Steve Lewis 00:09
Welcome to Speaking of Mol Bio, a podcast series about molecular biology and its trending applications in life sciences. I'm Steve Lewis and I'm so excited to introduce you today to two of my favorite people on the planet, Dr. Ryan Burnette and Dr. Lauren Richardson. Ryan is the Senior Vice President of Life Sciences at Merrick and Company, and Lauren is the director of his science and technology team. I had the pleasure in a past life of working with Ryan and Lauren on multiple biosecurity-related activities in support of the US government, including the Department of Defense, Department of Homeland Security, and the United States Department of Agriculture. We had a really great time, and I'm so excited to share this conversation with you.

Ryan Burnette, PhD 00:58
I have the pleasure, if you will, of being in charge of a business unit that solely focused on life sciences facilities and programs. What we enjoy the most is the outputs of the projects that we engage in whether those are academic, government, international, commercial, is we get to see the outputs of those labs with the potential for good therapeutics, good treatments, good research. So, we like to think we're doing good stuff. We're a unique collection of architects, engineers, commissioning agents, and a variety of folks in the sciences, including, you know, veterinarians, epidemiology, biosafety and biosecurity. And what all that does together is we really try to bring all aspects of life science facilities to bear.

Steve Lewis 01:52
You just mentioned that Lauren is a is a testament to the uniqueness of some of the folks on your team, do you want to explain why?

Ryan Burnette, PhD 02:00
It's hard to quantify her uniqueness adequately. When we when we created the division that now Lauren runs, which is the science and technology consulting arm, to my knowledge at the time, it was the first time we had an in-house collection of, of scientists and public health folks and biorisk management folks in house working side by side with the laboratory designers and the laboratory commissioning agents. That was kind of a new thing. One of the things that is most unique about Merrick is the fact that we've got this in-house team of high-powered nerds, right, that are not engineers, and not architects. And yet they fit very comfortably into a company that for the better part of seventy years has been a pure engineering firm.

Steve Lewis 02:46
It's very interesting. And Lauren, and in your case, as the Senior Director of the Science and Technology team, you along with Ryan, I know, get to see a really interesting part of the life sciences world and the laboratory operations. I'm interested to hear your lens because I know you have such a vast knowledge in veterinary medicine and of course human and public health as it relates to the different aspects of biosecurity. Do you mind kind of taking us through what it looks like to work at the government level? And then how that kind of translates down into the science and technology aspect for what relates to the topic of our podcast, molecular biology?

Lauren Richardson, DVM,MPH,DACVPM 03:33
Sure, you know, this is something that we think about a lot in terms of how do we translate those science needs and requirements into a facility piece. But we also, a lot of the time we're talking through one end to the other. And I really think of it as starting a continuum from theory. What is the theory that is associated with whether it's biosecurity or whether it's a life sciences discipline, molecular bio, what is the theory? How does that inform policy at a government level, sometimes at an international level? Then how does that feed into the strategy at an agency or ministry level, depending on where you are in the world? And then once you get into the facilities, how do you operationalize that? How do you turn that into something that operates a lab and designs how the lab will function? And then that goes down to the bench. So, how does that technical, kind of tactical level operation, nest within all of those different components? And what we often see is that there's really a disconnect between that policy theory and the technical side. So, a lot of what we look to do is figure out how do we support the mission, the policy drivers that are coming through those federal government clients or through some of our private clients or our academic clients, how do we support that from the end user science side so that what we are doing in the lab, whether it's, you know, selecting the equipment that will allow you to do the science you need to do, how does that feed into the larger goals of the of the institution, and then of the agency or entity?

Steve Lewis 05:19
Tell us about some of the functional areas that you work with in the lab.

Lauren Richardson, DVM,MPH,DACVPM 05:24
So I really divided it up into a few different streams of work. We talk about things in terms of facility support, science support, and then science augmentation or science support itself. So you've got facilities, you've got science, and you've got science support. So under facilities, you might have the operations and maintenance, how is the facility running? How does the equipment operate? How do you make sure that the lab works to enable the science that you need? In terms of the science, this is what I think probably most of your listeners are used to. What are you doing in the laboratory? Whether it's a research laboratory and you're doing whatever your basic research is, or your applied research. And then you've got those science support functions. So, things like your quality management teams, all of those things that enable science but require a background knowledge to be able to facilitate whatever's happening in your institution.

