



Lauren:

Good morning and welcome to today's webinar on Reaching the 90-90-90 Targets: the Implications of HIV Misdiagnosis. My name is **Lauren Alexanderson** and I am the Knowledge Management Communications Manager for the AIDSFree project. Before we begin today's presentations, I'd like to quickly review the Adobe Connect environment and set a few norms for today's webinar.

Today's webinar has four presentations, followed by a discussion period during which our speakers will address your questions. Within the webinar environment, please make use of our question and answer box on the bottom right side of your screen to share your thoughts, note your questions, or ask for help with sound during the presentation. Questions you ask are only visible to you, our presenters, and our technical support. If you're experiencing difficulties, our technical support will respond to your question privately.

We will collect your questions from our speakers and save them for the discussion period at the end. It's great that we're able to connect people from so many places today but your experience may vary, based on your internet connection and computer equipment. I will briefly go over a few trouble-shooting steps, should you have technology changes today. If you do lose connectivity or can't hear, close the webinar; reenter the meeting room in a browser other than Google Chrome by clicking on the webinar link we provided. Use the Q&A box to ask AIDS-Free techs for assistance.

If the trouble-shooting steps are not successful, please rest assured that the webinar is being recorded and you will receive an email with a link to the recording following today's events. And any questions that don't get answered during our discussion session will be compiled after the webinar and shared with our presenters, and any responses will be shared with the participants.

To get us started, I will hand it over to our co-moderator, Vincent **Wong** of **USAID**.



Vincent: Hello, everybody. Can you hear me okay?

Interviewer: Sounds great.

Vincent: Okay, fantastic. Hello. My name is Vincent Wong. I am a Senior Technical Advisor here at USAID Washington and today's webinar has been really organized primarily by AIDSFree but I'll be co-moderating with my colleague Cheryl Johnson from WHO from Geneva, who is on the line. And we've got a really good panel today. We've gathered four experts in the field looking at the evidence around HIV testing and misdiagnosis. So as we all know, the levels of HIV testing that are happening globally within **[Inaudible] [00:02:59]** alone were up to about 65 million individuals tested yearly, and globally I think that number is exceeding 160 million. So there's a lot of testing happening.

And as we continue to accelerate that to try to obtain the three 90s goals where we've got 90 percent of individuals diagnosed and enrolled in care, and couple that with policies of test and start and treat all where we're moving people from diagnosis into treatment immediately, it becomes just paramount that we ensure that the quality of the testing delivered and the test kits used are high, and that we are not misdiagnosing individuals as we move towards those aims.

So we've got really four speakers today to help speak to those topics. And as many have seen in the program, we have Anita Sands, who's going to be speaking to the normative structures that help ensure the test kit quality. We'll have some field evidence presented from MSF from Dr. Leslie Shanks, MOH perspective on it from Dr. Khumbo Ng'ona from Malawi, and then also some thoughts on regulatory challenges from Russell Dacombe.

So we'll get started today with Anita Sands from the WHO, speaking extensively on testing strategies and algorithms, procurement of diagnostics, postmarking **[audio cuts out]** all from the—with the global view in mind. So we'll turn it over to Anita and then continue on. And just a reminder, if you have questions along the way, please plug them into the Q&A box on the right and Cheryl and I will moderate them at the end.

Anita: Okay, thanks very much Vincent. This is Anita Sands. Can you all

hear me?

Female Speaker: Sounds great.

Anita: Okay. So I'm going to talk a little bit today about some of the work the WHO is doing around ensuring the quality of the test kits, obviously that being one of the fairly major drivers of the quality of the testing events and accurate testing is indeed the quality of the test kit that we use. So WHO has actually recently done quite a bit of work in this area, trying to have a bit more of a systematic review of the way in which misdiagnosis is actually being published about in the field.

We recently did a review where we found that misdiagnosis of HIV status was relatively common, and ranged anywhere from .3 percent up to over 10 percent. And what that means is that people were diagnosed as HIV positive when indeed they were not. They were HIV negative. But for some reason, either test kit quality or another part of the pathway led to them having an incorrect test result.

Obviously, that has got quite a long range of repercussions for the testing program. So we then went and looked at a number of the national testing policies to try to understand what would be the likely drivers of the misdiagnoses that we had observed in the systematic review. And what we found of the 48 national policies that we reviewed, only 17 of these actually adhered to the WHO recommended testing strategies. And I'll talk in a few slides about the testing strategies and what WHO actually recommends.

But these have been generated through a petition modeling process and have been recommended for a number of years by WHO. Just a particular note, we noticed that quite a number of the countries were using the third assay of the algorithm as a tiebreaker to rule in HIV infection, which WHO does not recommend. We do know that that is a very big driver of false positive statuses.

We also found that in a number of countries the testing algorithm that was being used, so which products are being used have not been validated. We saw there was poor training and supportive supervision of testing providers, both in the laboratory as well as

those they provided in community testers. And at a product level, we also **[inaudible] [00:07:18]** well aware of the impact of end-user areas, mainly around not observing the instructions for use play when testing for HIV.

And so some of the pieces of evidence that came up very commonly in our systematic review were the **[inaudible]** reading, very weakly—positive or weakly reactive test lines. We found a number of studies where results were read before the minimum reading time had been reached. So the second that a positive test was being seen, that person was being diagnosed from that result.

We also note that in a lot of countries, it's very difficult to store the test kits within the claims made by the manufacturer. And they normally say that a test should be stored between 2 and 30 degrees, and we often observed that the test kits are stored well above 30 degrees and often even in direct sunlight.

So there's a number of likely drivers that probably are contributing to this misdiagnosis, and there are a number of tools which WHO has. But one of the ones which we had recommended for a number of years, and we also realized in the course of the systematic **[inaudible] [00:08:27]** had not been widely implemented with the recommendation for all HIV-positive, newly diagnosed to actually be retested before they were initiated into care and treatment. So I'm also going to talk a little bit in a few slides about what retesting is. But we did find that that was poorly implemented. Only two of the 48 policies we reviewed actually had retesting as an objective.

I'm going to also talk a little bit on a more scientific level. And I realize that perhaps this might be very interesting to some of the audience and a little bit more difficult for other members of the audience. But what we do know is that the landscape is changing. The propel of people who are coming for testing is changing. We now have much more coverage of antiretroviral than we ever had before. And antiretroviral do have a great effect on the body, I that they do help your immune cells to fight off the HIV. But they also mean that they have an effect on the tests that are used to diagnosis HIV.

