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Center for Biologics Evaluation and Research (CBER)
159th Vaccines and Related Biological Products Advisory Committee (VRBPAC) Meeting

TOPIC II OPEN SESSION

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This transcript appears as received from the commercial transcribing service after inclusion of minor corrections to typographical and factual errors recommended by the DFO.

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DR. EL SAHLY: Any other parting thoughts on the strain selections for the flu vaccines? Okay. So moving on to topic two of this meeting, Laboratory of Respiratory and Special Pathogens Site Visit that was performed a few months ago. The LRSP is a Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccine Research and Review, Center for Biologics Evaluation and Research, CBER. Kathleen will read some housekeeping items and the conflict of interest statement regarding this topic two.

CONFLICT OF INTEREST STATEMENT

MS. HAYES: Thank you. I'm just going to give

a couple minutes for people to clear the room and for the lab to come in and be seated. Just as a reminder for individuals on the phone, you have a separate access code for this session since part of it's confidential. So if you could please hang up and then call back in using that second access code that you were provided via email, that would be great.

So all the presentations for topic two should be in your folders. Welcome to topic two, everyone. In this session, as Dr. El Sahly, mentioned, we'll hear from the Laboratory of Respiratory and Special Pathogens, from the Division of Bacterial Parasitic and Allergenic Products, and we will discuss recommendations from the committee regard the site visit report. In terms of housekeeping, just as a reminder, if everyone could ensure that your cell phones are still on silent, that would be great. And I will now read the conflict of interest statement.

The Food and Drug Administration is convening today, March 4th, 2020, for the 159th meeting of the

Vaccines and Related Biological Products Advisory Committee under the authority of the Federal Advisory Committee Act of 1972. This afternoon, for topic two, the VRBPAC committee will meet in partially closed session to hear overview presentations on intermural laboratory research programs. Per agency guidance, these sessions are determined to be non-particular matters which would have no impact on outside financial interests. Hence, no affected firms are identified, and members are not screened for this topic.

In the afternoon, the meeting will be closed from 4:10 p.m. to 5:10 p.m. to permit discussions where disclosure would constitute a clearly unwarranted invasion of personal privacy. With the exception of the industry representative, all participants of the committee are special government employees or regular federal government employees from other agencies and are subject to the Federal Conflict of Interest Laws and Regulations.

Mr. Sheldon Toubman is serving as a consumer

representative for this committee. Consumer representatives are appointed special government employees and are screened and cleared prior to their participation in the meeting. They are voting members of the committee and hence do have voting privileges, and they do participate in closed sessions, if held.

Dr. Paula Annunziato is serving as the industry representative to this committee. Dr. Annunziato's employed by Merck. Industry representatives act on behalf of all related industry and bring general industry perspectives to the committee. However, industry representatives are not appointed as special government employees and serve as non-voting members of this committee. They are not authorized to attend any closed sessions. Therefore, industry representatives are expected to leave when the open session ends.

This conflict of interest statement will be available for public viewing at the registration table, and this concludes my reading of the conflict of

interest statement for the public record. At this time, I would like to hand the meeting over to Dr. El Sahly. Thank you.

OVERVIEW OF RESEARCH/SITE VISIT PROCESS, CBER

DR. EL SAHLY: Thank you, Kathleen. Dr. Carolyn Wilson, who is Associate Director of Research at CBER will do an overview of the research site visit process.

DR. WILSON: Thank you and good afternoon. I apologize for those of you who've been members for a while as I know the presentation probably will, especially for Dr. El Sahly who's heard it a million times now -- but for those of you who are new members, I hope that this can orient you a little bit to the later discussion about the site visit report, why we do site visits, and your role here today. So all righty.

So just to give you a quick overview, I know, obviously, you're well aware of the work we do in

vaccines, but we also regulate a variety of other products like blood, blood components, blood derivatives, cell and gene therapies, certain human tissues, various related devices and xenotransplantation products. In addition to vaccines, of course, are live biotherapeutic products and allergenic products, each of which raise a number of complexities.

