David Phipps): Okay great. Thank you for the information.

Coordinator: Thank you. Our next question comes from (Nicole Crump) from Lab Services. You may go ahead.

(Nicole Crump): For the infection control, the cleaning and disinfection should the entire device be used for the cleaning and disinfection testing or can the individual materials from the device be tested?

Leslie Landree: Right, hello. This is Leslie again. There are two aspects to that testing for the disinfection efficacy where you're demonstrating that the disinfection effective hepatitis B. You can use parts of the meter so just – it's called coupon. So different – every external part like the buttons, the display, the case can be used but you don't have to use the complete full device. But for the robustness testing which is the second component to the testing the entire complete device should be used.

(Nicole Crump): Okay thank you. I have one follow up question then. So the pieces of the device and the materials, should that be – can they be new materials or should they be the materials that were used in the robustness testing?

Leslie Landree: No. Typically they're new materials.

(Nicole Crump): All right, thank you.

Coordinator: Thank you. Once again if you have any questions or comments please press star 1. Please un-mute your phone and state your first and last name when prompted. (Michael Chibero) you may ask your question from Nimco Health.

(Michael Chibero): Hello there. So the question – one of the questions we have is how does the guidance document play into a special 510K for a currently cleared device? If we're submitting a special 510K do we have to comply with the new guidance or will it be assessed against the guidance and standards in place when it was cleared?

Courtney Lias: Hello this is Courtney Lias. So guidance documents really are meant to outline the types of studies that we think that manufacturers should do address certain risks or performance evaluations for that particular type of device and the type of submission doesn't actually matter with respect to a particular study.

So if – for the change you're making, one of your verification validation activities requires some sort of study that you do to address the risk you've identified. We'd recommend you follow the guidance document and performing that study but as you know for a special 510K, if you're modify a product you'd do a risk analysis to identify the types of verification and validation activities that are necessary for that change.

So like I said when you're doing a study that's addressed by the guidance it's part of your V and V activities. We do recommend you follow the guidance. Certainly there are other activities that are V and V activities that may not be

addressed by the guidance also. We're also happy to help with any questions on particular situations that you have that might be unusual as well.

(Michael Chibero): Okay great. I have one other question as well if that's okay, different topics. So when we're doing the accuracy studies the guidance document just says that all data must meet those 95%, 99% requirements but you're using a comparator. Is it okay to essentially lump all the data together for that assessment or should it be assessed in each comparative value?

Woman: I'm not sure I understand your question. Are you saying – what are you saying you'd lump together?

(Michael Chibero): Say that I test against the comparator at 30, 50, 75, 100 on milligrams per deciliter. Should the comparison be made at each one of those comparator values or can I put all that data that I collected together and say I need it 95% and 99% of the time?

Woman: When you're doing the analysis each patient result should be compared to the respective comparator result. When you analyze it and present it you – the tables are combined for the different glucose ranges but each individual result should be compared to a comparator result. Does that answer your question?

(Michael Chibero): Not really. Maybe this is something that I need to take up on an individual basis or with you directly.

Courtney Lias: This is Courtney Lias. The method you'd use to do this isn't different than the method that you use now to do it so for each person that's in your study you take a meter measurement and a comparator measurement. You assess the difference between those values and then that difference is what you look at to

see how many of those subjects have a difference greater than or less than the goal.

(Michael Chibero): So I guess – say I tested 1000 subjects just to make it easy, then I could just for all 1000 subjects we met the 95% and 99% requirements.

Courtney Lias: Yes. If I'm understanding your question correctly but I'm not sure that I am so maybe it'd be good for you to follow us up on that. I do want to emphasize this isn't different than the way that people typically analyze the data for the current submissions.

(Michael Chibero): Okay great. Thank you.

Coordinator: Once again if you do have any questions or comments please press star 1. At this time I am showing no further questions. Again that's star 1 if you do have any questions.

Irene Aihie: Operator, are there any more questions?

Operator: At this time I'm showing no further questions.

Irene Aihie: Okay thank you. Thank you. This is Irene Aihie and we do appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CBRH learn webpage at www... seems like we have a few questions.

Coordinator: We do. One moment please.

Irene Aihie: Okay.

Coordinator: (Ginny Tammy) you may go ahead.

Woman: I'm not sure the company was.

(Ginny Tammy): Yes. We're from archive and we're calling because we have a question regarding the control solution with every strip. Could you elaborate more on that requirement in the guidance?

Woman: Yes. In the public meeting we received feedback that it'd be helpful if when users purchased their meters and test strips that they had small amounts of control solutions to use for their testing. So the guidance is intended to address that by suggesting that glucose control solutions be included in each test strip vial package.