We know that antibodies, which is what most of the rapid tests are looking for, but we know that antibodies and their production is very much affected particularly by early initiation of ART. For example, a very recent paper published by Michael **Desusier** and colleagues shows that early initiation of ART during acute infection phase actually led to cure a high rate of nonreactive **[audio cuts out]** results. So these people were coming up negative, when indeed they were not. But the influence of the antiretroviral had had an impact on the RDT that was used.

We find that this is more a problem with the older generations of tests; the first and second generation RDTs and more of an issue with all fluid tests done with whole blood tests. We also know that nucleic acids, so the focal viral load assays and **EID** assay are also quite affected by exposure of ARV. And so unfortunately, these can neither be considered to be a gold standard when ARVs are working well. Their whole objective is to reduce the amount of virus in the blood to being undetectable, which means it would also be undetectable by the kinds of tests that are available.

We also—so that's on the sensitivity side. But on the specificity side, we also see there's potential—and this is the missed diagnosis that's been much more widely published, which is the main part of our—main findings of our systematic review was around the influence that cross reactivity and **express** reactivity has on the test. So this means that the test comes up falsely reactive, so it's falsely positive or the presence of antibodies to HIV.

This is why we recommend testing strategies where more than one assay are used to come to that final diagnosis. What we have seen is as the marker for HIV rapid test has expanded, the number of manufacturers has expanded. But also we have an increase in what we call rebranding agreements, where companies will buy a test kit from another company and rebrand it with their own brand and their own product code and their own product name. And so you might not actually know if you're indeed using two of the same product but just with different brand within your testing strategy.

So it actually makes the product selection very, very difficult unless one does a validation study. And also, we know that certain

interfering substances can, in fact, induce false reactive results in concomitant infections. We know that sleeping sickness, and more recent with this evidence even malaria infection does actually because it is working on stimulating immune systems that we do see false reactivity.

And so a lot of this is actually well documented, and it is certainly these are the **[inaudible] [00:12:26]** aspects that during prequalification, we looked to see if the manufacturers considered these particular shortcomings of the test.

So in terms of talking now about how we would actually be able to assure quality, I'm going to talk a lot about test kit quality. But I just first wanted to situate it in this broader picture of quality assurance. You probably hear people say QA, have you got a QA system very often. And often this is a little bit hard to understand exactly what that means. And I've got a figure here, and unfortunately in an effort to try to make the font size a bit bigger, some of the letters are falling off the side.

But there are 12 basic aspects that you need to consider, and this is irrespective if you're in a laboratory, if you're a community-based testing; the principles of quality assurance need to be upheld in order to give the best chance that you avoid a misdiagnosis.

I'm just going to pull out a few little things here because these are actually topics I'm going to focus on. So purchasing and inventory; if you don't buy a good test, you can do all of the training in the world and have the best strategy and approach. But if the test itself is of not good quality, you won't get a good result. And that's what I'm going to then move on to talk about.

But I'd also just like to pick out that personnel, and having adequate training, supportive supervision so not **community** supervision but having someone that if you are conducting a test and you think actually, something doesn't look right, you kind of ask someone. And having that kind of regularized manner so that when and if problems arise, that testing providers have someone they can turn to for support.

We talk about a piece called assessment, and it's very important,

actually and it has been a good way for us to be able to have an understanding of the amount of misdiagnosis that's happening. Some of you might know it as EQA, or proficiency testing. But what that basically means is in order to be able to test the proficiency of a testing service to provide an accurate, correct diagnosis, we send out a panel, a specimen. They're normally blinded so they're labeled 1 through 10. You wouldn't know which ones are positive and which ones are negative.

And we ask a testing service to simply test them as they normally would on a normal client coming in through the door to see if they get the correct result. This is a great way for us to be able to understand if there's misdiagnosis happening or not. It's a really critical part of a quality management system. The next part obviously is then mounting an investigation and potentially corrective action to find out what it was that might have led to this misdiagnosis.

I alluded earlier to the fact that WHO recommends testing strategies. As I mentioned, you can't just rely on the result of one test alone to provide a definitive HIV diagnosis. Again, this slide is a little bit small; I tried to put the two strategies on the one slide. We have one strategy we recommend for high prevalence settings where the **[inaudible] [00:15:25]** prevalence is above 5 percent. And we have a second strategy for low prevalence. So this is when those results go back to the individual. So if you're even working in a surveillance setting but you know you're going to give your results back to the individual, this is the type of testing strategy you should use.

And as you can see here, we actually labeled the boxes as A1—that means Assay 1, Assay 2, Assay 3. We don't need to be so specific about which exact RDT it is; it's more about the statistical way in which we decide that these three tests in this order is adequate to help give an accurate diagnosis.

I've circled in orange the three times when unfortunately you cannot give a same-day diagnosis. This happens in very few people, but there are certain people where you would only be able to have inconclusive results for the first testing event. The high prevalence is individuals where assay 1 is reactive, Assay 2 is

nonreactive, and then Assay 3 is reactive. And this, in some settings, is called a positive result; what we call a tiebreaker result. It's not correct. You really should call that person HIV inconclusive, and ask them to return for testing in 14 days.

The specificity that the false positive rate of most ART is between 98 and 100 percent. That means we do expect that there will be some false positives. That's why we have three tests built in rather than just one.

And this is the low prevalence. It's where we see that the testing results don't come forward to all be the same. So we have Assay 1 reactive, Assay 2 reactive, but Assay 3 nonreactive. The other part of the algorithm—other strategies I'd like to point out is for those people who are identified as HIV positive but it is really critical to retest those individuals before they go onto ART. Sometimes it can be very difficult to understand the difference between retesting and repeat testing. Obviously, in English they can mean pretty much the same thing, and I'm sure when you translate them they can mean the same thing.

But for us, they actually have a very specific definition. When we say retesting, what we mean is to be retested on the exact, same testing algorithm so the exact, same test in the same order but on a different day, preferably at a different testing site by a different provider. The reason for retesting, the objective of retesting is to find an error.

An error in the way the test was performed, an error in the way the specimen was collected, the **[inaudible] [00:18:13]** was collected, potentially a transcription error. This would not control for when there is an algorithm that's used that is incorrect. So retesting is really to find simple errors and transcript errors happen much more often than we realize.

When we talk about repeat testing, this is for a very usual lab practice that when you get a result that you don't expect, like an HIV positive result, you repeat it just to double check that it is true and correct. So you'll notice that throughout the testing strategies we talk about repeating results when we see discordance. And so we're building many times little quality checks to make sure that

when we come to a final diagnosis where we're as confident about it as we can be.

In addition to these two approaches for diagnosing individuals, we are also working to expand the way in which testing can be conducted even further and further into the periphery. In some countries where laboratories have traditionally been the venue for testing, the test for triage approach has been something that has had quite some interest. And this is where performed either in a community or by lay provider, or even as self-test, and then the result of that allows that person to be triaged to the health facility for **[audio cuts out] [00:19:43]** to confirm their result. And this is the strategy I have here on the left of the slide.

