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Center for Biologics Evaluation and Research (CBER)

143rd Meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC)

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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PROCEEDINGS

Agenda Item: Call to Order and Opening Remarks

DR. EDWARDS: I welcome everyone. I would like to call the meeting to order of the Vaccines and Related Biologics Products Advisory Committee meeting. The goal of this meeting through teleconference, is to discuss the Office of Vaccines Research and Review of the Division of Bacterial, Parasitic, and Allergenic Products in the Laboratory of Bacterial Polysaccharides.

Before we start our discussion we need to have a reading of the conflict of interest.

DR. VIJH: Thank you Dr. Edwards. Hello everyone. I am Sujata Vijh, the Designated Federal Officer for today's meeting of the Vaccines and Related Biological Products Advisory Committee. Ms. Rosanna Harvey is the Committee Management Specialist for VRBPAC, and she is being assisted by our colleague Ms. Denise Royster.

On behalf of the FDA, the Center for Biologics Evaluations and Research and the Office of Vaccines Research and Review, we would like to welcome everyone to the 143rd VRBPAC meeting described in the Federal Register notice of March 16, 2016.

Members are participating via phone today, and the meeting is also being webcast live. Before proceeding

to administrative remarks and reading the COI statement, I would like to take a quick roll call of members on the phone for the record. I will be using the roster that you have to follow to check who is on the phone.

Dr. Edwards was on. Dr. Ruth Lynfield.

DR. LYNFIELD: Yes.

DR. VIJH: Dr. Karen Kotloff.

DR. KOTLOFF: (No response)

DR. VIJH: Dr. Patrick Moore.

DR. MOORE: Yes.

DR. VIJH: Dr. Janet Englund.

DR. ENGLUND: Yes.

DR. VIJH: Dr. Ofer Levy.

DR. LEVY: (No response)

DR. VIJH: Dr. Sarah Long.

DR. LONG: Yes.

DR. VIJH: Dr. Mark Sawyer.

DR. SAWYER: Yes.

DR. VIJH: Dr. David Greenberg.

DR. GREENBERG: Yes.

DR. VIJH: And Dr. Arnold Monto.

DR. MONTO: Yes.

DR. VIJH: I see that Dr. Karen Kotloff has joined. Dr. Karen Kotloff.

DR. KOTLOFF: Yes, I am here.

DR. VIJH: Wonderful. Also Dr. Ofer Levy has also joined?

DR. LEVY: (No response)

DR. VIJH: Okay. I now invite Dr. Kathryn Edwards to handle the introduction of the members on the phone.

DR. EDWARDS: I believe the first order of business will be an overview of the CBER Research/Site Visit Process by Dr. Wilson.

DR. VIJH: Dr. Edwards, you need to introduce the members on the phone because the public is watching the webcast so they need to know who the members of the VRBPAC Committee are. So if you use the roster perhaps they can just go through their introductions.

DR. EDWARDS: So you want me to list the number of all the members on the VRBPAC. I am Kathryn Edwards and I am a professor of pediatrics at Vanderbilt University.

Do you want each of the members then to introduce themselves? Is that what you are saying?

DR. VIJH: Yes, please.

DR. EDWARDS: Dr. Lynfield, would you please introduce yourself?

DR. LYNFIELD: Yes, thank you. This is Ruth Lynfield. I am a member of VRBPAC and I am the State

Epidemiologist and Medical Director at the Minnesota Department of Health.

DR. EDWARDS: Thank you. Dr. Kotloff.

DR. KOTLOFF: I am Karen Kotloff. I am professor of Pediatrics and Infectious Diseases at the University of Maryland School of Medicine.

DR. EDWARDS: Dr. Moore.

DR. MOORE: I am a professor at the University of Pittsburgh Cancer Institute and in the Department of Molecular Genetics and Microbiology at the University of Pittsburgh.

DR. EDWARDS: Thank you. Dr. Englund.

DR. ENGLUND: I am Dr. Janet Englund, Professor of Pediatrics in the Division of Infectious Disease at the University of Washington and Seattle Children’s Hospital and adjunct at Fred Hutchison Cancer Research Center.

DR. EDWARDS: Dr. Levy.

