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TRANSFUSION MEDICINE

**Podcast Transcript:**
**A Conversation on the Background and Implementation of Resolving Discrepant NAT Testing Results**
**by Sam Rose, PhD & Nico Lelie, PhD**
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**Shawn:** Hello and welcome to the Grifols Academy of Transfusion Medicine podcast series. My name is Shawn Leonard. I am the Senior Manager of Global Education and Medical Affairs.

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This podcast is titled, "A Conversation on the Background and Implementation of Resolving Discrepant NAT Testing Results." Our host speaker today is Sam Rose, PhD, and is joined by our guest speaker Nico Lelie, PhD.

Dr. Sam Rose is a medical biochemist with extensive technical knowledge and experience in the interface of molecular diagnostic and pharmaceutical science. He has experience in both diagnostic and pharmaceutical research, as well as commercial medical device and pharmaceutical operations environment. He has 33 years of research and medical affairs experience in commercial in vitro diagnostics, focusing on molecular testing technology using signal or target amplification technologies and 20 issued US patents in nucleic acid detection technologies. Dr. Rose is currently Director of Medical Affairs Donor Screening and is responsible for medical affairs support of global business for Grifols blood donor screening assays and instrumentation.

Dr. Nico Lelie is an internationally recognized expert in transfusion science whose career has been focused on innovation and quality regarding donor screening technology for infectious agents. He received his PhD in 1989 at the University of Amsterdam studying a heat-inactivated hepatitis B vaccine. Dr. Lelie was initially employed at what is now the Sanquin Blood Supply Foundation in the Netherlands, where he was head of the Viral Diagnostic Laboratory supporting WHO Collaborative Studies and International Proficiency Program for Viral Serology and NAT Laboratories in the early days of NAT. He

has been a member of the WHO Expert Committee of Biological Standardization and other expert groups for advice and regulatory management of technical diagnostic and donor screening assays. At the time of introduction of the first automated NAT screening systems, Dr. Lelie was Scientific Affairs Director of Chiron, supporting blood centers in several countries with NAT evaluation studies. Since 2010, he is working as a consultant and more recently, in 2017, he became CEO of Biologicals Quality Control, a company providing external controls and reference panels for validation of blood screening assays. He is author or coauthor of almost 200 peer-reviewed scientific publications.

Thank you, Dr. Rose and Dr. Lelie, for joining today.

**Sam:** Thanks very much, Shawn, for the kind introduction. And I think the first thing that I have to do is mention disclosures. The opinions expressed on this episode are those of my guest and I alone and do not reflect those of the organizations with which either of us is affiliated. And regarding financial disclosures, Dr. Lelie is being compensated for this educational podcast, and I am an employee of Grifols Diagnostic Solutions, Inc.

So hello, everyone again, and good afternoon, Dr. Lelie. And I guess my first question for you is, can I call you Nico?

**Nico:** Yes, please do, Sam.

**Sam:** It feels a bit awkward to do otherwise. We've known each other for so many years. Thanks for joining me, Nico, in a conversation on a subject that interests many people in the blood bank and donor testing industry, especially those that are new to nucleic acid technology, or NAT, testing. The topic of how to resolve test result discrepancies is of fundamental importance to him, and being in medical affairs, it's a question that gets elevated to us almost several times a year, especially from people who are new adopters to the technology. Let me first define, before we get into our conversation, the kind of testing that we're going to be talking about today. We're going to be trying to talk about how people resolve discrepant or unexpected test results. One type of discrepant result that can happen is a reactive or positive result on a NAT screening test, but a non-reactive (People call it negative) on the subsequent NAT test, a discriminatory test, or a repeat of the screening test (laboratories do it differently) such that the reactive screening test, but no reactive results on the three discriminatory tests for HIV, HBV, or HCV or their repeat. When there's a discriminatory test following the first initial screening test, that's reactive, and then a non-reactive in the discriminatory test, these are commonly called discriminatory test non-reactives because the second test was a discriminatory test. More frequently, when people talk about this and the screening test, what they do is that the screening test is repeated automatically when there's a reactive and that screening test, the second screening test, is non-reactive. That's normally and commonly called a nonrepeat reactive. And we'll use both of these names for the kinds of second test non-reactives. But mostly what people are talking about is nonrepeat reactives, I think, in the context of this conversation. And of course, that's confusing to a lot of people, how can a first test be reactive and a second test non-reactive? So we'll discuss that. A second discrepant type is when a NAT test, nucleic acid technology test result, and a serology result, either antigen or antibody immunoassay test, from the same donation, do not agree, such as a NAT reactive but immunoassay non-reactive. This could be a