Coordinator: Would you like to go to the next question?

Irene Aihie: Yes please.

Coordinator: (Unintelligible) from Alkali. You may go ahead.

Woman: Hello yes. I have a follow up to what was just asked. When the control solution is in each of vial package with the test strips will they test one strip from each of the vials or each of the bottles?

Courtney Lias: Courtney Lias. I think probably we believe that most manufacturers will choose to put a smaller than the typical current vials amount in the vial with the test strips. And manufacturers, they'll typically now tell users how many control solutions to do but they do make recommendations in the labeling about control testing. So manufacturers should assess what type of

instructions they should provide to users and we do recognize that control materials are also available for the users who may want to test more often.

Woman: Okay. I just wasn't sure what to tell the clients when they ask how often they should test their control solution.

Courtney Lias: Right. The guidance document doesn't recommend any changes to the instructions. The concern I believe was with the availability of control material for users to purchase new test strips.

Woman: Right, okay. And then my second question is this is going to be for name brand meters as well as drug store meters, generic meters?

Courtney Lias: Yes, all.

Woman: Okay so all of them will have the accuracy requirement on their boxes moving forward.

Courtney Lias: Yes.

Woman: Okay. Thank you.

Coordinator: (Dennis Gunnel) from EPAC. You may go ahead. Sir your line is open, (Dennis Gunnel). Once again if you do have any questions please press star 1.

Irene Aihie: We'll give it a few moments to have people log in if there are any questions.

Coordinator: One moment. (Charles Ryan) from (unintelligible) you may go ahead sir

(Charles Ryan): Yes. I have a follow up to the control solution discussion. I was just wondering if FDA would allow entertaining an alternative such as providing a coupon in with product rather than the physical control solution.

Courtney Lias: This is Courtney Lias. The concern that we heard at the public meeting was related to individuals who wanted to do control testing and also you may be unaware of the subsidy for control testing but didn't have within (unintelligible) control materials available to them. So we're definitely happy to address or to discuss things that may be alternatives to address the issues that we discussed in the guidance document. So we're happy to discuss that with you.

We'd want to understand how the proposal that you have like a coupon would address that type of concern. So we're happy to address that. I think that they'd still not have the control material there to test with a coupon. They still have to take an action to order it but I just wanted to clarify the concern that we were trying to address there. Does that help?

(Charles Ryan): Yes. I think there's ways that we can still arrange that but okay. Thank you.

Courtney Lias: Sure. We're happy to discuss.

Coordinator: Thank you. (Dennis Gunnel) you may ask your question. Please state your company name.

(Dennis Gunnel): I think it's Bennet Dunlap. They're a patient advocacy coalition. Hello?

Woman: Hello caller. We lost you for a second. Can you repeat your question?

(Dennis Gunnel): Bennet Dunlap. Can you hear me now?

Woman: Yes we can hear you.

(Dennis Gunnel): I feel like I'm on a cellular commercial. Thank you. In the – it's Bennet Dunlap with the Diabetes Patient Advocacy Coalition and the guidance process patients should express concerns both to the over the counter and the point of care use devices.

I think it's interesting that the first question we had today was apparently a healthcare professional that was concerned about the over the counter devices being used in clinical settings and I'm curious as to what processes there would be to enforce the correct devices used in the correct setting and the concern over transmission of infection and cleaning that there'll be consideration of vectors other than the actual device such as the supplies because there's evidence that suggests that supply can be a vector for transmission of disease.

In the over the counter area labeling I think is something that patients were very concerned about in the guidance and we noted a few years ago that FDA used guidance to say that the device wasn't approved for care adjustments and not approved to do calibration of the CGM and I'm curious if the FDA is open to dissentative labeling claims by manufacturers with a device is approved to make their adjustments and is approved to calibrated CGMs so that we can clearly differentiate devices that are approved under this new guidance from devices that are (unintelligible) some previous generations of guidance. Thank you.

Courtney Lias: Hello Bennet this is Courtney. I've got a few questions in there. Let me try to get some of it and then you can let me know if I missed any. First you expressed some concern about the other product that people use to test and

whether or not they may be vectors for infection and of course the other products, other types of supplies that people with diabetes use have some of the same issues but cleaning disinfection is necessary for all types of medical devices that are being contacting.

These guidance documents address blood glucose meters and those products. There are other parts of the FDA that address cleaning and disinfection requirements for other types of products. So it's definitely a concern and we hope that the efforts that are underway to address those for all products are effective.

(Dennis Gunnel): Yes. I guess Courtney what I really meant was the supplies that travel with the glucose meters so if a can of strips is moving from hospital room to hospital room to hospital room and a gloved hand is going into that can a strip or under that container of strips if that container of strips then can become the vector.

