This content was published before guidance to change "monkeypox" to "mpox" was delivered to CDC programs in December 2022

CDC Town Hall Meeting on Laboratory Biosafety – Use of Laboratory Instruments, June 24, 2022 Meeting Transcript

NANCY CORNISH: I am Nancy Cornish. I'm a pathologist, physician, and clinical microbiologist. I work in the Division of Laboratory Systems. I am very pleased to announce the start of the CDC Town Hall meeting on laboratory biosafety. I'm also very pleased that everybody is attending. I would like to introduce Dr. Reynolds Salerno, who is the Director of the Division of Laboratory Systems in the Center for Surveillance, Epidemiology, and Laboratory Services at CDC. DLS improves public health, patient outcomes, and health equity by advancing clinical and public health laboratory quality and safety, data and repository science and workforce competency. Dr. Salerno is also the lead CDC official for the Federal Tri-agency Clinical Laboratory Improvement Amendments program, or CLIA, and the designated federal official of the US Clinical Laboratory Improvement Advisory Committee, CLIAC. He is also an expert in biosafety and biosecurity. And so, I'm very pleased, without further ado, to introduce him and have him give the opening remarks.

REYNOLDS SALERNO: Thank you, Nancy. I'm pleased to open this CDC Town Hall meeting on Laboratory Biosafety and the Use of Laboratory Instruments. It's really great to be here with all of you and I want to express my sincere appreciation to all of you for attending today's town hall. We will focus on laboratory biosafety, but specifically the design and use of laboratory instruments. I'm just really thrilled to see how many people are here today. It's awesome that we have representation from both the diagnostic manufacturers, from our clinical and public health laboratory professionals, federal partners from across the interagency, as well as industrial hygienists, but also clinical and laboratory professionals from many, many jurisdictions from across the country. So, we're really happy with this broad group who is convened here today.

The purpose of this meeting is to provide an overview and discussion on laboratory biosafety when using laboratory instruments to test human and biologic specimens. From a historical perspective, the field of laboratory biosafety was originally designed to address the dangers of working with particularly dangerous pathogens in research laboratories, not clinical laboratories. Clinical laboratories were, really, for a long period of time, left out of the field of laboratory biosafety. In fact, the so-called bible of laboratory biosafety, the BMBL, which both the CDC and NIH have published since 1984, did not include a specific chapter on clinical laboratory biosafety until its sixth edition, which was published just last year. For years, laboratory biosafety as a scientific discipline was focused almost exclusively on research facilities. In fact, it was the biological weapons programs of the US and UK, primarily, that created the field of biosafety because they were researchers and scientists who were on a daily basis, working with the most dangerous pathogens. So, their lives were literally at stake every single day that they went to work. And that's where we owe them a debt of gratitude for creating things like the biosafety levels and pathogen risk groups and so on. But recently, there's been a wider recognition that clinical laboratories can also encounter dangerous pathogens at any time. A laboratory accident or a laboratory-acquired infection could affect not only the laboratory staff, but others around them. Fears about inadequate biosafety can paralyze a clinical laboratory and jeopardize patient care. Now, largely as a result of the COVID-19 pandemic, our understanding of clinical laboratories has evolved to include testing that occurs in nursing homes, schools, shelters, correctional facilities, and even parking lots. Any and all of these settings could present biosafety risks to personnel. So, we must broaden our application of biosafety, including guidance and training and procedures, to address all types of clinical testing locations. The

underlying weakness of clinical laboratory biosafety in the United States became particularly clear when Ebola spread from West Africa to the US in 2014.

Soon after the first Ebola patient appeared in the United States, many of the largest commercial laboratory companies, all of whom were well versed in handling specimens that contain dangerous pathogens, publicly announced that they would not accept blood or tissue samples from Ebola patients. Many laboratory instrument manufacturers followed suit. Some indicated their warranties called for incineration of their equipment after use with samples from Ebola patients. Others explained that their technicians would not service equipment from isolation wards used for Ebola patients.

In 2014, during the Ebola crisis, CAP conducted a survey of 28 health systems and more than 350 hospitals. Only 4 of the 17 respondents indicated that they would allow suspected or confirmed Ebola virus disease specimens into their laboratories. Of those four, one would restrict testing to a BSL3 laboratory. And one would strongly discourage sending clinical specimens to the laboratory for testing. This almost complete shutdown of clinical laboratory testing in the US for suspected Ebola patients had significant consequences. Between July and November 2014, local health departments and health care providers acknowledged that complete blood counts, liver function tests, and serum chemistries were regularly deferred until there were assurances of a negative Ebola virus test result. Individuals who had recently traveled to or from Africa with fever and malaise symptoms were routinely refused malaria testing until Ebola had been ruled out. As a result, a majority of malaria patients did not receive the proper and timely intravenous antiviral treatment. According to one CDC study, at least two persons who tested negative for Ebola died from other causes because of severely delayed diagnoses and treatment. In 2016, the Clinical Laboratory Improvement Advisory Committee, or CLIAC, which is a federal advisory committee, declared that biosafety in clinical laboratories is a critical unmet national need. And CLIAC has pressed CDC and the federal government to take action on clinical laboratory biosafety ever since. Have we made progress advancing the importance of biosafety and clinical laboratory testing since 2016? Well, I hope so. And I think so. But I would welcome discussion on this point today.

One thing we can say is that the clinical laboratory community has performed extremely well during the COVID-19 pandemic. Clinical laboratories did not refuse to perform testing. And there have not been any documented cases of laboratory-acquired infections with SARS-CoV-2. And in my opinion-- I'm a little bit biased, we at CDC did a better job, perhaps even a much better job, of providing laboratory biosafety guidance during the COVID-19 pandemic than during the 2014 Ebola outbreak in the United States. This town hall collaboration is designed to foster mutual understanding of various perspectives on biosafety as it pertains to laboratory instrumentation.

Our goal today is to collaboratively develop practical solutions to address issues or gaps and to improve pandemic preparedness. Today's agenda will include presentations and discussions on four topic areas-- medical device design and incorporation of safety and biosafety, perceived risk to laboratory personnel and impact on testing, independent assessment of risks and instrument design, the discussion of potential areas for improvement. Throughout this meeting, we will have prepared presentations, discussions among presenters and panelists, and a period of questions and written public comments. I look forward to today's discussions and encourage you to think about how we all can ensure safety is integrated into instrument design and instructions for use. I'll now turn it back to Nancy Cornish, who I think will introduce our other opening remarks from my colleague at FDA.

NANCY CORNISH: Thank you very much, Dr. Salerno. That was an excellent opening presentation. Now I would like to introduce Dr. Timothy Stenzel. He directs the FDA'S Office of In Vitro Diagnostics and has an extensive

background spanning more than 20 years in executive leadership, innovation, companion diagnostics, research, development, FDA regulations, and clinical laboratory operations. He received his MD And PhD in Microbiology and Immunology, focusing on molecular biology of DNA replication from Duke University, after graduating with honors in Chemistry from Grinnell College. As the director, Tim advises FDA leadership on all regulatory, premarket and post market, for in vitro diagnostics, radiologic, and medical devices, as well as radiation-emitting product issues that have an impact on center- and agency-level decisions, policy development, nationwide programming, execution, and short- and long-range program goals and objectives, as well as providing executive leadership and scientific direction to the Office of In Vitro Diagnostics, Office of Product Evaluation and Quality (OHT7) and Office of Information and Regulatory Affairs (OIR) staff. Timothy, the floor is yours.

TIMOTHY STENZEL: Thanks, Nancy. I have a fairly deep and broad responsibility. I'm fortunate to have been a long history of experience in the lab, as many of us have. And first off, I want to say that Ren's remarks were spot on. Happy to be a part of today. CDC came to the FDA a while ago and said, we're hearing from laboratorians that we really want to talk about this issue. And we fully supported the development of this workshop and look forward to it. It looks like it's going to be a great day.

Hello to everyone and good morning. And then also to those who are far west of us even-- I don't know if we have anybody participating from Hawaii. But obviously it would be very early morning for them. But even on the West Coast, earlier than usual. So, I just I wanted to start out with lab safety and biosafety. For those of us who are scientists, it began in high school, or even earlier. And it's a shared responsibility. For example, one person cannot follow procedures and put the whole lab at risk. For me, it began in high school and well trained in science classes and went to-- and then college. And then the first time I was really concerned about biosafety was in medical school, graduate school, and residency in pathology, where in anatomic pathology, obviously handling tissues and being present in the autopsy suite. Biosafety is very important and was drilled into us. And, in my rotations through the clinical labs during my laboratory medicine training and residency and joining the faculty at Duke and being responsible for multiple labs research and clinical, I was then responsible for the safety of the staff that worked in those labs and for the procedures that we put in place to be safe. And then when I moved to industry after my time at Duke, safety of the instrumentation is built into the design and into the assays and the quality systems. The FDA-compliant quality systems require in design that user safety is a key part of the development of those assays.
As an MD, I was involved many times in examining it from a medical perspective, estimating risks. And we did have safety complaints. We were required to investigate those if they were not insignificant. We, of course, required to report it to the FDA. And my experience and history was that when there was a potential safety issue, we dealt with it appropriately and quickly. And so, I learned a lot from all those settings, as perhaps many others have been here. And the purpose of this meeting is really bringing the stakeholders together to bring issues or potential issues to light and for all of us to play a role with finding and implementing solutions to any identified issues.

The discovery of issues, however few or many they may be, and the dialogue that will start today-- or it has been going on and will go on-- will bring us forward together. The FDA does stand ready do our part. Likewise, we've seen evidence during the COVID pandemic and Ebola and other times, where we're laboratorians are rightly concerned about biosafety. And some were concerned about actual testing. We know that from prior emergencies and other situations. And we want all laboratorians to feel safe, prepared, and ready to test, now and in the future for routine testing in between outbreaks and during outbreaks because we do need, as a laboratory industry, to respond to these appropriately so we can mitigate the morbidity and mortality in our country and perhaps others' as well. When we look at the FDA device reviews, tests, and instrumentation, we do look at if there's a potential for cross-contamination. Of course, we're looking at whether you might get a false positive in a negative sample when

it's near a positive sample. And so, there's various techniques to do this. They've been done for years. And if there is cross-contamination discovered or potential discovered, those would need to be addressed through the review process. And if they are not discovered, then it is an indication that there's less likely to be a biosafety issue. It doesn't completely eliminate it. And of course, biosafety begins at the patient-clinician interface. And it goes all the way through a sample that is processed and any derivatives all the way through to appropriate discarding of those samples. And then also after a device is authorized by the FDA, we monitor that, the safety of that device, through our MDR, Medical Device Review program, reporting program.

The FDA's ongoing monitoring of MDRs has not yielded a significant issue that has needed a resolution. That doesn't mean there aren't issues out there. But if there is underreporting of issues, we would not be tracking those. And we would not have the ability to investigate them. So, manufacturers, of course, are required to relay significant complaints and concerns that are of importance to the FDA in a timely manner through the MDR systems. As well, the labs can report. It's voluntary for the labs. They can directly report issues directly to the FDA through the MedWatch program. And we do strongly encourage that because it may be that a manufacturer hasn't or won't report it to the FDA. But the FDA will nonetheless-- if there's a significant concern, the FDA will look at that and investigate if appropriate. So, like I said at the beginning, I said we're all in this together. So, it's important that these issues do come to light as soon as possible. So, then they can properly be addressed through-- and the FDA can address them through our regulatory programs.

Finally, we have a new outbreak of significance, the monkeypox outbreak. CDC and the FDA are already thinking about lab safety here. And the CDC test looks at how you inactivate monkeypox in a sample before you begin extensive reprocessing of that sample. And that is going into the instructions for use of that monkeypox test. The Orthopox test has being used largely in the LRN. It's now, of course, being rolled out to clinical labs, five major reference labs, as reported earlier this week. And so, the inactivation of that virus prior to extensive processing of that example is very important. We, together, know what-- the CDC did the work. And the FDA has reviewed it. We know how to inactivate that virus. There are those out there. The FDA has said that LDTs for monkeypox are under the routine enforcement discretion so that labs can develop a monkeypox test of their own and validate it and begin testing without even notifying the FDA. We do urge, of course, in those situations, where the FDA doesn't actively oversee those, that lab safety is addressed there as well. And with that, I want to turn it back over to you, Nancy. And it was great to be able to be here today and to share these opening remarks. Thank you.

NANCY CORNISH: Thank you very much, Dr. Stenzel. We really appreciate your presence and your remarks. I will now introduce Ms. Yvonne Walker. She is our CDC moderator. And she will set the ground rules for the presentations and the discussions that follow. We urge that everybody be respectful and listen to each other. That is the goal of having a moderator present. Ms. Yvonne Walker is the Lead Facilitator for the Office of the Associate Director for Policy and Strategies Program, Performance, and Evaluation Office. She serves as a public health analyst in PPEO and as a cross-team liaison working with the monitoring and evaluation and policy and strategy units. Her work allows her to assist the office in process and technology improvement, operational streamlining, and assisting other offices with cross-cutting agency-level work. She also has a microbiology background. Yvonne, are you ready to take over?

YVONNE WALKER: Sure. Thank you very much, Nancy, for that introduction. Today, myself, along with my colleagues, Katie Busalacchi and Mica Jamison will be co-facilitating this session. However, we wanted to make sure that with the size of this town hall, we wanted to lay some ground rules for presenters and for panelists alike when we're going through, especially when we're doing the discussions. So, some of the dos that we would like for

everybody to consider is to listen when others are speaking. Understand that we're not always going to agree on everything. And that's OK. Ask questions, share ideas and stories. Use the camera during the discussion so that people can see your lovely faces. And ask for help whenever you're having some technology issues. There are some people that are producers that are behind the scenes that will help. Please mute yourself when you're not speaking. Or we can accommodate you by muting you if you forget, which is no problem. And if you do have a question or have something constructive to add to the conversation, please use the hand-raise feature. We've seen that a few people have already used it. We only have a few don'ts. One of the biggest one's is don't refuse to listen. And that means just keep an open mind and don't listen to formulate an answer. But listen to what the presenters and the other panelists are trying to say so that you can formulate a very clear answer or response to whatever questions or comments they may have. Also, please don't attack people personally, that myself and Katie will handle people who do. And we'll make sure that this is a very constructive and civil conversation that'll be had. And one another big thing is we're not going to solve everything today. So just bear in mind that everything will not be solved today and that we'll be able to have further conversations later down the road. And for our audience, any questions, or comments that the audience have please understand that your opinions are valued. And we would like for you all to actually send those comments and questions to the DLS Biosafety inbox. And they will definitely make sure that they get a response to you after the meeting. And that goes for any of the presenters as well, anything that you may have heard during this presentation in this town hall. And so, with that, I'll go ahead and turn it back over to you, Nancy.

NANCY CORNISH: Thank you very much, Yvonne. We will now move to our colleagues from AdvaMed and learn about how AdvaMed supports manufacturers. Mr. Andy Quintenz serves on our CLIAC committee and does a wonderful job. He has been very helpful with this town hall and has an excellent presentation ready for you. He will introduce himself and Ms. Jamie Wolszon, who is one of his colleagues.

ANDY QUINTENZ: Thank you very much, Nancy. I'll let you start, Jamie.

JAMIE WOLSZON: OK, great. First of all, thank you everybody. I'm Jamie Wolszon, vice president of technology and regulatory affairs at AdvaMed. Very pleased to be here today. And today I'll be speaking to designing instruments with safety in mind.A few disclosures before we begin. I'm here with my colleague, although he's not officially with AdvaMed. But he's a wonderful resource and ally, Andy is our officially designated liaison to CLIAC. We are lucky enough to have an industry representative to CLIAC. That is Andy. He has served for many years, and he's done a stellar job. So, he is here in that capacity. He's not here in the capacity of his individual company. He is here on behalf of AdvaMed Dx, along with me. And the points that we're going to present today are a compilation of points and suggestions by what we call our diagnostics task force. We have a group of regulatory member experts who I convened to discuss this issue and this topic. They had suggestions, and that's what you see here in this presentation.

AdvaMed Dx, for those of you who are not familiar, is a division of the larger advanced medical technology association. AdvaMed generally represents over 400 manufacturers, but of course the ones that matter the most today are our In Vitro Diagnostic (IVD) friends. I provided the link to our website here, but AdvaMed Dx represents over 75 manufacturers of IVDs in the United States and abroad, including many instrument manufacturers, many of whom you know and recognize. And our job is to promote innovation and expanded access to quality testing.

We are involved in as many areas as we can, including coding, coverage, and payment, although that is not my job personally. Collaboration with regulatory bodies to understand and clarify regulations. That is a key aspect of my

job, and I am pleased to recognize friends here today. Promotion and communication of the value of IVDs. I think one of the silver linings of COVID, right, and there aren't many, but is the real recognition of the value of diagnostics, right? For so long I think most people, or many people, did not know really what a diagnostic was, and they certainly didn't necessarily recognize the value. And I think that has changed, right? Through the pandemic, it's become a household, understood term. Promotion-- COVID-19 response. I mentioned that a little bit. But we have been involved, working with multiple entities in terms of response to COVID-19, including there was a registry where we detailed sort of how many various tests were out there for COVID to better understand the footprint. And supply-- that should be chain-- I think I accidentally deleted the N. This is something that I'm sure many of you are aware has been a real issue of late to our manufacturers. Challenges with the supply chain. You've heard, I'm sure, about the chips issue. There are other emerging issues, and this is something that we've been trying to work on as well.