You may also be aware that WHO has been working for quite some time now to review the evidence and to establish recommendations around HIV self-testing. HIV self-testing strategy also mirrors a little bit what we're thinking with test for triage. So these are ways that one can **[audio cuts out]** in the community testing with perhaps less proficient testers where you can at least get a signal that the person potentially is HIV positive, and then bring those people to the facility to have the additional testing to confirm their status. So we're always trying to find different modes to meet different needs in different settings.

I've already mentioned a little bit about this, so I can perhaps move around it very quickly that retesting, I mentioned a little bit on that side about testing **[inaudible]** about what is retesting.

But just to run through again, **[inaudible]** retested, which is the third bullet point on the bottom there. We talk about individuals who have an inconclusive status. So these are people who we think potentially might be undergoing seroconversion. Seroconversion in that first few months of HIV infections and might be positive on one test but negative on another test. So we do ask that those individuals to come back in 14 days for retesting.

We also ask obviously all of the newly diagnosed individuals to have to be retested, and of course anyone who's HIV-negative but remains ongoing we recommend to undergo retesting. **[Inaudible]** guidelines have quite a lot of specificity about who we

would recommend retesting.

So in terms of what is prequalification, WHO has spent quite a bit of time to **[inaudible]** to what is it that we do to assure test **[inaudible]**. **[Inaudible] [00:21:36]** prequalification is an assessment of the safety, performance and quality of HIV **[inaudible] [00:21:43]**. It's a bit similar to a regulatory approval and it is **[audio cuts out]** for procurement decision making. I'm not going to run in a lot of data out here because I know we're running out of time. But just to say that the prequalification process has three arms.

We have a dossier review section, we have a site inspection where we go onsite to the manufacturing facility, and we also do performance evaluation to evaluate the product. A product would have to meet all three of these components of prequalification to be considered prequalified and to therefore be eligible for UN procurement. So when I say UN, I mean **[inaudible]** procurement, UNICEF, UNSTA, UNDP and MSF.

[Inaudible] that another part of assuring test kit quality is the premarket assessment, the prequalification but also very much around the **[inaudible]** market aspect. So unfortunately, nothing stays the same over time no matter how much we try to. Tests can always be improved. Test production can be made cheaper. And so the kinds of tests are actually changed over time. So it's really important that you have in place a system for post-market surveillance to be able to understand when there is a problem with testing quality.

In the interest of time, I won't go over this in too much detail. You can perhaps re-read the slides later on. But we do have quite a large piece of guidance that the prequalification team has developed on post-market surveillance. We work with the manufacturers of the product and also with the regulators in your countries, and with you as the end users as program managers to be able to see this information **[inaudible] [00:23:27]** very simple labeling misinterpretation is very useful to be fed back to the manufacturer for them to be able to make changes until it is very clear and comprehensible.

This is my second to the last slide and I just sort of want to commission back and reiterate that the quality of testing has a continuum. Test kit quality is obviously very, very critical. We can obviously try to rule out products that are poorly designed and poorly manufactured. We would hope that prequalification or the National Regulatory review would be able to identify tests that don't meet those standards. Obviously there's always the test there could be a production defect, and obviously that's where having a good quality system or participating in proficiency testing, as well as the post-market surveillance allows you to then monitor the test kit quality.

And unfortunately, none of these tests are infallible; they do have certain storage conditions and they have very explicit instructions. So if the tests are not stored correctly, normally at 2 to 30, during transportation but even as well when they're in use. And if the test kit is not followed exactly correctly as per the instructions, they can be testing quality issues that can contribute to misdiagnoses.

I have exhausted my time and that's my last slide. We do have a mailing list that if you want to have more information about products that WHO and the activities that WHO is doing for test kit quality, you can sign up to our mailing list by emailing diagnostics@who.int. Thank you.

Cheryl:

Thank you, Anita and please continue adding your questions for Anita in the Q&A box for our discussion session. And the next presentation **[audio cuts out] [00:25:35]** Leslie Shanks of the Inner City Health Associates. Leslie was also previously with MSF, so I'm sure that should just be an acknowledgement to some of her really important work on misdiagnosis.

Leslie:

Thanks so much, and I have to say that I'm very excited to hear that this is going to be the topic of a webinar. This is, I think, an extremely important topic as has already been outlined. But it's often a deeply unpopular topic. So I think there's just so much work to be done in getting the message out that this is an issue that it doesn't need to stop all of the important efforts to scale up and to get people tested. But instead, that we need just to include the crack in getting to the 90 target.

I'm going to speak about my experience working with MSF Operational Center Amsterdam and the journey that we took as we discovered there was a problem with misdiagnosis in our program. And this takes us back some time. It was the early days of our treatment programs to address HIV in the early 2000s and we started to hear rumors from various countries that there were patients being included in our programs who did not have HIV.

I'm going to take you to the story of Bukavu, which was an HIV project that we were running in the Democratic Republic of Congo in the time period of 2000 and 2005. This was a time that I was on the ground that I first came face to face with people who had been misdiagnosed and could actually see the consequences that this had for individuals impacted. This project that we had was the first to start addressing HIV in the area.

We were the first to start ARV. So it was very early days. We noticed as we were testing people and when we introduced our CD4 machine that there were some people whose CD4 counts remained stable or were actually quite high. So some of these were retested and found to be falsely positive.

The impact of this news that we had people in our program who did not have HIV at a time when the stigma was incredibly high in the community really had a major impact on our program team in the field, and also all the way through headquarters. We felt that our labs were, for the most part, well managed. We were doing quality control were in place. They were being monitored. We had training and supervision. We were doing all of the tests in front of the client. And that, of course, eliminated the opportunity of administrative errors.

Finally, we were also retesting everyone who was coming to our program who had been tested elsewhere. So we couldn't figure out what was going on. We looked at our test kits and our agents. We looked at all of our test procedures. And we did detect some supervision and testing problems, and we worked to improve those and tighten them up. We also introduced retesting or repeat testing, sorry, of all our VCT positives and all of the discordant or discrepant test by the laboratory, because remember the tests were being done in front of the client. Some samples were sent to

the lab to just make sure that the quality of the testing hadn't been an error in that testing.

However, we recognized that the problem was still going on. So we decided to introduce a confirmatory algorithm. This was very similar to what the testing algorithms that were done in non resource limited settings. So we looked at introducing a Western blot and then we also tried serological confirmation test which was possible to do at a level 2 lab. So it was feasible for field use. I'm not going to spend much time on this test because it's just recently been discontinued.

