DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
National Center for Toxicological Research

Ranch Hand Advisory Committee Meeting

November 18, 2005
Rockville, Maryland

Certified Verbatim Transcript

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Opening Session

[CONVENE 8:34 A.M.]

M. STOTO: There we go. Everyone, please remember to turn your microphone on before you speak. I'm Mike Stoto, the Chair of the Committee. I'd like to call the meeting to order. David Butler, who's going to be presenting the report from the Institute of Medicine needs to leave by a certain time, so I want to make sure we have that discussion and the subsequent discussion from the Air Force that relates to it as soon as possible. So I think we'll try to keep this first part relatively brief and come back later to finish up things that we might have to do otherwise.

So let's begin, if we could, by just going around the table and then the room with people introducing themselves. I'm, as I said, I'm Mike Stoto, the Chair of the Committee and I work at the Rand Corporation.

P. CAMACHO: I'm Paul Camacho and I'm at the William Joiner Center at the University of Massachusetts.

L. SCHECHTMAN: Okay. I'm Leonard Schechtman, FDA's National Center for Toxicological Research, Deputy Director for Washington Operations, and the Executive Secretary of the Ranch Hands Committee.

S. LEFFINGWELL: Sanford Leffingwell. I'm a consultant in occupational and environmental medicine, formerly with Centers for Disease Control.

R. TREWYN: Ron Trewyn, Kansas State. I'm here to be as far away from Paul as possible so we behave ourselves today.

D. JOHNSON: Dave Johnson, Florida Department of Health, Executive Medical Director for the Division of Environmental Health and Acting State Epidemiologist.

E. HASSOUN: Ezdihar Hassoun, Professor of Toxicology, the University of Toledo.

K. OSEI: Kwame Osei, Professor of Medicine, Chair of Division of Endocrinology at Ohio State.

R. SILLS: Robert Sills, head of molecular pathology, National Institute of Environmental Health Sciences.

J. ROBINSON: Julie Robinson, I'm the Branch Chief for the Air Force Health Study.

K. FOX: Colonel Karen Fox, Principal Investigator for the Ranch Hand Study.

K. CAMPBELL: Kim Campbell, Food and Drug Administration.

D. BUTLER: David Butler, National Academy of Sciences, Institute of Medicine.

M. OWENS: Maurice Owens of Science Applications International Corporation. I'm a Program Manager for the Ranch Hand support contract.

J. MINER: I'm Jay Miner, Operational Technologies. I work in the Air Force Program Support Office.

W. GRUBBS: Bill Grubbs, also with SAIC. I work with Dr. Owens.

M. YEAGER: Meghan Yeager, SAIC.

M. PAVUK: Marian Pavuk, SpecPro Corporation. I work on the Air Force Health Study.

S. LEVY: Lieutenant Susan Levy. I'm the Deputy Program Manager for Ranch Hand, the Human Systems Group, at Brooks City-Base.

M. STOTO: Okay. Thank you, everyone. Okay. Did everyone get — introduce themselves? Yes. Okay. Len, you want to begin with the household — housekeeping items?

L. SCHECHTMAN: Household is good. Okay. We're — we don't really have very many housekeeping items today. We — I just want to inform you that we are going to have a working lunch so that we can get through this agenda and I will be reading the conflict of interest statement before we — before we get started. But I do want to point out that I'd like everyone to be thinking about future meetings or meeting singular before

the closure of the — of this effort. So we will get to that item toward the end of the meeting, but please be thinking about it as we progress through today's agenda.

Okay. The following announcement addresses the issue of conflict of interest with respect to this meeting and is made a part of the record to preclude even the appearance of such. Based on the agenda submitted for today's meeting, all such government employees have been screened for their financial interests related to the topics at hand. FDA has determined that all financial interests and firms regulated by the Food and Drug Administration present no potential for a conflict of interest at this meeting.

In the event that the discussions involve any other products or firms not already on the agenda for which a participant has a financial interest, the participants are aware of the need to be excluded from further participation. Such an action will be noted for the record. In the interest of fairness, all other guest participants are asked to address any current or previous financial involvement with any firm whose products upon which they wish to comment.

M. STOTO: Okay. Thank you. Since we don't have any products, we're talking about that's not as relevant. But conflict of interest is an important issue, so I'm glad that we had a chance to do that. I think we're going to hold the approval of the minutes until later so we can get right into the — into Dr. Butler's presentation. So David, if you're ready?