window period where NAT detects, because of its sensitivity, but the immune response hasn't happened yet, and so immunoassays cannot detect the infection. Those are called NAT yield cases, and we will talk about NAT yields. Further, the immunoassay could be reactive, but the NAT screen is non-reactive. That's a possible serology yield case, and those certainly occur. We will talk mostly about the first NAT test results that are inconsistent, just speaking about NAT and NAT as a first and second test. But all discrepants obviously are important. We should also acknowledge that in most instances we are talking about situations where individual donation NAT testing is being performed, where we are often more likely to encounter the NAT nonrepeat reactives. So correct me if you'd like, Dr. Lelie, but at least with those definitions, can I ask you to give us some background on the common causes of such nonrepeat reactives?

**Nico:** It is a complex area and I think it's difficult for a podcast to discuss, but let's try to do that. You have, of course, screening algorithms that differ, but what you are talking about is more like the resolution algorithm. Once you have an initial reactive result, the issue with resolution testing algorithm is the purpose. The main purpose is to discriminate between a true and false initial reaction. In that case, repeat tests are used, as you have said, and there is a certain probability or certain chance that you will encounter inconsistent results. And that happens when the viral load of the test sample is low, below the detection limit of the NAT assay, let's say 20 to 50 copies per milliliter. In those cases, a repeat test can be false negative and that you cannot avoid that. This happens most of the time with HBV infections and not so much with hepatitis C and HIV infections because the viral load in window period with those viruses is much higher. And did you already address that? You have different of those resolution algorithms, and if people directly use the discriminatory test, you say it is a nondiscriminatory repeat reactive, or if people use more like a serology-like repeat algorithm. That means if the test is initial reactive, then you perform a duplicate repeat test, let's say then you say it is a nonrepeat reactive and that's correct.

**Sam:** My experience has been when people are trying to resolve discrepant results, often what it is, is hepatitis B and not just early infection, but occult hepatitis B. When the person is infected with hepatitis B and they have a low but steady viral load of hepatitis B circulating, can you explain why discrepant results are more often found with hepatitis B than with other viruses?

**Nico:** Yes, of course. With HIV and HCV window period, the viral load is often very high. And in the past when there was no hepatitis B testing, the people used the duplex test, and then often in mini pools. And the discriminatory tests were then used for resolution testing at the individual donation level. And then the viral load was often high enough to have consistent results because viral loads are often very high. But with hepatitis B in the window period, normally you have a viral load below 1000 copies per milliliter. And in a later stage of HBsAg-negative infection, you have even lower viral loads that often the majority below 100 copies per milliliter, but more than half below even 10 copies per millimeter. So you cannot avoid with those very low viral load donations that you will find inconsistent results because of the Poisson distribution with such low viral loads. This always has led to confusion. In the very beginning when ID NAT was introduced in 2004, 2005, I remember workshops with opinion leaders and they complained about the test and said, well, I don't know what to do with your test because I had a healthy donor and she was positive in the test and I know this was an approved carrier and he was discriminatory test, non-

reactive. So this issue of low viral load donations that are not always positive is a problem that exists for a long time. And yeah, of course, you also have false positive reactions on the initial screening test, and those often are negative in repeat tests. But even with sample contamination, you can have false positive as well. And so you always have to do in fact, for confirmation testing, you have to do a follow up testing and take a second sample of the donor.

**Sam:** No test is 100% sensitive and no test ever will be. So when there's a viral load that's so small that a qualitative test like a screening test will sometimes be reactive and sometimes non-reactive, that's going to be the world we live in. And if the prevalence of hepatitis B infection is relatively high in the donor population, then one's going to get this kind of nonrepeat reactive or nondiscriminatory reactive result every once in a while. And it's irritating and confusing but difficult to avoid but understandable. And what we're going to talk about today is what people do in order to resolve those. We just can't avoid inconsistent results with repeat NAT testing when the viral load is low. I'd like to begin to explore maybe based on history, what people do to overcome this problem of false negativity and say the discriminatory test. And the problem becomes even more confusing because we know that we can also have a false positive reaction. You've already described that there were those in past meetings when first using the test, that they were confused about what to do. What might be the role of companion serology testing or direct antigen testing like anti-hepatitis B core, for instance, in non-repeat reactives? What have you seen? Or what would you recommend that people do for their serology testing to resolve discrepant results?