And so the products that we regulate are often things that can't be terminally sterilized, are very complex, living cells, living viruses, and living bacteria. And these novel products that are being developed in response to major public health concerns also raise a number of questions when they come to us for -- first in human clinical trials or even as the clinical development continues through in terms of things like what's the mechanism of action and how do you develop a potency assay.

So these regulatory challenges we address through what we call regulatory science, which is a

combination of both discovery science and targeted development of new tools, sometimes reference materials and other very dedicated specific methodology that can help support development of these new products. And as we have better science and tools at our hands, we're in a better position to make regulatory policy and decision-making. And that allows sponsors then to give us improved data to inform our benefit risk decision-making. And it doesn't stop there because, once the product is licensed, hopefully both safe and effective to address this public health need, we continue through post-market surveyance of that product.

So our research goals, which are shown here -- we're in the process of actually revising them this year. But they aren't out yet, so I'll show you our current goals, which are to advance the scientific basis for regulation of biologics, human tissues, and blood by developing and evaluating technology reagents and standards to inform and improve chemistry, manufacturing, and controls; developing and assessing

non-clinical models and methods predictive of clinical performance with respected toxicity and effectiveness; improving clinical evaluation pre- and post-licensure through use of big data, innovative designs, and statistical, analytical, and modeling approaches; and preparing for future regulatory and public health challenges.

So I wanted to mention a couple of a new scientific initiatives which we've really launched, primarily in FY19. The advanced manufacturing is a new intramural research program. We've brought in two new principle investigators to work on advancing manufacturing for influenza vaccines, which is, of course, a topic of interest to you today, and also in the area of hematopoietic stem cells.

And then a new program which we're launching in this FY20 is regarding pathogen reduction technologies. The idea is, even though we have some licensed technologies for plasma and platelets, to expand these technologies to hold blood so that you

could then reduce pathogen load in whole blood and then fractionate to the various components. And we think that would be of great public health need and address -- also save money.

So within our research program, in addition to these new initiatives, we have a variety of applied technologies and things like high resolution NMR mass spectrometry to evaluate structural components of biologics we regulate. We have core facilities for things like flow cytometry, microarray, high throughput sequencing, and the related bioinformatics and IT infrastructure. As you can imagine with the kinds of products we regulate, we have a lot of microbiology, immunology, biochemistry, and molecular biology, cell and developmental biology, including a relatively new program in micro physiologic systems, epidemiology, biostatistics, and bioinformatics.

So here at White Oak, we have a lab facility just down in the southeast quad here on campus, and, as I mentioned, we have core facilities for a variety of

different technologies and a state of the art vivarium, which allows for imaging with MRI, digital x-ray, intravital imaging systems, ultrasound, and CT, as well as ABSL-2 as well as ABSL-3 capacity, which is really important for certain infectious agents research, as well as a transgenic derivation facility. We also have a PI networking and information group to provide peer mentoring and information sharing. It meets monthly to discuss and share general issues that come up in the life of PIs. Our principle investigators are what we call researcher reviewers, so they have all the same review activities as full-time reviewers while still trying to manage their research laboratories. So some of the issues that come up in our environment may be unique to our situation.

We also do a lot of work with external collaborations within the U.S. and internationally and with a variety of different sectors, as you can see in this graph. And we also do formal leverage mechanisms through contracts, grants, and tech transfers shown

here. And we also take advantage of intellectual property that has been developed here in compliance with the Technology Transfer Act. We file employee invention reports on things that we think have intellectual property implications and, on some occasions, actually file patents and receive royalties, which are then funneled back to help support the research endeavors.

So our research management processes include the CBER Regulatory Science Counsel, which develops research goals and objectives, develops an evaluation framework and criteria to measure scientific and regulatory impact and performs a portfolio review. In addition, there's management review of the research program and internal and external peer review. And so I'm not going to go through this in great detail but only to say that the site visit, which is what you'll be talking about later today in the closed session, is something that we do every four years as part of a broader program of management and peer review. And the

output of your report becomes part of a large package that goes through an internal peer review committee called the Committee for Promotion and Evaluation of Researcher Reviewers.

Our evaluation framework is based on four major areas, mission relevance, dissemination, scientific impact, and unique contribution and regulatory practice. So the site visit is a really critical component of looking at our research reviewers. We do senior staff fellows and staff fellows who are in the service fellowship program. This is an FTE-based program, but these are temporary appointments. And in CBER, these are up to about seven years.