DR. LEVY: Hi. I am Dr. Ofer Levy. I am a faculty member in Human Biology and Translational Medicine and an Associate Professor at Harvard Medical School. I am a staff physician and director of the Precision Vaccine Programs in the Division of Infectious Diseases at Boston Children’s Hospital.

DR. EDWARDS: Thank you. Dr. Long.

DR. LONG: I am Dr. Sarah Long. I am a member of VRBPAC. Professor of Pediatrics at Drexel University College of Medicine and Chief of Infectious Diseases at St. Christopher's Hospital for Children in Philadelphia.

DR. EDWARDS: Thank you. Dr. Sawyer.

DR. SAWYER: Mark Sawyer, Professor of Pediatrics in the Division of Infectious Disease at UC San Diego and Rady Children's Hospital, San Diego.

DR. EDWARDS: Thank you. Dr. Greenberg.

DR. GREENBERG: I am the industry representative at VRBPAC. Vice President, Scientific and Medical Affairs at Sanofi Pasteur and adjunct Associate Professor of Pediatrics at University of Pittsburgh.

DR. EDWARDS: Dr. Monto.

DR. MONTO: I am Arnold Monto. VRBPAC member. I am Professor of Epidemiology in the School of Public Health, University of Michigan.

DR. EDWARDS: Dr. Andrews.

DR. ANDREWS: I am Ellen Andrews. I am a temporary member and a consumer representative. I am the Executive Director of the Connecticut Health Policy Project.

DR. EDWARDS: Thank you very much. I would like to now introduce the FDA participants who will be providing information and discussion. The first will be Dr. Carolyn

Wilson, Associate Director for Research for CBER, who will be giving us an overview of the site visit process.

Dr. Wilson.

DR. VIJH: Dr. Edwards, I still need to finish my administrative remarks and my conflict of interest statement before we move on to having the presentation.

DR. EDWARDS: Great. Go ahead.

DR. VIJH: Because this is a format where people can't really see what is going on, we just have to be very clear about what is going on in the room so the public has an understanding too. There are FDA staff sitting at the table that I would like to quickly go through for the introductions.

Dr. Gruber.

DR. GRUBER: My name is Marion Gruber. I am the Director of the Office of Vaccines Research and Review at CBER.

DR. WILSON: Carolyn Wilson, Associate Director for Research, CBER.

DR. BURNS: Drusilla Burns, Deputy Director, Division of Bacterial, Parasitic and Allergenic Products, CBER.

DR. SLATER: Jay Slater. I am the Director of the Division of Bacterial, Parasitic and Allergenic Products at CBER.

DR. VANN: Willie Vann. I am Chief of the Laboratory of Bacterial Polysaccharides, which is in the Division of Bacterial, Parasitic and Allergenic Products at CBER.

DR. VIJH: Thank you. I would like to go through the meeting format. We will begin today's meeting with a session that is open to the public, followed by the open public hearing session. Both of which are available by live webcast. It is anticipated that the open public hearing will take place about 30 to 40 minutes ahead of schedule. So if there are members of the public that would like to present oral comments please sign up outside at the registration table. If there are no comments from the public, the meeting will go to the closed session. That is not webcast.

For the closed session, the FDA staff being evaluated for personnel actions will leave the room. Dr. David Greenberg, who is a VRBPAC industry representative, will also disconnect from the phone before the closed session starts.

Dr. Ellen Andrews is a temporary voting consumer representative for the meeting. Ms. Debra Gilliam is the transcriptionist, seated in the room and will be present during both open and closed sessions. Please check your cell phones to make sure that they are off or are in silent

mode. Members via phone, please mute your lines and unmute to speak as needed.

Participants in the room are also requested to state your name and speak clearly and loudly into the phone or microphone, so that the transcriber and other attendees and those watching via webcast can hear your comments. I would now like to read the Conflict of Interest Statement into the public record.

Agenda Item: Conflicts of Interest Statement.

DR. VIJH: The Food and Drug Administration is convening today's meeting of the Vaccines and Related Biological Products Advisory Committee under the authority of the Federal Advisory Committee Act, FACA, of 1972. With the exception of the industry representative, all participants of the committee are special government employees from other agencies that are subject to the Federal Conflict of Interest Laws and Regulations.