**Nico:** Yeah, you're right. People use different algorithms because there is no algorithm prescribed in the package insert so people design their own resolution algorithm like with the serology test you see in the package insert that people have to repeat the test in duplicate and then the test, if it is non-reactive in the repeat test, the final result is non-reactive. Such sort of indication is not given because there is always a probability that an initial reactive, even with multiple replicate tests, will be missed just because of the nature of NAT testing. So there were different algorithms designed including anti core as an assay. But in the beginning I would say if I go a little bit around the world for those that use individual NAT testing because of course you have mini pool NAT testing and in that case you often see that people do first serology testing and then only subject the serology negative donation to pool testing. And then the resolution testing on individual donation level is in fact much easier because the viral loads are often then higher. But with ID NAT you also detect the very low viral loads and then the problem kicks in. So in Italy, they were one of the early adopters. They started to use quite early on this serology-like algorithm where they did repeat tests if the initial test was reactive. So the same screening test was repeated twice and if it was non-reactive then it was over. But if there was repeat reactivity on the primary test tube, then they did further discriminatory testing on a second sample, often from the plasma bag for example. But others they wanted to follow more the suggestion in package insert to do immediately discriminatory test. But they like the idea of repeat test as well. So some countries like Poland or South Africa or also Ireland, I remember they started combining repeat tests on the primary test tube but also discriminatory test. So that means you need a large volume vacutainer tube to perform five tests to resolve the initial reactive result. And you're right, in some countries - I think it were the Australians that were one of the first ID

NAT adopters as well, and they started using on what they call the initial reactive or the nondiscriminatory test reactives to perform the anti-core test because then they immediately started to recognize occult carriers because it was clear in different settings that if you looked at the nonrepeat reactives so ID-NAT nonrepeat reactive or non-discriminatory test reactives and you compare that with the ones that were discriminatory hepatitis B reactive, you saw an increased anti-core prevalence like in China where between 30% to 40% of the donors are anti-core positive. At the time that ID NAT testing was introduced, the proportion of anti-core among the discriminatory HBV-positive was approximately 80% and almost the same if it were initially reactive discriminatory test non-reactive. So you see this issue and algorithms were designed at different places in a somewhat different manner, but they all addressed the same issue. They wanted to early on try to identify if there was presence of virus or not. And by doing repeat testing often and I think they involved also samples from the plasma bag. But this then is more for confirmation testing because there were some countries even that did repeat tests and if the test was nonrepeat reactive, they used the blood for transfusion. But in most of the countries this does not happen. If the test is initial reactive, the blood is not used, but if it is nonrepeat reactive in their algorithm, they do not inform the donor and the donor is not deferred and the next donation the donor can be tested again. I hope that I answer your question.

**Sam:** You did. We'll talk about elements of this again as we get deeper into it. But let me speculate for a moment and ask you about the speculation. If, for instance, a multi-signal screening assay so that it could discriminate in the very first time that you test in the screening test, it could discriminate between hepatitis B, hepatitis C, and HIV. Would that solve the problem of non-repeat reactives or the confusion just all by itself?

**Nico:** Yeah, I think that is an advantage, especially with the serology positives. If you want to exclude double infection and you immediately see that the reactivity is HCV or HBV, that helps. But in a seronegative NAT yield case, in a low viral load, hepatitis B, that often is the case. You cannot with one test say it was hepatitis B. So stop now. It could very well be false positive. So you need to do repeat tests anyhow. So it is an advantage, but you should not overestimate the value of direct discrimination and multidye technology. And yeah, if I think about the algorithm, you could, for example, say okay, rather than using the discriminatory tests when the test is initial active, you better can do three tests because then you repeat for hepatitis B three times, and if it is then non-and perhaps also immediately do the anti-core test as people in some countries do. So if all is negative, you could even decide to transfuse the blood because the incremental risk is so low that it's comparable what happens with resolving a mini pool of six, for example? But still, you could still decide no, for legal reason whatsoever, we do not want to transfuse initial reactive donations, even though overall the residual risk is far lower than with the mini pool test protocol. But still, just because it was once found initial reactive, we never will use that blood. Then of course, you throw out you discard the blood without informing the donor. And that has been some of the time. Also some discussion. But yeah, you could for example, say we use the plasma for fractionation, for example, because if there is any virus, the chance is extremely low, but also the viral load will be very, very low. So that could be an option as well.