Senior staff fellows are what we call independent principle investigators. They receive independent resources to support their research program in terms of personnel and space and budget. And staff fellows, or visiting associates, are support scientists that are working under a principle investigator.

In order for them to be considered for promotions or if they were to apply for a permanent position, we want them to have gone through a site visit so that there's external peer review of the work they're doing. Once individuals are on our permanent staff, they're called either principle investigators or staff scientists. And again, we want them to continuously go through the external peer review process every four years in order to gain the critical expert input on the direction of their program and so on.

So the site visit report that you have before you today is a draft report, and you have three options. You can accept the report as written, you can amend the report, or you may reject the report and send it back to the site visit team. Once it's approved by the full advisory committee, as I mentioned, the final report is submitted as part of a larger package to the CBER for personnel actions. The PIs take all of the scientific recommendations into account to improve

their own research program and by management when thinking about resource allocation decisions.

So to finish, the benefits of the CBER research program is the integration of research and review in order to ensure relevance, expertise, timeliness, and usability of the science that we are doing. It fosters rational policy and decisions based on sound science, law, and public health impact. It also prepares for future innovative products and public health challenges.

For example, the diversity of virology expertise that we have in Division of Viral Products has actually put us in a very excellent position. We happen to have somebody with prior experience working on Merck's coronavirus, not the subject of his current research at CBER but who has now quickly tacked and is up and running starting a research program to address the new SARS-CoV-2. So this is really important to have a facile and flexible approach to the research program -- developing tools and data that are available

to all stakeholders and support development of product classes and recruit and maintain highly trained scientists with the necessary expertise we need to review regulatory submissions.

So I'll finish with a thank you. I want to specifically call out Drs. Levine and Wharton, who are the co-chairs of this particular site visit, for their time to prepare for today's discussion but also, of course, for the time that they spent doing the site visit and preparing the report. So thank you. I'll stop there and answer any questions.

DR. EL SAHLY: Thank you, Dr. Wilson. Any questions regarding the process?

DR. WILSON: Okay, thank you.

OVERVIEW OF THE OFFICE OF VACCINES RESEARCH AND REVIEW (OVRR) & OVERVIEW OF THE DIVISION OF BACTERIAL, PARASITIC, AND ALLERGENIC PRODUCTS (DBAP)

DR. EL SAHLY: Okay, thank you, Dr. Wilson.

Dr. Jay Slater, who is the director of the Division of Bacterial Parasitic and Allergenic Products at CBER, will do an overview of the Office of Vaccine Research and Review, an overview of the Division of Bacterial Parasitic and --

DR. SLATER: Thank you very much. So in a few minutes, Dr. Michael Schmitt, who's the head of the lab that's being reviewed, is going to orient you about his lab program. And it's my job to bridge Dr. Wilson's talk to his talk and bring you down to the level of LRSP, which is really going to be the focus of your activity. So I'm going to start out by talking about the Office of Vaccines, Research, and Reviews Research Program. OVRR regulates vaccines, as you well know, but also allergenic products, live biotherapeutic products including probiotics and fecal microbiota for transplantation and, most recently, bacteriophage.

The OVRR mission is to protect and enhance the public health by assuring the availability of safe and effective vaccines, allergenic products, and related

products. And the research program that we're focusing on today is designed to complement and support the regulatory mission. So the OVRR core activities, obviously, are review, to review and evaluate and take appropriate actions on all sorts of regulatory submissions, to develop policies and procedures governing the premarket review of regulated products, and also to conduct research related to the development, manufacture, and evaluation of vaccines and related products.

This is the OVRR organizational chart. The director of the Office of Vaccines is Marion Gruber. Deputy director is Phil Krause. And the three relevant divisions that I've put under here, to the far right is the Division of Vaccines and Related Product Applications headed by Dr. Doran Fink and Dr. Loris McVittie. But the two research divisions are the Division of Vital Products and my division, the Division of Bacterial Parasitic and Allergenic Products, which one of my colleagues felt we ought to

rename the Division of Not Viral Products.