The following information on the status of this Advisory Committee's compliance with Federal Conflict of Interest Laws including but not limited to 18 U.S. Code Section 208 of the Federal Food, Drug, and Cosmetic Act, is being provided to participants at this meeting and to the public.

FDA has determined that members of this committee are in compliance with Federal Ethics and Conflict of Interest Laws.

Today's agenda includes an overview of the research programs in the Laboratory of Bacterial Polysaccharides, Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccines Research and Review, of the Center for Biologics Evaluation and Research.

This overview is a non-particular matter. Based on the agenda, it has been determined that this overview presents no actual or appearance of a conflict of interest.

In closed session the committee will review and discuss the draft site visit report from the site visit concluded on February 4, 2016.

Dr. David Greenberg, serving as an industry representative, acts on behalf of all related industry. He is employed by Sanofi Pasteur. Industry representatives are not special government employees and do not vote.

This conflict of interest statement will be available at the registration table for review. We would like to remind members, consultants, and participants that if discussions involve any products or firms not on the agenda for which an FDA participant has a personal or imputed financial interest, the participant needs to

exclude themselves from such involvement and exclusion will be noted for the record.

FDA encourages all participants to advise the committee of any financial relationships that you may have with firms that could be affected by the committee discussions.

Dr. Edwards, I now hand over the meeting to you to introduce Dr. Carolyn Wilson for her presentation.

DR. EDWARDS: Thank you very much. I now would like to introduce Carolyn Wilson, Associate Director for Research at CBER at the FDA, who will present an overview of the CBER Research Site/Visit Process.

Dr. Wilson.

DR. LONG: This is Sarah Long. May I just ask you – I am still on the title page. Is there something that I need to do here?

Topic: Presentations of the Laboratory of Bacterial Polysaccharides, Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research

Agenda Item: Overview of CBER Research/Site Visit Process

DR. WILSON: We see the title page here too, in the room so don’t worry. We will catch up.

While those are being brought up I wanted to provide a special thanks to Drs. Levy and Moore for co-chairing the site visit. We always rely on the good graces of our Advisory Committee members to step up and be willing to chair these site visits throughout their tenure. So we really do appreciate the time and effort involved in doing this.

I will try to go through very quickly a quick overview about the Center for Biologics and particularly about our regulatory science and research program. For those of you who are relatively new to the committee what I want to emphasize is that science and regulation really go hand in hand as we look at how the Center for Biologics can advance product development.

DR. EDWARDS: We can't hear you.

DR. WILSON: You can't? I wonder why.

DR. EDWARDS: We can now hear you.

DR. WILSON: You can? Fantastic. Everybody can hear me now. All right, I will just try and continue since all you missed was an introductory statement.

What I was saying is we think of science and regulations as going hand in hand in advancing product development and the role that CBER plays in that process. We think of it as starting with the public health problem that drives the development of novel products. Those novel

products may sometimes pose a challenge to us as regulators because we don't always have all the best information or models available to us or tools even, to assess how these products may perform in the clinic.

So that is where regulatory science through a combination of both discovery science and targeted development of new tools, for example, reference materials, perhaps a new animal model that can help assess product pre-clinically, a better mechanistic study to be able to advise sponsors on potency assays and so on. These kinds of studies can help address product issues that would impact a whole class of products, as opposed to what industry does, which is very specific to one product.

As we generate this new science and information and tools, it also informs our regulatory policy and decision making and as we get better guidance out to sponsors they are then in a better position to provide improved data to allow us to make a benefit risk decision.

So that in the end, we hope that we are licensing a product that has a positive impact on that public health issue that drove the development of that new product. The cycle doesn't really end there as we continue post-marketing to do surveillance for adverse events and in some cases, gaining additional information about efficacy of the product as well.

CBER scientists are what are called researcher or regulators or researcher or reviewers. These individuals perform all the same activities as full-time review staff. Meaning that they review submissions, regulatory submissions, participate in inspections, write guidance documents, organize and participate in advisory committees and workshops.

While they are firmly rooted in the regulatory processes which allows them to have a view of what is in-house, they are also active engaged members of their own scientific communities; going out to meetings, interacting and collaborating with members of academia and other government agencies. This allows them to also be looking forward in thinking about issues that may face the agency in the future so that we can make sure that we are using our scientific staff in the most useful way in being able to be both proactive and addressing issues as they arise.