So we followed all of our clients who had been tested over a period of time, and we accumulated almost 3,000 samples. Out of those, there were 229 who were positive on a serial algorithm for Determine/Unigold positive. And then we put them all through a Western blot. And we found quite astoundingly that over 10 percent—10.5 percent—were either Western blot negative or indeterminate.

One of the other things we realized when we did this analysis was the importance of the strength of the test line. Our staff noticed that some of the test lines were weaker than the control line, as you can see here on the left picture. They felt there was potentially a relationship with the false positive results. So here we see that all the results with one or more weak positive lines were false positive.

However, I think it's also important to say that even when we eliminated all the weakly reactive test lines, there was still a number who had double RDT positives or algorithm positives who were false positives.

So this brings us to the issue of cross reactivity, which I think many of you are familiar. But for those who are not, we're really talking about where an antibody will bind to an antigen that differs from its originator antigen. So instead of a malaria antibody binding to a [audio cuts out] [00:32:35] ...so instead of a malaria body binding to an HIV antigen—it binds to an HIV antigen. But there's also postulated [inaudible] [0032:47] broad spectrum antibody response to infection, whereby you get these nonspecific binding

of antibodies to the test antigen. So here you can't correlate it specifically, for example, with people with malaria are more likely to have false positive tests if you're looking at this mechanism.

So recognizing that this was all going on in our program, we rolled out some new policies based on this experience in Bukavu that I've just been outlining for you. This was really to strengthen all the aspects of our testing service that all of the tests would be repeated in the lab when they were done in EDCT, that we were going to introduce a confirmation test for the algorithm. And then we also looked at retesting the cohorts who had been tested before and diagnosed before we'd introduced these changes.

So this is some of the data of that experience of introducing the confirmatory test to the algorithm and looking at retesting. And there are two things I wanted to highlight here. One is experience in Zambia. When we looked at that, there were 19 cases of false positives that we identified on the retesting. And these were very simply due to administrative errors. It was simply a question of that the individuals were not tested. They were tested at the lab rather than by the counselors themselves. And these were labeling errors on the tube or transcription errors. So very simple errors that had resulted in 19 people being included in the HIV program who did not have HIV.

The other thing I wanted to highlight here is that we were able to retest. And you can see in Ethiopia, we retested those who were already in our program in Burundi; we did this in Bukavu. And we were able to do this successfully without undermining our program or impacting on the uptake to our testing program. Because this of course was the great fear; that we were going to have a negative impact on our scale-up efforts by doing this retesting. And in fact we found that did not happen.

I also want to mention the issue that Anita mentioned on the tiebreaker algorithm. And this was not an issue in the MSF programs that I'm describing for you now because we were not using the tiebreaker algorithm. But many of the countries that we worked in, that is the national algorithm. We looked at evaluating HIV algorithms in Ethiopia, together with our Ethiopian partners. And we found, in fact, what we knew which was that the tiebreaker

algorithm did not perform well and here was a 7.3 percent false positive rate on the tiebreaker.

The other thing I want to highlight from this is that we looked at fully a three-test algorithm. When you looked at the serial algorithm, in this case it was KHB and **stat pack**; they actually performed fairly well. There was only one false positive in that group. But then when we switched the order of the tests and had KHB and Unigold as the second test instead of stat pack, then we were up to again 16 false positive tests. So the importance in the order of the tests in choosing your tests appropriately is really highlighted in this work. We also found that all of the false positives had at least one falsely reactive—a weakly reactive test.

The other thing I want to talk to you about is the variability in test performance that we found in our projects. We were very often doing parallel testing and we were monitoring in all of our projects the discordance or discrepancy rate between those two tests. And we noticed huge variability. So it wasn't always that one test Assay 1 was positive and Assay 2 was negative; this was actually change over time.

We asked a modeler to come in and to look at what all of this data could tell us. And I won't go into the details of the modeling, and this is written up in the paper we wrote about it. But we ended up looking at 51 test centers in ten countries with seven different RDTs. And we were able to show through this modeling that the specificity was varying by location of the test center, and that was both within and between different countries. Also I think very importantly, and something that needs to be looked at further is that the specificity varied over time within a particular location.

And finally, that these variations were not confined to a single test. So I think this really highlights some of the challenges we have using RDTs in an algorithm to diagnose HIV.

I want to finish by talking about the consequences of the false positives, because I think this is what really spurs us on to make the changes that are needed to improve our testing programs to improve the accuracy of them. Across our programs we heard many stories of abandonment, of divorce, of violence when people

were diagnosed as HIV positive.

We had people who were diagnosed as HIV who were peer support workers, very prominent in the community, took great courage **[inaudible] [00:39:25]** that time as HIV positive. And then we were faced with telling them that actually there had been a misdiagnosis and they did not have HIV. One woman had been divorced when she was diagnosed with HIV. She had remarried someone HIV positive and then found out that she was HIV negative. These are not uncommon stories.

There was also, of course, exposure to unnecessary medications, particularly ARVs but also **coltree** as well, women who stopped breastfeeding because they thought they were positive. I think for the program, there was also this sense of loss of faith in the testing. We were always amazed that the community knew what was going on. They knew that there were false positives; they knew there were concerns. They were going around to different test centers that were giving different tests.

This was really an issue that we found we needed to just confront head on by making the changes in our program and being clear about the chance, however small it was, that the initial test was not positive. I think there were also myths of cure, and really from our program perspective, this is something we weren't able to quantify. But this misuse of scarce resources have people in your program who don't have HIV.

I want to just finish up by going through the conclusions that really comes from our experience of facing this in the field. We clearly, as Bonita has highlighted, there are many issues linked to misdiagnosis. We know that quality assurance programs are really key to improving performance. It's absolutely vital that the tiebreaker algorithms are abandoned and the WHO-adopted algorithms are taken onboard. I think this is something that is really impacting and causing a lot of misdiagnosis right now.

The issue of cross reactivity is a challenge; it's going to remain a challenge for us and we need to be aware of that. But the bottom line is that it is possible to dramatically reduce the risk of misdiagnosis out there. And I think the cost of not doing so is not

addressing this problem and allowing it to remain hidden are just too great for us to not face this head-on. Thank you.

Male Speaker: Thank you, Leslie for the concise and sobering summary of the data. It's interesting and I encourage everybody to enter their questions on this and on Anita's and on the other presentations down on the lower right hand side. And just one correction; **[inaudible] [00:42:29]** Dacombe will be presenting on HIV self-testing quality, rather than on regulatory structure. So please stay tuned for that.