Update on the Air Force Health Study Disposition Study

D. BUTLER: Good morning, everyone, and thank you for accommodating my schedule by allowing me to present first thing this morning. There we go. I have prepared a set of slides; I also have copies of these slides should anyone need to take a look at them. What I'm here to talk about is an interim letter report from the committee on the disposition on the Air Force Health Study, a National Academy of Sciences, Institute of Medicine study that was tasked to address the disposition of the AFHS.

I will just run through these quickly since everyone has seen these slides before. They're our standard opening slides on what the National Academies is, and specifically, what the Institute of Medicine does. As I've mentioned before, we have a process whereby we form volunteer committees of experts and write reports based on their systematic review of available scientific evidence. Those reports are then subject to an external peer review.

The Congress tasked us, and more specifically, tasked the Department of Veterans Affairs to ask us to address five separate topics related to the Ranch Hand Study: the scientific merit of maintaining the data assets collected in the course of the study; whether or not any obstacles existed to maintaining those data assets; the advisability of providing independent oversight of those materials past the time of the scheduled end of the study and the mechanism for doing so; whether there should be any further study of these materials; the advisability of extending the study itself, and if

so, who or what should be responsible for extending the study; and finally, the advisability of making the materials collected in the course of the study available to outside researchers.

In order to accomplish this task, the committee on the disposition of the Air Force Health Study was formed. You'll see the names of the individuals there. Their expertise ranges from epidemiology through biostatistics, occupational environmental medicine and bioethics.

The interim letter report that I'm talking about today is a very small document and it'll probably take longer for me to talk about it than it would take for you to just sit down and read it. It is a highly focused document that addresses only one component of that charge that I just ran through a moment ago, specifically whether or not any obstacles exist to retaining and maintaining the electronic data, the paper records that have been rendered in pdf form, and the laboratory specimens that have been collected in the course of the study.

The committee — and you'll note most of what I have here is in quotes both because it makes sure that I get things across clearly and also because it saves me trying to rewrite what's already been written anyway. The committee thought it was important to offer its findings, conclusions and recommendations on this topic alone because they were aware of the fact that the time clock on the study is running very rapidly and very loudly at the moment. And they wanted to make sure that their

recommendations would have a chance to be considered while the individuals, the investigators with the AFHS who are most familiar with those data assets and the funding to support them were still available.

In gathering information for this letter report — and I should add the final report that we're working on — the committee held meetings earlier this year, including workshops where we invited parties, including Dr. Stoto, to come and talk with us and also conducted a subcommittee visit to the research facilities in San Antonio in May. We also asked a number of questions to the AFHS staff, which they were terribly patient about answering. And we really appreciate all of the efforts that they have put forward to make sure that we got all of the information that we requested.

Two working groups went to San Antonio and they looked separately at the data and at the laboratory specimens. I'll start out with the bottom line and then just drop down into a little bit of detail that's in the report. The bottom line was that the committee found that the data and the specimens had been maintained at the level typical of most epidemiological research.

Now because this is a study that's gone on for so very long, the state-of-the-art has changed over the time; computer programs have changed; the ability to manage data electronically have changed over time. And as a result, you have a data set which was collected at various points in history and is in various states of electronic documentation. The subcommittee noted that study personnel weren't tasked with

rendering all of those data assets accessible to outside research — researchers over time and that their findings concerning it should not be viewed as a criticism of the AFHS staff.

Instead, what they found were a set of working principles for managing and analyzing the data and specimens that works very well for the AFHS investigators. Every — the committees, the subcommittees asked staff to go through a series of exercises that were intended to elicit how easy it would be to access certain data and to analyze that data. To do so, what they did is they asked staff to write a small SAS program to randomly draw case numbers from five of — five Ranch Hands and five comparison subjects and use those case numbers as sort of the example population for the particular exercises.

In the course of going through those exercises, the committee found that data, especially data that had been collected earlier in the studies wasn't necessarily documented in electronic forms. So if you were wondering what particular code was associated with a variable that had been collected in an early stage of the study, you might pull out a book where it had been — that information had been hand-annotated.

Over the course of the study, the collection of variables changed. Variables that might have the same name over the course of the study might've been coded in different ways over its history. That's, again, researchers responding to the incentives

and the local conditions when they were doing the work rather than looking to do some grand overarching data set.

With the laboratory specimens, a system has evolved whereby the data were, at the time the committee was there in May, where you had to go through a two-step look-up process to find a particular sample: both consulting an original database and then consulting exceptions to that database that had occurred over time as specimens had changed because a particular freezer might've failed or a specimen otherwise had to be moved.

