

FOOD AND DRUG ADMINISTRATION

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH
VACCINES AND RELATED BIOLOGICAL PRODUCTS
ADVISORY COMMITTEE MEETING
OPEN SESSION

9000 Rockville Pike
Bethesda, Maryland 20892
Thursday, December 4, 1997

ATTENDEES:

L. PATRICIA FERRIERI, M.D., Committee Chair
Professor, Departments of Laboratory
Medicine, Pathology and Pediatrics
Director, Clinical Microbiology Laboratory
University of Minnesota Medical School

NANCY CHERRY, Executive Secretary
Scientific Advisors and Consultants Staff
Center for Biologics Evaluation and Research
Food and Drug Administration

DENISE ROYSTER
Scientific Advisors & Consultants Staff
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ADAORA A. ADIMORA, M.D.
Clinical Assistant Professor of Medicine
Department of Medicine
University of North Carolina
School of Medicine

BASCOM ANTHONY, M.D.
Division of Bacterial Products

MICHAEL A. APICELLA, M.D.
Professor and Head, Department of Microbiology
College of Medicine
University of Iowa

MARY LOU CLEMENTS-MANN, M.D.
Professor, Departments of International
Health, Molecular Microbiology and
Immunology and Medicine
Schools of Public Health and Medicine
Johns Hopkins University

KATHRYN M. EDWARDS, M.D.
Professor of Pediatrics
Department of Pediatrics
Vanderbilt University School of Medicine
ATTENDEES (CONT'D):

BILL EGAN, M.D.

MARY K. ESTES, Ph.D.
Professor of Molecular Virology
Division of Molecular Virology
Baylor College of Medicine

BILL FREEZE
Food and Drug Administration

NEIL GOLDMAN, M.D.

HARRY B. GREENBERG, M.D.
Acting Chair, Department of Medicine
Division of Gastroenterology
Stanford University School of Medicine

CAROLINE B. HALL, M.D.
School of Medicine and Dentistry
University of Rochester

CAROLYN HARDEGREE, M.D.

ERIK L. HEWLETT, M.D.
Chief, Division of Clinical Pharmacology
Department of Internal Medicine

University of Virginia

ALICE S. HUANG, Ph.D.
Senior Councilor for External Relations
California Institute of Technology

DENNIS KOPECKO, M.D.
Laboratory of Enteric and Sexually
Transmitted Diseases

GREGORY A. POLAND, M.D.
Associate Professor of Medicine
Clinical Pharmacology
Chief, Mayo Vaccine Research Group
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P R O C E E D I N G S

DR. FERRIERI: I'd like to call the session to order; and, other than my greeting to everyone, including FDA, I'd like to now turn it over to Nancy Cherry for any official announcements.

MS. CHERRY: The only announcement I have is to welcome everyone, as well and to tell you thanks for taking the time for this when I know you'll all be coming into town next week as well.

I have a conflict of interest statement to read, mercifully short. This announcement is made a part of the record at this meeting of the Vaccines and Related Biological Products Advisory Committee on December 4, 1997.

Pursuant to the authority granted under the Committee Charter, the Director of the Center for Biologics Evaluation and Research has appointed Dr. Erik Hewlett as a temporary voting member. I do hope we can get Dr. Hewlett on with us.

Based on the agenda made available, it has been determined that all Committee discussions at this meeting for the review of the Intramural Research Program of the Laboratory of Enteric and Sexually Transmitted Diseases, Division of Bacterial Products, Office of Vaccines Research and Review present no potential for a conflict of interest.

In the event that the discussions involve specific products or firms not on the agenda for which FDA's participants have a financial interest, the participants are aware of the need to exclude themselves from such involvement; and their exclusion will be noted for the public record.

With respect to all other meeting participants, we ask, in the name of fairness, that they address any current or previous financial involvement with any firm whose products they wish to comment on. That's the end of the Conflict of Interest Statement.

Before I return this to Dr. Ferrieri, I will say that the purpose of this teleconference is to complete the review of the Laboratory of Enteric and Sexually Transmitted Diseases. We started this process with a site visit on August 19.

Today, you, as the Committee, will be taken action on the Site Visit Report. Because this is a teleconference, we ask that you announce your name each time you speak.

If you are cut off, the number to get back to the conference is 1-800-545-4387. You ask for Conference No. R29125. You can use the mute button on your phone; but, please, do not use

a hold button.

UNIDENTIFIED SPEAKER: Could you repeat that number?

MS. CHERRY: Call 1-800-545-4387 and you ask for Conference No. R29125. Please, no cellphones. Do not use the hold button; and, if you have a chance to close an office door, it will help by eliminating some of the background noise.

We'll have a short Open Session. Dr. Kopecko is joining us via teleconference. He's in Florida today, and then this will be followed by closed committee deliberations. That's it. Back to Dr. Ferrieri.

DR. FERRIERI: Thank you, Nancy. Could you identify for me who is in the room, then, from FDA other than yourself? I assume that Dr. Anthony is there?