So we're going to move on to a talk from Dr. Khumbo Ng'ona from the Ministry of Health Malawi and I'll turn it over to him to take it away, so please, Dr. Ng'ona.

Dr. Ng'ona: Thank you very much. Can you hear me?

Cheryl: Yes, we can hear you.

Dr. Ng'ona: Thank you so much. My name is Khumbo, as already alluded, from the Ministry of Health Malawi. I work as the HIV Testing Services Officer within the Department of HIV **[inaudible]**. The topic that I'll be speaking on today is on the misdiagnosis of HIV status in Malawi experience. Basically what we've actually gone through in terms of HIV testing as a program from the time that we had the program, we've already shown up-to-date what were the issues and all that was involved in terms of HIV diagnosis.

So in terms of the presentation, I'll actually do a bit of introduction on what actually transpired in the program **[inaudible]** and also a bit of a background on that, and some of the misdiagnosis reports that we actually captured from the field. And also, some of the factors that we observed to be part of the contributing issues on the misdiagnosis. And also, some of the lessons learned from the program evaluation and from **[inaudible] [00:44:08]** itself and some of the reports, and also on the way forward; what steps as a country, as a program we have incorporated in our policy; so I'll share on that.

So Malawi as a country, we have a population of 17.4 million people. And as of now, we have approximately 1 million people who are living with HIV. And if you look at the trend, it's actually a bit of stable since 1995 **[audio cuts out] [inaudible]** up to 2015.

So we also adopted the UN **[audio cuts out]** and it's hoped that by **[audio cuts out]** we should be able to reach the 1990 targets. And that by 2030, we should be able to have an HIV-free generation.

So as a background, Malawi as HIV testing services, we started doing the rapid testing in 2000. **[Inaudible]** which is the Malawi **[inaudible]**. So after that, we adopted whole blood rapid testing. So in 2004, that's when we had a massive increase in HIV rapid testing. **[Inaudible]** And in terms of sites, we started very **[audio cuts out]** and as of **[inaudible]** 2015 we had **[inaudible]** 847 **[inaudible]** sites, and one **[inaudible]** **[00:45:47]**. And to date, more than 5.5 million people have been tested since the introduction **[inaudible]** in July, 2004. And you can see from the data that we've already tested a lot of people. We've increased the access and the scale-up in terms of HIV testing.

And for the provider testers who have been trained, **[audio cuts out]** we've actually task shifted **[inaudible]** HSAs and **[inaudible]**. And out of these 5,000, most of them are the **[audio cuts out]** providers, who are the HSAs and HDAs. So **[inaudible]** HIV—the **[inaudible]** assistance and the HDAs **[inaudible]** system. And all of them are non-health provisions. But out of the 5,000 some of **[audio cuts out]** **[inaudible]** the doctors. **[Audio cuts out]** **[inaudible]**.

[Audio cuts out] **[00:46:55]**. So we visited six sites, or six facilities including the central hospitals, district hospitals and some health centers. So if you look at the sites of just actually A, B up to F, I did actually want to include the action **[inaudible]**. But if you look at the numbers, we actually **[inaudible]** to F. If you go to—we tested—like for D, **[audio cuts out]** **[inaudible]**. And those who tested positive on **[inaudible]**. And if you look at those where **[inaudible]** it was actually 215, meaning that out of the 258 who **[audio cuts out]** **[inaudible]** eight actually came up to be distance.

So if you look at H, which is 3.1 percent, it's actually on a bit of a higher find, looking at the ratio of discordant. The same with E and F. And for F and E, actually, it be tied with 25 percent, which is actually the most high out of all of those that are listed here. So

this actually alarmed us as a program to say what is actually happening; why all these discordant results? And at that point, we were using **[inaudible] [00:48:22]** tiebreaker.

So if you at those that were given negative results, out of those that came accordant, **[audio cuts out] [inaudible]** percent it was actually all of them were **[inaudible]** results **[audio cuts out]** 100 percent. So those are just some of the findings that we observed from the field.

Some of the issues, as well, that we identified with misdiagnosis were the issues of **[inaudible]**. We observed that most of the **[inaudible]** were incomplete. If you look at in terms of the test gives details, the load numbers and the like, they were actually missing. And the most important issues that you would want to capture when a client comes to you for **[inaudible]**, most of them were **[inaudible]**.

The other issue **[audio cuts out] [inaudible]**. I'll give an example. For example, **[audio cuts out]** of five providers. And out of the five, all of them for example **[audio cuts out]** 80 percent and they would actually fill the same finding. In Malawi we give the five **[inaudible]**. So just for example, **[audio cuts out]**. So it was actually showing that all the counselors we—depending on one person to **[audio cuts out]** all of them were actually calling from individual. And it was an individual-based **[inaudible]** is also what we observed.

Another organization **[inaudible]** and you may know this facility. If you look at the picture below, you see that there were a lot of clients which were taking the evaluation. A lot of **[inaudible]** but you have two providers and maybe just one room **[audio cuts out]** looking at an eight-hour shift, that that individual has **[inaudible]** all of these clients. And as a result, it resorted to contesting where they would do a couple of tests at the same time. They would just collect blood **[audio cuts out]** as you can see on the picture, and sample parts. The test **[inaudible] [00:50:30]**.

So it was actually difficult if you **[audio cuts out]** or maybe the wind has blown them. The test **[inaudible]** you come back and

someone has mixed up this. You wouldn't actually know which one belongs to which one. Because if you look at the picture, it actually **[audio cuts out] [00:50:49]**. So that was some of the issues we observed **[inaudible]**.

[Inaudible] there was also more stories of the test **[inaudible]**. If you can look at the picture, you **[inaudible]** but the way they've been placed in the waiting area, they've actually not been separated and they are not in the **[inaudible]**. And if you look closely, you'll see that they've actually placed samples on those determining strips. So there were **[inaudible]** tests without separating the strips. This was also one of the contributing factors to the diagnosis. Like Leslie pointed out there is a cross-reactivity and there are issues of cross contamination. These were just some of the issues we observed.

And in terms of interpretation of the results, like for the same lines, it was actually difficult for others to integrate when we're faced with such **[inaudible] [00:51:47]** lines. The other observation was that the providers **[audio cuts out] [inaudible]** whatever discovered, whatever they thought the results were without sometimes actually doing the actual test. For example, when they get **[inaudible]** results, they just assume maybe this one is **[inaudible]** positive and just **[inaudible] [audio cuts out]** go back and do the test—repeat the test so that they get the actual result. So these are just some of the issues that we observed from the field.