Our research mission is designed to complement and support the regulatory mission. Did I go backwards? No, I didn't. The OVRR research goals are to focus on safety, efficacy, and availability of these products.

So the importance of research in the regulation of vaccines and other products -- and I apologize if this is self-evident for you, but I think it sometimes needs to be restated explicitly. First of all, the vaccines, there is an emphasis on safety that really isn't present in the rest of the agency. These are products that are intended for mass use, often universal use. The recipients are healthy individuals, often children. And so the tolerance for safety signals is really quite low, and I think our research really helps us with that.

It's also a field in which in technology is moving very quickly, and our research program helps us to keep pace with that technology. Obviously, vaccines

are subject to an extremely high level of scrutiny by the public. It's really critical that our regulatory decisions be absolutely bullet proof in terms of their science base. And we think that our engagement in active research science really helps us with that.

And then finally -- and of course this talk was put together back in November, so I don't have specifics here -- but we need to be able to respond to public health threats. And it's not just the emerging viral infections, which are, of course, what we're all thinking about today, but issues of antibiotic resistance, C. diff, and other infectious problems. Our research program in OVRR is broad. We can't cover everything, but we need to cover as much as possible within the scope of our responsibilities. It is collaborative. We collaborate with scientists around the country, as Dr. Wilson explained, and around the world to leverage our investments and research.

It's important to note that our research is really investigator initiated. This allows our

researcher reviews to anticipate regulatory needs and proactively address important questions. We expect our research to be excellent. Our motivation is the regulatory mission, but our research is published and broadly cited and used.

Our research scientists are members of the broader scientific community, and we expect them to be well-known and well-regarded experts in their fields. And finally, our research is flexible. Our scientists work on topics that allow rapid adaptation to emerging needs.

Dr. Wilson talked about the researcher regulatory model. We are very committed to this. This is a model that integrates regulatory review responsibilities with our mission-directed research. Our researchers actively review IND and BLA applications. They're active participants in product-related -- as subject matter experts on inspections. They perform relevant research to evaluate specific issues of safety, efficacy, or manufacturing issues.

So I'm now going to zoom in one last time before Dr. Schmitt's presentation on the Division of Bacterial Parasitic and Allergenic Products, which I head. We have four laboratories within the division. I am the director. Dr. Drusilla Burns is the deputy director. And the focus of your attention today is the lab in the upper right-hand corner, the Lab of Respiratory and Special Pathogens.

Of note is that Dr. Schmitt is the Chief of that lab. Dr. Burns, who's my Deputy Director, is also a PI within that lab, as is Dr. Tod Merkel. Likewise, even though I'm the head of the Division, I'm also an active researcher in the Lab of Immunobiochemistry in the lower left-hand corner. It's all a little bit back and forth organizationally, but it has worked for many years so far.

I'm going to review very briefly in just a handful of slides the DBPAP regulatory research portfolio. And the shorthand that I have found most useful to explain it to people is to give you on this

slide the full range of organisms that we regulate in terms of either our research, upcoming aspirational vaccine research, or, in some cases, many cases, long established vaccine targets. And you have the non-invasive toxin producers, the invasive organisms for which the protective responses are to polysaccharides. You have intracellular pathogens, enteric pathogens, parasites, and then, of course, there has to be a group of other that don't quite fit neatly into that.

The Lab of Bacterial Polysaccharides, LBP, focuses, as you would expect it to, on that small group of invasive organisms for which the protective responses are to their polysaccharides, H flu, Neisseria meningitidis, strep pneumoniae. And in addition, among the enteric organisms, there is a salmonella vaccine that is directed to the polysaccharides specifically, and LBP regulates those. The Lab of Immunobiochemistry, that's our somewhat fancy name for the Lab of Allergenic Products.

We regulate allergenic products, which seems

like only one entry on this slide. They are actually over 800 different allergenic products, and it's a technologically very rapidly moving field. So we are kept quite busy regulating those. And the research that we do, both Dr. Rabin and I, directly focuses on ways of improving this very heterogenous group of products.

The Lab of Respiratory and Special Pathogens is the one that you're going to focus on today. By and large, this lab focuses on non-invasive toxin producers, anthrax, pertussis, botulinum toxin, tetanus, and Corynebacterium diphtheriae. In addition, this lab is part of a consortium of two labs that we've put together to deal with issues having to do with staph aureus vaccine development.