**Sam:** Yeah, this was always my feeling is that to resolve a nonrepeat reactive test or test discrepant nonrepeat result, repeat testing of the specimen is just going to be required. That sometimes, as you've touched on, means that the repeat testing is utilizing an aliquot drawn from the specimen tube, the primary specimen tube, but sometimes from the blood bag and not the specimen tube. Since contamination of the tube is a formal possibility, what are the concerns? What are your thoughts about when to go back? When is it appropriate to go back to the original vacutainers and, for instance, collection tube? When is it appropriate to go back to the blood bag itself and test your follow-up testing from either of those two? What are the positive things about choosing one or the other? What are the negative things about choosing one or the other?

**Nico:** Yeah, I think if, for example, the regulators would accept, as with serology that a nonrepeat reactive result, let's say on three repeats could be used for transfusion, then you should not involve plasma units to finish that algorithm. Then you use the primary barcoded tube in order to avoid administrative errors, et cetera. And all the testing comes out of that dedicated test tube. You if you then go to the freezer and take the plasma bag and take samples from the plasma bag, you have to label those samples as coming from the right donation. So this includes a lot of processing. During that processing, you can actually contaminate the test samples also. In discriminatory test runs, you also could introduce contamination with high viral load samples that are serology positive, et cetera. So my personal preference would be to do the repeat test on the dedicated primary screening tube. And once you see repeat reactivity, then you start to do the confirmation testing, in fact. Taking, for example, samples of the plasma bag where you can do the viral load test, you can do supplementary serology testing. And of course, as we said in the beginning, for real confirmation, certainly for window period, you need to recall the donor and do testing on a follow-up sample in order to confirm seroconversion, et cetera.

**Sam:** Yeah. By then, they've probably become reactive both by serology, if not also by NAT later on. And so that is a reasonable way to go forward. And if you can get them to come back and either give us a specimen or wait until they donate again. The repeat testing that resolution algorithms can call for can be quite elaborate. And they can include, say, three separate specimens tested in parallel. And if any of those tests test reactive, then the donation is designated as infected. One in three is enough to confirm that it's an infected donation. But if all three test non-reactive, the donation might be designated as not infected. And as you say, in some places in the world, the blood could be released for transfusion. It may be possible in some countries to ask the donor to go to a diagnostic lab for further testing with, for instance, diagnostic nucleic acid amplification tests. I know that happens in the United States. The first test in the United States, if it's reactive, is called the test of record and that means that blood cannot be used in a transfusion at all. The donor is often told by letter often that they were reactive for something for some infection and they should go to their physician and be tested, but they may be deferred forever. It depends on the algorithms used and et cetera, what the resolution algorithms may be, but that's pretty much the way it is in the United States. So the donor could be allowed to donate again in some countries, depending on how the resolution testing comes out. Do you have a feeling about how the prevalence of one virus or another that we're testing for, how the prevalence in one country or one region versus another determines the algorithm for resolving NAT test discrepant results? Can you name or describe

some countries or regions where the resolution algorithms differ and how they differ based upon prevalence of, say, HIV or hepatitis B in particular?

**Nico:** Yeah, it's often said that testing algorithms, the most optimal testing algorithm depends a little bit on the prevalence of viral markers in the donor population, but I think that may hold for the screening algorithm. For example, if you have a low prevalence of HBV, it's more easier to do anti-core testing, for example, as happens in France, Netherlands, and then in combination with mini pool testing, because that they think is more cost efficient because you use less reagent or whatever. Well, in other countries where you have high prevalence of hepatitis B, like Asia, Africa or hepatitis C like Egypt and Pakistan, India, some areas, or HIV. Of course, in Africa the prevalence is high, so even ID NAT resolution algorithms start to change a bit. But for the seronegatives, I would say the choice of the algorithm is not so much. I think dependent on the prevalence, it is a matter of what is the most optimal and efficient way to discriminate between a true and a false initial positive, reactive or reactive result. I think the difference in algorithms more often happens in seropositives with the discriminatory test. For example, I remember in Egypt there's quite a high prevalence for hepatitis C & B, and it mounted up to, let's say, 4% or 5% of the donations. So to do discriminatory tests on all the seropositives was just not possible. So in that case, if you have an HBsAg positive and reactive, that then thought it was hepatitis B and no further confirmation testing was done. But if you had a seronegative, we did triplicate, repeat tests and if it was one of the triplicates were reactive, we did further confirmation because to do further confirmation involving, for example, the plama unit and use viral load test, et cetera. This helps us to understand what is the viral prevalence in the country. If you do ELISA testing, for example, and don't use the donations and only apply mini pool test on the seronegatives, you never will have a good picture of what is the prevalence of infection in the donor population and how it is spread among occult carriers, window period infections, et cetera.