MS. CHERRY: Yes.

DR. FERRIERI: Is Dr. Goldman there?

MS. CHERRY: Yes.

DR. FERRIERI: Dr. Hardegree?

MS. CHERRY: Yes. Dr. Egan and, from my office, Denise, Bill Freeze, and me and the transcriber.

DR. FERRIERI: Thank you, Nancy. Well, I'd like to start, then, by having the overview of the Division of Bacterial Products by Dr. Anthony. Good morning, Bud.

DR. ANTHONY: Good morning or afternoon, Pat, and everyone else. I will be very brief. We have five laboratories. Of those, the Lab of Enteric and Sexually Transmitted Diseases is really the newest. It was created as a successor to the Laboratory of Microplasma as part of the reorganization of CBER which occurred in 1992 and 1993. Dr. Kopecko was recruited to head this group and arrived in 1994. So it is a fairly new operation.

DR. CLEMENTS-MANN: Hello.

DR. FERRIERI: Hi, Mary Lou.)))) the program. Dr. Anthony is speaking.

DR. CLEMENTS-MANN: I'm sorry)))) that I got cut off.

DR. ANTHONY: This does have the largest number of INDs to review of the laboratories in this Division. They also have had a few product license applications. The most significant active one right now is an application for a new cholera vaccine.

I won't say anything about the research programs. I will say that the lab has experienced some unfortunate loss of resources since Dr. Kopecko first came. They certainly went through a growth phase. He has lost some key people. Dr. Ann Juris was here for about a year and we lost her to an academic job. Then Dr. Elkins relocated to another laboratory.

The good news, in spite of those losses, is that Dr. Carolyn Deal, who's been with us in a temporary capacity for most of this calendar year, is now or will in a matter of days be a permanent FDA employee. She will wear several hats in the Division. She will be our expert on sexually-transmitted diseases. She will be a major reviewer of product applications in this laboratory, and I expect her to help me with some Division responsibilities. I think with that I'll turn it over, unless there are some questions.

DR. FERRIERI: Thank you very much. Dr. Kopecko, are you with us?

DR. KOPECKO: Yes, I am.

DR. FERRIERI: Great. Good morning or afternoon. Could you give us, then, an overview for the research activities and goals of this entire laboratory?

DR. KOPECKO: Thank you for the opportunity to take a few minutes. I know the advisory panel here has two issues that they bring up and probably do not have a good feel for

what it is we do with the research and some of the regulatory products that have not --

DR. FERRIERI: Excuse me. We're having trouble hearing you. If you could speak a little louder?

DR. KOPECKO: In addition to a research program, also the variety of products that fall outside the realm of what you would expect from)))).

As Bud mentioned, the Lab of Enteric and Sexually-Transmitted Diseases was created in 1993 in place of the former Microplasma Lab. I came in 1994 and at that point there were five individuals within the lab, so I was the sixth member.

The Lab, I understand, was created because of the large number of regulatory actions against enteric diseases and with the expectation that there would be an increase in submission for sexually-transmitted diseases.

In fact, we were beginning to see the trend. We were getting an increase in enteric submissions. The laboratory, then conduct research on)))) regulatory responsibilities in the broad area of enteric and of STDs.

Probably, in terms of our research, we have two major research thrusts or areas that we're working on. In my research program, we're conducting studies aimed at analyzing the properidic euperidic mechanisms in function involved in bacterial invasion of mucosal epithelial cells. The process)))) the early step in disease)))). We are currently focusing on two organisms, salmonella)))), which triggers the microfilament-dependent update process similar to)))).

We are also using)))) as an example where we've identified a very novel microtubule-dependent update)))) quite different from some of the enteric pathogens. We are analyzing those two systems in detail.

The second major research thrust is carried out in Dr. Stibitz's lab, and that involves studies of the global regulation of gene expressions)))) and different bacterial)))).

As I think most of you know, when pathogens have been analyzed all of them have been found to carry two component regulatory systems that control)))) and they have a membrane sensory component that senses the environment and)))) an activator inside the membrane that controls transcription of a variety of genes around the chromosome that need to be turned on in a certain temporal fashion in order to trigger the progression of disease.

Scott has been)))) . That system is very)))) and homologous to all the systems that have been found in a variety of different)))).

I want to mention that we feel that the two research areas are highly related to our regulatory commission in that many of the vaccine products that we review are invasive)))) pathogens for which we need to understand the invasion process)))) fully)))) of the organism. And many)))) created using genetic mutations of either)))) genes or)))) system. We feel that both of these areas)))) relevant to our regulatory duties.

During the past three years, we've also had for one year an STD research program carried out by Dr. Ann Juris. She, obviously, only had a chance to get some preliminary studies conducted. She was able to look for)))) factors of)))) gonorrhoea. She found some interesting pH-regulated outer membrane proteins; and she is now pursuing those and she is also pursuing a study that she started on the development of a mouse model for)))).