The committee found, after its review of the subcommittee information and its review of the reports and other documentation that had been prepared over the course of the study, that the medical records, other study data and laboratory specimens — you'll notice I echo those words because those are the words that are in the charge — collected in the course of the study have been properly maintained. But they are not currently organized or documented in a manner that would allow them to be easily understood, evaluated, managed or analyzed by persons outside of the AFHS.

Therefore, the committee concluded, again addressing a specific item in the charge, the present state of the documentation and organization is an obstacle to retaining and maintaining these materials once the currently scheduled termination date of the study occurs. The committee therefore formed a primary recommendation that actions should be taken prior to the scheduled termination date to reorganize and

document the data assets in a form and format that does allow them to be easily understood, evaluated, managed or analyzed by people outside of the AFHS staff.

It proposed a number of specific recommendations separately addressing the electronic and paper records that have been rendered in pdf form and the laboratory specimens. For the data, first of all, they proposed that a comprehensive inventory of master data files be created. Let me explain what that means. Over the course of the study, a rather large number of data files had been collected or generated. These include the raw data files that were the original input for these data, the cleaned up version to those files that were used for — as the basis of analyses, and files that were generated in the course of particular analyses.

What the committee refers to as “master data files” be the — that subset, that small subset of the rather large number of files generated over the course of the study that staff consider to be the definitive files, the files you would start every study with if you were going to conduct a new study. And what they’re asking here is that those files simply be identified in a clear manner and inventoried. So if one wanted to look at pulmonary assessment data from Cycle 3, you’d be able to pick up a book and immediately say this is the definitive file you would use to study those data.

Second, to create a comprehensive inventory of the variables contained in the master data files. Now this is something that has been done over the course of the study, but not necessarily consistently over the course of the study. The committee

wanted to make it clear that a number of their recommendations stemmed from looking at materials that had been prepared as part of one cycle's examination or another, but weren't necessarily identifiable in easy — in an easy way in other cycles.

A comprehensive inventory of variables — the data dictionary that was produced for the Cycle 6 examination is an example of the document that they're looking for there: something that tells you what the variable names were, what the descriptions are, what the codes were used — the codes that were used to summarize the data that were collected and the like.

A master data code book containing the name of data variables — this is basically a document that would be generated from the requests above it, simply having sort of a one-stop shop where the files and the variables were associated in a single document so that somebody looking to do a particular analysis over time or of a particular cycle would be able to identify those pieces of information they needed in order to do the work.

Finally, for the documents that have been scanned into image pdf files, a document containing the content, format and location of those materials. Again, what we're not talking about is something where you go through the — Joel liked to talk about the "linear mile" of paper — not a document that goes through every last piece of paper there, but simply the type of materials that the AFHS investigators prepared in response

to questions to us when we asked about how those information — that information had been inventoried to begin with.

This is not an effort, the committee wants to make clear, where it believes you would need to go back through every one of the thousands of data files or the thousands of reports and rewrite them or make every last piece of information consistent. Instead, this is a documentation effort: take those key pieces of information, the key documents which have, in some cases, already been prepared, and identify them clearly and say this is the definitive piece of information you want to pick up if this is the thing you want to analyze in the future.

As I said, the committee noted that some of these documents already exist in some form and the documentation for the later examination cycles exhibits many of the features that the committee suggests. The concern — their concern is simply that information for all the cycles be compiled into easily identified, definitive reference documents with uniform information content. And what I didn't write down here, but which the committee suggested, is that these be in an electronic form, searchable pdf files, for example, that would facilitate someone finding a particular piece of information that they were looking for.

The committee also had a few suggestions regarding laboratory specimens. Let me cut to the bottom line here before I go through these. These recommendations were based on the state of the laboratory specimens at the time the committee visited. The

committee understands that since then, there has been a reorganization of those samples which addresses many of the items that are spoken of in the report: to do an inventory and create a single specimen database.

The committee also suggests to compile the information regarding specimen history into a reference database. If someone is going to — were to want to analyze these specimens in the future, they would want to know what the specimen history was to be confident that they could do good analysis work and to compile all the protocols regarding the receipt, the maintenance, the dispersal and the return of the specimens where specimens had been sent out to other investigators and have not yet been destroyed into a single reference document to document the status of those to performed — perform the planned re-assay to aid in the evaluation of specimen stability and condition.