And then finally, the Lab of Mucosal Pathogens and Cellular Immunology, this is the lab that is largely focused on enteric organisms and intracellular organisms that are listed here. But this is also a lab that focuses on C. diff as a pathogen and on malaria

research. In fact, one of our most recent recruits is a PI who will be focusing exclusively on issues having to do with malaria.

LMPCI also was fortunate enough to deal with the lion's share of the other classification. In addition to working with LRSP on staph aureus, this is also the group that focuses on live biotherapeutic products or probiotics, phage, and the microbiome-related products. At the LRSP site visit several months ago, there were five presenters, and Dr. Schmitt, who you'll be hearing from momentarily, spoke and presented his work and an overview of the lab. Dr. Drusilla Burns and Dr. Tod Merkel are the other two PIs in the group. And then staff scientist, Dr. Anita Verma, and staff fellow, Dr. Eric Peng, presented their work as well. I would be very happy to field any questions at this point before I turn this over to Dr. Schmitt.

DR. CHATTERJEE: So I'm new to the committee and was just curious to try and learn a little bit more

in terms of your collaboration with other scientists. Does that extend to scientists who are engaged in industry, or is this confined to people who are in academia and in other government agencies like NIH?

DR. SLATER: That's a great question. Collaborations within government tend to be the easiest and the smoothest, and obviously we have collaborations with colleagues at the National Institutes of Health and other government scientists as well. When their interest in working with us is very close, we sometimes benefit from interagency agreements in which case we can get funds. But most of the collaborations are less formal than that. I'm working my way to answering your question.

Academic collaborations are very widespread. Our scientists really have a great deal of interest in collaborating. We can sometimes actually benefit from that as well. We can't be principle investigators on their NIH grants, but we can benefit in limited ways from participating in their NIH grants. And that is

useful. But again, most of the collaborations with academics are on a relatively less formal level. We try to formalize them to the degree that they become more intense.

When we're asked to collaborate with industry, obviously, we're concerned about both real and perceived conflicts of interest. Depending on the extent of that kind of research, we sometimes worry about it more and sometimes less. We are capable of constructing CRADAs, cooperative research agreements, with industry. The advantage of that is not only that we get money from the industry partners to support our research but that we really formalize and draw lines as to what we do and what we don't do.

And you know, one of the decisions that, you know, when somebody comes to me and wants to collaborate with industry that first I and then Dr. Gruber have to sign on to is whether this will require us to recuse this investigator and their staff from reviewing products that come in down the line. And

again, you know, we err on the side of appearance. We really want to make sure that there's no perceived conflict of interest, even if there isn't a real one. But typically, if our research is very early in the product development, then we will be more eager and active participants in that then certainly later. There have been several examples where we have worked with industry under those constraints. Thanks.

DR. CHATTERJEE: So a question about the priorities as to how you decide which of these organisms you're going to prioritize, what type of research you're going to prioritize. How are those priorities set?

DR. SLATER: So as I said, really the lion's share of the priorities are set by the investigators themselves. We largely trust them. Now, that said, in addition to the quadrennial review that goes on at the site visit, there is an annual review that goes on for all of our labs. In our labs, all of the PIs need to submit reports to a centralized research reporting

database in which they report their progress and their plans for the next year and ask for money for the next year. That's reviewed very closely by their lab chief and then by me and then ultimately by the office and the center.

I've had conversations with PIs about the direction of their research, but, typically, the PIs exercise really, really good judgement on this. And for the most part, it's set by them and, of course, informed by the regulatory worth that they see coming in. They're the ones on the front lines of the regulatory questions, and so I think, for the most part, they're pretty sensitive to what the issues are.

DR. WILSON: Just to add that a little bit at a broader level. In terms of research priorities, in addition to what Jay described that goes on in sort of a micro level for the PIs who are already here and have active and ongoing research, we also do think strategically about future recruitments and try to identify what are some new priority areas that, if

resources arise, where we would invest those in terms of future PI recruitments. And so the divisions and offices periodically do this kind of review and discussion. It's brought up to the Regulatory Science Counsel.