In 2016, we stood up a new body called the Regulatory Science Council, which is composed of Office and Center leadership. One outcome of that is we developed four new regulatory science and research goals. For the sake of time I won't read through these but they are in your slide set for reference if it is useful.

The process that we use to review our research involved an annual process as well as a cyclic process

every four years. The annual process is facilitated by an online research reporting database where PIs provide progress reports, future plans, budget request, presentations, publications, and other output may include things like an employee invention report, a patent application, and so on.

The information is reviewed at multiple levels. There are lab chief, division, office level supervisory chain, and they are looking for the relevance, productivity and quality of the science. Then funding decisions are made in accordance with those reviews.

The cyclic review, which I mentioned, occurs every four years. The site visits, which you are looking at today, is the external component of that whereby the research program is looked at very in-depth through a peer review by scientific experts. That site visit report becomes part of a larger package reviewed by an internal peer review committee called the Promotion, Conversion, Evaluation Committee.

These individuals look not just at the research program and the accomplishments, but also at the individual’s regulatory performance and accomplishments as well.

This year we also developed a research impact framework, which we look at from both the portfolio and

project level. The portfolio level includes looking at alignment with major Center and Office-wide strategic initiatives and priorities.

We also want to make sure that we have the scientific expertise to address the review needs both currently and anticipated. And we also want to make sure that our research program provides us an agile set of internal capabilities to address unexpected urgent public health needs.

Individually, we also want to make sure that we are looking at scientific gaps and questions that are of importance to our regulatory mission. Then of course, also on the project level we need to take into account the scientific merit and the PIs historical productivity.

The site-visit report that you will be reviewing today is a draft report generated by the site visit team. Your goal here is to review the final report. You have several opportunities – three different outcomes of that review. One is to accept the report as written. Second is to provide an amendment to the report. Third, if you feel major changes need to be made you can reject the report and send it back to the site visit team for revision.

The report is very important for both as I mentioned, the internal peer review process by the PCE. That is of particular importance for those involving

personnel actions for promotion or conversion. The PIs obviously take the scientific input very seriously to improve their own research program. Then management is also, obviously, taking into account the important input as well.

I will stop where I finished with a large thank you to the site visit team, which was chaired by Drs. Levy and Moore. In case you did not hear at the beginning, I started the talk by thanking them for their time and effort. The site visits are fairly significant in terms of the amount of time it takes to perform these. We really rely on the volunteerism of these Advisory Committee members to chair these site visit teams.

Thank you very much. I will stop there and answer any questions.

DR. EDWARDS: Thank you Dr. Wilson. Are there any questions?

DR. WILSON: I just wanted to mention we are right next door to a fairly noisy meeting so when you hear huge rounds of applause and laughter, that is not in here.

DR. EDWARDS: Thank you very much. If there are no further questions then we will ask Dr. Gruber to give an overview of the OVRR.

Agenda Item: Overview of OVRR

DR. GRUBER: My name is Marion Gruber. I will provide, as Kathy stated, with an overview of the OVRR Research Program. I will abbreviate this presentation to allow plenty of time for the closed session discussion.

OVRR's research mission and its program is designed to complement and support the regulatory mission. It focuses on issues that are related to the development of safe and effective vaccines and other biological products that this Office regulates.

The Office is organized in the immediate Office of the Director. We have three different Divisions. The Division of Bacterial, Parasitic, and Allergenic Products is one of our two laboratory based divisions. Dr. Slater will talk a little bit more about the organization of this Division in the next presentation.

We regulate a very complex area and range of biological products. We not only regulate licensed investigational preventive and therapeutic vaccines for infectious disease indications, but also allergenic products and diagnostic tests. Lately we also regulate a new class of products such as fecal microbiota transplantations as well as probiotic products.

Our core activities include the review and evaluation of investigational new drug applications,

biologics license applications, and supplements for vaccines and related biological products.

We develop policies and procedures that govern the pre-marketing review of regulated products. Of course we do conduct research that is related to the development, manufacture, and evaluation of vaccines and related biological products.