Our goal today is to present a snapshot of how instrument manufacturers incorporate biosafety when designing an instrument, and when modifying biosafety protocols to address emerging pathogenic threats. I think Tim was reminding me that this is an ongoing discussion, right? It doesn't just end at the pre-market step. It's not intended to be comprehensive. Again, we consulted with member experts but you're not seeing them today. So, while other than Andy with me. But he's here in his, again, as an AdvaMed DX representative, not in his capacity as an individual company. As was alluded to earlier, instrument manufacturers follow well-established regulations and harmonize international consensus standards to protect users from reasonably foreseeable biohazards during normal use. International consensus standards. I'm not sure how many of you are aware of this, but FDA has a recognized consensus standard approach where they will essentially say, you don't necessarily have to use this standard, but we recognize this international voluntary standard as something that is very good for you to use. And if you use it in your regulatory submissions, your life will be easier. A key one that is instrumental is ISO-14971. It's the risk management standard. Medical devices, application of risk management to medical devices. And I heard Tim mention assessment of risk. It outlines processes for managing risks, primarily to the patient, but also to the operator, other persons, other equipment, and the environment. It includes provisions such as information for safe use to be provided to the end user, risk control options, analysis including protective measures for the operators, risk analysis performed on the intended users, including the operator, health care providers, and patients. And this is a key standard that is used throughout industry. Also, ISO-62366-- medical devices, application of usability engineering to medical devices. Again, these are not mandatory. They're international consensus standards. But again, they are extremely widely adopted.

Turning to FDA regulations and guidance. Again, Tim teed this up. There's the FDA requirement of design controls per 21 CFR-6 and 820.30. Right, it outlines a number of considerations that must be included in the design. There's also FDA guidance, applying human factors and usability engineering to medical devices, which talks about eliminating or reducing design-related problems that contribute to or cause unsafe or ineffective use is part of the overall risk management process. Just talked about the risk management process and how important that is. And it includes biological hazards, including allergens, bio incompatible agents, and infectious agents as one of the hazards traditionally considered in the risk analysis and management. So, I realize that I jumped here to European. Listening to Tim, I realized. I think we focused a little bit too much on the pre-market, to the exclusion of the post-market. So, I think it's important to reinforce some of the points that he mentioned, because I think there are really good ones. One is the requirement of complaint handling. That's, I believe, 21 CFR 20.128. But a requirement for the QSR, Quality System Regulations, that a manufacturer investigate complaints, right? You can't just pretend they're not there. I mean, not that a good company would do that anyway. But per the regulations, companies are required to investigate the complaints that they receive. He also mentioned the MDR, right? This is the adverse

event reporting, which does require reporting to FDA within specified time frames for adverse events. But I think it's also interesting, the device framework does something that you don't see in the drug side. Which is, you're not just required to report to FDA in the event of an adverse event, but also for what I'm characterizing very loosely as near misses. These are the malfunction reporting requirements, which essentially say that if a medical device-- which includes an instrument-- if it malfunctions, AKA it does not perform as intended and to its specifications. And what happens rises to a level, I won't bug you with the language. But enough of a level that if it were to occur again, someone probably would get hurt. That is, even though if someone didn't get hurt, that is something that also must be reported. That is not something that's required under the drug framework, and I think is also important to keep in mind.

So, I just heard a lot of good points from Tim, and I realized that I'd focus too much on the pre-market. So wanted to talk about the post-market as well, because I think there are a number of protections that are relevant to our discussion today. I also wanted to briefly mention the-- that there are applicable European requirements. Not so much to focus on the details, but primarily to mention that most of our companies-- most of the big instrument manufacturers-- are international, global players, right? And they are required to meet the varying regulations of the jurisdictions in which they participate, many of which have varying regulations both on the pre-market and the post-market side. So, I mention here Europe, which is currently going through a transition from the IVDD to the IVDR. You don't need to know the specific details, but it does also include incorporation of biosafety. There are other jurisdictions not included on these slides as well. For instance, China. But just to make the point that it is-- FDA has a very key role, and you know, but there are also other jurisdictions to be considered as well. And it's also-- right, this is more my laboratory community friends than it is me, but I think it's relevant to mention as well. The regulations and standards protecting against biohazards as part of the laboratory operations, right? So, you also have CLIA, OSHA, CLSI standard. So, I think it's important to keep that in mind as part of the overall picture. And this is where I turn it over to Andy. Essentially the transition is from my discussion of AdvaMed Dx and also the general regulatory requirements to how this works in practice. Andy?

ANDY QUINTENZ: Sure, thank you Jamie. So as Jamie walked through a number of regulations that manufacturers must adhere to if they want to put their products on market. Sometimes our eyes glaze over when we read regulations, and we try to think about what they all say. But if we think about putting this in practice from a manufacturer's viewpoint, when an instrument is designed, there's a number of considerations that are taken into account. And the engineers, the industrial hygienists, the various disciplines that come together to develop the design, to develop the final look and feel of the instruments all have to take into account how the instrument is actually being used in its setting. So, you see here a handful of the factors that we think about when we design instruments. There are certainly the materials, and the components are used. If it's a very simple instrument, it might just have a few different types of components in it then more complex, large-scale instruments. There's tubing, there's pipe headers, there's a number of moving parts. All these things are considered from the viewpoint of, will somebody have to interact with them? And if they interact with them, how can we interact with them safely? If an instrument has a panel that can be opened and a component cleaned or changed, we have to consider how is that-- what sort of decontaminants are going to be involved with that? And how can we ensure that it's rendered safe for the user? The user environment is also taken in account. And CLIA complexity may seem an odd term here, but whether it's a waved instrument, if it's an instrument that can be used by waived users, it would be more likely to be a layperson or somebody without the higher skilled training as somebody who's operating an instrument in a high-complexity laboratory. And somebody who is a medical technologist or clinical lab scientist has a great deal more training and understanding of what the risks are for themselves as they're doing things in maintaining the instrument. And then certainly, if it's a point of care instrument in a physician's office, the considerations for the

types of decontaminants that are used, or who might be coming in contact with it and the level of knowledge that they have, would play a factor into the recommendations and the design considerations for decontamination. And then another, the usability. So, user interface, more so than just what we typically think about it in looking at a software screen. User interface is just, how is the user interacting with the instrument itself? Are there panels that have to be opened, are there components that need to be changed out? How do they install their reagents? And then if those things and all the components that come into contact with the specimen from the patient. How are those all decontaminated as well?

Additionally, manufacturers have to think about, how are we going to communicate these considerations, how are we going to communicate the steps that need to be taken for decontamination, the risks that may be associated, and things that we want the users to think about and consider before they undertake a certain maintenance or cleaning procedure. These are all well detailed, what we need to do, how we need to frame these up in the various regulations. It's all-- any of these sorts of, like the cleaning procedure, is considered part of labeling. Instructions for routine maintenance, warnings, precautions all have very, very clear and strict regulations or guidelines behind them as to what we need to do.

We're getting more to the challenge that was raised for this webinar. When we think about outbreaks or we think about viral contaminations from patient samples, we certainly want to make sure that we are designing and recommending procedures that would render the part, or the instrument, safe for the users. There's a wide variety of decontaminants that can be used. Sometimes we discover that a laboratory may have chosen a decontaminant that was not on our list and not evaluated for cleaning the instruments. And some of those decontaminants are harmful to various components, whether it's electronics or tubing. It may be a different decontaminant that you would use on those versus the decontaminant you would use on a surface part. And then also, some decontaminants should be used with certain transport media. We saw in the coronavirus, a CDC communication about this specifically. Where labs were using bleach to decontaminate their instrument, and that was having an effect on the transport media and then affecting patient results. So, decontamination procedures, decontaminants really vary depending upon where-- what part of the instrument it's being used on, and where it's being used. But regardless of what the type of decontaminant is or what the procedure is, the manufacturer has to validate these. The manufacturer has to be able to reassure the users and demonstrate to the FDA when the instrument is submitted for review that the procedure has been tested and that it is guaranteed to work. But the bigger challenge comes when we have an emerging crisis like Ebola. In the early days of an outbreak, certainly manufacturers are getting phone calls from laboratories to ask the question, how can I be sure that my instrument isn't at risk for affecting my employees? That it's safe for-- that it's safe to-- that it's safely not transferring any of the patient sample into a place where somebody else could touch it and potentially become infected. So, the problem in the emerging crisis is-- just as Ren and Tim mentioned-- there's a lot not known in the early days. And the instrument manufacturers are trying to understand this and learn about the pathogen at the same time that the CDC is doing their studies, at the same time that research laboratories are studying the pathogen as well. And additionally, in order to determine what a safety contamination procedure is and what decontaminants can be used, the manufacturers also have to be able to have access to the pathogen. And access to samples is very difficult in the early days of a crisis. So as mentioned before, before a manufacturer, before we can say to a laboratory, for the Ebola virus or for whatever pathogen it is, here are the steps and here are the decontaminants that you need to use in order to safely clean the instrument, we have to be able to validate that and confirm that it works in multiple use situations. And that takes time.

So, kind of going back to the story that Ren mentioned earlier, and just as an example of what happens in the early days, we had the USA Today story. Here's the headline. Latest Ebola Fear, Safety of Lab Equipment. Very long article, very alarming. All based in facts, all based on things that actually happened. But if you read the article, quickly on it says that the manufacturers, instrument manufactures, refused technical service and one was said to destroy their point of care instrument after use. That they could not-- they could not guarantee that it could be decontaminated. Very alarming, but true statement. And something that unfortunately happened in the early days of the outbreak. Reading down through the article, that same CEO, that same company's CEO, said that when he learned about their communication that the instruments should be destroyed, he thought that was, and I quote him, that it was the dumbest thing that he had ever heard. And he quickly repealed that statement and then told the laboratories that they were evaluating decontamination procedures and ultimately replaced it with a validated procedure that actually would be able to decontaminate the instrument. And then later on in that article, again, people remember the headline. But later on in the article, it recognized and said that many manufacturers' policies were evolving as fears were alleviated by facts coming out from research laboratories, facts coming out from the CDC about the Ebola virus. And the misinformation was starting to subside. And as Ren mentioned earlier, there were still some labs who were limiting their patients, their access to testing for some patients, until they felt that the patient was certified Ebola free. Out of concern for both staff and patient safety. And I think this is an excellent-- I like the fact that this article starts off, it has this very alarming headline. And then, as with many articles, the really good details are further down, which a lot of people don't read. But what this demonstrates is the issue that still, even instrument manufacturers have, as we're dealing with outbreaks, in the early days when customers, just as patients in the laboratories.

In the early days, the laboratories are looking for a guarantee that they can do testing and that the instruments are safe for use. And there's not enough information out there. There's not enough understanding about the pathogen. We saw this early in the AIDS epidemic when labs were refusing, or labs were refusing to do certain tests on-- to do testing on certain patients, or that even when we saw some labs-- lab staff leaving the-- leaving the field out of fear of infection. And to some extent, in the early days of the coronavirus pandemic-- if we think back to two years, some of the things that we were told to do about washing down all the surfaces and how often you need to do it and what you need to do it with, it was an overabundance of caution because there wasn't enough understood yet about the virus itself.

And we think about today and a lot of those cleaning protocols, just in our own offices and homes and things that we used to do, when we didn't understand the virus very well, have gone by the wayside. So, I want to say that, to sum this slide up. When we think about the things that happened in 2014 in the early days of the Ebola virus, those are very different than what the considerations would be likely today if there were another outbreak, or an Ebola virus patient appeared in an appropriate institution for care. And the concerns about the testing would still be there, but they would not be as heightened and overly sensitive as they were in those early days of that outbreak.

So, as we move on to the panel discussions, there's just some final thoughts from the AdvaMed diagnostic task force. There are numerous regulations that guide instrument manufacturers in the development, in the testing, in the design, and in the ultimate validation of the instrument before the technical package is sent to the appropriate government for review. Many of those have some elements of biosafety requirements in them and refer to other documents that are specifically designed and written for biosafety guidance for instrument design. Again, as I mentioned before, when we're talking about some of the issues that happen to the laboratories and the concerns that some of the laboratory staff had very well-founded concerns, very understandable. But in the early days of an outbreak, there's a lot of misinformation that goes around. Again, instrument manufacturers were required to

validate decontamination procedures before dissemination. If somebody calls up to our technical support teams, the technical support person can't tell them, this is what we think might work. We can only tell them either we don't know and we're studying it, or once we have a validated, approved, released procedure can we make a recommendation for how we do that. At the same time that-- in these days of early outbreak-- our scientists, just as the scientists at the CDC or in research labs, they're really working hard to understand, to read as much as they can, and to get samples to test with these new pathogens so that they can validate, they can determine what are the best procedures to decontaminate the instrument and keep the lab professionals safe. And the last closing thought on this is that this is a shared responsibility. We as instrument manufacturers have a responsibility to design our instruments as safe, with the information that we have at hand, with what we know about the pathogens that are out there, with the expectation that if our procedures are followed. If we write procedures that are well followed, that the laboratorian and the patients will be safe. That responsibility also applies to laboratory communities and public health authorities, that they reinforce the proper use of procedures and that laboratory communities follow those procedures. I would venture to say everyone on the call today has certainly experienced at least at one time or another where maybe there was a deviation from a procedure that wasn't expected, procedure wasn't well written, somebody didn't follow it, and there was an unexpected consequence.

So again, we thank the CDC for inviting us to participate in this very important discussion today. We have a number of our colleagues who are on this webinar who are very eager to hear the discussion and allow us to take some of the input back to our own companies. And we hope that this is the first step to a greater understanding of how best to protect our staff and our customers and our laboratories during an outbreak. As we are listening to this webinar during the rest of the day, I think that these are three things that we're going to be thinking about and we would ask our fellow presenters and panelists to also be thinking about. What safety measures can be taken before the pathogen is well characterized? Before we understand everything there is to understand about that, how can we best protect those users of the instruments? From a manufacturer's viewpoint and also from a lab director, lab leader's viewpoint.

What safety measures can be added while we're validating our decontamination procedures? What can the lab do, in the time frame before they get a solid decontamination procedure, to help protect their staff? And then ultimately, from the viewpoint of the laboratory, what additional mechanisms could be employed to disseminate the information of a validated protocol? All companies have protocols in place about how we communicate new information to our customers, to the laboratories who are using our instruments. Sometimes we find that those communications are sent to the appropriate person that was designated at the time of the purchase of the instrument, but they don't make their way down to the people who are actually using the instruments in a timely fashion. So, it would be really helpful to understand what additional mechanisms could be employed. And with that, I thank you all again for allowing AdvaMed to have this opportunity to share our viewpoint, and to listen in on today's discussion. Thank you, Nancy.

NANCY CORNISH: Thank you Andy and Jamie. That was an excellent presentation, and I really appreciate the questions at the end, which we will keep in mind as we continue the discussions. Now I would like to introduce our second panel. Perceived risks to laboratory personnel and impact on testing. And I'm going to turn it over to Dr. Sheldon Campbell, Dr. Peter Iwen, and Dr. Mike Pentella to introduce themselves and do their presentations.

DR. MIKE PENTELLA: Thank you very much, Nancy. I'd like to start by introducing myself. I'm Mike Pentella. I'm a clinical professor here at the University of Iowa, and the director of the state hygienic laboratory. I've been a clinical

microbiologist since the 1970s, and I've worked in both clinical laboratories and public health laboratories. I'd like to pass it next to Dr. Sheldon Campbell.

DR. SHELDON CAMPBELL: Hi, I'm Sheldon Campbell. I'm a clinical pathologist at the department of laboratory medicine at Yale School of Medicine and at VA Connecticut Health Care. And like Mike, I've been practicing laboratory medicine longer than I care to admit.

DR. MIKE PENTELLA: Dr. Peter Iwen

DR. PETER IWEN: Yeah, good morning, everybody. I'm Peter Iwen, I'm the laboratory director for the Nebraska Public Health Lab. I'm also a professor in microbiology at the University of Nebraska Medical Center. So, everybody would call me a card-carrying microbiologist. But I've also served a role for 15 years as the campus biosafety officer, and I'm currently the senior biosafety officer on campus. And I have been a responsible official for a Tier One select agent program for the past 15 years. So, I've got a lot of experience in the biosafety world as well.

DR. MIKE PENTELLA: Thank you, Pete. Dr. Campbell will go first.