**Sam:** Let's turn the conversation something that's rather more practical and that is this issue of resolving discrepant results. It's often, in my experience, happening to people who are new to laboratory testing in the blood bank or the associated blood bank laboratory or it's people who have been doing a lot of serology testing and they're used to those kinds of algorithms and then they begin to be exposed and to be running nucleic acid technology, NAT testing, and it's a different recommendation. If it's a different resolution and those kinds of backgrounds, it can be confusing. It's a different kind of qualitative result in NAT testing. You usually have zero signal or you have a whole lot of signal due to the power of the amplification. But for those who are new to NAT testing, wherever they're coming from and they're learning how to run the NAT instrumentation, can you suggest or do you happen to know of any resources that are available to them to learn the prevalence of tested infectious agents in their locality or what appropriate algorithms can be applied to their location for test resolution?

**Nico:** Yes, there are a number of publications, national blood center publications where people have their own testing algorithm and often in the method section they describe what they did or they referred to previous papers. There's one paper that of a multi-center hepatitis B study involving 10 million donations where I in a figure, remember, have presented the different algorithms that were used and that we already have described in the conversation before they could look at that publication. But they can also approach me

if they want and I can send a paper or something. But perhaps this is also available with the Grifols Medical Affairs Department. I don't know.

**Sam:** It can be. Yes, it can be. Yes, that's true. I think there hasn't been anything yet put together that is a comprehensive look at discrepant testing algorithms all over the world yet. And I think that that's something that's badly needed sort of. First, Besides this podcast as an introduction to something that they can look at and start to see what much of the world does, depending on whether they use it or not, the amount of circulating in the donor population, hepatitis B, hepatitis C or HIV or combination, there would be something that they could go to and learn. Resolution testing is just not in textbooks. It's something that we have to teach one on one. And this podcast being available will be something that I think we can be proud of and people will at least be able to start there.

**Nico:** Can I ask you a question? Sure, of course, Sam. Because I remember the discussion when I was working for Chiron many years ago. Why are we not giving a little bit more guidance on resolution testing algorithm in the package insert? Because if you, for example, look in the serology test, people say, well, the test was initial reactive, then you do repeat test, for example, and if the repeat tests are negative, the result is called non-reactive or non-repeat reactive. You don't say anything how to do the donor management or whether or not to release the blood. You just give a sort of an algorithm that you use. I understand, of course, that's difficult, that if you also include different algorithms depending on the serology status, it becomes difficult. I understand and from a regulatory perspective it becomes difficult. I read before this podcast the package insert and I saw there was very little information, but it was also not said that people should immediately use the discriminatory test. So obviously labs or blood banks are free to use the serology like approach of first do repeat test. That is not forbidden, it is not prescribed. You have to do immediately discriminatory test because when the first users start doing that, then they run into the problem with a lot of false negative occult carriers.

**Sam:** That's right. Non repeat reactive or non-discriminatory reactive. It's a completely fair question, Nico, and I can only tell you a few things. Being familiar with obviously the manufacturer of my employee and also familiar with interactions with regulatory agencies, I've gone back through package inserts as well of people who offer NAT tests around the world and I haven't been able to find in any package insert any kind of explicit algorithm of how to resolve the discrepant results. And I think I know why. Let me try to explain that. Let me make a few points here. It's a completely fair question and I know our customers come back to us and say help us with this all the time. A manufacturer the first thing a manufacturer really can't write specific algorithms for specific parts of the world because it's just asking too much for a manufacturer to do. When we have a quality control release of a lot of product and that lot can go to any of a number of countries, it will often be C.E. mark designated, but it can go to quite a number of different countries and exactly where in the world and which countries that lot of testing might be used can't be known by the manufacturer. And to the extent that prevalence is a big determinant of the type of algorithm used, sometimes it is and sometimes it isn't. Then the manufacturer can't write in their package insert, which is a document that goes to say all of the EU or all of the United States can't give an algorithm for resolution that would be truest or most accepted in those regions. They just can't know the prevalence of each virus type in each country that they're selling a lot of released product.

**Nico:** All right, Sam. But this then assumes that the testing algorithm is dependent on the prevalence of the viral markers. I don't think that is the case, but go on.