It is very important to conduct research in this Office because as you all appreciate, preventive vaccines administered to healthy individuals, the majority perhaps being children, and then place a special emphasis on the safety of these products. There is a high-level of scrutiny by the public. And of course we have to keep up with the pace of technology as new manufacturing technologies are rapidly evolving.

There is a wide variety of rapidly evolving technical and scientific issues that concern the safety, purity, potency, and effectiveness of vaccines and related biological products. That of course, does require knowledge of new developments in basic research in these disciplines.

Our research program addresses the scientific aspects of regulatory issues, as stated by Dr. Wilson. We evaluate and implement when applicable, innovative technology to improve testing methods for both currently

licensed products and those that are currently under development.

The purpose of the OVRR Research Program is stated in the slide.

. It contributes to the regulation of vaccines and related products by addressing scientific aspects of critical regulatory issues.

. It maintains and develops the scientific base for establishing methods and standards that are designed to ensure the continued safety, purity, potency and effectiveness of the products that we regulate.

. We recruit and maintain highly trained scientists who possess the expertise that is necessary to review these rather complex biologic products submissions.

. Of course, we provide scientific expertise and advice to our stakeholders.

I am going to skip this slide and go onto the next slide that gives you an overview of OVRR's research goals and objectives. In the interest of time, I am only talking about the goals and objectives associated with what is on these slides.

Research goal #1 is safety. We thrive to enhance the safety of preventive vaccines and related biological products through the development of methods and models and

reagents that are needed in the manufacture and evaluation of the products that we regulate.

Research goal #2 is efficacy. We try to improve the effectiveness of vaccines and related biological products through the development of models, methods and reagents that are needed to measure and predict the effectiveness of these products.

Finally, research goal #3 is to develop and study approaches to enhance the availability of vaccines and related biological products.

As Dr. Wilson stated, the function can be described using the research regulator model. The research regulator model integrates regulatory review responsibilities with mission-directed research. And in addition to performing research that is relevant to the evaluation of specific product safety and efficacy, or manufacturing issues, our researchers also review investigational new drug applications, BLA applications, and they participate as subject matter experts in inspections.

Of course, there is always the challenge to balance and integrate investigator-initiated research with the need to address public health threats, as illustrated by the Ebola epidemic in the past year or two, where OVRR research was really integral and played an integral part of

the regulatory review team that critically evaluated investigational products.

OVRR has established a research management process. Its function is to periodically review research priorities, identify gaps and unnecessary redundancies, and also to assure uniform approaches to the allocation of resources.

We have established a process for resource allocation by investigators request funding of their projects in connection with research reporting, that was described by Dr. Wilson. The requests are evaluated by lab chiefs, division directors, and office management, and recently by our newly formed Regulatory Science Council.

This will be my last slide, in the interest of time. We evaluate the validity of research projects, taking into consideration the following factors; public health significance, scientific merit, as well as qualifications and productivity.

Thank you very much.

DR. EDWARDS: Thank you, Dr. Gruber. Are there any questions? If not, then we will go onto Dr. Slater, who will give us an overview of the DBPAP. Dr. Slater.

Agenda Item: Overview of DBPAP

DR. SLATER: Thank you very much, Dr. Edwards. The purpose of all of these introductory talks is to hone

in on the activities of LBP. We are now at the stage of talking about the Division of Bacterial, Parasitic and Allergenic Products.

My purpose here is to really give you an idea of what the scientific environment is for LBP and its members in terms of our regulatory and research function.

The Division of Bacterial, Parasitic and Allergenic Products is itself a product of a merger of the old Division of Bacterial Products and the Division of Allergenic Products and Parasitology.

You can see on slide two the four laboratories that are in this lab now. Of course there is the Immediate Office of the Director, which consists of me and my Deputy, Drusilla Burns, and six other FTEs that assist us in our activities.

Of the four laboratories, the one in the upper left hand corner is the Lab of Bacterial Polysaccharides. I am not going to say anything more about that because that is the one that you are going to learn the most about in terms of presentation today from Dr. Vann. That is the one that the site visit committee focused on on February 4th.

Another lab in the lower left hand corner of slide two, is the Lab of Immunobiochemistry. Ron Rabin is the Chief of that Lab and I am a principal investigator in that lab as well.