DR. SHELDON CAMPBELL: Thank you. My boards are in clinical pathology and medical microbiology, but here at VA Connecticut, I'm director of chemistry, microbiology, and point of care and whatever else I need to do this week. I'm kind of a generalist in the laboratory realm. And this is designed to be sort of a broad overview of the clinical laboratory perspective on biosafety and emerging infections. Infections have had an impact on human societies throughout our existence. And this is a painting intended to represent a theme from the Book of Revelation where the horseman on the left is the pale horse that is death, or plague.I'm hoping in this presentation to help you recognize the potential routes of spread of emerging, or for that matter, endemic pathogens within the laboratory and talk about the different laboratory activities where biosafety concerns arise, particularly related to instrumentation. And then talk about different levels of safety from the laboratory perspective. So, laboratory-acquired infections are still infections. And this image describes the different things that you need to have an infection. You need to have a susceptible host, a pathogen, a reservoir, a place where the pathogen resides, a portal of exit from the reservoir, a mode of transmission, so a mode of entry into-- mode of transmission, a way of getting from the reservoir to the susceptible host, a portal of entry into the susceptible host. So, in the clinical laboratory realm, the reservoirs are almost always people. Because we-- except for veterinary laboratories, we don't test animals or soil or food or water. The portal of exit can be anything because we get everything. But also-- and the panel in the middle there is, we get lots of blood and urine. But we get less, but still, some of, everything else. So, we get nasopharyngeal things and respiratory things and practically any other bit of the body you can imagine.

The modes of transmission are all in play in the laboratory, mostly direct and indirect contact. Vectors, not so much. We mostly try and keep flies and mosquitoes out of our laboratories, and usually successfully. So direct and indirect contact are the most important modes of transmission. And then all the available portals of entry, mouth, nose, eyes, cuts, and skin, are available. We don't have infants in the laboratory, but our laboratory population of workers is aging. It certainly has immunocompromised persons. So, plenty of susceptible hosts in the clinical laboratory. The other thing to recognize and that sometimes gets less attention than it deserves is that particularly for emerging pathogens in the clinical laboratory, there may be routes of transmission that are not epidemiologically important outside of a laboratory environment. So, a pathogen that's not normally bloodborne may be bloodborne if you're handling 10,000 bloods a day. A pathogen for which urine is not a particularly important route of spread in the

environment may nonetheless provide risk via the urine, even if it's not always present. So, laboratory people divide the universe into the pre-analytic, analytic, and post-analytic realms. The pre-analytic realm includes everything from sample collection to transport to reference laboratories. And there are places on that continuum for exposure of laboratory staff and others at every step. From collection to transport to reception and unpacking to centrifugation, uncapping, aliquoting, and various bits of transport of specimens. In the analytic realm, we have a whole bunch of different laboratories that do different things, that have very different instrumentation in them, that handle different specimens in different ways. And there are unique biosafety issues in each of the areas of the laboratory. And then there are even post-analytic biosafety issues in terms of waste management and sample storage and retrieval. Next slide, please.

Focusing on the analytic phase where many, but not all, of the instrumentation related risks reside, I mention that chemistry has got by far the most complex instrumentation. General chemistry and hybrid general chemistry, immunochemistry analyzers, have multiple sampling stations, they've got multiple aliquoting events, and they have waste pathways for liquid waste, as well as for tubes. And often in the case of laboratory automation, for caps as well. Most chemistry instruments cannot perform closed tube sampling, so there is a decapping step. These instruments, as I tell my non-laboratory colleagues, are worth more than my house and are extremely complicated. So, they require a lot of attention. They're extremely expensive. And even if you could use them safely for your high consequence pathogen patients, they're critical for care for large numbers of patients. So, taking a risk with a chemistry analyzer is not only putting that instrument at risk, but it's putting the care of a large number of patients at risk. And once you get beyond a single instrument to large scale automation, there are many interaction points, both with the sample and with users, in large scale laboratory automation systems. And I'll show an example of that in a minute. Blood gases is its own little fascinating area of the laboratory. Samples are submitted in syringe, mostly without needles. Mostly. But it's an extremely labile sample and it has to be handled rapidly. So extra handling steps are a problem in the blood gas realm. Hematology, in addition to many of the same issues as chemistry analyzers, also have either manual or automated slide making associated with them, including glass slides, including sometimes assemblies for drying slides by blowing air over them. In the bacteriology lab-- everybody's favorite because we're mostly microbiologists here-- we don't necessarily know how well viruses survive in culture systems that are used for bacteriology. But it's likely that they do survive pretty well. Old studies show that HIV, a relatively fragile virus, survives pretty well in blood culture systems. So even though we are taking a sample and plating it and going on and doing other things with it, those viruses may well not go away, in addition to we may be cultivating high consequence bacterial pathogens like Bacillus anthracis or Francisella tularensis. There is a lot of manual handling of samples and cultures in bacteriology. Plus, complicated analyzers like MALDI-TOF systems. Particular to virology, but waning in importance, is the growth of emerging pathogens in viral culture. Routine clinical virology laboratories, in many cases, have abandoned viral culture entirely or only have very limited use of viral culture. Still, something to keep in mind, as well as the issues related to instrumentation of all the other sections. Molecular diagnostic sections also have really complicated analyzers that are much more manual, in many ways, than are automated general chemistry and hematology systems.

There's also the specific question, particularly related to molecular diagnostics, since that's how we mostly approach novel pathogens, these days is how we evaluate and validate EUA tests for dangerous rare pathogens. Exactly how do we do that safely? In transfusion medicine, two based methods that are still widely used, likely generally droplets. There is no sealed road or blood bank centrifuge currently available. I still haven't found one. And risks associated with gel and instrumented methods are unknown in the transfusion medicine realm. The laboratory community has not been terribly aggressive about investigating these hazards. There's a whole literature on laboratory acquired infections, and they don't seem to be common. But they're not monitored, either. But this is

one of the better studies that the laboratory community has done, looking at potential viral pathogen contamination of a total laboratory automation system running automated clinical chemistry. Looking both at baseline and after running-- intentionally running high titer HCV samples through it. One thing about HCV is you can get samples that have got 30 million copies per mil. They put glass slides in place where droplets might go. They also swab parts of the system, and then did PCR to detect HCV, RNA. Next slide.

And the short answer, though the paper is well worth the reading, is that they found both Hepatitis B and Hepatitis C nucleic acid during routine usage and in additional sites after processing high titer HCV. And they were in-- mostly in the places where you'd expect. In the waste shoots, in the places where tubes are directly sampled and handled. But not always. You could find RNA in some out of the way places in their total laboratory automation system as well. It's an important caveat of any such study using nucleic acid amplification is that it's not clear whether it represents infectious virus. But that doesn't necessarily-- shouldn't reassure us too much because different pathogens are going to have different levels of environmental stability and infectiousness. So even if it's not infectious HCV, it doesn't mean it couldn't be infectious monkeypox or whatever the next damn thing is.
And as our colleagues from AdvaMed have reminded us, there's lots of situations where instruments are handled and managed and interacted with by people. But I want to emphasize that from the clinical laboratory perspective, we don't always know what we're working with. We may get samples from patients with a known high consequence pathogen. We might get samples from patients under investigation for a high consequence pathogen. If they tell us. Not always what happens. And we might get samples from patients not under investigation, who still might have pathogen X. And then, in addition to hazards during use, there's the after use and decontamination of the instrument Before more use, before servicing, and at the end of the instrument life. So, all of these are things that we and our industry colleagues think about. So, I want to sort of describe what I think of as the partnership going forward. To some extent, the risks right now are unknown. The laboratory community has not been great about studying these risks, and there is not extensive documentation for the instruments that I have in my laboratory of risks, particularly related to biosafety in those instruments. So, the first step, I think, for both of us, is to do a better job of describing the risks. What elements of instruments are associated with what risk? With droplet production, with percutaneous exposures, potentially with aerosol production. What degree of risk and contamination occurs in routine usage? And this is something that's going to require a partnership between industry and the laboratory community. To do this, to be able to describe these risks. The next step, of course, is to mitigate them. To identify-- to address identified risks, to continue to address identified risks with the clever engineering, as described by the folks from AdvaMed.

And for us in the laboratory to mitigate other risks with improved laboratory practices. And it is worth mentioning that eliminating all risk is not an attainable objective, but that nonetheless we continue to work to mitigate those risks. And that's the 30,000-foot viewpoint from the clinical laboratory.

DR. MIKE PENTELLA: Thank you very much, Sheldon. Dr. Pete Iwen is next,

DR. PETER IWEN: Good morning, everybody. It's my honor and pleasure to be here, to talk with you about some of my experiences in caring for patients who actually had Ebola. At the time that we dealt with the Ebola patients, there was very little information on how to provide laboratory care for patients with a high consequence pathogen. And then throwing in a high consequence pathogen that's in a risk group 4 for added a whole other level of complexity to this. So, I would like to give you a little bit of an overview of my experience in caring for these patients with Ebola virus from the standpoint of the laboratory. My laboratory was asked-- since I worked with a public health lab, I had access to a level three facility-- was asked to provide the laboratory testing for the Ebola patients.

And interestingly, at that time, we thought more of the microbiology testing, but weren't really up to date on the chemistry, hematology, blood banking for my laboratory. So, we had to get competent in those areas as well. I'd like to also talk about some of the laboratory challenges that we encountered. And I will tell you that there were a lot of challenges. We learned a lot of things with this process. We had challenges with select agent issues. We had challenges with transportation. We had challenges with staff wanting to quit because they didn't want to handle these samples in the laboratory because of the risks. But I will dwell on the challenges involved with the instrumentation as well. So, there were a lot of challenges involved in caring for these patients.We had 11 people with Ebola show up in the US during this 2014-2015 issue with the Ebola outbreak in West Africa. And of these samples, seven of them were expatriated to the US from West Africa. Three of those patients ended up in our biocontainment unit here at the University of Nebraska Medical Center. Four of them ended up at Emory University. And on the right here is just a picture of our unit. At the time, we had a 10-bed patient biocontainment unit that was actually available to care for patients with a high consequence pathogen. It was the largest unit in the United States, and it may have been the largest unit in the world at the time.

But one thing we did not have is we did not have a laboratory set up, available to test our patients within this unit. And we, at the time, determined that we really needed a point of care lab within the unit, which we did set up. So, we were trying to prepare and care for our patients as easily as possible with handling these specimens.
We knew that the risk to handle Ebola virus infected specimens was high. The high viral load in a symptomatic patient is an eye-opener to me, but greater than 100 million plaque forming units per mL. And the infectious dose is less than 10 viable viral particles. So, if you do the math, you could almost take one tube, one mL of sample, and infect many, many people. Certainly, everybody probably, almost, in the United States. And the microdroplets produced from blood could easily contain enough virus to cause infection. Now this figure below was put together by the CDC in a document that's listed below there.

But it's Ebola virus RNA copy levels in sera over time from Ebola virus disease infected patients. And you can get a feel here during the period, just within the first 10 days, that you could easily have 10 to the eighth viral copies per mL in the serum. So, handling these samples was a risk to the laboratorians, and we were concerned about that. So, what level of risk are we willing to accept? Well, I had administration come to me and say, there is no exception here. We can't have a laboratory professional get infected with Ebola virus. And we knew that the specimens contained high concentrations of Ebola virus. And we also knew that there was an OSHA general duty clause that basically says that the employers need to have a safe environment for the employees. I am paraphrasing here.
We also knew that there was a lot of tests that needed to be run that the clinicians-- if they wanted a test, they're going to get a test run, in their mind, whether we were prepared or not. So, we had to sit down with the physicians and say, you know, we really need to design a list of tests that we can perform safely within the laboratory that will support your care and the optimal care of your patients.

So, we actually sat down and designed a list of tests that could be run safely in the laboratory. This, of course, involved the testing of known Ebola virus patients. But this test list was limited and would certainly expand if we included patients with other diagnoses. The on-site risk assessment, then, to look at which of these tests could be run safely with the instruments that we had, and was there a change that we need to make in the laboratory to be able to run these tests? While doing the risk assessment on site, we found out that the chemistry automated analyzer in our core lab had an initial centrifugation process with no sealed rotors.

And that was a problem that we weren't sure how we were going to deal with. And basically, what ended up-- and I'll show you how we mitigated some of these risks-- ended up using point of care devices to help run these tests.

We had a coagulation automated analyzer that required open tube testing as well. Again, what are we going to do about this? We had the blood bank where the crossmatch required open tube centrifugation. What are we going to do about that? And you'll see the slide in the upper right that we actually started by using an agglutination test to do typing for the blood. Kind of an old school method, but it did work. And also, on top of this, even though we had biosafety cabinets available in our facilities, a lot of the facilities within the state who were doing PUI testing didn't even have biosafety cabinets. So, it was really a concern. And the conclusion was that not all laboratory sections could safely handle specimens from a patient that had a potential to have Ebola virus disease. So, mitigation. Mitigating the safety. Well, certainly, you look at engineering controls. You look at your equipment. You look at your facilities, whether you have negative ventilation. You look at administrative practices, the training, limiting access to what we're doing. Testing, writing protocols, policies, having a medical surveillance program in place for the employees, and making sure that we had the appropriate PPE. So, these are all processes we looked at to mitigate the risks. And mitigation involved for the equipment involved looking at the instruments that we now determined were aerosol producing and coming up with an alternative approach. And some of these alternative approaches involve using point of care instruments. Some of these instruments are CLIA-waived instruments, some are not. We made a decision in our laboratory that the laboratories would run all of these instruments, even though some of them, such as the iStat, were waived. And that we would run them in the laboratory. And that we would run them under a biosafety cabinet. So those are some of the things we looked at for mitigating the risks of the instruments. So, the learning issues from what we did was that, first up, we developed this essential list of tests. And we looked at a risk assessment, determined what we could do and how we could do the tests that the physicians needed. And we also looked at making sure that we met CLIA standards, such as competency, verification testing for the different types of cartridges, for instance, that were used on the point of care instruments.

We looked at a risk assessment process throughout. Any time we changed anything, any time a physician asked for a new test, we looked at the risk assessment process. We opened up lines of communication, which were very important with the medical staff. Again, physicians said, if we want a test, you're going to run it. Well, the point was that we couldn't run all the tests that they wanted. We opened up lines of communication with the equipment manufacturers, and as well with the CDC. And we, again, determined that all not all tests could be performed safely. So, we had to come up with alternatives. We looked at our flat lab policies and procedures that needed to be fluid. And basically, we needed to be prepared to provide optimal patient management in an environment that was safe for the employees, students, and visitors.

Mr. Quintenz already talked about this article that was put out by the USA Today, The Latest Ebola Fear, Safety of Lab Equipment. And he talked about the issue of some of the CEOs saying that this was the dumbest approach imaginable. Well, my boss actually had a comment in here in the last column. And his comment that if this unfounded behavior continues, it could significantly impact the way hospitals care for these patients. Well, where are we at today? Dr. Gibbs is going to talk about a paper that we wrote looking at the manufacturer's response, and responses to a survey that we put out, which avoided answering some of the questions that we brought to the manufacturer's attention. There were no protocols for some of the high consequence pathogens, no protocols for decontamination, manufacturers would not service some of the instruments, invalidated warranties. He will talk more about this issue. But I would like to close by saying that it seems that we're still dealing with these issues today with the monkeypox. We're getting questions from laboratories again, wondering how can we test certain samples within our core labs now that they may contain monkeypox? So, this has not gone away. And I think we are now looking again at the risk assessment process. One concept that might be something we could talk about or look for a solution might be that if we could actually collect samples of specimens within a matrix that inactivates any of the pathogens within that collection device before it's ever put on an instrument.

It's something that might be a consideration as well. So, I'll close there. That's my talk. I look forward to the panel discussion on this. Thank you.

DR. MIKE PENTELLA: Thank you, Pete. I would like to thank the organizers of today's town hall for the opportunity to speak. Biosafety has been a significant area of interest and concern for me from the start of my career, which dates to prior to the HIV epidemic. Studies have shown, and I have observed, that after a clinical laboratory scientist has an exposure or has acquired an infection, they often leave their position, and even the field.
And in these days of the critical workforce shortages for the clinical laboratory, that is very stressful for us to consider. When they explain their reasons, though, it's the stress of the exposure. Having to take antibiotics and the potential to bring their infection home to their families. The thought of future risk to their health and safety that weighs heavily on them and leads to these transitions. In the US, exposures and even lab acquired infections are not reportable events. Therefore, we don't have any idea how often this occurs.

My hope for today is to bring your attention to planning to test for an emerging pathogen. There's a certain amount of fear associated with handling potential infectious material, but we do get used to it. But when you see a new emerging pathogen, those fears reappear. And for an emerging pathogen, it's different for each scenario of the pathogen. The nurse pictured on this slide in the upper right is demonstrating to the Massachusetts legislatures that the gown that she's provided to use to care for patients who may have Ebola is very flimsy, and it's not sufficient to protect against blood and body fluids. And that is the situation in laboratories as well. While laboratories are dedicated to providing test results for patient care, to place that person at risk of disease, or even death, to meet the mission of the laboratory is completely unreasonable. So, our laboratory directors, understandably, while dedicated to the mission of the lab, are dedicated to protecting their staff.

