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CENTER FOR BIOLOGICAL EVALUATION AND RESEARCH

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VACCINES AND RELATED BIOLOGICAL PRODUCTS
ADVISORY COMMITTEE

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MEETING BY TELECONFERENCE

OPEN SESSION

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MONDAY, JUNE 11, 2001

The meeting came to order at 11:30 a.m., in Conference Room 1NN06, Building 29-B, National Institutes of Health, 9800 Wisconsin Avenue, Bethesda, MD., Robert Daum, Committee Chair, presiding.

PRESENT:

Dr. Robert Daum, M.D.	Committee Chair
Dr. Kathryn Carbone, M.D.	Chief Laboratory LPRVD
Dr. Bill Egan	Deputy Director Research of Influenza Vaccines
Dr. Neil Goldmark	Associate Director Research
Dr. Karen Midthun	Director, Office of Vaccines Review Research
Dr. Peter Patriarca	Director, Division of Viral Products
Ms. Nancy Cherry	FDA/CBER/SACS
Ms. Denise Royster	FDA/CBER/SACS
Dr. Steve Kohl, M.D.	Member
Dr. Dixie Snider, Jr., M.D., M.P.H.	Member
Dr. Walter Faggett, M.D.	Member
Dr. Diane Griffin, Ph.D.	Member
Dr. David Stephens, M.D.	Member
Ms. Barbara Lou Fisher	Member
Dr. Pamela Diaz	Member
Dr. Judith Goldberg, M.D.	Member
Dr. Samuel Katz, M.D.	Member

C-O-N-T-E-N-T-S

P-R-O-C-E-E-D-N-G-S

(11:43 a.m.)

MS. CHERRY: Okay. Dr. Faggett?

DR. FAGGETT: Here in Washington.

MS. CHERRY: Okay. Dr. Diaz?

DR. DIAZ: Here.

MS. CHERRY: Dr. Griffin?

DR. GRIFFIN: Here.

MS. CHERRY: Dr. Daum?

CHAIRPERSON DAUM: Yes.

MS. CHERRY: Ms. Fisher?

MS. FISHER: Yes.

MS. CHERRY: Dr. Katz? Dr. Katz? Well he was here, he was the first one. I guess he'll be back.

DR. KATZ: Can't you hear me? I'm here.

MS. CHERRY: Okay. Dr. Goldberg?

DR. GOLDBERG: Here.

MS. CHERRY: Dr. Stephens?

DR. STEPHENS: Here.

MS. CHERRY: Dr. Kohl?

DR. KOHL: Here.

MS. CHERRY: And Dr. Snider?

DR. SNIDER: Here.

MS. CHERRY: Okay. And when they find Dr.

Kim he'll dial in. And Dr. Manley could not be with us. Okay. All over to the Committee chair.

CHAIRPERSON DAUM: Okay. I would like to go around the table and -- I'm just joking. The first act I guess is to tell everybody welcome and thank you for making the time to participate in this teleconference style, which is a little less satisfying than face to face I think but probably saves a lot of effort and travel.

And then to turn the floor over to Nancy for announcements and conflict of interest statements that apply to today's session.

MS. CHERRY: It does. Well, first of all, let me mention who's in the room here. We have Dr. Goldman, Dr. Egan, Dr. Patriarca, Dr. Carbone. We have a reporter, right? Okay. And we have Bill Fries from my office and, of course, oh Denise back here, I didn't see. And we have the court reporter and that's it.

When you all speak would you please identify, okay, and Dr. Midthun will be coming in I understand. When you speak, would you please identify yourselves for the benefit of the court reporter, since he can't look down the table and see who's talking and, of course, I have a conflict of

interest statement, Bob, how could you say otherwise?

CHAIRPERSON DAUM: I'm sure that's probably true.