Steve Lewis 06:23
So right off the bat, I think one of the things that's really interesting about your line of work at Merrick and Company, but in the broader sense of the biosecurity world is today, a lot of people actually know what you all do. And that relates specifically to the COVID pandemic that we're on, on the heels of. Do you mind sharing your unique lens about everything from medical counter measure development all the way to regulatory and policy impact?

Lauren Richardson, DVM,MPH,DACVPM 06:58
It's been a really interesting journey to watch how people have interacted with the science from the public perspective, as well as from the science perspective itself, from within and from without. Anybody who has been in laboratories or in healthcare over the last few years has really found themselves in

the, in the spotlight. So I think there's a little bit of a disconnect in terms of what are the expectations of what is happening and what is the reality of what it takes to get to a countermeasure that can be used. Whether that's a vaccine, or whether that's a medication, or whether that's a diagnostic. So, translating that expectation into something that is palatable, I don't particularly envy our policymakers, our representatives at the agency level. From what does that look like for us as consultants and folks who are helping out those individual institutions, we've come in in a few different ways and we've found that different folks have different struggles. It's been difficult to actually find new ways of working in a new occupational health environment. So, whether that is we didn't have enough biosafety cabinets to be able to process the number of samples that were necessary. Whether that was trying to deal with heavier diagnostics load that was brought in because of actual response to the pandemic. Or whether it was the supply chains dried up because of either inability to move materials, because of impacts of the pandemic. Or whether it was because of resource drains from other areas that then impacted research, impacted the non-COVID science that was going on. The other thing that we found was that folks had to use the facilities that they had used for a long time for something completely new. So we would come in and figure out alright, well, what do we need to do in this space to allow for operations to change and people to work safely, but maybe that wasn't what the facility was designed or fit for purpose intended to do. So we've seen a lot of different pieces. What are those pieces of equipment intended to do? How are they used? We also got a lot of questions about risk. And a lot of what we do is in the risk sciences. Questions from either occupational health perspectives or from facility perspectives and in understanding what the what the aspects of risk that we should be concerned about whether it's waste management or whether it is the way that you're actually operating within a facility? We got a lot of questions on risk from that perspective. We also got a lot of questions from areas of the public that we don't normally interface with. Typically our clients are scientists. We ended up having questions from schools, from high density facilities, the understanding of biosafety and biosecurity was really just being introduced to folks. So having to talk through some of those things. So, it was a really interesting time. And I'm sure it was incredibly frustrating for a lot of the folks who were coming to realize that there is a large amount of work that goes on that we only really see the wave tops.

Steve Lewis 10:31
That's really insightful. And I think pulling on that thread a little bit more for something like a potential outbreak, Ryan alluded earlier to a biocontainment facility. Do you mind sharing, Ryan, a little bit deeper into how that's defined from your viewpoint and then also the biosafety levels associated with that, and then maybe even shed a little light on, I'm sure what will be everyone's favorite topic from this episode, which is a biosafety level four facility and the unique operations around that?

Ryan Burnette, PhD 11:09
The bio containment spaces, you know, as the name implies that the job of that facility is to contain the biological agent of consequence. Most commonly, we're talking about bacteria or viruses. So the containment aspect of it is really just intended to keep those things secure. The hallmarks of a containment laboratory, we need to make sure those the surfaces, whether it's bench tops or floors or walls, you know, are sealed and easily cleanable. Where the engineers have a lot of fun designing them as in the air handling systems. We have to think about the direction that air flows, we have to think about how the air is filtered. For basic classes, BSL-1, not a whole lot different than then your kitchen, right? There's no special requirements for operating in a BSL-1, and that would be your

equivalent high school biology laboratory facility. You start to get into level two, now you have some things that are a bit more desirable in terms of equipment that you will use in those laboratories, such as biosafety cabinets or other types of isolators. By the time you get to level three, now you have some requirements for directional airflow. How liquid waste is treated, coming out of those laboratories. The number of checkpoints that you'll go through from an entry perspective and an exit perspective. And then depending on the specific agents that are being worked within that facility, might even have some very specific requirements in terms of personal protective equipment or egress, you know, disinfection, emergency response. By the time you get to a BSL-4, this is the maximum containment laboratory. This is usually restricted for use with agents for which there are no current or known therapeutics or treatments for those agents. The engineering controls are quite robust, the training requirements are quite, quite robust. I think what's interesting for, you know, an audience that is savvy in the molecular biology front is oftentimes that biocontainment laboratory operates in distinct parallel, but separation, from those molecular spaces, right. Where you've got the containment lab really is intended to isolate, you know, those agents of interest. Been a while since I was at the bench, but I do remember contamination being an issue during my own molecular escapades. And so containment and molecular don't always play nice together. But they're both required for what is today happening. And that is the juxtaposition between the diagnostics that have, I think, really been revolutionized by molecular but the fact that we still have to have basic containment laboratories for the collection, propagation, and culturing, and identification of the of the agents themselves. So we spent a lot of time looking at that interface and of course, probably one of the best known in the world for the containment labs.