And sometimes the only way to do so is not to perform the test. And of course, that leads the situation, as Ren described in his opening comments. Where tests are performed, is also changing. So, we have to consider that we're moving from traditional laboratory to a point of care test done in pharmacies, in some situations.
So that moves the risk to those environments as well. But when is the right time to decide that a risk exists? Is it at the time when the test needs to be performed? That is too late. I would venture to say that the design phase is the most important phase to determine that there is a risk to the end user. This gives you a list of emerging pathogens by decade. And it's a reality of life that we are going to be facing an emerging pathogen. The list is not inclusive, by any means. But we need to consider the next emerging pathogen, and not design for the known pathogens, but design for what we may be facing in the future. And that's really hard to do.

All right. This has already been brought up, that during 2014, Ebola in the US took us by surprise. Yet, it really shouldn't have been a surprise. We should have recognized that we're going to face an emerging pathogen like Ebola that's life threatening, that there's not a treatment, there's not a vaccine. And SARS-CoV-1 presented that exact same scenario to us in 2000. So, we were surprised, though, by the reaction from the manufacturers. Let's go on to the next slide.

This documents a case of a four-year-old girl who had recently returned from West Africa, and she was hospitalized. And it was that situation where they were fearful of testing samples from this four-year-old, so they wouldn't even insert an IV. And turned out that she had malaria, and she did not get the standard of care that she deserved. She survived, and that's great, but others did not, as pointed out on the next slide.

And then this situation, there are reports where people didn't receive the standard of care and they did not get the test they needed. And they were negative for Ebola, but sometimes other diseases were not recognized sooner. So, we had specific laboratory concerns related to Ebola. And we've tried to address many of those concerns. And as Dr. Salerno said, I too am convinced that we're in a better place than we were in 2014. And that's great. And I did see a lot on listservs when COVID appeared where people were talking about doing a risk assessment. And we're talking now about a risk assessment from monkeypox. But I'm also very concerned about risk assessments for point of care environment in other locations, such as pharmacies. Because I don't know the knowledge level that we have. But one of the things I want to point out is, there's no oversight of those risk assessments. We don't know what quality of the risk assessment is being performed. And we don't know the quality of the person, or the knowledge of the person who's performing the risk assessment. We have these recommendations for when to perform a risk assessment, and one of those recommendations is to perform it before you acquire the new instrument. The third bullet when new equipment is being considered for purchase. And I think that is a very good thing to do for laboratories, and we should emphasize that. When you're in a rush though that doesn't always occur. In the next slide,

I will share with you that we were selecting a new instrument for COVID testing. And we were in the midst of doing about 20,000 tests a day at the time. And we were moving to more high throughput instrumentation, which we were glad the manufacturers were putting out there. Unfortunately, though, we didn't do our risk assessment. Then when we got the instrument, we recognized that there was a risk to staff of exposure to positive samples. And because of that risk, we had to add another step to our procedures to inactivate the virus by adding guanidine to the sample. This took additional time. We estimated at least an hour was added to the procedure before we could start the testing. And this really slowed us down, and added an additional cost, more handling, more risk of errors. So, it really was something that we wish the manufacturer had considered before we got the instrument. But unfortunately, it was handed to us. Fortunately, we recognized it, and no one was exposed.All right, so looking at these, I want to point out that it's not just the acute disease. It's the long-term consequence. COVID 19, as I just spoke about, has a side effect of Long COVID. And also, something like Hepatitis C, a bloodborne pathogen, has a side effect of leading to cancer. Although rare, it does occur. I want to next introduce our panel, but I'd like to emphasize that laboratorians understand that there's a risk. But we have to do everything we can to mitigate that risk. And I'd like to end my slides now and go on to the panel discussion and introduce Laura Nolte and Dr. Andrew Bryan. So Dr. Bryan, you're on the slide. Could you introduce yourself to the town hall?

DR. ANDREW BRYAN: Yes. Thank you, Dr. Pentella. Andrew Bryan, clinical microbiologist and faculty in the Department of Laboratory Medicine and Pathology at the University of Washington, where I serve as medical director for our main University Medical Center clinical laboratories.

DR. MIKE PENTELLA: Thank you, Andrew. And Laura Nolte, please introduce yourself.

LAURA NOLTE: Hi. I am Laura Nolte, and I am the manager of the microbiology molecular and special procedures laboratory for Texas Health Presbyterian Hospital within Dallas. And we had the fun experience of hosting several Ebola patients back in 2014 and have had numerous experiences with additional emerging pathogens since then.

DR. MIKE PENTELLA: Welcome Laura. And now, Dr. Iwen and Dr. Campbell, could you join us on camera and off mute for our next portion of this? Thank you. So, I'd like Doctor Bryan to start by asking the first discussion question.

DR. ANDREW BRYAN: Yes. Thank you so much. So, the CDC has biosafety guidelines. There's the general, and then you've come out with specific Ebola, SARS-CoV-2, Monkeypox. And any of those specific guidelines are often calling out the routine laboratory tests. You know, hematology, chemistries, routine bacteriology cultures. And then often the pathogen of interest. But the guidance often distinguishes less clearly, between manual and automated methods. And with this section around instrumentation, I think that's a key component. Particularly, there's commenting on an unsealed centrifuge rotor. Well, there's a huge difference in where that is in that actual workflow. And sometimes the guidance has a preference for point of care testing. So as the study that we did, that Dr. Campbell mentioned, we saw on our automation line that there is quite a bit more contamination around the decapping components of that workflow relative to the actual centrifuge, even though that was an unsealed rotor in our system. And so, our own risk assessment at our institution, when we recently redid this for monkeypox, as we thought through that, is that the risks associated with manual handling of the tubes to be much greater than automated instrumentation. Even if that had included an unsealed rotor. Just like everyone to think through the exercise of, OK, if you have a sealed rotor, you spin it, great. Or you have an unsealed rotor, spinning that down manually. You still have to get that cap off that tube and onto the actual analyzer. So, you may be left with taking that rotor into a biological safety cabinet, uncapping it there, and then manually walking it across the lab in your hand or on a cart. Open it when your face is right in front of it. Or you're taking that tube with the cap on right in front of your instrument and then you still have to take off the cap that's in your hand, now outside of the BSC, the most dangerous risk for droplet generation before you put it on the instrument. So, some additional follow-ups to this, I think, is where our discussion may go. But I'd like to ask any of our other panelists here, how would you integrate these manual versus automated workflows into your risk assessment in your lab, when deciding both your routine, safety protocols, as well as for a high consequence pathogen?

DR. SHELDON CAMPBELL: Well, you don't ask any easy ones, do you? I think your point is really well taken that whenever you can let a machine handle a tube, it's better than having a person handle it, even if the machine has gaps in its safety processes. Because the machine can't get anything, and people can. But I don't know how you balance, will I open the tube in the BSC and then I walk it to the instrument open, and trip over something and, you know, spray the lab with it. Versus I carry it close to the instrument and open it there. I don't know how you address that question.

DR. PETER IWEN: I think what we want is we want truly automated instruments that do the pre-analytical and analytical processing. But I also recognize, from our facility, that the core chemistry areas didn't even have biosafety cabinets to process the original pre-analytical step of decapping tubes.
So that was an issue for us as well.

DR. SHELDON CAMPBELL: And as a smaller lab, I'm not going to be, in the foreseeable future, able to have space or money for a true Total Laboratory System (TLA) system either.

LAURA NOLTE: I think that, especially in a smaller lab, not just having space for a TLA system. But even having a space for a hood, even a small hood. I think, though, to try to begin to answer that question is within the risk assessment of the space and what you need to be continuing to do for other patients at the same time, are you able to shut down where you're working in order to remove all nonessential personnel from doing that particular test? Have a tester and buddy. And what can you do to mitigate the trip? To mitigate how they're exposed. What kind of PPE are you wearing, how do you transport it? Because you don't want to necessarily transport something in your hand. Is there something that you can contain to stabilize that tube? If, in fact, you have to open it with-- in a safety cabinet or somewhere else and transport it. So, I think every lab is going to be extremely different with that,

just based on their set up. And just even the knowledge and comfort in the training level of their personnel. We are constantly-- even now in our own lab, and just finished another round of this. And every time we do this, we find something different that we could do better. And I think that just goes to continually looking at risk assessments as well.

DR. PETER IWEN: I don't know, Laura, if that was a yes or no question. But do we-- do we have-- can we dedicate a space, for instance, that only one or two employees are working in to run these samples? And the answer is, probably no. The other issue that comes up that came up with the monkey pox just recently was-- the core lab asked if you have a PUI that might be monkey pox through your core analyzer, do you need to decontaminate your analyzer after the sample was run through? Well, the decontamination process step would have shut the instrument down for one to two hours to decontaminate it, and they can't afford to shut the instrument off that long. So, there's a lot of processes involved there.

LAURA NOLTE: Correct. And we have the same issues and the same questions as well. And had to deal with monkey pox last year as well. So, when you look at labs of various sizes, some labs may be able to do something over here and work with everybody over here, but it is kind of the whole shutdown process and what do you have in between? Or can you just do everything on a point of care? Well, no, not necessarily. You can't do that. Because as you even said in the presentation, which I wrote down here as I wholeheartedly agreed, because the doctors want what the doctors want. Right now. So, it's how do we get around that and appease them at the same time?

DR. SHELDON CAMPBELL: The other thing that comes to mind, for me, as I listen to this conversation is that there are a lot of good ideas here, particularly on the sort of detail level. You know, how do I transport a tube from a biosafety cabinet to an instrument? Can I shut down my lab for 30 minutes for everything else, and do a dedicated run of a PUI? That maybe are not widely published and publicized. And how we do this research and publish it, I think, is still something that is worth us talking about.

LAURA NOLTE: And I really think that we have to differentiate when we're looking at this between a PUI and someone who is known to us at the time. So, a PUI for Ebola with us is handled differently than a known patient with Ebola that's going to be here for a long period of time. And so, to me, they're two very different things to look at.

DR. MIKE PENTELLA: I just wanted to add that I think it's a really good point to our manufacturing colleagues that having conversations with us in the design phase would really help. Because if there was a way to have a rapid decontamination of the instrument so that you wouldn't have to shut it down and it could be designed in, that would be really helpful.

DR. ANDREW BRYAN: I was just going to follow up and that was a perfect segue to what I was going to say is, a lot of what we're talking to here and-- risk assessments or device design phase are kind of these extra asks to our manufacturer colleagues, which may be challenging for them to do, particularly for a for profit company that may have obligations to their shareholders. So how do we take these, and rather than simply applying extra layers of regulation that incentives may not be there as far as alignment for meeting a bare minimum. How do we spin this in a way that incentivizes these risk assessments and turn it into a selling point for that, so that we can be safe in our labs, our regulatory colleagues can be comfortable that we're doing the right thing, and then the companies can achieve their aims as well?

DR. PETER IWEN: I agree, Andrew. And just to add to that, I'd like to say that biosafety in the laboratory is certainly, as Sheldon said, is not a new concept. I mean we've been thinking about these for years and years and years. But the point in my mind is that we're talking about high consequence pathogens here. What about the things that we don't know? In other words, every specimen that goes through the clinical lab has a potential to have something bad, right? And they all should-- we handle them under body fluid, bloodborne pathogen precautions, right? We know that. But we should be prepared-- every risk assessment should prepare us for the fact that anything bad could happen in the laboratory, right? And instruments need to be thought of from that standpoint, in my mind.

DR. MIKE PENTELLA: One of the things we have to recognize, too, is the manufacturers could look at this as a selling point. Because if all things being equal, you-- I would select the instrument that had the safety features that I wanted to protect my staff over and above one that did not.

LAURA NOLTE: I agree. In addition to a risk assessment and what manufacturers have done to provide guidance as a selling point, I think that it really needs to continue to be ongoing. And I know that was something that Andy had mentioned earlier, as an action item, was to determine what is the best route of communication. And when I look at as route of communication, from the manufacturer to us in the clinical laboratory, I'm thinking on levels of not just selling but ongoing from a Factory Service Contractor (FSC) who is coming to service my instrument. And for us to have that clear communication of expectations on both sides to keep them safe. But as well as, if we must troubleshoot an instrument and I call technical service, or I have off shift personnel and they're calling technical service, are they getting someone who can also help protect them on the phone when they're asking them to open this part of the instrument and look at it. Are we taking those measures all throughout that process as well? And is technical service trained on that? As far as the question that Andy had about better communication, because he is absolutely, 100% right that the letters of communication will go out to somebody who may have-- not be here anymore, who may have made a purchase above us, and their names on the contract. That might be who gets the information when they have an update. And it doesn't trickle down. So where does that kind of fall in place? I think that is in combination with the FSC and whoever your immediate sales rep is. So, I know that was a lot of communication packed into one thing.

DR. SHELDON CAMPBELL: I was on a committee a long time ago with a guy whose favorite expression was, the word of the Czar is law, but Moscow is far away, and the roads are bad. It's one thing to put things out and it's another to have them get where they need to go.

DR. ANDREW BRYAN: Extending Laura's comment about the technical service. We've had some vendors come into the lab performing that service, and without the appropriate PPE. So, while we're talking about risk assessments and establishing standards for the instrumentation, there's that other key parallel to the staff. In their clean room building the instruments and training, they're not exposed to the same things that we are in the clinical lab. And so, we need to make sure we match that, you know, precautions for all the interactions. You know, I see a big difference, for example, in our micro staff walking around the lab and their habits compared to the main lab. Where even after doing that study, had someone grabbing a centrifuge rack off the line with bare hands. I'm like, I think you want gloves with that. And so, it's just not built into that mentality and that training, whereas like our micro folks would never—I hope they would never do that. And so, we need that it really spans across different areas of the laboratory, not just those that are very aware of contamination in the micro lab, but our core laboratories, our instrument technicians, et cetera.

DR. PETER IWEN: That was the eye opener to me because I'm a microbiologist. And I thought biosafety goes with microbiology. And to find out that all these other labs, this is a really big issue that, quite frankly, I don't think they were prepared to discuss biosafety as much as my microbiology folks were. So, it opened my eyes up to find out that there's a lot of things going on in the chemistry, blood bank, transfusion medicine, et cetera, where there are unsafe practices were being done. And I think we're more attuned to that today. I think that's a good thing. But we still have older instruments that run the same way they did 10 years ago. So, we've got issues to deal with there.

DR. SHELDON CAMPBELL: And it's really important to make sure that not just microbiologists come to the table. Because microbiologists don't necessarily know what's going on in the chemistry lab and in the blood bank.

DR. MIKE PENTELLA: Yeah. We have had the same issue here that our field service representatives who visit our lab have not always been trained well enough to recognize potential hazards. And it's hard for us to have to teach them, because they don't always want to accept what we're asking them to do. So, it really behooves the manufacturers to do a good job of training them and ask them to follow our requests when they come into our labs, for safety.

DR. ANDREW BRYAN: Just looking at the time there and making sure we can hit a couple of different topics. Laura, do you want to ask some of the other talk topics here, as far as a follow up question?

LAURA NOLTE: Sure, I can. One of mine-- and this is-- this is more, really, for clinical labs to resolve. But I think just for manufacturers to keep in mind is the landscape of the laboratorian is changing. It-- we have a lot of laboratorians that have retired, we have a lot of new laboratorians that are coming in. And every facility has so many different knowledge bases. And not every facility has PhDs that you can rely on as well that kind of have a little different level of expertise. We do have colleagues that we can call on and ask questions within the field. But I think that also sometimes puts especially smaller labs without a lot of that expertise at a disadvantage. And I would hope that as manufacturers are developing new instrumentation, it becomes more and more complex, that they're kind of taking all of that into account. And I know we've all, I think, said at one point that we really need to have the manufacturers work with us directly in clinical labs before they roll something out. And really, my reason behind that is just because of how we are all so different in those different knowledge phases.

DR. MIKE PENTELLA: So right. I come from a state where there's many, very small, rural laboratories, and rural hospitals. And it's imperative that we consider them and their needs. Because they do not have the resources. They have to look to others. And one of their major sources of information is the manufacturer's reps. And so, it's very valuable to them to have the manufacturing rep point out the biosafety risks and how to mitigate.

DR. PETER IWEN: And they are the front-line laboratories, in my opinion.

DR. MIKE PENTELLA: Yes.

DR. PETER IWEN: Things are going to happen in those rural labs before they ever show up in the big commercial labs.

DR. ANDREW BRYAN: So, I mean, and along with the-- maybe the non-microbiologist lab director, that rural hospital, and the instrument vendors, they're really relying on that clinical guidance from the CDC, as far as the biosafety guidance that we have. I think-- and apologies, I can't remember. It may have been Ren Salerno in some

of the introduction about the BMBL, as far as the biosafety and microbiology and biomedical laboratories guidance. And that the BMBL has generally not been focused on clinical labs. And so, I think we see that, too, in some of the Ebola, initial SARS CoV-1, and particularly now with Monkeypox. Where in the example of the Monkeypox, we have a non-clinical division of the CDC writing the biosafety guidelines for clinical laboratories. And I think there are some components of that that don't really make sense for those of us on the ground in the clinical laboratories. And it would be helpful to reconcile. So how would-- I guess to the rest of the group, what's that ideal group of stakeholders to really compose those biosafety guidelines? Both that guidance for the manufacturers, as well as then for those public health or CDC guidance to the rest of us in the clinical labs, whether you're a large academic or a small site.