MS. CHERRY: Okay, here goes. This announcement is made a part of the record for the meeting on June 11, 2001 of the Vaccines and Related Biological Products Advisory Committee. Based on the agenda made available, it has been determined that the committee discussions on the scientific research programs of the laboratory of pediatric and respiratory viral diseases present no potential for a conflict of interest.

Should we discuss specific products of firms not on the agenda, for which you all have a financial interest, then please exclude yourself from the discussions and we'll not your recusal for the record. With respect to anyone else in the room, we ask if they speak that they state their name and affiliation and any current or previous financial involvement with any firm whose product they wish to comment on.

And as I started this little reading, I'll remind you one more time to please identify yourself when you speak. That's it.

CHAIRPERSON DAUM: Thank you very much, Nancy. I think we'll now ask Dr. Goldman to introduce us to the laboratories and CBER in general and then we'll work our way down more specifically to the group that's the subject of discussion today.

DR. GOLDMAN: Yes. Well, thank you, Dr. Daum. Good morning. I am Neil Goldman, the associate director for research at CBER and I'd like to thank you for joining us in what will, hopefully, be a short advisory committee, at least we hope so.

The purpose of this teleconference is ultimately to present the report of the site visit team's evaluation of the research programs in the laboratory of pediatric and respiratory viral diseases, and the four members of the laboratory who were formally reviewed. This lab is in the division of viral products under the direction of Dr. Peter Patriarca and within the office of vaccines research and review under the direction of Drs. Karen Midthun and Bill Egan.

As you are already aware, product review and approval are among our primary responsibilities. We have scientists and medical officers who do full time product and clinical review, but in addition we have lab-based senior investigators and conversion

track fellows spending about half of their time on product and clinical review and half of their time on regulatory research related activities.

We refer to these latter staff as our researcher reviewers and, parenthetically, many of our researcher reviewers spend now probably more than half their time on regulatory matters.

Currently at CBER we have approximately 420 lab-based scientists of which about 76 are permanent career appointment principal investigators, and about 58 are what we refer to as conversion track investigators which is similar in academia to what you refer to as tenure track investigators. We also have approximately 96 contract post doctoral fellow and about 193 technical support and staff scientists.

Now the types of research performed in the center include, first, research on a specific product, including for example such aspects as mechanism of action, potential toxicity or surrogate measures of efficacy. Second, research on a specific policy issue which may be related to a product class, disease area or therapeutic modality. And, lastly and of course of major importance to regulatory agency like ours, research associated

with the development and validation of methods and standards to maintain product safety and quality. In fact, these categories I think will be exemplified by the four research programs being reported on today.

The vigil and oversight and quality control of our research programs are maintained through our continuous intramural review of our research. We site visit review our laboratory research programs, and the individuals who guide them, every four years by an external peer review committee composed of members of our advisory committee in concert with outside experts. For example, those from academia and other research institutions, or in the particular field of study of the laboratory being reviewed.

For our approximately 30 laboratories, this turns out to about 6 to 7 lab reviews per year. In addition, internally our office directors for each of the product offices with research using criteria for mission relevance and scientific excellence, have been annually prioritizing their research projects and funding them accordingly.

Lastly, we underwent an external review of the center's entire research program by our blue

ribbon panel, this was back in 1998, which included review of our 12 research divisions.

Now a site visit team, a subgroup of your advisory committee, so a subgroup of VRBPAC, was charged to assess, and that is assessing both strengths as well as weaknesses, the quality and appropriateness to the regulatory mission of the research being conducted which includes the relevant scientific rationale, validity of approaches, creativity of design and solution, and level of sophistication.

And also to evaluate the accomplishments of the individual scientists, that includes demonstration of his or her abilities and experimental design and performance, independence of effort, originality, stature and recognition amongst his or her peers and productivity.

In addition, we ask the site visit team to provide us advice on current scientific direction of the research program, whether new directions should be considered, any changes in the way the research program is administered, or the level and utilization of resources in that program. And, lastly, any advice on promotion or conversion of an eligible candidate, particularly the appropriateness

at this time for such a personal action.