Steve Lewis 14:19
One of the things where this biosecurity world really overlaps in molecular biology is at the DNA level. In recent years, we have had a number of new developments in technology related to oligo synthesis, its accessibility, and then its cloning and assembly as it relates to making ultimately synthetic DNA. And a few years ago, coming out of the J. Craig Venter Institute was the actual working organism that was built synthetically, I believe it was for basically a skeleton of E.*coli*. So Ryan, do you mind sharing a bit about the kind of impetus that started the ultimately, the IGSC at the case study level, and then ultimately, where we are today as it relates to synthetic DNA?

Ryan Burnette, PhD 15:17
You know, today when we think about biosecurity, we really think about, and in the traditional way, it was much what I was saying about the containment laboratories. Not only do we have to keep, you know, the people like laboratorians, and the public safe from the biological agents, we have to keep the biological agents safe from people, because they do have that dual use component. To your point, Steve, it doesn't end at the organism level, right. It comes down to the genetic level. And I think that that has been a bit of a paradigm shift, I'll say in the past fifteen or so years, is really recognizing the inherent vulnerability of the DNA sequence itself and what that entails. So this is where you know, the IGSC has become pretty, pretty pivotal in this is, you know, newsflash, science moves faster than policy can. Particularly when we talk about international policy. Our view on what biosecurity is as it relates to a hog down to a bacteria that could be a pathogen against a human, now down to a very specific gene sequence. So our definition in our lens of biosecurity keeps getting smaller as we go down to this thing. The bottom line is today, we still don't have at a true policy level, in terms of you know, codes of federal regulation, outside of the federal select agent program, of things that truly

regulate access to genetic sequence, right. And this is where the IGSC comes in, in terms of, you know, banding together from an industry perspective, best practices. And so I think that's pretty powerful. But I think that we have to continue to look at the security and the information security issues, all rolled up in that newer, more modern definition of bio security, which is a pretty small, pinprick now. We're looking at specific DNA sequences, and what that should have.

Lauren Richardson, DVM,MPH,DACVPM 17:15
Alternatively, while it's gotten really, really small, it's also gotten really, really big. Because the realm of what we might consider valuable biological material is no longer your hog farm. It's not even really your lab. It's, it's where you're storing your digital information and all of the associated data that is linked to some of these materials. It's an interesting space to talk about in terms of definitions. And I think we're often limited by our own understanding of those definitions. And the fact that people are so expert in things that are so detailed, and technical, often means that we miss the spaces in between. So those silos of excellence are often where we find connections that offer vulnerabilities for some of the work that we do.

Steve Lewis 18:10
We're excited to be in season three of Speaking of Mol Bio, and we know that we have you, our loyal listeners, to thank for the growing success of our podcast series. As a thank you, we're offering a free portable wireless speaker so you can listen to the podcast or your music anywhere. I have one at my desk, and I love how easily it connects to my phone. It's nice when I want to break from my headphones or want to share what I'm listening to with others. I hope you'll visit thermofisher.com/molbiopodcast to request yours today. Please note this item is only available in some regions and only while supplies last. Again, visit thermofisher.com/molbiopodcast t to request yours. And now back to our interview.

Steve Lewis 18:57
It's a really fascinating concept that the data itself, meaning like in this case you we were talking about sequences, can be as both valuable and potentially have the same level of risk as the organism or biological material. Ryan, have you seen blurring of lines between low level data meets biology or information technology meets biology and almost like a sound like a blurring of those lines?

Ryan Burnette, PhD 19:35
To Lauren's point earlier, the regulatory aspects really only hit at the threshold of an organism level. When we start thinking about what does it take to look at that through the lens of the of the information, you know not to being too hard on the COVID pandemic, but that was the currency. That information was the currency. You know, first the sequence, obviously from a therapeutic value, right? But I think there was also the nefarious aspects of that. The examples that we run into mostly in in the laboratory environment is we work, obviously, with a lot of federal clients who happen to be in this federal select agent program. And people who have access to those agents and information about those agents are required to have various levels of suitability through the federal government. I think it's clearer today than it was but I think initially, as we were going through this realization, that the information about, you know, the organism or even the genetic code of that organism being something that needed to be protected, that was not always the case. And there's been more than one example, where we've had to

catch up to this realization, right. We, you know, through some contacts at some, some other three letter agencies where it really became an experiment to see where those triggers were. Actually ordering sequences from organisms and not in a real obvious way either, right. Trying to order those sequences and seeing at what point would that individual perhaps be stopped for security reasons. We've taken a lot of those lessons learned now and we've tried to de-blur those lines. But I think there's I think there's still a long way to go.