And out of the **[audio cuts out]** that we had, we also learned some lessons which were very helpful for the program. The first lesson that we learned was that the massive expression **[inaudible]** actually a significant accomplishment. But **[audio cuts out]** compromises use of quality. You know, and programs sometimes just focus on getting the numbers, getting people **[inaudible]** people accessing the services, reaching them everywhere **[audio cuts out] [inaudible]**. But the aspect of quality is actually overlooked most of the time. So this was one of the lessons that we learned.

And another organization was in terms of the screening. As a program at that point, we were using **[inaudible]** of the first test, Unigold test and then byline of the **[inaudible]**. And if you look at the time our providers spent with clients, it would be more than an hour. And if you look at the numbers **[inaudible]** for testing **[inaudible]**.

So the other **[audio cuts out]** either we could have a screening test, like maybe one or two with less **[audio cuts out] [inaudible] [00:53:35]** so that we actually saved a lot of clients without compromising the quality. Another aspect that we learned was **[audio cuts out]** we must and that will be done by a different tester. And as of now, this is what we **[inaudible]** as a country. It's part of the HTS guidelines of the policy.

If one is tested positive, another provider has to come in to do a **[inaudible]**. The initial arrangement, the confirmatory should be done at the clinic. But the issue of space, and you know the **[inaudible]** were built a long time before we actually thought of HIV and AIDS. So there's that challenge of space. And now the policy is that the confirmatory has to be done at the HDS room by a different tester.

And conveyor belt testing, we also observed that it actually comprised testing quality, and that it has to be stopped. And it's actually clear in our policy that providers are not supposed to be doing conveyor belt testing.

As a way forward, looking at the reports that we got from the field and from the whole analysis of the data from the evaluation, as a program we took a step of retraining all of the testers. So I'm talking about all the site **[inaudible][00:54:56]** testers who were there, including the trainers. And if you talk with the trainers **[audio cuts out]** as well as the **[inaudible]** trainers. And the curriculum which was developed, which was called the skills intensive training curriculum, it was indeed intensive and it was actually for three **[inaudible]**. And it was interesting to see that all the trainers, even the lab trainers, would actually fail the skills intensive training.

So this was a **[audio cuts out]** to say maybe the people we

entrusted were not capable of doing the test and actually training others. And the passing mark for the skills intensive training was 80 percent for **[inaudible]** and 100 percent for **[inaudible]**. **[Inaudible]** the PT part of it. And it was actually interesting to see that most of the trainers actually failed the skills intensive training.

But for the writers, the score for the **[inaudible]** was **[inaudible]** to 70 percent. As I mentioned, most of the providers are lay providers; they are not health personnel. So the passing mark was reduced to 70 percent. We didn't want to go below 70 percent because as a program, we felt that it actually compromised the quality. But at least at 70 percent, we were at least sure that we would get people of high quality.

This **[audio cuts out] [00:56:21]** revised 2016 HTS guidelines. We are actually strengthening the compliance by doing the dissemination meeting. And since we devised the 2016 guidelines, we shall be in line with the WHO guidelines, the **[inaudible]** 90-90-90 target, our own **[inaudible]** structure plan.

The program we also revised the training for new providers as well as the supervisor curriculum, which we're actually using as of now. And also we strengthened the supervision and mentorship, both at national level, **[inaudible]** level and at facility level. **[Audio cuts out]** we are continuing to implement the PT at least twice a year, and the emphasis is on individualized PT panels. We also changed the testing algorithm following the evaluation. We **[inaudible]** **[00:57:11]**...

[Crosstalk]

Female Speaker: It sounds like you're starting to cut out a little bit.

Dr. Ng'ona: For the tiebreaker, we are using both Determine and Unigold in parallel. We removed the **bioline** to the algorithm. Can you hear me?

Male Speaker: Yes.

Female Speaker: Yes, we can hear you now.

Male Speaker: Yes, loud and clear.

Dr. Ng'ona: Alright, thank you. The issue of having a lot of clients coming overcrowding the facilities and the HT sites, we thought of coming

up with a group retest education effort where the high volume sites would actually do the group retests. And then shortening the time for the one-to-one discussions at the testing so that we could actually capture more clients without compromising the quality. And also the strict monitoring of the **[inaudible] [00:58:12]** from all sites.

And our HTS **[inaudible]** as incorporated a column where a **[audio cuts out]** is supposed to confine effective **[inaudible]** and if the results are actually in line with what the QC was supposed to reform. And if there are any other errors, corrective actions are taken with the immediate supervisors as well as the national **[inaudible]**. We revise data over time to see the performance and where we are as of now, just rule out all errors in terms of the quality controls.

[Audio cuts out] [00:58:44] to the DTS for both PT and QC **[inaudible]** but now we just do DTS and as of now, the PT and the QC, we actually perform a bit better than we used to before the evaluation. And also issues of data analysis we got from the field, we actually are not waiting for evaluation. But as a program, we are doing it periodically and **[inaudible]** the data and looking at the issues **[inaudible]** misdiagnosis that come from our team.

So the strict monitoring of the turnaround time for the PT scores. So in terms of the PT, those were all less than 100 percent, a great deduction is supposed to be taken. **[Audio cuts out][00:59:28]** fail for two consecutive quarters, the failed PT less than 80 percent, they're supposed to stop practicing until they undergo a **[inaudible]**. That's how we've actually structured our policy following the evaluation that we had. Over to Vincent to continue with the rest of the program. Thank you.

Vincent:

Thank you, Dr. Ng'ona for the presentation. So we're going to turn it over to our last speaker, Russell Dacombe from the Liverpool School of Clinical Medicine. He is going to speak to HIV self-testing and potential for misdiagnosis. And then we'll get into a brief period of questions so put in your questions if you have them. We'll get to as many as possible. Take it away.

Russell:

Thank you very much indeed. Sorry for any confusion. My job role

is part of the startup which is involved with stimulating the market for HIV self-testing. And I'm involved in the regulation of HIV self-testing, so hopefully I'll manage to cover a bit of both in this presentation. So first of all, I just wanted to give a definition of HIV self-testing and some of the complexities around the different models.

The definition for HIV self-testing is the person takes the specimen, performs and interprets their own test in private. Though the definition **[audio cuts out]** quite a bit between the different models **[inaudible] [01:01:00]**. Also, it's worth **[inaudible]** in some models the individual will be responsible for storing their own for some periods of time. That's also an issue that needs looking at. As Anita said in her presentation, it should be used as a screening test. And it's also worth noting that HIV self-testing, one of its objectives is to reach those who wouldn't normally do HIV testing, or don't normally access testing. So it's worth bearing that in mind; **[audio cuts out]** adolescents and men in many countries.