Our final draft report is prepared by the chair of the site visit team, in this case Dr. Snider, with the aid of his ad hoc reviewers and presented to this full parent advisory committee to the VRBPAC.

Now as the parent advisory committee, you, VRBPAC, have the duty to accept, reject or modify the site visit team's report in part or in its entirety.

Then, lastly, you, VRBPAC will provide a final approved report which is then sent to our center director who will then pass it down the chain of command to the particular investigator who was reviewed.

If a recommendation requires a response, one will be prepared and sent back to VRBPAC.

Now our internal promotion and conversion evaluation committee will use the final approved site visit report from VRBPAC as significant evidence to support either a candidate's conversion to permanent employment status, or his or her promotion to the next grade level.

So, in conclusion, I'd like to thank Dr. Snider for his excellent shepherding of the site

visit review of the laboratory of pediatric and respiratory viral diseases, and also our gratitude to the expert members who made up his review panel.

And I lastly would like to express our deep appreciation to VRBPAC for supporting our need for peer review of our research programs, which is particularly critical in these times of fiscal austerity. So thank you, Dr. Daum and I turn it back to you I guess for the next speaker.

CHAIRPERSON DAUM: I must say, Dr. Goldman, that it's a resource and a chance to really focus one's efforts, if one's a laboratory researcher, to have this process go on and I'm sure there's many of us in academia who wish that we had a similar mechanism in place at such regular intervals because it's very helpful to direct your efforts and helpful just on the quality and relevance of what you're doing.

DR. GOLDMAN: Well, thank you, it helps us in prioritizing.

CHAIRPERSON DAUM: We now get a little more focused on the target of this morning's discussion and we'll call on Bill Egan to tell us about laboratory research in OVRR. You're on, Bill.

DR. EGAN: Yes, thank you. Well Dr. Goldman has just given a very nice and thorough overview of the research programs within the center and Dr. Patriarca is going to be speaking about the laboratory viral products in a few moments. And, if I recall, one of the things I learned in logic a long time ago, there's the law of the excluded middle, and I think some variant of that applies here. So I only have a very brief remark to make and that said, I'd like to reiterate the remarks I made at the time of the review about the importance of the research programs and indeed the laboratory programs in general within the office of vaccine to the regulation of vaccines.

These research and laboratory programs are integral to the regulation of vaccines. And I'd like to just thank everybody for their participation in the review of the laboratory programs. The feedback that we get from the reviewers is really necessary for maintaining the high quality of the programs and for giving us very sage advice with regard to directions for these programs and the directions that the individual researchers are taking.

And then the quality of the individual

researchers which are so important in our decisions with regard to promotions and conversion. And, again, I would like to thank all of the reviewers who participated in the review of the laboratory and pediatric and respiratory viral diseases and, again, Dr. Snider for shepherding everybody through the process. That's all I'm going to say, just my thanks again.

CHAIRPERSON DAUM: Thank you, Bill. We'll go right on I think to asking Peter Patriarca to now get us a little more closer to target, and that is to discuss the laboratories in the division of viral products.

DR. PATRIARCA: Thank you, Bob. I too would like to extend my thanks and welcome to all of you for taking time out, not only for the site visit but also for meeting today.

I just want to provide a very brief overview of our division. Our division is one of two so-called research divisions within the office of vaccines review and research. It's divided into eight components, including the office of the director and seven laboratories, one of which you will hear about in detail today. At the moment we have a full time staff of 68 with about another 30

or so contract employees. Our budget this year is approximately $1 million dollars, which is supplemented as it has for about the past five or six years by about $3 to $5 million dollars for targeted projects that are funded by other sources.