LAURA NOLTE: I think when I think of the stakeholders, it's kind of who you just listed. It's manufacturer, public health, and clinical lab all together in combination. And we take our guidance as clinical laboratories from public health, but I completely agree with your point. When I go and look at the BMBL it is more research-based. And if I'm cultivating Monkeypox, for instance, and some of that. I think it really is the three together, as with all facet's representatives.

DR. PETER IWEN: We need-- we need the users to be involved in the discussion.

DR. MIKE PENTELLA: The end users.

LAURA NOLTE: The end users.

DR. MIKE PENTELLA: And it needs to start at the design phase. Because as you were describing….

DR. SHELDON CAMPBELL: Not just the design phase for the instruments, but the design phase for the processes and the logistics.

DR. MIKE PENTELLA: Right.

DR. ANDREW BRYAN: That entire, I think, Sheldon, your slide with the pre-analytic, analytic, and post analytic. That it's follow the specimen, I mean, like we do in a CAP inspection. It's follow the specimen for-- it's not just about the instrumentation or what may be in the package insert, as far as intended use and hazards. It's everything around it that could be just as hazardous as the actual analytic phrase itself.

LAURA NOLTE: Correct. And I think you have a perfect point with it needs to be at the design phase. Really before engineers take over. Because the engineers are the ones that ne going to come up with these wonderful solutions for us. But we need to kind of come up with the big, overarching ideas of what it is that we need. Because it's only the users that do know exactly what they need.

DR. MIKE PENTELLA: And document that biosafety aspects in the instrument manuals for everyone to clearly pull that information out. I think that those are our two big asks of the manufacturers. A, work with the users and experts, biosafety professionals, et cetera, at the beginning to design phase. And then B. document in the instructions, the biosafety measures that people should be taking so that they will know exactly what they need to do, before they have an emerging pathogen, basically.

DR. SHELDON CAMPBELL: And not merely during routine use. But during troubleshooting and servicing and at end of life.

DR. ANDREW BRYAN: And I mean, I think that it's also important to emphasize that it doesn't have to be perfect, right? It's always-- it's a risk assessment. We don't want to have undue liability on the manufacturers of the instruments. It's just acknowledging the risk and the best guidance for how to mitigate that, as best we can. To support all of our patients.

LAURA NOLTE: Even if it's not that we're seeing the actual risk assessment from the manufacturer. But I think every lab has an obligation to consult with the manufacturer as they are doing their own risk assessment. That really is on us to reach out. But when we reach out, we have to be able to get an answer.

DR. SHELDON CAMPBELL: But we ought to recognize that liability issues and concerns about liability drive some parts of this conversation. Not only from the manufacturer side, but even from the lab side doing the research.

DR. ANDREW BRYAN: Right. Being the CLIA director, I feel that. That's for sure.

DR. PETER IWEN: But we want to provide optimal care for our patients as well.

LAURA NOLTE: Yeah. I think the ultimate goal is to be prepared at all times for anything and be able to serve all patients equally. What we don't want is-- my two main goals are, I don't want a laboratorian to be infected, and I don't want to be in that situation where I'm not providing care to someone, and they do die.
As you pointed out, Dr. Pentella, in your presentation with-- during Ebola with the patients that had to wait for treatment.

CDC MODERATOR: OK, thank you everybody. That was a great discussion. We are now going to take a 30 minute lunch break.

CDC MODERATOR: Good afternoon, everybody. Welcome back to our town hall meeting today on laboratory biosafety. We're going to go ahead and get started if Dr. Gibbs is ready. We'll go ahead and turn it over to you for our third session on independent assessment of risk and instrument design.

SHAWN GIBBS: Excellent. And I'm happy to be here. Please let me know if you've got any difficulties hearing what I'm having to say. So first, I'd like to thank you to the CDC for hosting this workshop. It is extremely timely and very necessary. I'd like to start off with just saying we're all in this together, and we can come up with a lot of solutions together that I think will help make this process a lot easier and a lot safer. So just a little introduction of myself. I'm Dean of the Texas A&M University School of Public Health. But I'm here, as I am also a certified industrial hygienist whose research focuses on the disruption of the transmission of highly infectious diseases.

I'm faculty in the National Emerging Special Pathogens Training and Education Center, also known as NETEC. And I'm also with the National Institutes of Environmental Health Sciences Worker Training Program, P2R Academy. Previously, I've been director of research for the Nebraska Biocontainment Unit and have supported treatment and transports of Ebola and other highly infectious disease patients into the United States.

This is just the obligatory slide brought to you by as these are the groups that have also supplied my funding and so on, to be here. Earlier today, Dr. Pentella mentioned the importance of risk assessment but also knowing the quality of risk assessment and the person conducting it. And I want to say I could not agree with that statement more. I think the industrial hygiene field needs to actively increase its capacity and the quality of members to do these, both in operational risk assessments, as well as in the development phase prior to manufacturing and marketing of equipment.

I know that as an industrial hygienist, I bring a different perspective to these challenges than some other people do. And remember, as an industrial hygienist, we're not only here to identify what the potential exposures are but to help design and implement solutions to mediate those potential exposures, as well.
So later on, one of the panel members we'll be talking with is Dr. Le, who I also wrote the articles that you're seeing here. And what we're wanting to do is essentially challenge industrial hygienists to become more involved in infectious disease response.

When we survey the various high-level isolation laboratories, you see the importance of clinical laboratory and point-of-care equipment in their treatment plans. We are often tasked with assessing equipment within the laboratories and helping them set up processes so that tests can be run as safe as possible. When supporting laboratories to determine the processes, understanding the manufacturing recommendations are essential to moving forward into developing laboratory processes and procedures. However, there's still a whole lot of unknowns in these situations. Hopefully, this workshop will push things forward and will help to address some of those unknowns. And I think, as we've seen through some of the earlier discussions and panels today, we not only have to address these issues for the patients who are suffering from these highly infectious diseases but also making sure that their clinicians who make treatment decisions have access to the same laboratory test results as other patients, as well, and that testing for patients with highly infectious diseases does not disrupt the ability to provide those laboratory assessments/tests to those patients who do not have highly infectious diseases. Whether going down two floors within your own facility to your own clinical laboratory or whether you're shipping laboratory specimens across the country for CDC confirmation testing, handling these specimens requires following strict procedures to comply with both internal policies but also various state and federal regulations. All of these components have to be considered, whether it's the laboratory systems themselves, handling of the specimens, the prep that goes into it. All of these have to be considered and brought together. And they have to come together and fit together like a nice jigsaw puzzle.

So, I want to spend, essentially, the last portion of my time here talking about some articles that we've written, primarily this article. And what I want to focus on is the ambiguity around manufacturer policies for usage of clinical laboratory equipment in the treatment of highly hazardous communicable disease patients. And the usage of this equipment is really a must for the treatment of these patients. And it can be done safely. These processes have to be worked out in advance. And once they are worked out, they need to be clearly and easily accessible. And they need to be clearly and easily accessible in advance. One of the biggest headaches in the US Ebola response was the ambiguity around the decontamination of the equipment used for the care of these patients. As previously stated by a number of our other colleagues, in some cases, manufacturers told facilities that they would have to destroy very valuable equipment or that their warranties would be voided if the equipment was used for these clinical specimens. All parties here want to do the right thing when it comes to the safety and health of those that we're responsible for. However, there remain a lot of unknowns that I believe can be addressed in advance, and have to be addressed in advance, in order to be prepared to actively treat patients in a highly infectious disease scenario.

I would say communication is a big issue that can be corrected with minimal cost and effort. In the study we conducted and our own personal experiences, there was not a clear route to ask questions or to obtain written documentation from some manufacturers. Often, questions were routed through multiple individuals and not in a timely manner. In multiple cases, we waited days to get responses. And in some cases, no response came. And when we were doing this study, it was in 2019, several years after the Ebola responses. So just imagine the consequences if these are time-sensitive questions that you're trying to get answers to very quickly.

There was also a reliance, what we found, on oral communication from the on-site sales team, which did not always match when we were able to receive later written documentation-- when, later, documentation was identified. I think we all know oral communication drastically increases the chances for miscommunication. We've all, at one time or another, played the telephone game, or at least know how it works. So, I think the importance of having policies and procedures clearly available ahead of time is paramount as we prepare to support laboratories to treat these patients. There tends to be a lack of planning in this area on everyone's part's, not just the manufacturer. Someone earlier mentioned that we need to think beyond Ebola and beyond COVID. And that's completely true. We tend to focus on the last, or the latest, organism instead of looking forward on how we handle all organisms or categories of organisms or planning for that unknown that may pop up. At the end of the day, if you have a policy that addresses how to decontaminate equipment, then it should be effective, regardless of organism. This is because you never know when you will run a sample, and then the organism of concern will be identified after the fact. The process also must be very clear so that the equipment's not down for too long and that the decontamination process isn't damaging the equipment. Now, I know a lot of these are huge wants and not always possible. But I think we can balance these amongst ourselves to get to the best possible solution.

In our survey, for example-- just to give a story of one of the things that we encountered-- in our survey, one of the manufacturers recommended the decontamination of their devices after usage of it on a patient with Ebola virus disease. They recommended ethylene oxide gas to decontaminate, which is a very effective decontaminant. But they also specified that it would void the warranty and damage the equipment. So, while ethylene oxide was recommended for the decontamination method and was then excluded-- now, this exclusion was disclosed in the manufacturer's warranty and in their communication-- essentially, what they were recommending at that time was a terminal decontamination and not a decontamination for continued use of the equipment. So, I think we need to get together and get to a situation where we can agree upon what the needs are for decontamination and the potential exposures associated with working with this equipment and really come to solutions in advance that can then be brought out based upon what we're seeing with new or emerging infectious diseases.

So, in summary, I'd like to say that advanced planning and clarity of information and communication is key. I would say this is something, if nothing else comes out of here, I think that our communication strategy would just be a huge success, just coming up with and figuring out a proper communication strategy. The ambiguity around communication further underscores the need to improve clarity and expanded dissemination of manufacturer-approved decontamination methods that are easily accessible, and not only easily accessible for current customers but also accessible for those who are in the planning or the purchasing phase. One of the difficulties we had was accessing information about these pieces of equipment when we were in the preparation phase to look at purchasing. So, the equipment must be used for the benefit of all patients. And its usage on specimens from highly infectious disease patients must not void the warranties. We have to figure out ways in which we can properly decontaminate this equipment for turnaround for use of all patients. And I'll turn it over next to Kurtis.

KURTIS STRAUB: All right. Hello, everyone. I'm Kurtis Straub, a senior microbiologist with CDC's Division of Select Agents and Toxins. For my presentation, I'll briefly introduce both the Federal Select Agent Program and its use of APHIS/CDC Form 3 to record incidents of release, loss, or theft of a select agent or toxin. We'll then turn to a preliminary analysis of Form 3's that were submitted in 2021, particularly those with narratives of release or exposures suffered by laboratorians when identifying BSAT from unknown patient specimens. As you'll see, use of automated identification instruments is frequently associated with the incidents that required reporting to our program. So, let's begin.

The Federal Select Agent Program, or FSAP, which was established in response to a congressional mandate, regulates the possession, use, and transfer of Biological Select Agents and Toxins, AKA BSAT. Now, BSAT are agents with the potential to pose a severe threat to public, animal, or plant health. Some examples of BSAT include the organisms that cause anthrax, smallpox, the plant pathogen Ralstonia solanacearum, as well as the toxin ricin, so a diverse array of agents. The FSAP is jointly managed by the US Department of Health and Human Services through the Centers for Disease Control and Prevention, specifically the Division of Select Agents and Toxins, or DSAT, and by the US Department of Agriculture through the Division of Agricultural Select Agents and Toxins. My preferred pronunciation, for lack of something better, is DASAT. The select agent regs roughly mirror the joint management of the FSAP program. DASAT enforces rules governing the BSAT that impact plants or plant products and animals and animal products, respectively. DSAT enforces Part 73 of Title 42 covering BSAT capable of impacting human health. The FSAP operates as a list-based program, where the laws require the program to review and republish the lists of select agents and toxins on at least a biennial basis, following public input. Currently, we stand at 68 regulated agents and toxins.

Now, select agents or toxins, or products containing BSAT, can be exempt from the select agent regulations through the circumstances listed on this slide, most of which need not delay us. What's really important for this audience is the first bullet. Any entity that identifies BSAT through diagnostic, verification, or proficiency testing is not held to the requirements of entities registered with FSAP, to possess BSAT provided that, upon identification, they securely store the identified BSAT, report any theft, loss, or release using Form 3, transfer or destroy the BSAT within seven days of identification, and complete an APHIS/CDC Form 4 within seven days detailing the identification. So this approach is very common to labs conducting clinical or diagnostic assays that are critical in informing patient care decisions or other disease surveillance. The select agent regulations require the reporting of the release of a select agent or toxin causing occupational exposure. These are things like needle sticks, animal bites or scratches, failure of personal protective equipment, or release of the select agent or toxin outside of the primary barriers of the biocontainment area. That could be a spill outside of a biological safety cabinet.

When a release occurs, this would require an immediate notification to FSAP, typically by email or telephone, followed by the entity sending, within seven calendar days, a completed APHIS/CDC Form 3 that describes the event and what actions the entity has taken as a result of the event. We use the information submitted on this form to ensure that the proper actions have been taken and that the appropriate federal and state authorities have been notified. So why look at releases or exposures, as reported by Form 3? Well, Form 3 reports represent a pretty unique source of information on laboratory incidents that resulted in potential exposures of BSAT to laboratory workers, including not just a description of activities leading up to and following the release event but also the entity's investigation of the root cause underlying the incident and the corrective actions that the entity has implemented in order to mitigate the risk of recurrence.

So what we did was look at 171 Form 3 reports of release. That's what you'll see in the first data slide. We then quickly zeroed in on a core set of 104 reports of release submitted to DSAT that involve specimen manipulation outside primary containment. And again, this is just reports that were submitted to DSAT in 2021. Unfortunately, we didn't have time before the town hall to integrate those reports that were sent to DASAT or USDA. Much of the information in the Form 3, such as the agent involved in the release, was tabulated directly from each form using what's called the Electronic Federal Select Agent Program database, or eFSAP.

To analyze the laboratory activities, root cause, and corrective actions associated with the report, we made use of several sources of information. The Form 3 has multiple free-text fields, particularly appendix 1, or at the time this screenshot was taken, appendix A, that asks for a detailed summary of events. There's also block, or section, C8, reporting the details of an entity's internal investigation of the incident. And then, beyond the form, we also screen the entity response to what's called a Request For Information letter, or the RFI. If there's any missing or inaccurate information from the Form 3 after we review it. Or if we want more details on how the entity is investigating the problem, we will send a Request For Information letter, or an RFI. And often, that response to RFI will add more information on exposure activities than we get alone from the Form 3.

So let's turn to the results of this analysis. Here we have the total of 171 Form 3 reports of release for exposure to BSAT submitted in 2021, split between two bars where reports from entities that are registered with FSAP are shown in blue. Our reports from non-registered entities are shown in orange. The non-registered entities, as we mentioned previously, tend to be clinical or diagnostic laboratories that, while not registered with FSAP to store or manipulate select agents, do frequently identify BSAT in the course of conducting diagnostic work. Now, on top of each color bar is the exact number of Form 3 reports and, in parentheses, the distinct entities that generated that total number. So on the right, we have 103 reports that were submitted by 91 distinct Non-Registered Entities, or NREs. This represents a majority-- about 60%-- of the 171 total reports. Registered entities, by contrast, reported 68 release events in 2021, or about 40%. And as you can see, since only 30 entities reported, most of those registered entities submitted multiple reports. If you look at the specific underlying incident types from those 2021 release reports, a clear distinction emerges between those submitted by registered entities and those from NREs. Starting with the blue columns from registered entities, you get a very mixed picture. There's no clear dominating type of incident that prompted the release report.