We may think of misdiagnosis, would we get them or wouldn't we get them? Anyway. So as I said, there's a number of different models for providing HIV self-testing. I'll just go through them in a bit of detail because it's worth knowing there's some depth to understanding the different issues in misdiagnosing HIV or potential misdiagnosis.

So the continuum of HIV self-testing is here in this slide, taken from the WHO guidelines on testing. So the top is supervised. So I talked a little bit about how private I private. So in the supervised self-testing line, you have community health workers or people in the facility providing a degree of supervision to the person who is conducting the test. They would keep their results private but they would have a degree of support on the conduct of the test.

When we're looking at unsupervised self-testing, again community-based workers and clinics can also distribute the test to people they're able to access. But there their role ends and it's up to the individual to carry out their test correctly and interpret their result correctly. And this also includes another **[audio cuts out] [01:03:03]** not possible with supervised HIV self-testing,

which is completely open access so the ability to get the test over the counter at pharmacies, such as you would do something like a pregnancy **[audio cuts out]**.

So a lot of **[audio cuts out]** for misdiagnosis in HIV self-testing. The test characteristics, which some detail **[audio cuts out]** also play a part within HIV self-testing. So I won't go into too much detail on them because they've already been covered. And then the test **[audio cuts out]** individuals on ART. Obviously, the window period plays a significant part, as well. But possibly also there's some evidence that literacy levels may also play a role in allowing the person to use and interpret the test correctly. So these could link correct performance test or incorrect interpretation.

So test characteristics, as Anita has already said, all the tests are sensitive. Evidence around RDTs, less sensitive in those on ART and generation of kit will determine window; the earlier generation, the longer the window. And I'm glad that me and Anita agree on that, so that's good.

So I'm just going to speak a little bit around the accuracy of HIV self-testing in intended users and the individuals using it. I'm going to use **[inaudible] [01:04:31]** presentation that was given **[audio cuts out]** by Cheryl **[inaudible]** colleagues and herself, **[inaudible]** Carmen Figueroa. Just to give you an idea, because there are 18 studies included in a literary review looking at accuracy of self-testing.

The majority **[audio cuts out]** were oral fluid, a minority were blood, and one was both. Specificity was pretty good across both oral and blood-based tests. Lowest 94 **[audio cuts out]** was in the upper regions.

So the issue of sensitivity was different as you went back to some degree between the oral fluid and the blood-based test, with the blood-based test coming out much higher in the mid high 90s. but quite a range on the oral tests; more so than you would expect just from variations in the kit. So seeing the information that Cheryl and Carmen and their colleagues extracted from the papers that they reviewed, and apologies this is a little bit small. So I'm

just going to say that the line that you probably can't read **[inaudible][01:05:49]** encompassed a majority of the test is the oral based test, and the little one encompassing three tests at the bottom is the one for the blood-based test.

But we see here that there is a number of tests that actually the sensitivity for the oral test is actually pretty good. And this may well be to do with the model of testing that was used and the population that was tested. So if you look at the third and fourth ones down **[inaudible]**, which was done in Zimbabwe, I believe, with a supervised model but there's quite a great difference between the sensitivity **[audio cuts out]** in the rural based population. But it is worth noting that huge variation on the confidence interval if you look at the **[inaudible]** to the right as well as the numbers.

If you look then at the Marley paper that I believe was done in China, you can see there that there is again a lower **[inaudible]** and this was done unsupervised in an urban environment. And if you look at the Choko studies, which was done in Malawi with quite a high level of sensitivity and specificity, these were supervised. And again, you can see in the Asilmwe studies from Uganda that there is a slight variation in sensitivity between the urban and the rural.

So I guess what I'm saying by this is there's a fair bit to kind of pick apart on the impact of different models of delivering HIV self-testing is in terms of potential for misdiagnosis. So I just want to share some of the experiences that people have on the star project and some of the experiences that came through those papers. So there's a number of performance errors that have been documented, issues around packaging, issues around the specimen collection, especially it seemed to be from blood-based test; spilling of buffer, the reading of the time, and indeed the instructions for use themselves, which are obviously pretty critical.

There's also issues around interpretation errors. Again I've stressed that a lower education level may be associated with the misinterpretation. But also there's been a slightly higher number of invalids associated with the blood-based compared to the oral tests.

So moving quickly on, just to show you some examples and I'd like to thank my colleague, Moses Kumwenda in Malawi for giving these pictorial examples and just to say that we're using OraQuick for all the studies at the moment, so we're not singling out OraQuick particular; it's just the ones we have pictures of. So you can see that many people recognize the little nick in the package, which is where you would normally tear it if you use these things. But this participant is using a much more old school method of ripping the packaging with their teeth, which potentially could be quite a painful experience.

Opening the tube, again no demonstration on how to open the tube means that people try and pull the tube off by the top, which again could lead to potential spillage of buffer. And particular issues around putting the tube in the stand. So you put the tube in the stand to then put the swab from the **[inaudible] [01:09:26]** in the kit into the buffer. If it's put in at 90 degrees, it can tip over and you can spill everything all over the place. And the stand itself, which is designed with cost as well as efficiency in mind, again because it has to in an L angle, a lot of people try and put it in at 90 degrees or turn it upside down, and again that can lead to overbalancing, spillage, and so on.

And as we go out to the performance/interpretation of errors, this is again from the **Icosa** presentation and this is—just to let you know this is across ten studies in which interpretation errors were documented. You can see there's a fair spread base across supervised and unsupervised, and this is actually the number of papers that it was reported in, rather than the number of errors. People seem to generally read or follow instructions for use but there was lots of issues around collection, use of buffer, and interpreting of the results.

Just one last piece of information on literacy level, this is from a study that happened in Zimbabwe that's available on the HIVselftesting.org website. Again, they looked at urban and rural populations and they did a bit of work looking into the reasons why. In the urban environment, the false positive and false negative results were due to anti-retroviral treatment and incorrect transcription; the **[inaudible] [01:11:05]** wrote the wrong

thing on the form but thought they were negative. So those were very kind of unavoidable errors in some respects.

And the rural ones, they were much more around interpretation and performance. So that's for that.

So how would we mitigate these kind of amplified risks around HIV self-testing? So obviously clear messaging is very important. People really need to know that if you're on ART, you could get a negative result but it doesn't mean you're cured, and this is obviously a very critical message to get across. The window period is important because it will vary between generations of tests used. And very clear that it's the screening test. Obviously, anxiety around getting a positive—or a reactive result on a screening test is not great, but it's—obviously if you then assume that you're positive, that's really not good.

Obviously because certainly the unsupervised models, it's all really about the instructions for use. They need to be very well designed, and they need to go through a good process of refining to make sure that they are applicable to the context in which they're going to be used. Some studies **[audio cuts out] [01:12:29]** videos, and obviously with the supervised model and in some respects the unsupervised model distributed by health workers, you can add a demonstration step to that.