We actually discuss it at the center level to identify where we might need to engage or identify new opportunities to address new challenges. And the offices also present to the Regulatory Science Counsel a sort of research program portfolio review to look at potential gaps in areas that they would want to address in the future.

OVERVIEW OF THE LABORATORY OF RESPIRATORY AND SPECIAL PATHOGENS

DR. EL SAHLY: Okay. Thank you, Dr. Slater. Dr. Michael Schmitt, Chief of the Laboratory of Respiratory and Special Pathogens at CBER, will give us an overview of the Laboratory of Respiratory and

Special Pathogens, LRSP.

DR. SCHMITT: Great, thank you. Thank you. Good afternoon, everyone. So I'm Mike Schmitt, Chief of the Laboratory of Respiratory and Special Pathogens, and I'd like to give you today just a brief overview of the research and regulatory activities of the laboratory. Let's see. I think I'm -- wouldn't you know, I'm the one that can't get it to turn. Is this it? I'm hitting the wrong button. Okay. It's just this one over here. Got it. Okay. Thank you.

Okay. So as the other speakers have indicated, the principle investigators in LRSP are what we refer to as research reviewers, and they have two primary responsibilities: that is to develop and direct independent research programs but also participate in the regulatory activities of the laboratory. So the current research programs in LSRP cover a broad range from basic studies in bacterial virulence and pathogenesis to research that examines the characteristics of current and future vaccines. We

feel the research is supportive of the regulatory activities in LSRP, as seen the product-specific research programs but also in the expertise of the investigators in fields of bacteriology, immunology, and biochemistry.

So on this slide I wanted to just touch on some of the vaccines that fall under our purview of review responsibilities, and I've divided it into three categories here. The primary license vaccines, which primarily exist as combinations, and these are vaccines against diphtheriae, tetanus, and pertussis. The second group are the biodefense vaccines. This includes vaccines against anthrax, plague, and the botulinum and ricin toxins. The last group is just other vaccines that are also very important in part of our portfolio. This includes vaccines against staph aureus, staphylococcus aureus disease, and also various streptococcal pathogens and clostridium difficile.

So I wanted to get into a little more detail of our specific regulatory activities on this slide,

and I've divided this also into categories, two categories. These are the preapproval submissions that we receive -- and these are primarily pre-licensure submissions -- and then also post-approval which are our licensed vaccines. So under the preapproval, these are mainly INDs, investigational new drug applications. And we'll get these coming in as either pre-INDs, that is, before the actual IND is submitted where we will provide advice to the investigator or company regarding their product.

We will then receive the IND and then subsequent amendments to that IND. And our primary focus for review is product oriented, that is we will review manufacturing and testing issues regarding the vaccine. The other type of submission would be the biologic license application itself, and this would come in as what we refer to an original submission BLA. And this is when a manufacturer is coming in to request a licensure of their product.

The second group are the post-approvals, and

these are the licensed product, the licensed vaccines that we look at. And in the primary submissions that we get here are what we refer to BLA supplements. So any time a manufacturer makes a significant change in manufacturing or testing for their vaccine, they will need to receive approval from the FDA, and this will come in the form of a supplement. And again, what we would review is the product associated aspects of this submission, again, manufacturing and testing issues. We're also involved in lot release issues and also in the inspection of vaccine manufacturers.

So what I've shown here is the current organization of the laboratory. We have three PIs: Drusilla Burns, who also serves as the deputy director of the division, Tod Merkel, and myself. And here is the full staffing chart for LRSP. Directly under my responsibility, I have two full-time regulatory reviewers and then under the PIs are shown the various staff members for them and these include staff scientists, staff fellows, and also research associates

in their laboratory.

So what I want to outline here is the specific research and regulatory responsibilities of each of the individual lab groups. So under Drusilla Burns, she primarily focuses on her -- her research primarily focuses on three areas: looking at anthrax vaccines, pertussis vaccines, and also vaccines against staph aureus disease. Tod Merkel focuses almost exclusively on issues related to pertussis vaccines, while my group looks at diphtheriae vaccines and other issues related to C. diphtheriae pathogenesis.