The next is the Lab of Respiratory and Special Pathogens. Mike Schmitt is the Lab Chief. Drusilla Burns, who is the Deputy of the Division, is also a PI in that Lab, along with two other PIs.

Finally, the Lab of Mucosal Pathogens & Cellular Immunology, with Scott Stibitz as the Chief, and three other principal investigators.

This is the group of organisms, both licensed products and investigational products, that roughly speaking, covers the ground of DBPAP research and regulatory portfolio. As I go through it you will see the color change on the slide to demonstrate which laboratories cover which organisms. So for example, on slide four we are going to the Lab on Bacterial Polysaccharides. You can see that the organisms mainly focused on in that Lab include three organisms that are invasive and for which the protective responses are to the polysaccharides. That includes Haemophilus influenza, Neisseria meningitides, and Strep pneumoniae.

The Lab also is involved in the regulation of one of the vaccines against Salmonella typhi, the injected vaccine, since that is a polysaccharide vaccine.

Next slide is the Lab of Immunobiochemistry. This is the Lab that I am a member of. Our Lab covers allergenic products, which although it only occupies one

line in slide five, is a group of products of great complexity and diversity that occupies us quite a bit in both research and regulatory activity.

Next is the Lab of Mucosal Pathogens and Cellular Immunology. This has an interesting portfolio of products due to the fact that it also is the product of a lab merger between a lab that previously had regulated intercellular organisms such as MTB and bovis, and investigationally, Francisella tularensis, as well as collaborative activity with the Office of Blood on research involving malaria.

The other lab involved in that merger focused on enteric organisms; Salmonella typhi, as well as Campylobacter and Shigella and new research interest in that lab in Clostridium difficile.

That Lab is also part of a collaborative effort across the Division, in addressing issues related to Staph aureus. That Lab also is involved deeply in regulation of probiotics and the emerging fields of fecal transplant and bacteriophage associated products.

Finally, in slide seven, we see the Lab of Respiratory and Special Pathogens. This is a lab that has focused on non-invasive organisms that produced toxins. You can see a list of those in the upper left hand corner of slide seven, including obviously, pertussis, tetanus, diphtheria, and anthrax.

Other emerging organisms covered by this Lab include collaborative effort on Staph aureus, as well as some interest in Yersinia pestis.

On February 4th the site visit committee heard from the people listed on this slide in terms of their orientation regarding LBP's research activities. It included Willie Vann, Margaret Bash, Marcos Battistel, John Cipollo, Daron Freedberg, Wei Wang, Mustafa Akkoyunlu. I will turn over the podium after your questions, to Dr. Willie Vann, who will tell you more about LBP's research activities. Are there any questions?

DR. EDWARDS: Thank you. Any questions? Dr. Vann, would you provide us overview of LBP?

Agenda Item: Overview of LBP

DR. VANN: Yes. The Laboratory of Bacterial Polysaccharides investigated the biochemistry, biology, chemistry, and immunology of virulence factors of encapsulated bacteria.

These virulence factors include capsular polysaccharides, lipopolysaccharides, and outer membrane proteins.

These basic research fields are related to the regulatory activities of the Laboratory of Bacterial Polysaccharides which include, review and approval of BLA and IND submissions related to polysaccharide and

polysaccharide conjugate vaccines in addition to non-capsular immunogens of encapsulated bacteria.

We have product responsibilities for a number of products; licensed polysaccharide vaccines, which include polysaccharides for pneumococcus, meningococcus and Typhoid Vi. The more recent vaccines are licensed Glycoconjugate vaccines and we have responsibilities for several conjugate vaccines, two meningococci, pneumococci, Haemophilus, et cetera.

We also have responsibility for two new recombinant protein vaccines. Again, it is meningococci. Responsibility for BLA supplements, inspections, lot release, et cetera, for all of these products.

Some of our major regulatory accomplishments since the last site visit include the licensure of a meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine in June of 2012.

Then in October of 2014, Meningococcal Group B protein vaccine was licensed. And a second protein vaccine against Meningococcal Group B was licensed in January of 2015.

The Laboratory is organized into several research groups. Structural Biology, which is headed by Dr. Daron Freedberg. Vaccine Structure, headed by Dr. John Cipollo. Cellular Immunology by Dr. Mustafa Akkoyunlu. Molecular

Epidemiology by Dr. Margaret Bash. Bacterial Pathogenesis by Dr. Wei Wang, and Glycobiology by myself.