Now, some leading contenders include equipment or mechanical failures, where storage vessels for BSAT or other equipment that's designed to hold BSAT were compromised, and PPE failure, which denotes a failure of personal protective equipment, such as gloves, or the PPE becomes compromised during BSAT manipulations. The category All Other Types on the right include types of release that were mentioned earlier, such as needle sticks, animal bites, scratches, things that happen far less of the time than the PPE failures or the equipment failures. I'll note before going forward that registered entities indicated multiple, or two, incident types in four reports of release. Those are all captured in the All Other Types blue column. So just note the total number of reports that are categorized by incident type, the numbers you're seeing on top of each column, does not reflect the exact number of reports received from registered entities. That mixed picture is not the case with non-registered entities. Except for one report, the only type of release involves circumstances where specimens were not known to have BSAT at the time and were manipulated outside of a biological safety cabinet or other primary containment device designed to protect laboratorians from infectious aerosols generated by those manipulations. It was these types of reports we chose to focus on as most applicable to diagnostic work with unknown specimens. And so this made the core of 104 reports analyzed in the following slides. So the total number of reports is now just 104. And from that total, we quantified the select agent or toxin most frequently listed. As you can see, bacterial BSAT are predominant for

NREs. And they were the only BSAT listed for the two reports from registered entities. This tracks well with the most commonly identified BSAT, as seen in Form 4's, which are any of the three regulated Brucella species, be it abortis, be it melitensis, or be it suis. There's also Francisella tularensis and Burkholderia pseudomallei. The asterisks denote a subset of BSAT considered to be Tier 1 agents, those that require additional security and biosafety provisions on the part of the entities since they present the greatest risk of deliberate misuse and have the most significant potential for mass casualties or devastating effects to the economy.

OK, so here is our busiest slide. And we identified which of the 104 reports had a narrative associating the release or exposure with the use of automated instruments. So we identified 59 such reports. That is the bottom set, or the bottom solid green bar. This was a majority of 56.7% with the other 45%-- on top-- associating the release with strictly manual activities, such as preparing a gram stain, culturing bacteria from patient specimens, opening culture plates to review for the presence of colonies, or conducting a necropsy outside of primary containment. Now, it's tempting to see the number of reports and the multicolored bars underneath the bright green bars as components of those bars in bright green-- AKA those that had narratives saying the release was involved or associated with automated instruments or not. That's not quite the case. For each category-- 45 or the 59-- we took that set and screened the narratives further to identify all the activities associated with exposure, trying to identify what specific steps of automated identification were associated with the release.

So from this, we'll note two results. One, several reports feature release events stemming from multiple activities, not just those using automated equipment, which is not really surprising. Opening culture plates, which is the red bar, and preparing gram stain slides outside of containment-- that's the light green bars-- occur the most frequently, whether or not automated work also created a release event. Second thing to note is that the most commonly reported step in automated work that led to release was spotting organisms onto a target plate for testing outside the container. Finishing up this analysis, from the 104 reports, we calculated the total number of individuals exposed to BSAT. This was 551 individuals. And then we identified from that total which were identified as exposed while performing activities associated with automated instruments.

Now, that total came to 98 staff. That's 17.8% of the total, which is significant if not staggering. Now, this likely represents an underestimate, as highlighted by the asterisk. For 21 reports, the entity reported exposure associated with automated instrument work, but they didn't specify how many people were exposed as a result and were thus counted as only one exposure per report. Some reports did actually identify, or give the number of, everybody that was exposed as a result of the automated work. Now, this limitation could be addressed in future versions of the Form 3 where entities must report how many exposures were associated with each activity rather than leaving it up to the entity to offer that specific information as part of their broader narrative. Now, in screening the various incident narratives, we came upon certain root causes that were frequently reported. And to illustrate, I've selected a few quotes pointing to the problem underlying the release. The first quote, in the upper left, states the technologist did not follow the procedure that states that any culture plates demonstrating growth of slow-growing gram-negative rod should be opened in a biological safety cabinet and should be treated as a potential bioterrorism agent until ruled out-- i.e. All manipulation of culture will be done in the BSC.

So this points to a deviation from existing policy where retraining is likely needed. Many entities communicated something like this second quote. It says there was no expected diagnosis for the select agent. No one knew the patient harboring the select agent was infected. Indeed, the need to improve communication with providers was highlighted in 68 out of the 104 reports we focused on. The providers' suspicions of BSAT were not received by the

laboratory doing requested testing. And quite often, the entity stated on behalf of the providers that BSAT was not suspected. And that was pointed out in 40 of the 104 reports.

Finally, at the bottom, we have an instance of repeated organism misidentification by the automated instrument-- in this case, Corynebacterium or actinomyces when Brucella suis was actually the agent present. Now, misidentification is by no means limited to Brucella, but it does represent another significant focus for reducing the risk of incurring a release when analyzing specimens that may harbor BSAT. So how do entities that didn't know BSAT was contained in the material they were working with improve following a release? We see corrective actions falling into three main categories, none of which are mutually exclusive. Naturally, if unknown specimens will be processed using procedures that can generate aerosols, such procedures should be performed in primary containment devices, which aligns with the safety standards published by the BMBL. Training should be frequently conducted to facilitate recognition of BSAT by microbiology staff. BSAT growth characteristics, common misidentifications, including by automated instruments, and rule-out algorithms should be emphasized. We also recommend microbiology labs improve their coordination with the providers that send them samples to test. If suspicions of BSAT exist, they should be made known to the micro lab to minimize the chance of manipulating BSAT outside of primary containment.

So the analysis that we've just gone over reinforced how important entity narratives of each release event are in identifying courses of corrective action that entities, as a whole, can pursue. We appreciate opportunities like this town hall to increase awareness on safe work practices in the lab to reduce the number of occupational exposures. So to recap our analysis, a majority of the releases reported a DSAP in 2021 were submitted by non-registered entities-- 60%-- with work outside primary containment the predominant incident type-- 60 and 1/2%. Brucella species, the regulated ones, and F. tularensis are the most commonly reported BSAT in the releases that involve work outside primary containment. And the majority of the reports include, or mention, the use of automated instruments as release events in their narrative. It came to about 56.7%, where, again, sample inoculation, or spotting, is what was most commonly done outside the biosafety cabinet. Automated processes, at least looking at the total number of exposed individuals, accounted for at least 17.8% of those reported exposures. And then one last but very important point that was not directly communicated on the slides is that none of the releases reported resulting deaths or transmission of pathogens outside of laboratories. All right. So that concludes this talk, I want to thank everyone for their attention, and I hope that my presentation will plant the seeds for a useful discussion.

SHAWN GIBBS: Well, thank you, Dr. Straub. If members of the panel could now turn on their cameras, if possible. And I'll do a quick introduction to the members of the panel. So joining us via phone and the person you just heard from, is Dr. Kurtis Straub. And he is a microbiologist with the Centers for Disease Control and Prevention. As a microbiologist/inspector for the Division of Select Agents and Toxins, he contributes to public health, laboratory safety, and biosecurity through oversight of facilities registered to work with select agents and toxins. He coordinates and conducts regulatory on-site inspections of BSL-2 and 3 laboratories to ensure compliance. Also joining us is Dr. Nancy Burton. Dr. Burton is a certified industrial hygienist with the CDC's National Institute for Occupational Safety and Health. She has worked for 31 years conducting field studies in many occupational settings with the Health Hazard Evaluation program. Her research interests include the evaluation and control of potential exposures dealing with microbial agents in the workplace environment. Her current projects include potential laboratory exposures to pathogens, cannabis growing and processing, indoor environmental quality issues, especially mold, and Welder's anthrax. Our next member of our panel is Dr. Aurora Le. Dr. Le is the John G. Searle Assistant Professor of Environmental Health Sciences at the University of Michigan School of Public Health. Dr. Le's interdisciplinary research is centered around highly infectious disease mitigation and management with a

focus on training, education, prevention, and bio-preparedness. Her experience in this area includes previously assisting the Nebraska Biocontainment Unit with their research and programmatic activities during the 2014-2016 West African Ebola outbreak, serving as a subject matter expert for the National Disaster Medical System, and continuing as a sub award principal investigator and trainer for the National Institute of Environmental Health Sciences Worker Training Program. And as I introduced myself earlier, I'm Dr. Shawn Gibbs. And I'm dean of the School of Public Health at Texas A&M University, but I'm here as an industrial hygienist whose work focuses on the disruption of highly infectious diseases. So, thank you to all of our panelists. The first question I'll go ahead and toss out to the group to answer is there's been a lot of focus been placed on risk assessments. And that is something that industrial hygienists do regularly. So particularly to Dr. Burton and Dr. Le. What are your thoughts on the potential for usage of industrial hygiene, industrial hygienists, and risk assessment in the equipment development process?

NANCY BURTON: I think it's very important to be included in the process development because there are a lot of different factors. The usage in the actual environment needs to be easy also, but the maintenance needs to be something that can be done fairly quickly, either by the staff that's using it or by the manufacturer's representative. So, it's important to include all of that so you don't have any unknown issues that might crop up during the field use.

AURORA LE: just to add on to that, obviously, I'm biased as somebody who works in industrial hygiene. But I think that we are highly underutilized. And that is, to a great extent, a lot of folks outside of our field don't necessarily understand what it is that we do or what our entire skill set comprises. Really, we are considered occupational health scientists with a broad skill set. And as Dr. Gibbs mentioned earlier, we wrote a couple of pieces about how industrial hygienists can be incorporated further into pandemic response and infectious disease response. Traditionally, for this laboratory manufacturing equipment, they default to engineers, which is great. And now they're trying to incorporate more of the perspective of user friendliness and different ergonomic considerations. But I think that since we are indeed trained on risk assessment, why not capitalize on the expertise that we have and incorporate us in, whether or not we're already existing at some of these facilities as industrial hygienists with other functions or tapping on us as consultants?

SHAWN GIBBS: Dr. Straub, I wonder if I could get your perspective, coming as someone who's done inspections for these different types of laboratories. So, in particular, one of the earlier people earlier today talked about the importance of doing risk assessments but also maintaining the quality and maintaining consistency of those risk assessments, as well as the personnel doing them. I wonder if we could get your opinion on that.

KURTIS STRAUB: As far as risk assessments and the laboratories that are registered with the Select Agent Program, they do have to have as part of the regulations, is that they have a biosafety plan in place that is sufficient to contain the select agents and toxins that the entity possesses or manipulates. And usually, as part of that, as part of when we review biosafety plans, there will be an expectation of a risk assessment to account for the agent hazards, not just those specific to the agent but also the particular manipulations, including those that are done if there is diagnostic work, what may be encountered. We would expect that to be covered in the biosafety plan. For the majority of the Form 3 reports discussed in my presentation coming from non-registered entities, we don't typically review, or have submitted to us, any risk assessments. But we'd agree it is an important step. And any time that there's a significant change, whether it's a new project, a type of equipment that may introduce new avenues of exposure via use of that equipment, we would expect the risk assessment for registered entities to account for those hazards.

SHAWN GIBBS: So, one of the other questions I'd like to put out to the team is there is a small number of facilities in the United States that have been essentially designated as hospitals or health care systems that are expected to treat highly infectious disease patients. Earlier, these were referred to as Ebola treatment centers, or regional Ebola treatment centers. So, they're preparing to treat infectious diseases. My question is, when working with an organization setting up or determining their laboratory capacity for such a response, what information would you like to have available from the manufacturer? I think one of the questions I had going back to the study we did was, for example, information on proper decontamination that wouldn't damage the equipment and being able to access that easily in advance.

AURORA LE: just to add to that, Dr. Gibbs, based on the study that we did and you presented earlier, I think having readily available information in some kind of repository online, either by the manufacturer or for the type of equipment would be extremely useful just because of the challenges that we encounter trying to contact manufacturers for these types of nuances. And now I would say, with the day and age that we live in, 2014 seems like so long ago with Ebola, but now with COVID and with monkeypox, the ability for us to get information that a potential pathogen is going to be a threat to a certain portion of the country or even multiple countries is more rapidly ascertained. And if manufacturers are able to get ahead of that a little bit and start even putting out quick announcements or updates on their website on how to perhaps encounter some of these questions that may arise, I think that could help mitigate some of these issues.

SHAWN GIBBS: Thank you, Dr. Le. All right, moving on to another question here. These risk assessments of clinical laboratory equipment are being done across the country. And they're being done in various different types of facilities. Each facility tends to be fairly unique. As you've done these risk assessments or had colleagues communicate them to you, what has been your biggest takeaway, either from an assessment you've done or that's been shared with you, that you've heard about or seen and you thought, I wish more people knew about this potential issue?

NANCY BURTON: One of the issues that I've come across is the placement of equipment, especially if it's not in the biosafety cabinet is actually including in your assessment the ventilation and the layout of the laboratory and how it's going to be used with the employees, where they're placed. Because that can add to the potential exposures if an accidental spill hits or something like that.

SHAWN GIBBS: I think that's a wonderful comment. And it goes along with what I was thinking when we put that question together where I think we've all seen a scenario in which the person working is essentially in the path of the airflow that's being pulled off the piece of equipment. So, it's almost pulling the airflow towards the person. So, I think that's a wonderful comment there, Dr. Burton.

KURTIS STRAUB: Can I go back to the prior question? I was trying to look up the regulatory language regarding decontamination and information expected from manufacturers.

SHAWN GIBBS: Yes, go for it.

KURTIS STRAUB: OK. There's a clear difference between the entities that are registered with our program and those that are not registered. The same regs that stipulate the biosafety plan require written procedures for each method. And it must be validated for disinfection, decontamination, or destruction of the select agent that is being used by the registered entity. And the entity doesn't necessarily have to validate their method for decontamination

in-house. In those circumstances, they could rely on either published methods-- so what is well-established by publication-- or from manufacturer guidelines. We would expect that information to be part of what is reviewed. In the non-registered entity examples where, for the first time, generally, we're encountering what experience these folks have with exposures and also the need for decontamination of equipment, we will ask them frequently, how was the work area where the exposure occurred outside the biosafety cabinet decontaminated? And how did they know that it was effective for the select agent that was identified?

SHAWN GIBBS: But wonderful, wonderful point there. And I think that's going to be one of the key differences throughout this is those who are intending, as Dr. Straub-- laid out there, those who are registered and those who are unregistered so those who are responding because monkeypox showed up in their facility versus those who have been actively and intentionally working with it. So, we've been discussing a lot of these policies and procedures from the standpoint of how things are supposed to work. It's important to think about what happens when things don't work. So just opening it up to the panel, can you discuss how you've evaluated the risk when you have equipment breakdown? For example, it wasn't necessarily an equipment breakdown, but I was working with one facility, and their laboratory facility suffered a clogged drain that was not a result of anything that the laboratory had done. It was a result of the building they were in. And then we were assessing the potential implications for that clogged drain. So, I'm just opening up to the group, as you're working through the risks and how people are working with these pieces of equipment, how, in your mind, do you try to account for those breakdowns in processes or those breakdowns in equipment function that, unfortunately, happen?

AURORA LE: I mean, in an ideal scenario, everything works perfectly. But that's not the way that life works. So I know this sounds so basic, but having written standard operating procedures with contingency plans outlined and discussed so that if you don't necessarily have the industrial hygienist present at that time, or your workplace, or this workplace, doesn't even have an industrial hygienist, having one, if not multiple, people understand, at least at a basic level, what the particular steps are or who may be the appropriate person to contact in the event that scenarios have to change and risk has to be mitigated in the best possible way as you can. We're not going to have the answer right then or the perfect solution. But often times, many of these factors or these unfortunate circumstances aren't even thought or given any discussion or foresight. So, I think that's very critical.

SHAWN GIBBS: Thank you, Dr. Le.

NANCY BURTON: It's important in your risk assessment to also include the maintenance staff or the staff that actually services the laboratory and to have protocols in place. Because not only do they have to clean up whatever happened, whatever issue happened, but also how to protect themselves from what unknown might be there. And it's not necessarily included in their normal working procedures.

SHAWN GIBBS: That's a very good point. I once had a conversation with a plumber in a health care setting. And they were talking about items coming from the laboratory. And they rightfully were concerned about it being a biohazard. But in the course of my conversation with the individual, I realized they didn't consider anything else in the hospital a biohazard. And I very nicely and politely reminded them, this is a health care environment. Pretty much everything you're encountering is a biohazard. So we just got a question that came in from the group. And it says, similar to the discussion in previous session, the select agent regulations website verbiage in the Form 3 appear to not really be written with clinical laboratories in mind. For example, an exposure to a hematology tech doing a cell count on a specimen outside of a biosafety cabinet that was later determined to have been a select agent, the root cause of the exposure outside of the primary containment unit is simply that it's a clinical lab. So, it's

not likely we're going to realistically challenge the workflow anytime soon. So, I think this also gets into one of the questions that I wanted to ask, which is one of the examples I always highlight in regards to the unknown is, in 2016, a German funeral home worker was infected with Lassa fever from the remains of an individual that no one knew was infected with Lassa fever. I see this as very similar to what we need to prepare for in the clinical environment, which is it's very possible that the specimen will be run before the highly infectious disease is even suspected or known. So just open up to the group there, what are items, or what are thoughts that you have, in regards to things that should be done in advance just generally to protect from any of these types of exposures?

KURTIS STRAUB: I'll go ahead and start. I think we have to acknowledge the challenge, since these specimens or what people may encounter, often not knowing what is present before doing the analysis, it's where you can easily run into trouble. But as alluded to towards the end of my presentation in dealing with training, I think that clinical laboratories, they can be aware of what select agents are present. There are great resources for rule-out algorithms and, as I mentioned, growth characteristics that are typical for select agents. Labs in specific areas can inform themselves by what is known to be endemic in a certain area, what may be rising, what is the seasonality of particular agents, and thereby have some idea that, even if it is not immediately called out, what are some possibilities that they need to be aware of?