So under this, beneath the research program, I show the regulatory activities. And they, in general, reflect our research program, although there are a number of exceptions. So you can see with Dr. Burns, her primarily regulatory activities of her laboratory are anthrax, pertussis, and staph aureus vaccine submissions. But individuals in her lab will frequently review issues related to diphtheriae and tetanus and other vaccines.

With Tod Merkel, his primary focus is on pertussis and anthrax vaccine submissions. And my group, our primary focus is on the diphtheriae and tetanus components in vaccines, and we also look at the biodefense vaccines. But many people in my group over the years have been heavily involved with pertussis and anthrax and other vaccine submissions. So there is overlap, but our primary focus for the type of submissions we receive largely reflects our research program.

So I'm going to get a little more detail into the individual research programs in the laboratory, and here's a description of Dr. Burns' research program. So I said, it's divided into three areas: anthrax, pertussis, and then staphylococcus aureus vaccines. So under her anthrax work, she's primarily focused on the analysis of neutralizing antibody response to anthrax vaccines and other toxoid-based vaccines and also improving anthrax vaccine stability. With regard to her pertussis vaccine program, she's looking at vaccine

safety with the development of an invitro assay to assess residual pertussis toxin activity.

She also assess vaccine efficacy, and the development of corelates of protection are examined in those studies. With regard to her staphylococcus aureus vaccine program, it involves the development of animal models that represent different clinical presentations of staph aureus disease and also the elucidation of corelates of immunity. So overall our program provides information used in the development of quality control tests for anthrax, pertussis, and staph aureus and also supplies important information for assessing safety and efficacy of new anthrax, pertussis, and staph aureus vaccines.

So the Merkel program, which I have indicated was primarily associated with pertussis vaccines, is involved in the development and use of the baboon model of pertussis to study pertussis pathogenesis in the immune response to infection and vaccination and also the development of aerosol models of pertussis to

identify and characterize factors contributing to transmission of the bacteria. So this research program provides important insights into vaccine mediated protection against pertussis leading to enhanced understanding of the epidemiology of pertussis in the U.S. It also allows for the identification of immune responses required for vaccine mediating clearance of B. pertussis, which may assist in the identification of biomarkers to assess vaccine effectiveness. In his work, he is involved in studies in the impact of host factors in vaccination status on shedding of the B. pertussis organism, and this may facilitate the vaccine development and other public health measures to reduce transmission.

So my program primarily focuses on diphtheriae vaccines with the focus on acquisition of host iron by Corynebacterium diphtheriae. We finally study the analysis of factors that are coordinately expressed with diphtheriae toxin to focus on metal and heme transport systems. We view our system as a model

system to understand pathogenic mechanisms in chronic bacterium and, more broadly, in other gram-positive pathogens to help identify possible virulence factors in future vaccine candidates. My research program provides the scientific foundation for the evaluation of components for future diphtheriae vaccines as well as support for the review and regulation of the numerous changes in the production and testing required to maintain and improve the quality of our currently licensed diphtheriae toxoid-containing vaccines.

So I just want to close with the relevance of our research regulation. We feel the knowledge acquired from our research establishes a scientific basis for our decisions in the regulation of vaccines. It gives us an in-depth knowledge and understanding of novel products and methods, expertise to determine the suitability of tests that assess safety, purity, and potency of vaccines, and also an expertise to provide advice in the design of non-clinical studies for vaccines licensed under the animal rule. These would

primarily be the biodefense vaccines such as anthrax and vaccines against botulinum toxins.

It also gives us quite a bit of credibility in the scientific community. It provides assurances that we possess the scientific qualifications to assess safety and quality of current and future vaccines. Thank you and I'll take any questions.

DR. EL SAHLY: Questions for Schmitt from the committee? Okay. Well, thank you, Dr. Schmitt.

DR. SCHMITT: Great. Thank you.

DR. EL SAHLY: We have no one registered for the open public hearing session that follows these presentations. Anyone in the room for an open public hearing statement? Okay. So neither on the phone nor in person do we have a statement. We will now take a break, a ten-minute break, before we hear the report and deliberate on the matter in a closed session.

[END OF TOPIC II OPEN SESSION]