We're looking forward to hearing the report on the progress on that today. And simply in the reorganization, to make sure that individual samples are documented so that someone looking at them would know when they had been collected if there are any vials that aren't already marked with that information.

As I noted, the committee said that they were aware of the re-inventory and physical reorganization of the specimens and said that it was in agreement in the effort since it achieved the goals that it was looking for. The committee drew one final recommendation concerning these. We understand that the recommendations that are

being offered are not costless and do involve time and staff commitments when there's very little time left.

The committee recommended that the Air Force, as custodian of the research materials, take responsibility to ensure their proper documentation and their organization for historic reasons, and also to allow the possibility of future use, and indicted that if available program funds weren't sufficient to accomplish the actions that the committee recommended, that supplemental funding be provided to carry out such work in a complete and timely manner.

This is only one small part of the committee's final report on this topic, which is in advance stages of completion and which I'm working at basically on any moments that I'm not devoting to other things: eating, sleeping and the like. We are working to complete this report as quickly as possible and get it out so we can have conclusions on all of the topics that the committee was charged with addressing available for the consideration of the Congress and other parties.

The complete report is posted for download at the National Academies Press web site. That address will take you to a page that will allow you either to look at the report page-by-page on the web or allow you to download your own pdf copy of it after you provide your e-mail address or somebody's e-mail address to NAP.

And as before, this was part of a larger research effort regarding veterans' health that the Institute of Medicine has been conducting at the behest of the Department of

Veterans Affairs and others. And we have a comprehensive web site which pulls all the information from these disparate projects together so that people looking for information can, we hope, find it easily. That's the end of my presentation. I'd be happy to take questions.

M. STOTO: Okay. Thank you very much, David. Are there questions from the Committee? Ron?

R. TREWYN: It would appear based on the fact that the recommendation at this early stage is to reformat both the, you know, some of the aspects reorganized for both the data and the specimens that we can probably anticipate at the end of this that there's going to be a recommendation that the materials be maintained and be available to other than Air Force personnel. Otherwise, this initial stage probably would not have been recommended early on. Is that roughly a fair assumption?

D. BUTLER: Well, the committee makes clear in the interim letter report that it reaches no specific conclusion on that topic in this report. It notes that whatever recommendations it offers and whatever policy decisions are taken in response to those recommendations, the committee believes there's merit in doing a complete documentation of this data set. If nothing else, the committee understands that the electronic and paper records are subject to review by the national archivists for possible inclusion in the National Archives. That's an activity that's entirely outside of this committee's mandate.

The committee suggested that if for no other reason than to ensure a complete and thorough review of that issue by the national archivists that complete documentation was appropriate should the national archivists choose to make this — these data part of the archives. Having complete documentation would also facilitate its use at some point in the future were the materials to be made public.

R. TREWYN: Can I follow up just one more thing on that? I guess the reason for my — I just turned it off. Now it's on? Okay. I guess the real basis for my question is because it would be very clear that this would be a costly and time-consuming process between now and the end of the — end of the study.

And it would then, I think fairly obviously, mean that the Air Force would need to be directing as many of the unexpended resources as possible to this process, which would probably mean they would be putting less resources toward writing up additional things for publication. And so then the outcome, if then the ultimate outcome was, "No, we're going to then destroy everything and whatnot, it" — then there are some significant, potential concerns. Those are — those are not necessarily great alternatives then if, so ...

D. BUTLER: The Committee understood this and this is why they explicitly recommended that the Air Force allocate additional funds to manage these activities, you know.

M. STOTO: And Ron, you may want to ask that question again when the Air Force responds.

R. TREWYN: Right. I may do that.

M. STOTO: Yes.

D. BUTLER: Yeah.

M. STOTO: Robert?

R. SILLS: And I probably should know this, but as I was listening to your presentation, I thought the committee has done a really good job of identifying the issues and helping us solve them. The question I had is, do we have a home for the study? Is it the National Archives?

D. BUTLER: That is a topic that the committee will address in the final report. We were specifically charged with making a recommendation for a future home should the committee conclude that additional data analysis activities were appropriate.

R. SILLS: And the reason I brought this up is it seems as though since we are — since the committee's recommend — recommending, which I think is very, very important, that the data is accessible is to have the parties who are going to be the home of the study working with the — with the group that's organizing the data so that — so that there's a smooth transition and the new party could — will have — will be — will know exactly where those records are and how to access them. So, you know, an

important part of this process was, if possible, would be to have both groups working together so that, you know, we could really use this important information.