As Dr. Goldman alluded to earlier, although we are a research division, the better part of what we do has to do with review and regulatory activities. As Neil said, our top scientists now are in the range of 70 to 80 percent of their time on review activities. And a lot of what our division does is otherwise invisible to the public, namely we also have quite a bit of post licensure activities, including inspection and compliance issues, lot release testing and lot release protocol issues.

We also review various reports for those vaccines for which the division regulates, and we're also involved in label and promotional activity review. And I think Dr. Carbone and her laboratory sort of represent all of these activities in great detail. Her repertoire is probably larger than any of the other laboratories in the division.

That's all I'd like to say and I would like to turn it over to Kathy to talk to talk about

her laboratory.

CHAIRPERSON DAUM: Thank you very much, Peter. Dr. Carbone, are you there?

DR. CARBONE: Yes, I am.

CHAIRPERSON: It's still good morning evening your time zone. Good morning. I'd like to hear from you next so if you just step up and go, that'll be great.

DR. CARBONE: Good morning. Thank you. Thank you Dr. Daum and thank you to the site review committee and I appreciate everyone's participation and I hope the phrase that Dr. Daum used to refer to my laboratory as a "target" earlier is not taken too literally by everyone on the committee. But anyway we appreciate your comments.

I'd like to refer, I guess everyone received -

CHAIRPERSON: It's under review.

DR. CARBONE: Just kidding. Everyone should have received a black-covered little notebook that states DVP and LPRVD summary, and that will be the basis of my brief talk here. So that'll help people to sort of follow along. So if you want to pull -- and that's fortunately the thinnest one, if you want to pull that out.

Today I'd like to talk about the laboratory. Its large name is in part due to the fact that it's a joining of two separate laboratories, which also explains sort of the mixed nature of the review. We have a different agenda for virtually every investigator and, hopefully, this review will sort of unify and put everybody on the same track literally for the future reviews.

As a result, Dr. Atreya, who is being reviewed for promotion from GS-13 to 14 is undergoing a full review since his last review was a full four years ago. Dr. Levandowski is also being considered for full review and future promotion from GS-14 to 15, again it was reviewed fully four years ago, but Dr. Beeler and myself were reviewed in November of 1999 and, as a result, are only being considered for update only purposes. But, again, this review will put us all on the same track and the next review in four years will constitute the first time this laboratory will be reviewed on an even keel ever.

As Dr. Patriarca said, I think many people when reviewing labs like to know what the regulatory commitments of the laboratory are so as to put the research productivity in right, and I

think just suffice it to say that with approximately 20, 21 percent of the DVP's personnel we review about 30 percent of the INDs and about a little over 50 percent of BLA supplements. So you can just say that our regulatory requirements are substantial. So that just helps put our research productivity in light.

Between November of 1999 and February 2001, the LPRVD members produced 46 publications and have presented at many national and international meetings, including ASV, international double strand meeting, ICAAC, IBSA and conference on vaccine research and these included many plenary session presentations.

The research is accomplished with a baseline funding of about $7,000 to $10,000 per research position per year, but in addition we receive a substantial amount of funding, thankfully, from the national vaccine program office, as well as outside grants, including NIH extramural RO1 funding, and this year my laboratory received BTEP, a collaborative grant with Russia. I'm the principal investigator in a collaboration with CDC and Vector Laboratories in Russia with an approximately $2 million dollar grant. And it's

these sort of external funding that keep our laboratories going.

We have four research teams in the laboratory. There's my team which is neuro immuno pathogenesis team, and in my team we study the pathogenesis of virus-induced neurological disease. We use these data, studying the development of in vivo, in vitro and molecular biological assays in neurovirulences, how we apply these two vaccines.

It's important to know the pathogenesis of the disease process in order to develop a rational neurovirulence assay and we hope to move our assays from the animal to the molecular level.

We are fairly free with the viruses that we study in that these assays can be used, and are currently being used, to assess mumps virus, influenza virus, smallpox vaccines and we use Borna Disease virus as a mechanism to study development in the brain and apply neurovirulence assays to developmentally pertinent areas.