Currently, we do not have an ongoing STD research program.

Let me tell you a little bit about how we're divided. I mentioned a few names of some of the persons. The lab is somewhat informally divided into three sections based on physical

location, research area, and regulatory area.

For example, Scott Stibitz heads up what we call the Molecular Genetics Gene Expression Section. His labs are located on the fifth floor of Building 29. Next to his lab is the Sexually-Transmitted Disease Laboratory that Carolyn Deal is now acting head of. A floor below, I have my lab in the Enteric Disease Pathogenesis Section.

Scott works with a research associate, a very talented research fellow, Dr.)))))

In my lab, I have two Fogarty fellows, Drs.))))) and)))), who are both M.D. Ph.D. researchers, and the research associate.

MS. CHERRY: I'm sorry. Do you have a new research associate?

DR. KOPECKO: Yes. In fact, from a personnel standpoint, there are three actions that have actually taken place since August. Carolyn Deal was converted from detail to permanent; Dr. Lesley Ball, who left on detail to go to our Applications Division decided to formally leave. She actually administratively is gone now. I was able to obtain a master's- level research associate from another Division within CBER. That person is now on detail in the lab.))))) personnel.

I wanted to take a couple of minutes and just review some of the regulatory products that we have regulatory oversight over because there is quite a diversity. The typical enteric diseases, cholera, typhoid, salmonella,))))))). Also, we dealt with some brain replacement or competition therapy, the use of))))) and replacement therapy for a variety of anaerobic))))) for treatment of chronic))))). We also dealt with the))))) bacterial vaccine vectors))))). A number of sexually- transmitted disease agents are listed as))))) involving gonorrhea,))))) urinary tract infections pathogens))))). During the past three years, we've also handled tularemia,))))) fever, and))))) with regulatory responsibilities for these latter))))) three to the microplasm lab.

We also have a developing system))))) vegetables))))) experiments with))))) antigen that I think will take off over the next couple of years. We'll probably see a lot of increasing activity there. We regulate the use of the))))) bacterial product which is used to treat))))). We have also been involved in the development of new oral))))).

In consult with other arms of the FDA, we've dealt with a variety of specific))))) products from cattle or chicken directed at))))) a variety of different conditions or infection. Recently, we've had activity on an oral anticocaine vaccine, and we've also been involved in pre-IND review of a new oral streptococcus))))) vaccine vector))))).

In recent consult with the Food Safety Center of the FDA, we've worked with them on the addition of things like))))) bacteria.

I hope this gives you a broader picture of what kind of))))) we need to do handle our regulatory duty.))))) mentioned that we have approximately 100 INDs under our review at this time; there are three))))) the lab, Drs. Deal, Stibitz, and myself. Carolyn Deal spends approximately 80% of her time carrying out regulatory reviews administratively, but))))) and I spend approximately 50% of our time doing))))).

I think the only other point I wanted to touch on was future goals. From a research standpoint, we simply would like to continue our main research thrust))))) biochemical and genetic))))) as well as bacterial invasion mechanisms, specifically, on salmonella typhii and))))). I would like to see us restart an STD research.

In a nutshell, that's what we do. I would be happy to answer any questions.

DR. FERRIERI: Thank you very much. Now, Committee members, do you have anything specific that you would like Dr. Kopecko to address? If not --

DR. APICELLA: I do. What type of an SRD research program are you thinking of

developing? That's a big area. What are you thinking of focusing on?

DR. KOPECKO: I don't have any real specific thought. I think it depends on the individual. If we were able to obtain an individual or if Carolyn Deal hadn't switched her duties and was able to spend more time. If she can kick-))) some collaboration, it obviously would be in gonorrhoea along the lines in which she is currently handling a few collaborations. I think))) would be a very interesting system to develop. We're going to get into -- what it would really depend if we could pull someone in that had special expertise)))).

DR. FERRIERI: Other questions for Dr. Kopecko? If not, thank you very much. We'll move on, then, and have a break to clear the room.

MS. CHERRY: We don't need to clear the room here; but we do have to say goodbye to Dr. Kopecko.

DR. FERRIERI: Yes. I hope you're enjoying the sun down there Dennis.

DR. KOPECKO: Thanks for your complaining.

DR. FERRIERI: I'm seeing sun in Minneapolis; so --

DR. KOPECKO: There's sun in California. It was a good meeting.

DR. FERRIERI: So, everyone, including Dr. Goldman, attests to the validity of))) everyone in the room. I think that Dr. Anthony ought to explain what Dr. Kopecko was doing in Florida because I think it does show one of his other kinds of roles.

DR. ANTHONY: He's not on vacation, actually. He's attending the U.S.-Japan Cholera Conference which is a organization that meets periodically. Dr. Hardegree's been involved with that in the past.

(Whereupon, the ADVISORY COMMITTEE MEETING OPEN SESSION was adjourned.)

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