Steve Lewis 21:26
Our longer-term listeners will recall that I used to manage Thermo Fisher's gene synthesis portfolio. And the word that popped to mind that we kind of see in the gene synthesis industry is this idea of teleportation. You don't need to send physical samples if you know the sequence in theory, right? There's a few, I mean, probably decades to go before, it's as simple as you know, print out sequence and then ultimately, you have the same exact organism. But the idea that the data, the sequence itself, actually enables the biological development of whatever it is that could ultimately be made. So in our case, the spike protein for the Coronavirus, was a very important sequence for I think anybody who had access to it and was a big part of the medical countermeasure development in the form of of the vaccine, vaccines that ultimately came out. And so it's a really fascinating time to be a part of that world, but also a really very clear indication that sequences themselves actually have a role to play in the biosecurity space. And we happen to have Lauren on the call and so I'm going to ask her a little bit about digital biosecurity and how that relates to some of the molecular techniques that I know our listeners do on a day-to-day basis, whether it's PCR amplification or next generation sequencing and everything in between. So why don't you tell us what digital biosecurity is, and then share with us your perspective as well on the blurring of those lines?

Lauren Richardson, DVM,MPH,DACVPM 23:25
Yeah, I think, and I'll caveat this with you've may have heard of digital biosecurity, there's a lot of different terms. I don't really care what anyone calls it, as long as they are thinking about it and considering how to how to best secure their information. When we're talking through this, I really think of biological materials or valuable biological materials and their associated data. So whatever those data may be. In this case, in synthetic biology, especially, you've got a lot of access to digitized data. Ryan mentioned a few different ways that people started recognizing the significance and where do we want to protect it? How do we want to protect it? Is it a certain size? Is it a specific sequence that is what we should start to look at as the trigger or tripwire for us to recognize that something may be in need of better watching? And I know Steve, you mentioned the spike protein and I really think that's a really great example of when it became obvious to the general population that sequence information was valuable. In terms of what does digital biosecurity really entail, I think it goes beyond just sequence information to the integrated components of laboratories, involves different pieces of equipment, sharing of information, even epidemiologic data, patient information. There really is just a huge continuum of where that digitized information is vulnerable. In terms of how do we, how do we think about protecting it? There are a lot of things that I think people don't consider as vulnerable. I had an effort that I was working on about a year ago to understand what the perspectives of digital biosecurity were in different industries. And I got a lot of different responses that were somewhat alarming. Everything from a response of a very large company, saying, "Oh, well, we're not worried about the protection of sequence information because everyone who has access to it has signed an NDA." So I

think, you know, that type of misunderstanding or misapprehension of security is pretty widespread. But we also, it's a little bit difficult to determine who owns that responsibility for protecting data. Once it's in your hands, or in your system on your server, you can understand that that's probably something that needs to be protected. But what about all of these laboratory equipment pieces that are IoT. The hardware that allows for sequencing didn't have implicit protections for the data that was being put out until recently. So that was actually something that wasn't considered as who owns that security? Who is responsible for that security? And I think folks in laboratories make the assumption that the provider of the technology has already ensured protection. And so it's that space where no one asked the question of who is protecting this. But it's also that space of, you've got two different groups; you've got scientists, and you've got cyber professionals. And they have very different tacit knowledge that is difficult to express in a way that can be taught. So your laboratory staff will know through the way that they work with materials what's being put out, what is the value associated with that? And then you've got your cyber professionals, your IT professionals, who understand what's happening with the data as it comes out of machines, but don't really understand the significance of that from a value perspective. So, that requires that a pretty interconnected look to understand where those areas of vulnerability are, as those different silos of excellence meet one another.

Steve Lewis 27:37
It's almost like you all are like a cross between like, scientists, regulators, and honestly, like a think tank. Like that's, that's kind of what, my mind is blown, right. And I know you all so that I think in and of itself, you know, is just a just a testament to the kind of interesting vulnerabilities that you all think about on your day to day. And then also the real risk mitigation needs that there are in the bespoke disciplines, but also integration points between them.