We have had several publications since our last review, and you can see those listed in the summary, but the most interesting one is that recently at a WHO meeting in Geneva they presented our mumps vaccine neurovirulence assay development

and have a resolution to try an international validation of that study.

It turns out that many countries that cannot afford to use some of the more expensive vaccines and are using vaccines that have some small but significant association of meningitis neurovirulence outcomes, would like to try testing batches of vaccine with this assay to try and attempt to find batches of vaccine that are less of a risk of neurovirulence outcome. So we're going to attempt some international validation studies of our assay system.

In addition, we have the viral pathogenesis and vaccine adverse reactions teams which is headed by C.D. Atreya. They studied rotavirus vaccine potency and efficacy, elucidating molecular mechanisms associated with rotavirus vaccine-related adverse events such as intussusception. They studied molecular mechanisms of Rubella virus pathogenesis and adverse events and look at the etiology of Rubella vaccine associated auutoimmune in arthropathy.

I think what's particularly important about this team is that we decided that when rotavirus vaccines became a very important issue for

the FDA, C.D. Atreya who initially was quite established in the Rubella virus field took up de novo essentially rotavirus and became, has become in a fairly short time a significant player in the research field.

He was on the organizing committee for the recent double-strand RNA meeting and has published several interesting papers, including studies of mutations and rotavirus enterotoxin as well as finding some mutations outside the NSP4 cytotoxic domain and tissue culture adapted strains.

And his work continues and he has two publications that are now submitted to the Journal of Cell Biology and the Journal of Biological Chemistry. His work has been quite impressive in such a short time.

We also have the influenza team which was recently joined by Dr. Zhiping Ye, an M.D., Ph.D., well trained influenza virologist who has added his significant molecular biology skill to the laboratory and he and Dr. Levandowski have one publication Journal of Virology studying replication of influenza virus and how it relates to the matrix gene, and have now got a publication in virology with some small modifications and we expect that

publication to be accepted as well.

The importance of their work for vaccines is quite substantial because with modifications in the matrix gene, understanding how it affects replication, they expect to be able to tune up virus replication which will be helpful in activated vaccine production, as well as tune virus replication which would be helpful in active or live attenuated vaccine production.

So that work can be applicable to both and continues in quite some fine work.

We also have Dr. Beeler's antigenic structure and function team, which studies and understands better knowledge of virus receptor and co-receptor interactions which facilitate the ability to understand factors that contribute to tropism, virulence and attenuation in RSV vaccines. She studies unique ways to develop vaccines that are effective for RSV including antibodies that actually block virus receptor interaction, which is a novel approach to vaccines, which can actually block infectivity and contribute to infection.

The assays measure these specific antibodies may prove to be useful correlates of protection which we do not have currently for RSV,

and will help in clinical evaluation of RSV vaccines. She's had substantial achievements in this area and many of these articles are nearing, or have been published in the recent past.

And I think that overall, since our coming here in 1996, I think the laboratory has pulled together with the addition of several key people like Dr. Atreya and Dr. Zhiping Ye and we've had some substantial increase in research productivity, and Dr. Beeler as well, and the laboratory from a research point of view has pulled together. And I've been quite proud of a laboratory that has always had substantial regulatory input, now having substantial research output as well.

I thank you for your attention.

CHAIRPERSON DAUM: Thank you, Dr. Carbone for your presentation and I think I'll rephrase your unit as being the subject of the review.

(Laughter.)

DR. CARBONE: Thank you.

CHAIRPERSON DAUM: Okay. Are there questions and comments on the presentations we've heard so far?

DR. KATZ: Hello? Bob?

CHAIRPERSON DAUM: Yes?

DR. KATZ: Hi, this is Sam Katz. I'd love to ask Dr. Carbone a generic question which comes across in a number of the reports that we were sent to read, and which I think she touched on very tangentially.