Courtney Lias: Yes. Certainly that's a question we do ask when we look at meters designed for this type of use. So manufacturers have chosen individually packed strips and things like that which do help.

(Dennis Gunnel): I guess the transmission of supplies from room to room to room, it doesn't matter if they're in a can or individually striped or whatever. If it's not disinfected, it's just like the device itself.

Courtney Lias: Right. I actually heard some of healthcare facilities that don't transfer certain files across rooms in an effort to control some of this as well which is probably a good practice.

One of the other questions that I think I heard in there and I may have heard out of you now but one of the other ones is that you were wondering about the

separation between over the counter products and products intended for use at healthcare facilities, more prescription use settings.

One, this guidance specifies that if you have a product that's designed for use – in a prescription use setting that it should be labeled appropriately for that use. The labeling will be specific about what the device has been cleared for, what type of assessments are done and what the limitations of the device are and the control that's in place there I believe is largely going to be CLIA and in that the labeling statements that are made are taken quite seriously by CLIA investigators or their – the other bodies like cap joint commissions, et cetera, that look at these products in a healthcare setting.

For example if there's a recommendation on the labeling they really take that as a requirement. So if it's recommended that products are handled in a certain way and a facility's not doing that they can be cited under CLIA. If there's an intended use population that's not cleared and that's being used in that intended use setting under CLIA they'll have to take appropriate steps to control the risks or do their own validations and take their own responsibilities for that.

So with the prescription use settings there are definitely some controls in place that are intended to help manage that. I'm not sure I got all of your questions. Can you repeat them?

(Dennis Gunnel): Sure. So that was really great on the OPC. I guess the question then becomes on the over the counter side. Is there a similar process to not (unintelligible) but to CLIA where the recommendations for labeling become something that would be followed by a third party payer. My concern is that there's a definitive difference between new, more accurate devices using those to dose insulin, make therapy adjustments versus devices that you said in the past that

once it's approved, it's approved. So we can have technology from the 80s or earlier that's still approved. How do we differentiate with a label that these new devices are approved to make therapy adjustments and they're approved to properly manage diabetes with dangerous drugs like insulin and are approved to calibrate a CGM?

Courtney Lias: Sure. You're raising importance to questions that we're definitely discussing with patient community and healthcare provider communities that can't be addressed by guidance documents unfortunately. They'd probably require a larger change in order to make other types of requirements apparent for these but we're looking at other areas. These guidance documents aren't the only efforts that FDA has in order to try and increase transparency and consistency with glucose meters in a way that benefits all stakeholders. We hear a lot of the concern...

(Dennis Gunnel): Can a label be used to do this?

Courtney Lias: Excuse me?

(Dennis Gunnel): Can a label be used to do that, the positive version of the negative 2013 label?

Courtney Lias: Right. So the label – for example the over the counter, in the over the counter guidance there are labeling statements that we're asking people put in that will help so the warnings about use on single patient use only, if you're a healthcare facility and for example the state health inspectors find that you're using them on multiple patients I think that there would be some liability on that facility for doing that without proper controls. So I personally believe that even those warnings will help some of those situations.

With respect to designating certain meters for treatment decisions and other meters not for treatment decisions, we don't have plans to go in that direction because of the potential one – we only have one category with those meters at the moment so we'd need a regulatory change to create different categories with meters. But we are discussing different ways of moving forward. We're happy to hear feedback about what types of needs are still there that will need to be addressed in the future.

(Dennis Gunnel): Thanks.

Courtney Lias: You're welcome.

Coordinator: Thank you. Once again if you do have any questions or comments please press star 1. Again that's star 1 if you do have any questions or comments. (Charles Ryan) you may ask your question. Please state your company name.

(Charles Ryan): It's (unintelligible).

Coordinator: Please go ahead.

(Charles Ryan): Just with respect to the OTC guidance and the accuracy criteria there can you confirm that the intent is that the criterion of the 95% and 99% ranges would apply not just to the fingertip results but also to alternative site testing?

Courtney Lias: Yes. That's the intent.

(Charles Ryan): Okay thank you.

Coordinator: And at this time I'm showing no further questions. I'll turn the call back over to Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie and we appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CBRH learn webpage at www.fda.gov/training/cdrhlearn by Wednesday, November 30. If you have additional questions about the final guidance document please use the contact information provided at the end of this slide presentation.

As always we appreciate your feedback. Again thank you for participating and this concludes today's webinar.

Coordinator: And thank you. You may go ahead and disconnect at this time. This does conclude today's conference call.

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