Lauren Richardson, DVM,MPH,DACVPM 28:17
I'll just add one thing to that. And I think your point is that to bespoke disciplines. Everyone knows their discipline very well. You are the expert in your own work. We are not the expert in your work. But that gives us a bit of an advantage in understanding what could we borrow from a different discipline. What are the others doing? So we find ourselves at that interface. And the goal is to make sure that everyone's talking to one another.

Steve Lewis 28:49
And I'm sure the visibility into a few hundred labs annually gives you gives you a lot of unique insight into some of the trends. As we move toward the end of this interview, I wanted to take an opportunity to ask, Ryan, is there anything that you want to share with our listeners that we might not have covered today?

Ryan Burnette, PhD 29:12
You know, I think if I remember, you know, coming into graduate school and people, people identifying as molecular biologists were, was like a badge of honor, right. And you're surrounded by these biochemists and anaerobic microbiologists. And here you are, it's 1991. It's like, "Oh, I'm a molecular biologist." And I think about what that meant then versus what it means now, and where we've seen, you know, those advances. There was a responsibility, in my opinion, that molecular biologists in the, you know, as they were self-identifying almost back then had, and that was to sort of carry that carry

that field forward and, you know, in a responsible manner. Make it valuable. Right? And, and they certainly did, by an order of magnitude over. And I think what I would say today is that even at the bench level, that responsibility has not gone away, it may have changed, but it hasn't gone away. So, you know, for the world that I think Lauren and I live in, in that world of containment and biosecurity, there will always be some gap that exists between the best practices that, you know, an international consortium will put out, there will always be some gaps between what, you know, a federal government will mandate in terms of law. So, where does that really bring the responsibility back to? It comes back to the bench level. It comes back to the people who are in the trenches working with the organisms working with the technologies, working with the nucleic acids, right, in whatever capacity. So, I think if there's one thing that we can, we can bestow upon that, that audience that still today is the molecular biologist, it's understand that you too have that responsibility to think about things related to security and misuse. Because if you don't, it might be another decade before a voluntary consortium or policy maker gets to the same conclusion.

Steve Lewis 31:35
That is an excellent call to action, think for a really unique episode. One of the things we ask all of our guests on the show is what are your keys to your success? And what would you recommend to future generations who might be interested in your line of work?

Lauren Richardson, DVM,MPH,DACVPM 31:56
It's a really interesting question for someone who is a veterinarian working at an engineering firm. In terms of, of keys to success, I think one of them is ask a lot of questions and listen more than you talk. There's a lot that you can gather, that then can be used across different disciplines. You've got to build your toolkit as you go, this is something that I continue to build with every interaction. So, understanding what everybody brings to the table and adding it to your to your base of knowledge. The other thing that I would encourage folks to do, if they are in really any scenario, but especially a scenario where you're trying to come in and help to resolve a concern or to develop a new program, is to understand that everybody has very different challenges. And there are different limitations to each environment. So understanding the system as it stands, and what those different pressures on both the facility and on the people who are working in it is really, really integral to developing solutions that are going to be feasible and useful.

Steve Lewis 33:14
Ryan, what about you?

Ryan Burnette, PhD 33:14
Honestly, one of the things that's admirable about the life sciences, the biological, biomedical sciences in general is most of us didn't go into this to get rich, we got into this because we cared about, you know, the outputs of these things. And we were naturally curious, right? So I think curiosity, as Lauren alluded to, is one of those things that, you know, that is that's a key to success. Always ask why, why? I think that I also would encourage, you know, folks to explore alternative careers. I had always assumed I was going to be a professor at an academic, medical research institution. Clearly, I took a different path. Those alternative careers are and pathways are out there, so explore those. Keep your head up and look around at those things. But I think perhaps for this audience, the most important thing I think

about is, as a community of scientists, we're not necessarily known for our skills in communication, right. And I think that there are a lot of issues, as we've talked about today, whether we're talking about security or public health or perception, the better the science community can get at communicating, I think the more trust we can earn in a lot of these problems, we can overcome. So never, never underestimate the power of just good communication skills, right. And the ability to continue to work on those can be really pivotal, whether you're in a science career or otherwise. It's still a hallmark of success in my book.

Steve Lewis 35:03
That was Dr. Ryan Burnette and Dr. Lauren Richardson from the team at Merrick and Company. Speaking of Mol Bio is produced by Matt Ferris, Sarah Briganti, and Matthew Stock. We hope you enjoyed this episode and we look forward to our next one. Until then, cheers and good science.