And that is, I'm not trying to be an advocate, I'm just trying to get you to say what I hear so often, and that is is there sufficient personnel and is there a sufficient number of hours in the day, so that the people who are doing regulatory work and research can do both?

DR. CARBONE: Well, the answer to that is no. We desperately need more help in the influenza laboratory I think without question. As everyone knows, Aviron has announced publicly that they have submitted a license application for live attenuated flu vaccines. We have essentially no additional resources to deal with the regulatory efforts that are going to come along with that license application, and if the vaccine is licensed what follows.

DR. KATZ: That's going to be one of the topics of our agenda at the July meeting.

DR. CARBONE: Right. And that has

caused substantial ulcer-generating times for both Roland Levandowski and myself. We have a substantial number of activity in the rotavirus arena. Many people suspected, or predicted, that the problems with the -- vaccine in voluntary withdrawal would result in closing down activity in rotavirus vaccine but I think, as again stated publicly by at least Merck and Glaxo SmithKline actually other companies saw this as an opportunity and activity, at least from those two companies, has increased as they stated publicly. So that's a very active area.

We have many other areas that are active and, of course, our neurovirulence program, virtually every vaccine has to be run through at least mentally if not in the laboratory, for neurovirulence assessment. So we have a tremendous amount of work from the regulatory end, and the research end we're trying to hold it together.

So from a personnel point of view, we need substantially more resources and we've been blessed this year with additional research resources, but we're still making it on a shoestring. I think my academic background has made me frugal and a scrambler, but it's not easy. We

need more in both things.

DR. KATZ: Thank you very much for a very candid answer.

CHAIRPERSON DAUM: If I could just take a minute to let everybody know about an event that occurred, perhaps of some importance, I don't know yet. One of the things that comes with chairing this committee is to sit on the National Vaccine Advisory Committee, which met recently. And there's a usual sort of report from the acting assistant secretary for health, Dr. Lawrence, and there was a question and answer session after Dr. Lawrence's report which has to do with budget items for large, large things in the department.

And CDC's budget, for example, was brought up and discussed, and I actually raised my hand and began to talk to Sam about this very issue, that is to do with the situation with the research laboratories and FDA, Dr. Carbone, Dr. Goldman and many others, Dr. Egan, have been discussing with us over the while.

And I had the feeling that he was genuinely hearing something that he hadn't thought a lot about, and I had three or four committee members come up and thank me for raising it with him. He

promised to look into it, and maybe that's a step to getting some more public awareness or intra government agency awareness of what's going on here and what the problem is.

DR. KATZ: Well, I hope it's, you know, I realize it's just an acting appointment and until they appoint some people from the White House who have some policy clout, I don't know whether anything's going to happen.

CHAIRPERSON DAUM: Well, he seemed interested and seemed to be willing to look into it. And I agree with you though, it's not enough to just do that.

DR. KATZ: And I would hope that it's an appropriate role for this committee to advocate on behalf of the intramural program.

CHAIRPERSON DAUM: Definitely, and I would like to talk with you some other time about doing more in that regard.

DR. KATZ: Fine.

CHAIRPERSON DAUM: I have one question about procedure here. Can someone educate us as to what GS-14 and 15 actually mean?

DR. GOLDMAN: Yes. The GS-14 is roughly the equivalent in academia to the associate

professor level, and the GS-15 is roughly equivalent to a full professor.

CHAIRPERSON DAUM: So this is an important hurdle?

DR. GOLDMAN: Yes, this certainly is an important hurdle.

CHAIRPERSON DAUM: Okay, thank you. Other committee members with questions about FDA presentation so far? I'm not hearing a whole lot.

DR. KOHL: Just a quick question. Steve Kohl. I was somewhat concerned about viruses that can be represented. Hello?

DR. CARBONE: Were you asking -- is that a question for me?