The major research areas are as follows; the Cellular Immunology Group investigates the immunobiology of host response to capsular polysaccharides of encapsulated bacteria.

The Vaccine Structure Group uses a mass spec base approach to investigate the role and significance of glycoconjugates in the infective process.

Structural Biology studies the confirmation of bacterial polysaccharide antigens.

Molecular Epidemiology explores outer membrane protein diversification as it relates to vaccine safety and efficacy.

Bacterial Pathogenesis Group studies the role of nitric oxide metabolism in the pathogenesis of Moraxella catarrhalis.

The Glycobiology Group has two focuses, one, capsular polysaccharide biosynthesis and targeted design of conjugate vaccines and the development of methodologies for low cost conjugate vaccines.

Some highlights of research effort in the Laboratory of Bacterial Polysaccharides include the following:

Dr. Akkoyunlu has noticed a deficiency of TACI in infants. And his expiration of macrophage could explain the poor response of infants to polysaccharide vaccines.

Dr. Margaret Bash used an immunoassay that she developed to assess the effectiveness of meningococcal Group A conjugate vaccine in a clinical trial.

Dr. John Cipollo has developed glycomics platform where he is looking at haemagglutinin in flu vaccine and has revealed some of the impact of glycosylation on antigen exposure, interaction with host immune system, and the vaccine structural heterogeneity.

Dr. Freedberg had made some interesting discoveries on hydrogen-bonding of a very important polysaccharide, polysialic acid and has developed a model for the structure which actually could give us some insight into the interaction of these polysaccharides with antibodies.

In her co-cultures model to investigate the pathogenesis of Moraxella, Dr. Wang has shown that nitric oxide derived in co-culture arrests host cell proliferation and induces host cell apoptosis, which could explain some of the phenomenon observed in Moraxella infections.

Perhaps one of the most significant developments that has happened is the development of the meningococcal

Group A vaccine resulting in Group A epidemics in the Meningitis belt becoming a thing of the past.

In December of 2010, young people across Burkina Faso, Mali, and Niger became the first to receive the MenAfriVac vaccine. The technology for the development of MenAfriVac was developed in the Laboratory of Polysaccharides.

By 2015, not a single case of meningitis Group A in 250 million vaccinees in these hyper-endemic countries was observed. In the 1996 to 1997 epidemic – this epidemic resulted in 25,000 deaths.

The Laboratory of Bacterial Polysaccharides has regulatory responsibilities for vaccines against encapsulated bacteria and products containing bacterial polysaccharides.

The overall goal of this research program of the Laboratory of Bacterial Polysaccharides, is to understand the virulence factors that are components of vaccines against bacterial pathogens.

The research programs of the Laboratory of Bacterial Polysaccharides are directed toward understanding the physical, chemical, and immunological properties of bacterial polysaccharides, and vaccines against encapsulated bacteria.

The knowledge and expertise gained in this research endeavor provide a scientific basis for our decisions related to the review of manufacturing, purity, potency, safety and efficacy of vaccines against encapsulated bacteria.

I will accept any of your questions.

DR. EDWARDS: Thank you very much, Dr. Vann. Are there any questions? Are there any questions that have come up to any of the other speakers in the interim?

(Pause)

Agenda Item: Open Public Hearing

DR. EDWARDS: Okay, if not, then this is open for open public hearing. Are there any people who are going to be speaking in the Open Public Hearing?

DR. VIJH: Give us one second. We are going to check. I don’t believe there are any but we are going to check and then maybe take a break for five minutes if there is no person who would like to speak, to stop the webcast and then move onto the closed session.

Please give me one or two minutes.

(Pause)

DR. VIJH: So Dr. Edwards there is no member of the public that is signed up and nobody is here in the room to present any comments so I will not read the open public hearing statement. If the committee members can give us

about five minutes. It is 1:41 – maybe around 1:46 we can resume and just clear the room out and have the staff that are not supposed to be in the room leave the room. Plus we will just take a minute to stop the webcast because we are now going into closed session.

(Whereupon, the open session adjourned at 1:42 p.m.)