As Anita and others have said in their presentations, monitoring through quality assurance is important. But there may be some issues around doing that related to HIV self-testing. And obviously, the retesting using the national algorithm to detect false positives is very important.

So a little bit quickly around monitoring HIV test accuracy, monitoring it pre-market before it's distributed is fine. It would be the same registration regulatory approvals, and the same quality control as test lots that's already in place for RDTs. Obviously, there will be a different need for regulatory approval based on the fact that they're self tests. But if the system is in place, the system is in place. Post-market is more of a difference. Unfortunately, my color coding here didn't work too well; I was hoping for a kind of amber and red kind of look.

But cool chain, as has been mentioned before, is an issue and particularly when it comes out of the hand of the health system; how do you monitor that in individual **[inaudible] [01:13:49]** and individuals.

Panel testing, obviously sending panels out to people who are self-testing has a great degree of problems. Blinded rechecking may potentially be a model, and I'll talk about that in the next and almost last slide. And supervision is a problem in an unsupervised model because by definition, you're not supervising people.

So obviously rechecking interpretation, and the critical thing is kits need to be stable beyond their official read time. So a small number of studies have looked at this and there seems to be some variation between these studies but some used the interpretation of the readers, which may have its own issues and some actually used lab-based confirmation. It needs some more work to see if this would work.

So in summary, HIV self-testing aims to target those who otherwise would not test so it's important to bear that in mind. It may result in a lower sensitivity. You need clear messaging and clear IFUs. False negatives for those on ART are probably of great concern. And false positives should be picked up by confirmatory testing. And EQA is challenging; traditional methods will need to be adapted and tested.

Now I think I've just managed it within my 15 minutes so I'm going to hand it back to the moderators.

Female Speaker: Excellent. Thank you so much, Russell, and for the excellent **[audio cuts out]**. We are now going to take time for discussion so please have your questions for our presenters in the Q&A box. We will try to get to as many questions in the time we have remaining, so let's go to our first question.

[Crosstalk]

Male Speaker: I'm going to package up two of them. The first is from—and these are both directed to Malawi and the specific question for Dr. Ng'ona. The first comes from **Milesh [inaudible]** and she was asking about post-marketing evaluation of your test kits, and once the test kits are shipped from a manufacturer and enter the

country, what sorts of activities or interventions do you have around post-marketing evaluations of kits? And then related to that, Malawi is really an early implementer of retesting for verification prior to ART initiation.

One of the concerns that a number of us here have round that relate to a question from **Shal Kakan**, who's asking about how is that best implemented in the era of tests and starts, and how are we not introducing a barrier to treatment that people are initiating on the same day and need to be retested to verify their status and their diagnosis in Malawi?

Dr. Ng'ona:

Alright, thank you very much for the questions. Let me start by responding to the first one on the pre- and post-shipment evaluation of the test kits. Malawi as a country, in terms of the evaluation of the test kits, this is done by the national HIV **Reference** Lab. So whenever we have a shipment of test kits, the National HIV Reference Lab will actually do the evaluation of the test kits before they are distributed to all of the testing sites. Apart from that, I've also talk to the EQA, the PT, the QC and the post-market **[inaudible]** **[01:17:34]** as well that is also done.

For the confirmatory testing and the issue of **[inaudible]** that Malawi we are also implementing the retesting, which is the confirmatory testing. As I mentioned already, the initial plan was that the confirmatory test should be conducted at the ART site, where the ART initiation is done. Unfortunately, most of our ART facilities do not have space for HIV testing services. So the confirmatory test, whenever a client comes to the ART clinic and they have no documentation for the confirmatory test, that client is actually sent back to the HDS testing room for a confirmatory test.

If you look at the test **[inaudible]** and the way we provide ART in Malawi, it is not a day-to-day activity into ART. As I mentioned, the issue of space; for some sites ART initiation is done maybe twice a week or three times a week. So for example, if they come in on Monday and the ART clinic will be on Wednesday or Thursday. So when that client comes for the initiation, that's when the confirmatory test would actually be done. And in some facilities where we have more than two or three providers, the confirmatory

test is absolutely done on the very same day, for example, on the days where the initiation is actually taking place.

So after someone has tested positive, if another provider is available to do the confirmatory, they would actually do the confirmatory so that we do not deny them the access to ART.

As much as we are saying that doing the test **[inaudible]** **[01:19:25]** but the clients are also given some time to actually deflect and digest and make a decision to say I really want to start ART, and they need to undergo **[inaudible]** education; the whole process before they actually start ART. So basically that's how we are doing the test and such. And we instruct all the ART providers to say if someone comes with all the confirmatory test results documented, do not initiate ART. We have to send them back to the HDS room for confirmatory test. Thank you.

Vincent: Thank you, Dr. Ng'ona. Cheryl, did you want to chime in with a question?

[No Audio]

[01:21:03]

[01:27:08]

Vincent: Great. Thanks so much, Anita, for as always a very thorough response to the questions. We are out of time. I apologize. There's a survey up so please enter that to say whether or not this helps you in your work. We have a range of questions that are still up, and we intend to organize answers to those from the speakers. We'll post those to the community of practice, which **HP** should send a link to.

We'll try to get all the questions answered in some form or another so we address things. I know there were a lot of questions on self-testing and linkage. There was a webinar a few months ago on self-testing. Some of those questions might be answered by going and looking back at that webinar, but we'll try to provide some references to that, as well.

So in ending, we covered a lot of ground. There are policy issues and health systems issues around procurement, post-marketing surveillance, the algorithms. I had algorithm questions for

everybody, as well. There are implementation issues and factors that we control and others, like cross-reactive antibodies where we have less control and those need to be considered in any diagnostic process. And we've got emerging approaches like HIV self-testing, but needs for quality testing and test and start and those factors and approaches and issues need to be considered in how we're moving forward. And there are a lot of things we're doing well at, and other areas where we need more attention and work.

So I'd like to thank the speakers. I'd like to thank my colleague, Cheryl Johnson at WHO for helping co-moderate this session, and to AIDSFree for doing a fantastic job organizing and providing the logistic support to let this happen. So thank you, everybody. I'm just recollecting, Cheryl, did you want to mention—there is a misdiagnosis supplement **[inaudible] [01:29:02]** planning and we might not have mentioned that. But Cheryl, do you want to say a word about that before we close?

[No Audio]

[01:29:13]

Male Speaker: Great. Thanks so much and thanks everybody again for joining, and we will all be in touch. Bye-bye.

[End of Audio]

Duration: 91 minutes