SHAWN GIBBS: Thank you, Dr. Straub. So, one of the things that I'd like to say in the example I gave you of the 2016 German funeral home worker, also in that example, there was a second party. And the second party was the one who handled the remains initially and did most of the preparation of that remains. And that second party did not become infected because they had been adhering to, essentially, standard bloodborne pathogens protocols. They were using the proper administrative controls, engineering controls, and personal protective equipment. So, I think a lot of what we're talking about here is implementing and really preparing the equipment and the procedures to be prepared for that unknown exposure, whether that's a highly infectious disease or if it's simply an infectious disease that we're more likely to encounter in a laboratory environment, like MRSA or HIV or something else.

AURORA LE: I did see a question about maybe asking how to better tailor the Select Program for clinical labs. I'd maybe let him comment since this more is his area.

KURTIS STRAUB: Hey, Dr. Le. We do have several public health laboratories, usually with states, that are registered with the Select Agent Program. And as I mentioned before, their biosafety plans, their risk assessments, would have to account for the type of diagnostic activities that are done. And that can be a great resource, as far as how they've accounted for potential hazards or whether their use of standard bloodborne pathogen protection, that that can be used to be disseminated to more regional clinical laboratories. So, we often find that that coordination between the state lab and more local clinical labs is a key resource.

PANEL DISCUSSION for all presenters and panelists on Potential areas for improvement.

CDC MODERATOR: This is going to be a panel discussion for all of our presenters and panelists. All three sessions were very educational and very insightful, as well as the discussions that followed. The CDC Moderator/Facilitation team is going to ask some questions to help frame this next portion of this town hall. Because in this portion, we want to focus on next steps. We want to focus on, where does the conversation go moving forward? We've discussed everything that's happened in the past. We've identified issues, potential solutions. We want to take it that next step further. Where do we go from here? One of the questions that came up

that seemed to be an overall theme throughout is communication, planning, and preparedness. When you're looking at communicating, what roles are needed, and what information is needed to advance this issue?

MIKE PENTELLA: Well, I'll take a start at this. I think I'd like to see the manufacturers get involved with making the first step of communication. Because I think that they have the ear of, particularly, the small laboratories. And that community relies heavily on the manufacturers, so addressing the issues of what's missing in their instructions, the use manuals, and better instructions and service representatives, call center staff, and sales staff would be very useful at this point to get that conversation going. It would also serve to tell them more about what's happening in those laboratories because they can have a two-way communication.

ANDREW BRYAN: I would personally extend that a little bit beyond the manufacturers and say it's critical to have all the stakeholders involved in that, whether that's a scientific advisory panel for a manufacturer or the CDC or Select Agent Program biosafety guidelines. I think there's clear gaps in not having real clinical laboratorian representation in some of these groups that leads to a lot of the confusion that we have to really achieve the safety that we're trying to achieve.

LAURA KNOLL: I think it almost depends on what we're talking about in terms of communication. Are we talking about it at the time of development? Are we talking communication at the point of sale? Are we talking after? Because stakeholders' input is needed at all these different points in processes and points in time. And so, I think that, actually, the answer to this actually changes with each process and point in time.

CDC MODERATOR: That is a fair point. So, let's, because I think we address starting from the beginning with design. So how would the information communicated in real time or when there are situation changes and new information has to be disseminated from manufacturers to the laboratories, how would improving that communication look like for the clinical labs?

LAURA KNOLL: Well, I know, from my perspective, if something has changed with an instrument and equipment that I have, I appreciate hearing directly from my rep and/or field service representative or both. Simply an email or a letter that's mailed out sometimes just doesn't do it because it doesn't make it to me. So that one-on-one contact tends to work the best.

SHAWN GIBBS: Well, I'd also say that one-on-one contact but also a repository that you can go back to so that if that reach out doesn't get to the right person or-- in one of the panels earlier today, I think someone made a very good point about, hey, the person who purchased this may have moved on recently and may not be there. So, if there's a place that you can be directed to by the manufacturer on their website that just has those kind of updates or a central, easily known location that you can reach out to get that kind of information answered for you. Because I like the one on one. But the person may be on vacation. The person may have moved to another laboratory across town three weeks ago, and the information hasn't been updated yet.

SHELDON CAMPBELL: I think the point about redundant communication is important. We've talked about how verbal communication is good. But also, verbal communication tends to be evanescent, and you end up not knowing exactly what was said. So, both direct contact and something like a repository, I think, are both essential.

PETER IWEN: I also think part of the communication is what Sheldon's getting to-- written communication. But the manufacturer's instructions themselves, not always do the manufacturer's instructions describe the hazards when

using that particular instrument. They also many times don't describe what are the decontamination processes necessary to decontaminate that piece of an instrument. So, I think having well-detailed instructions on what are the hazards and how would you mitigate those hazards through decontamination with the instructions would be useful, as well.

CDC MODERATOR: I appreciate everybody's thoughts on that. Part of the discussion when we were talking about communication tends to center around being in a broader sense, so labs in general but based off some of the previous sessions that we were looking at, it came up, specifically, clinical labs and, specifically, labs that are in rural environments and labs that are all different shapes and sizes, so what are some thoughts on information being tailored, or even equipment being tailored, specifically for clinical labs? What would ideal group of stakeholders look like to develop or update guidance or even-- I think, Andrew, you were the one who had spoken about having people on advisory boards to assist. So is there a need to tailor to clinical labs? And if so, what does that look like?

ANDREW BRYAN: I think, just extend that question, I think from a perspective, really going to, let's say, a standard precaution 2.0 and using standard precaution, not BSL-2, BSL-2 being more about that research framework, standard precaution being more about that clinical framework. And then a lot of this has been about Ebola and they are highly infectious pathogens. But we have lots of points made that not every institution has the resources to do that. We're not going to know what the patient coming in may have. And even for an academic, highly resourced laboratory, doing non-standard workflows, approval processes, doing things off the automated analyzers all adds overhead and interrupts the workflow to all of our patients. And so we tend to err on that side of caution. But then we can end up delaying care for that patient and potentially impacting care for the other patients. I think having some basic discussion, what those standard precautions 2.0 that we can establish benchmarking for instrumentation, benchmarking for PPE and workflows that we don't have to worry about it as much if we happen to get that Ebola patient or that monkeypox patient or whatever comes next as a walk in through the door and we don't know about it.

CDC MODERATOR: What would tailoring to clinical laboratories look like? Any suggestions on what you would like to see, especially for labs that are rural or may not have the capacity of some of the larger laboratories that are better funded?

SHAWN GIBBS: So, this is just my perspective, But I think, particularly for those kind of labs that you just outlined, I think the preparation that Dr. Bryan just talked about is even more paramount and more important. They don't have the resources to respond in time as quickly as some of the larger ones do. So a lot of that preplanning across the board is just extremely important.

PETER IWEN: So, it sounds to me like a baseline of information that everybody should have. Is that what I'm hearing?

ANDREW BRYAN: I think a baseline of information but also defining those standard precautions a little bit more, as well as how to, let's say, audit that. For example, our infection control, our institution, we do hand washing audits. Doing that for PPE in the clinical lab when working such as use of gloves on that automated line or clean workstations, what are some things that we can-- some clear, standard practice that we can incorporate into that everyday workload a little bit more granular level than, I think, treating just bloodborne pathogen guidelines.

PETER IWEN: But whether we're rural laboratory, whether we're a large hospital laboratory, or whether we're a reference laboratory, there's a baseline of information everybody should know, correct, in using that particular instrument, for instance?

ANDREW BRYAN: Yeah, the instrument and the training and that, again, full, I think, workflow.

MIKE PENTELLA: Pete and Andrew bring up a really important point. We have competencies on how to use the instrument, but we don't have competencies regarding safety. And so, as we think about the competencies that we write to make sure that our staff are trained and knowledgeable to use it, then we should incorporate competencies for the safety portions of it, as well. So, it's extending it to that next level, as Andrew was bringing up with standard precautions 2.0, so that you have a competency-based evaluation system that can be used for training and evaluation on an annual basis.

SHELDON CAMPBELL: For low resource laboratories to do that kind of thing, they need templates and job aids and a lot of infrastructure. Because they really don't have the time or the skill set to do it.

ANDREW BRYAN: A key opportunity there that may, in some cases, be faster than incorporating to all new instrumentation or regulatory framework, I think, is College of American Pathology, or CAP, checklist item, including safety competency as a checklist item. And then CAP, for example, it has a template for root cause analysis, have a template for that safety 2.0 that make it really easy for that small lab.

PETER IWEN: It seems to me that the CAP regulatory environment, this CLIA regulatory checklist, for instance, kind of sidestep biosafety. There might be a checklist question about it, but it doesn't get into any details. Is that true, Andrew, Sheldon?

ANDREW BRYAN: Yeah, I think it's very much up to the medical director as far as how we apply both OSHA and CAP checklist items, as far as we have a responsibility to ensure we have appropriate PPE and safety. But it doesn't really say what that is, necessarily

PETER IWEN: It doesn't get into details.

MIKE PENTELLA: That's right. And I think the CAP-- I can't speak for the CAP-- but it would be reluctant to impose extensive additional burdens on labs without either the resources for those labs to comply with that or a regulatory mandate to do it.

CDC MODERATOR: Dr. Pentella, when you were talking about competencies, that brought to mind something that we had heard earlier about manual versus automated processes. This is for the whole panel-- what do we need to know to better differentiate between manual versus automated processes and guidelines and then integrate them in the workflows in the lab? Is there information that we're missing? Or does it just depend on the lab or the capabilities that the labs have?

MIKE PENTELLA: Well, I think it's very dependent on the scenario of the lab. Having both automated procedures here and a lot of manual procedures, they're all different. So, I tend to do a risk assessment procedure-based or instrument-based instead of lab section-based. So, I think you have to look at your circumstance and determine what's appropriate.

SHELDON CAMPBELL: And nearly every laboratory has both.

ANDREW BRYAN: Given that each of those labs may have a different workflow, maybe some challenges applying that broad guidance. But I think this is where we could have data to help support all labs, not just the smaller ones, do the risk assessment of, what's some general data on manual errors associated with handling tubes so that the select agent data, how many of those exposures were related to whatever, dropping a culture of Brucella versus, then, test data from the manufacturers of what's the rate of a tube exploding in that unsealed centrifuge and having some of that literature to really make it easier for everyone to do the risk assessments. Because we're all asking for the risk assessments. We're also mostly going on expert opinion for that and operating in a paucity of data.

CDC MODERATOR: Andrew, you brought up the use of data when doing risk assessments. Are there, other than the manufacturer or data that we may find within the CDC, are there any other areas where laboratories could obtain that type of data to do their risk assessments? Is there somebody they should reach out to at their institute or the hospital or wherever they're working at? Or are there resources online that they could potentially go to?

LAURA KNOLL: I think that there's a couple of resources just within a facility. Especially if you're in a clinical lab in a hospital facility, reaching out to infection prevention is a good first step, as well. Because they can think of things a little bit differently. And I know that sometimes in the lab, when we put a process in place, even after we've done a risk assessment and we think we've determined the right way to go and we have some other eyes on it, we get a different perspective. And so for us, going to IP or, even in the micro lab, I have a counterpart in the core lab who will come and watch, or I will come and watch them, and so that we have that extra set of eyes. And then we can kind of gather our own internal data, as well. And when we look at, over time, we can look at what kind of incidents have we had, if we've had any, in the lab, and what was the root cause of those? Because if we do have something, we should be doing a root cause analysis. So, what is your own internal data?

SHAWN GIBBS: Well, and I'd like to highlight something Laura said there, which is also over time. I think, too often, these are done once and then not revisited enough. And sometimes, situations, setup, configurations with a laboratory may, may adjust or alter with flow over time. And that could impact the risk assessment. And I think, too often, people don't go back to it and repeat it.

MIKE PENTELLA: I'd like to point out that there is not a lot of research in this area of laboratory safety. And more funding for research would be extremely helpful so that we can understand the risk.
Because at times when I'm faced with a question and don't have any data to back it up, I'm going to go with the most stringent precautions to err on the side of anyone not getting ill from this. But if I really had data to support lesser precautions, then I would save time, save money, and people would be more likely to follow the precautions because it was already a data-based decision.

ANDREW BRYAN: Emphasizing that facility information that Laura was mentioning from employee health, in our infection control committee, regularly review the sharp injuries, as far as the bloodborne pathogen exposure, expanding that. The challenge at the end of that is pretty small. And so maybe a national database with anonymous reporting so we can help get better data. Because too often, it's not systematic if we're just relying on small institution data, even if that's large number of bed hospital.

PETER IWEN: And the training processes involved in this should be ongoing. I think we've got a lot of turnover in the laboratories. And knowing what are the risks, telling them once isn't enough. I think it's an ongoing process. I'd like to weigh in again, we talked about manual versus automated testing in the laboratory. Recognizing that we all have automated tests, we all have manual tests, a scenario that comes up will be we have a patient that shows up in the emergency room that monkeypox is put on the differential. Well, now, we are sitting in the laboratory going, oh, well should we put this on our core chemistry analyzer, or do we have to use our point of care manual test to run this sample? And if we had the core analyzer being a safe instrument to use, we would stick it on that instrument. So why do we have to sit and make those decisions under those circumstances? That's what goes in my mind since we know that any specimen that goes on that core analyzer could have something bad, anyway. You get the gist of where I'm going? We sit and argue about, where do we run this test? Might have monkeypox or whatever. It just seems to me if our automated instruments had safety processes in mind that we would be able to use that instrument, no matter what. That's my thought on it.

LAURA KNOLL: I agree with you. And in terms of that kind of instrumentation, when you were talking about the analyzer, you're talking about a large analyzer. And there are some smaller that are used in a more-- not just in the point-of-care setting but in a more biocontainment setting that are geared towards that and do have safety measures. But those same safety measures are not in place for the larger analyzers. And when you think about that, especially smaller facilities, rural facilities, they don't have funding to have their main core analyzer and another analyzer in case they have to set up a biocontainment.

PETER IWEN: Right. And maybe I'm dreaming, but all instruments should be safe, I guess. I just think we're sitting here, picking specimens from, oh, this one might be more hazardous than another one, blah, blah. I get that. I get the standpoint of if you're working with a patient that is known to have Ebola is a different story. I get all that. But I also get the point is when we handle specimens in the laboratory, how do we know that sample's safe?

LAURA KNOLL: Well, and just as Dr. Gibbs said earlier, we don't. If you think about it, it's not just even a clinical laboratory. Think about a doctor's office and their--

PETER IWEN: Sure. Nursing home. How about the nursing home, too?

LAURA KNOLL: Yes, nursing home, all of those facilities. Any facility could have something walk in the door. And the lab is always the last to know. We just are.

CDC MODERATOR: we have discussed the lab and what the lab is doing and what the lab should do. Are there any potential solutions that are more systematic on a larger, grander scale, so to speak, of not necessarily accountability but how can we get to a solution with assisting these clinical labs in being safer? And I know we have talked about what the manufacturers have done and what they're currently trying to do to assist. We have the BMBL, the biosafety manual. Is there anything else that we can think of that would be worthwhile so that it's more of a collaborative approach to a solution versus the onus is on one person or it's on another person?

MIKE PENTELLA: I think we have to take a systems approach with this. Sure, it's the end user, a laboratory purchasing the instrument who has the lab setup who has to think of the design of that lab. That's a given. There are also the accrediting agencies. There's CAP and CLIA. They need to have a part in evaluating what those individuals have put in place. There are also the manufacturers as a role and FDA as a role in looking over those instructions and evaluating the practicality of what's being proposed. So, I think there's a piece of that so that we

create a system where safety is supported throughout so that the end result encourages data that we see less exposures. The Canadians require reporting of lab-acquired infections and exposures. And they publish that information. And it's very interesting. You can learn a lot from that. But it would be great if we had our own data in the US.

CDC MODERATOR: So, when we're talking about limiting exposures that are associated with the use of automated equipment and but asking laboratories to report laboratory-acquired infections, would we include near misses in that? Or would there be a cutoff? Is it you report everything? Or is there such a thing as too much data?

MIKE PENTELLA: Well, I would like to see reports of exposures like you're getting for the select agents. But I'd like to see it expanded so you see all exposures that are identified. Of course, I don't want to add a burden to all my laboratory colleagues out there. I'll be hung in effigy for adding more work for anybody.
But I really do think we can learn so much by analyzing. Because I found Dr. Straub's presentation really interesting because it brought up such really great data. And I hope that we can expand it beyond select agents.

CDC MODERATOR: Because a goal of this town hall was to hear different perspectives from various stakeholders. I would like to open it up to the rest of the panel. Did anybody else find anything, heard anything today, that surprised them or that made them think of this issue in a different light?