DR. KOHL: Yes. And I wonder if parainfluenza or adenovirus are covered in other parts of the --

DR. CARBONE: We cover parainfluenza, RSV. We do not cover adenovirus, the DNA laboratory covers adenovirus, but we do do parainfluenza.

DR. KOHL: Okay.

DR. CARBONE: Right now we are hiring a staff fellow from my laboratory to replace one that has left who will be doing parainfluenza review for us.

DR. KOHL: Thank you.

CHAIRPERSON DAUM: Thank you very much. Other questions?

DR. STEPHENS: Yes, hi, this is David Stephens. I have one question. There was a comment made, I think by Peter, suggesting that 70 to 80 percent of the individual's times are spent in regulatory activities. Is that in fact true for your laboratory, Kathryn?

DR. CARBONE: I would say that's not, if you take over the course of the day, I try and carve out an eight hour day, I would try and carve out an hour or two tops to spend in the research effort, so I think that's not an unusual percentage if you're going an eight hour day, you know, if you count weekends and whatnot --

DR. STEPHENS: Research efforts.

DR. CARBONE: And then there's the issue of emergencies come up that we have to just drop everything and deal with the regulatory issue. But it's quite a big of juggling, multitasking going on.

CHAIRPERSON DAUM: Other input from committee members? Okay. We'll now turn the floor over to Nancy for a somewhat macabre open public

hearing, macabre in that we're out there on our conference calls and I presume anyone who wishes to addresses the committee is there.

MS. CHERRY: Anyone who wishes to address the committee would be here. We have no one in the room that wishes to speak, so I think you're safe in declaring the open public hearing closed.

CHAIRPERSON DAUM: Then I'm going to do that.

(Laughter.)

CHAIRPERSON DAUM: The open public hearing is closed. And we now need to have about a five minute break.

MS. CHERRY: Well, since there's only one person here, I can tell you when she's gone.

CHAIRPERSON DAUM: All right.

DR. CARBONE: I have to go.

MS. CHERRY: Oh yes, Kathy has to go. Two people, I'm sorry. Dr. Carbone is leaving.

CHAIRPERSON DAUM: Thank you very much, Dr. Carbone. Who else is leaving?

MS. CHERRY: I'm sorry, Bob, I didn't hear what you said.

CHAIRPERSON DAUM: Who else is leaving, Nancy?

MS. CHERRY: Oh, okay, The reporter and Dr. Carbone. And let me mention that Dr. Midthun has joined us. She was here I guess right after Dr. Goldman spoke.

DR. MIDTHUN: Hi there.

CHAIRPERSON DAUM: Depending on where you are, good afternoon.

MR. MIDTHUN: Thank you.

MS. CHERRY: Dr. Egan has left the room momentarily, he'll be right back. He walked the reporter out.

CHAIRPERSON: All right. Well perhaps we'll go right on then unless someone needs to have a break.

PARTICIPANT: Can we take a five minute break?

CHAIRPERSON DAUM: Why don't we? Here in the Eastern Time Zone it's right around 11:15 and we'll just put our phones down and resume at exactly 11:20.

PARTICIPANT: That's the central time zone.

CHAIRPERSON DAUM: 12:20 at the FDA.

PARTICIPANT: Are you serving coffee?

MS. CHERRY: We're serving water. We

can send you some virtual water here.

CHAIRPERSON DAUM: Does that make sense for everybody? I have 11:14 central and we'll meet at 11:20 central, 12:20 FDA time.

(Whereupon, the above entitled matter went off the record at 12:15 p.m.)

CERTIFICATE

This is to certify that the foregoing transcript in the matter of: OPEN MEETING BY TELECONFERENCE

Before: FDA / CBER / VRBPAC

Date: MONDAY, JUNE 11, 2001

Place: BETHESDA, MARYLAND

represents the full and complete proceedings of the aforementioned matter, as reported and reduced to typewriting.

Eric Hendrickson