**Sam:** Yeah, it is. In some countries, especially with high hepatitis B, it does influence them we can debate forever whether that's right or wrong. But it's the right scientific approach. But people do. And a second point is that a manufacturer just cannot market any donor screening medical product without strict approval of regulatory authorities. And they do as they should, scrutinize every word of a package insert. And in my experience, regulatory authorities historically only want a manufacturer to talk about the analytical capability of a test and how the software and instrument determines whether there's a reactive or non-reactive they haven't allowed package insert insertion of any language on how to interpret the test results. You're supplying a product that gives an analytical result. What you write about should be about how to interpret the analytical result, but not how to interpret the test for true positivity or true negativity, and more specifically, not how to resolve discrepant results. They tend to leave that to the physician or the healthcare provider or the blood bank to decide, along with looking at serology, along with looking at the patient and their condition, along with asking the donor to come back and give a second test. They leave the interpretation of true infectious versus noninfectious donation to the medical community, not to a test. So that's been a barrier, too. That's a concern. So let me just say one more thing. Yeah. I'll repeat. I don't know of any major manufacturer that includes in the package insert instructions on test discrepant resolution these barriers. Well, I don't want to say barriers. These concerns from regulatory authorities and physicians affect all commercial test manufacturers.

**Nico:** Sorry. Yeah, go ahead. I agree with everything you say, but I think I would not say that there should be any interpretation. But I just compare it with the serology tests. You don't give any interpretation on confirmation or infection or whatever or donor management or the only thing you say, for example, is if the test is initial reactive, you should perform a three discriminatory test. Or if the test is initial reactive, you should do repeat tests. That is the case with serology. But with serology, you're right. The difference with NAT is if you have a weak reactive, low antibody or low antigen concentration, you will still have a weak reactivity in the repeat test. And that is the difference with the NAT test because of the Poisson distribution. With low viral load, the signal can be very high or very low, totally negative. And so that is the complicating factor. So I perfectly understand. But I think you could give some more guidance than it's given now. But without that, I think you're right. We need perhaps a publication that describes the different algorithms used and the problems that we're seeing and that paper is still lacking, for example, the proportion if the certain algorithm is used, how often the discriminatory test was false positive and how often that sort of thing. At some time we need to work with some people to put this together in a sort of a recent paper or something.

**Sam:** I agree. Again, the physician associations, regulatory bodies and others that Grifols has to listen to and must for regulatory authorities must follow in order to have an approved released product. Their behavior, and I'd say properly so of course is rather conservative and can be at least as far as the customer is concerned, can be a little slow in moving forward or in changing a common view about just how

conservative language can be in a package insert. I have long felt and I think it's probably a job of medical affairs in our companies. The way forward on this is to change the mindset or at least expand and understand the complexity to physician groups and regulatory authorities about resolution testing, about discrepant testing. It's hard for that to come from industry, frankly, anything that we might say would sound like we're trying to make our product easier to sell, which is not the issue. It's to find the correct and true result. That's better coming from the academic community, Nico, I think that's better. As you have said in a scientific paper that is not from a company but is from the academic community that says here's the state of the world with respect to discrepant resolution. Here's what seems to work for people under different conditions and people would be able to refer to that as an independent scholarly contribution. And I think what you say is perfectly fair and that's probably something that medical affairs should start searching for someone to write that paper and that might be the first go to source of information on independent thoughts about resolution testing and then that would become known to the regulatory community and the regulatory community could look at that and then say, okay, well, maybe some language can change in a package insert, but it's hard for industry to get that going. I think if the mindset changes in the testing community, that would come from the academic side. So I would push that back to you and people like you that maybe that kind of paper would be a great one for someone to write.

**Nico:** Okay. That sounds like a good conclusion.

**Sam:** Thanks for that. And I really want to thank you for your time, Nico Dr. Lelie. And this has been wonderful and I think the fact that it's going to be electronic and available to a lot of different people around the world is a step forward. I know that you and I have had similar experiences where we have to fly from one part of the world to another, which is even harder now with COVID and give these kinds of talks and have these kinds of discussions. Maybe this is a way to spread the word and to get even more of a dialogue going. So thanks very much for your preparation, for your writing, for your thinking, for your time, Nico and I'll turn it back over to Shawn to conclude this podcast.

**Nico:** Thank you. Thanks for having me.

**Shawn:** Thank you, Doctor Rose and Dr. Lelie, for this wonderful conversation. This concludes today's podcast. As a reminder, if you're interested in receiving continuing education credit for this podcast or if you would like other information about our education program, please email TSEC@grifols.com. Thank you for listening and we look forward to your participation in our future educational event.