LAURA KNOLL: I'm not sure that I heard anything that would make me think of anything differently or anything that was shocking to me. I think that I am glad to hear in one of the earlier talks of the day that-- and I wrote this down-- that the statement was that the response now, moving forward after Ebola, they predicted would be different, so if we had Ebola today that they expect that the manufacturer response would be different. I would like to say yes to that, that that is the case. I don't know, with all of us and what we've experienced with monkeypox lately, I don't know 100% if we can say that that's the case. But I really appreciated that statement and that sentiment and the hope that that is true. So that's just something that I took away from one of the earlier talks. And when I started thinking about that, I was thinking about how something that goes along with that, just for laboratorians-- and really anything, laboratorians are no different than the general public, the fear is real for the general public, and the fear is real for the laboratorian. I think we have to be cognizant of that and compassionate with that in what we're putting forward.

CDC MODERATOR: So if nobody else saw or was surprised or their viewpoint has changed in the slightest, what is something that you were hoping to see but you didn't get to see or hoping to hear that you didn't get to hear?

ANDREW BRYAN: I think, coming back to your question about, what are the action items? And so what we're all kind of talking about that. And that's what we want. One thing I was struck with through all our conversations and the CMI review that most on this panel participated in asking more questions. And we're not necessarily developing those answers. And this is among the best experts in the country on the topic. And so we're not necessarily doing a service for others who maybe have thought about this less. So I think having that, what's the revision process for the BMBL? When does version, or edition, VII come out? How do we get clinical lab representation on that? Can we get-- and, ideally, I think it could be someone from the CDC with that clinical experience, or it could be someone-- maybe CLIAC defines a designee to help sit on that panel board or whatever that word would be for the next version of BMBL. What are those requirements, for example? How do we want to clarify that package insert without requiring a whole bunch of extra definitions and requirements for manufacturers? Can we get some clarifying language from the FDA on the required hazard line item in the package insert saying that that hazard

must include biosafety assessment? So, I think pinpointing some of those options would be really fantastic to help get towards some answers.

PETER IWEN: I agree, Andrew. I think we're talking about communication amongst people like CDC, FDA, end users and manufacturers. I think we kind of each go off in our own direction sometimes, and we really don't communicate well with each other. My goal would be, from this town hall, would be is if we could at least get a line of communication out there to say, let's talk about it. Let's look for ideas. I don't have all the ideas in my mind right now, but I know what some of the problems are. Let's come up with ideas on how we might be able to solve some of these problems. We've got a lot of old instruments out there that aren't going to, tomorrow, change their way of testing to become safe. But in the future, maybe there's things we can do to make things better for the laboratory. With all this new technology we have, why can't we? I don't know. I think the line of communication would be a big step in the right direction, if we could all communicate together and keep communicating.

MIKE PENTELLA: I agree with you, Pete. It would be great. And I'd like to see more dialogue with the manufacturers on this. I'd like to hear more from them what the barriers they see to what we're proposing so that we can help them figure out how to overcome those barriers.

CDC MODERATOR: In addition to communication, are there any other knowledge gaps or practices that we feel are feasible that would help in the short term with this issue?

ANDREW BRYAN: Some of that knowledge gap in the data. For example, could we include laboratory-acquired infections as part of an NHSN reporting, ideally an ungraded fashion so we can get the most robust, including near-miss, reports without making it a penalty or some other existing framework that we can piggyback on, given that we're not as centralized in the health care system as the Canadian system. So how can we gather with our existing infrastructure?

MIKE PENTELLA: I would also think that we'd want to see the service representatives and the call center staffs better educated about infectious disease transmission issues from the instrument perspective. And I think that would be something that could be easily accomplished.

PETER IWEN: Andrew, I heard the word penalty. I mean, when it comes down to reporting from the laboratory, like NIH reporting, select agent reporting, we look at the consequences sometimes of that and say, oh, my gosh. Select Agent Program has monetary fines for people that do things wrong. You wonder how many things don't get reported because of the penalty side of things. That doesn't help anybody, either, in my opinion. I know we struggle with, oh, should we report this to the NIH? It's a laboratory research issue. It doesn't seem like much. We're not going to report it. Or Mike, you're suggesting laboratory-acquired infections reporting near misses, et cetera. People are going to maybe look at that and say, well, that's going to make my lab look bad because we've had X number of near misses. How can we incentivize people to do it, I guess, is what I'm getting at, without making them look bad?

LAURA KNOLL: I think it's not just a matter of making them look bad. I think it's a matter of how onerous is it on the lab to do it?

PETER IWEN: Yeah, paperwork, for one reason, yeah.

CDC MODERATOR: So along this line of trying to incentivize people with reporting when it pertains to incidences or near misses with automated equipment, is there guidance that should be in place or even enhanced that would help with that? Again, I know you brought up the select program because we're mandated to. If you have this, you've got to report it kind of thing. But I wonder if there is guidance that needs to come from other sources other than NIH, CDC, specifically, that would help with the situation, help incentivize or try to get laboratories to be more open with, we're having a problem. It's not necessarily us, per se, and not that we're bad people. It's just there's something going on. This is what's happening. Someone can review the data and be like, oh, it's not the people, it's a practice, or it's a piece of equipment, or it's a piece of PPE that's malfunctioning-- something to that effect.

ANDREW BRYAN: Thinking about the NHSN and reporting for other things, it's all about the penalties and if you don't live up to some metric. But instead of, if the penalty or incentive was instead of, for that, actual safety incident, it was for reporting. And you actually get more points for having a more detailed report. So, you get some portion of extra reimbursement. The idea, I think, would be line itemed for staff to help ensure that. You could apply this more broadly to employee health issues in the hospital, too, and maybe not make it necessarily lab-specific, as long as that's included, but using some of that existing incentive structure to really encourage that reporting aspect.

SHELDON CAMPBELL: Make it a reimbursable activity.

ANDREW BRYAN: We could bill a clinic pathology CPT code for a consult on it. But I'm curious to hear-- I feel like, at least, like I'm talking too much-- but from our industrial hygienist colleagues about the data and gaps that you see and how that can fit in. I know we don't-- we had, for instance, our institution, a industrial hygienist outside consultant hired for Legionella cases. But not aware of that as a resource in our institution. Did you get help from your field, support some of that data and communication dissemination?

SHAWN GIBBS: So, Nancy, feel free to interrupt me and hop in at any time, but no, Andrew, you're right. One of the issues, there's not a whole lot of industrial hygienists, and there's even less of us who specialize in these types of areas. And we're not very well-known, so a lot of people don't even know about us as resources to be pulled into these types of assessments. So I think one of the issues and, getting back to my presentation, one of the reasons why Dr. Le and I had written those two articles, one in 2018 and one in '22, pushing our field to kind of embrace the infectious disease area a little bit more is because we see needs not only within laboratories but within a whole host of other areas within the health care organization where the skill sets of the industrial hygienist aren't being brought into, either because we're not available or were not known of. And we would be able to, I think, provide a lot different of a perspective and not only perspective about the issue but about potential solutions. Nancy, do you want to weigh in? I don't want to speak for all industrial hygienists, so maybe if two of us weigh in.

NANCY BURTON: Well, part of it is that we look at the workplace as a whole. And part of what we like to bring in is actually discussing things with the people who do the work. And we need to include those in our risk assessment. Because if we make suggestions on how to improve the workplace and they don't feel that they're appropriate, then they won't be implemented that's very important for us to do as industrial hygienists. So, a part of being an industrial hygienist is trying to bring all the different components together for a risk assessment, including the employees that are the ones that actually are doing the work, they need to be included as part of it. So, we bring a kind of a different perspective as in bringing all parties together for our risk assessments.

LAURA KNOLL: I feel like that concept of bringing all parties together, and especially those at the bench that are doing the work, is kind of an overarching theme that we've said again and again throughout the discussions and the presentations.

SHAWN GIBBS: And I would agree there with Laura. And I think that starts in the design phase and looking at how these are going to be utilized in some laboratories. And I believe-- I don't know if it was Mike or Pete who earlier had talked about, really, once you can get ahold of some pieces of equipment and they were realizing that there's potential for exposure, that may not have been identified in the design phase but were identified very early in the operational usage phase.

MIKE PENTELLA: Yes, that was our experience, Shawn. And we did catch it. It did set us behind because we were trying to rapidly bring the instrument up for use. But fortunately, it was detected, and we put in that fix. I'm not sure how it would have impacted our decision to purchase the instrument, though. Because the extra step took us a lot of effort. And we weren't planning on that. So, it would have been wise for us to detect it before we actually made the purchase. But particularly when you're busy like that, nothing ever goes as planned.

SHAWN GIBBS: And I think we've all had experiences like that. I remember doing a risk assessment for one large throughput laboratory. And it was a piece of equipment that ejected cartridges out into-- used cartridges that were being ejected into a refuse bin in a closed container. They were ejected with quite a bit of force, such that there was blood spatter inside the cabinets which they were being ejected into. So, something like that you could have identified in the design phase with a different type of plastic tubing going directly into the thing or something like that, whereas the risk we're worried about is if someone opens it up at the wrong time, what's going to happen? And that's not just for a highly infectious disease. That's for hepatitis. That's for HIV. That's for any other number of things.

ANDREW BRYAN: One caution that I would have with emphasis on the design phase on that instrumentation, including a concern about actually being more strict about package insert, for example, is getting locked in of that or the manufacturer being strict, oh, it's in the package insert or not, and we're not going to speculate if it's not in there. And we want to acknowledge that we're going to have uses of these instruments-- they may be used in unintended use. And we may need that for patient care. So, I think we need manufacturers and the FDA to understand we can't just be locked into intended use in the package insert. Because we can't anticipate all of the uses for a piece of instrumentation when you're sticking that-- it's fine to say that in isolation. But when you're putting that in a big, complex laboratory, you can't anticipate, necessarily, all of the things. And so we might have some assessments and guidelines for how to mitigate that. But when we're doing that, don't want to lock ourselves into, oh, if it's not in that insert, then we can't do it, or we can't support it.

PETER IWEN: Just one comment for the group, I know that the title of our panel was Perceived Risks to Laboratory Personnel. I think we all agree that there are real risks to laboratory personnel. It isn't just a perceived issue we're talking about here. I just wanted to make sure we all understand-- I know we all understand that. But sometimes it kind of gets lost. There are real risks for working in a clinical lab and handling these specimens. My staff will remind me of that all the time.

CDC MODERATOR: So as we're starting to wind down with our discussion here, I wanted to ask, was there anything-- because there was a lot of great points that came up around communication and around having a seat at the table and making sure that the data is there, not just for risk assessments, just to know what's going on in the

laboratories here in the US versus in other countries, like Canada, for instance. So I wanted to ask the panel, is there anything that we've missed today or things that weren't brought up that would be a good thing to discuss in our last bit of time that we have or even in the future?

PETER IWEN: I guess one comment I'd make is-- I know it was brought up, and you just brought it up-- about Canada and their issues with laboratory. It'd be interesting for me to know, what are the processes in Canada in dealing with safety in laboratories, or maybe in Europe? Do we need to reinvent a wheel, I guess, is where I'm going? I mean, if they've got processes in place that are very good or better than what we have, why can't we learn from them, as well? That's just a thought. Mike, do you know? I don't know Canadian processes for the lab.

MIKE PENTELLA: No. But I'd love to-- I'm not an expert on them by any means, but I've learned a lot from my colleagues and ASM, who are from Canada. And they have a different approach to things there. And I think that would be valuable to engage in more discussion with them. I agree with you.

LAURA KNOLL: I think that's a fabulous point. And just one other thing that I think that we really haven't mentioned a lot of today is for all of us on the call, this is something that's near and dear to our hearts and is forefront in our everyday life. And in all labs, lab safety is taken extremely seriously. But I think that when we're looking at biosafety from this perspective, how do we make this front and center at all labs? Because when we're going through what we go through on a day-to-day basis-- and I know COVID kind of helped push biosafety to the front and center, but now that it's kind of taken a little dive-- of course, it's coming up again-- but I think it's very easy for public and labs and everybody else to kind of take a step back. So how do we make sure that this is constantly front and center as a priority, as something to work with with all of our daily challenges?

MIKE PENTELLA: Well, I'd like to add to that. What we didn't hear enough from today are those people who are doing testing in unusual sites, like the long-term care facilities. Now there's testing in some schools, pharmacies. There's so many different sites. What are they doing to prioritize biosafety?

SHELDON CAMPBELL: Another population of folks to talk to might be, though they practice in a very different laboratory environment, laboratorians from places where high-consequence pathogens can be endemic. If we see Lassa fever, it's something to jump up and down about and go screaming off into the woods because we've never seen one before. There are places in the world where it's not that unusual. And there might be lessons to be learned from the folks who do laboratory testing in that part of the world.

ANDREW BRYAN: I think getting that voice from the folks at the bench doing that, from that first-year tech out of school who has to apply and incorporate that into their workflow. I don't know everyone well enough, but I imagine Laura is probably in the lab more than many of us. And when our division heads comment about the carpet versus the tile staff, so have carpeted office here, and we can wax or have those opinions about the safety. But often times, we don't have to wear that N95 and thick lab coat with gloves throughout the entire lab with minimal structured breaks that the union negotiated with the hospital and so making sure that our guidance can realistically be taken up and doesn't further hurt the morale and staffing issues that we're currently facing in a lot of our labs.

CDC MODERATOR: Thank you all for letting us know, or giving us an idea of things that you feel like we missed or you felt like we needed to discuss further. I wanted to give all the presenters and the panelists a chance to give some final thoughts on the town hall, the presentations that were provided, and even our discussion here today.

MIKE PENTELLA: I'll go first. I want to thank CDC for hosting this event. I think it's very important that we think more deeply about biosafety from the manufacturing and instrument perspective. It brings a lot of value to this discussion in this. And it's also important as we get, now, eight years out from that immediate Ebola experience, the outbreak that we had here in 2014, that we consider again the implications of that so that we don't suffer from the same situation, and the patients don't suffer, in the next outbreak like that.

LAURA KNOLL: Sure, I can go. I just want to reiterate a thank you to everyone who's on this call and for the CDC for putting this together. I think that the discussions have been great, especially to hear from all different types of perspectives and in the presentations, as well. And I really hope that there are some good takeaways for the whole group and for anybody that's listening for where we need to go from here. And I hope we have a good list of action items.

PETER IWEN: I agree. I agree with Laura and Mike, as well. I guess what I would hope is that we got a ball starting to roll downhill here, and let's keep it rolling. Let's not stop. I'd hate to see all of our discussions just get put on the back burner. I'd like to continue this discussion, if we could.

ANDREW BRYAN: I guess I'd like to thank the participants in the call that aren't on the panel for your interest in joining discussions without us being able to actually give you a voice to chime in real time to ask questions and encourage you to reach out to those on the panel for any additional thoughts, feedback-- not just at the official DLS Biosafety email but to individual, as well.

SHELDON CAMPBELL: I'd like to thank CDC for organizing this and all the participants. One point I might make is that we shouldn't focus too narrowly on Ebola and similar pathogens or COVID and similar pathogens but make sure we're not fighting the last war and prepare more broadly for different kinds of routes of transmission, stability, and clinical presentations.

SHAWN GIBBS: So I'll be happy to go next. I'd like to reiterate again what others have said in regards to thanks for putting this on. I would also agree with what Sheldon just put on about let's not focus about what's been in the past or what we're dealing with today but learning from the past and learning from today to prepare for the future. And I think that there's a lot of problems in this world that aren't solvable. I think a lot of what we're talking about around this is stuff that we can address and stuff that we can solve in the near future and that there's a lot of smart people that we can pull together in order to do that. And I think it's about continuing the conversation, identifying the problems, and then just really working through the solutions together.

NANCY BURTON: I just want to say thank you to everybody. I really enjoyed listening to everybody's comments today. And I learned quite a bit from everyone and appreciate it.

CDC MODERATOR: Was there anybody on the panel that I missed that wanted to give final remarks before we move forward?

NANCY CORNISH: I want to thank everybody who put so much work into this presentation. It's much appreciated. Do Tim or Ren want to say anything?

REN SALERNO: I just wanted to thank all the panelists for their dedication and commitment to this topic, their preparation for their presentations, and the great discussion that we've had today, extend my gratitude to all the

participants on the line who are not panelists, who listened and joined the conversation. And I encourage you to engage CDC further on this topic if you have particular interests or ideas or suggestions on paths that we should move forward on. And then my final thanks is to my colleagues at FDA for helping us at CDC lay the groundwork for this meeting, helping us identify speakers, and with the agenda. And thanks to Nancy Cornish and to Yvonne and to everyone else at CDC who's made this event happen. So, thank you. Tim, over to you.

TIM STENZEL: Thank you, Nancy and Ren and everybody at CDC and Yvonne that made this happen. It was an excellent day. I'm glad so many could join us. Thank you for joining us. The panelists and their presentations and the discussions were really excellent and will provide a springboard to take things going forward. This is a very important area. The solutions are not necessarily easy. They're complex. They involve multiple stakeholders. So, I look forward to continuing to work with all of you to get it to an even better place than we are right now. And thank you. And back over to you, Nancy.

NANCY CORNISH: OK, we're going to wrap up. And everybody, have a good weekend. It is Friday, so we appreciate you spending your Friday with us. And thank you very much.