D. BUTLER: Well, the committee asked for a set of documenting activities which it intended to result in generation of a — of a bunch of pieces of information that would allow anyone looking at the records in the future to understand the material that's there. Clearly, there is a tremendous amount of knowledge and expertise embedded in the AFHS staff on these data. The committee was hoping that some of that information might be committed to paper for future use.

R. SILLS: Thank you.

K. OSEI: Robert, Michael, the — at the end of the study, where will — who will be or what will be the owner of the database? Is it going to still be AFHS or some other body who may have no connection to this study at all? And not being part of a study and just going to look at data without some connection to AFHS may create problems in even designing the potential of the data. So if you could help us with a recommendation or discussion about the ultimate ownership and the home for this?

D. BUTLER: That's a topic of the committee's final report and until that report has been reviewed and finalized, I can't get into the committee's recommendations concerning that. We were charged with offering such recommendations, and again, no matter what we recommend, we are not the policymaking body in this particular respect. We are simply — we will offer recommendations that can be considered by the

Congress and by other parties. And the committee felt, again, that no matter what they recommended and what policy decision was made that it was important to ensure that there were complete document — there was complete documentation at this point.

K. OSEI: Okay. So what — who will be the final, you know, body that will decide that?

K. FOX: We don't know.

D. BUTLER: Yeah.

K. OSEI: Oh, you don't? Oh, okay.

D. BUTLER: That's a topic for the final report.

K. OSEI: Okay. All right.

M. STOTO: And then clearly, we're going to have to schedule another meeting of our Advisory Committee too once that final report is out in the next couple of months to discuss this further. Paul?

P. CAMACHO: I have two questions I guess. Can you tell us what progress, or ideas or comments have been made by your committee about number five, "the advisability of having outside people look at this?" And once you make your final report, let's just pretend some — several groups or this group says, "No, we don't like that. You should be making a change." What are the chances of modifying your opinions after you've made them?

D. BUTLER: The committee's report is the committee's report. Again, we're not the decision-making body here; all we can do is offer recommendations. And charge five is one of the things that will be addressed in that final report.

P. CAMACHO: Are you going to have enough input from say, stakeholders, about number five?

D. BUTLER: We have been soliciting input from stakeholders throughout our information gathering process.

M. STOTO: And then, you know, whatever they say, we'll have a chance to say we agree or we disagree and it should be something else; that's okay. Were there other questions? Sandy?

S. LEFFINGWELL: I'm wondering if there's a potential dilemma arising here. A number of years ago the National Archives and Records Service concluded that long-term storage of records should be only paper or microfiche because electronic data formats were too femoral. When was the last time you saw a machine that could read an eight-inch floppy? Has that been resolved?

D. BUTLER: I can tell you that I spoke with the archivist who is responsible for storage of electronic data sets at the National Archives. The Archives have come out with a set of recommendations for how electronic data should be formatted and what media it should be placed on for submission to the Archives.

My understanding is that this is an evolving standard at the moment, but they do have an explicit set of recommendations right now for how electronic data should be submitted to them. And if you go to the Archives electronic data section, you'll find they now have a rather large number of sets, including epidemiologic data that they make available. They are strictly an archive though; they do not do anything in the way of support for any of the information that they hold.

M. STOTO: Okay. Other questions? Well, great, thank you very much, David, for joining us today and ...

D. BUTLER: Thank you.

M. STOTO: ... I know that either you or one of your colleagues will stay ...

D. BUTLER: Yes.

M. STOTO: ... for the rest of the discussion.

D. BUTLER: Amy O'Connor, who is here in the corner, a research associate for this study will be here for the entire length of the study. And she'll try to help you with any questions that you may have because I have to take off.

M. STOTO: Okay. Thank you.

Air Force Health Study Specimen Viability Study

M. STOTO: Let's now turn to the Air Force. We have a presentation from Dr. Pavuk on specimen viability and I think that's next on the agenda. Is that — you're ready to go?

M. PAVUK: Good morning, everyone. As most of you know, in the course of the Air Force Health Study, a lot of biological specimens — be it serum, urine, adipose tissue, blood and some other samples — were collected. Most of those were serum samples. Some of those samples, the study, first physical examination was in 1982 has been stored for more than 20 years. So the logical question arise, how will the samples be preserved and what are some of the samples could be used for the research?

This study was not designed to evaluate comprehensively all the samples and answer all the questions on all possible methods of how the samples could be analyzed for different analytes. We have selected one of the technologies that looks — which is called "multi-analyte profile" done by Rules-Based Medicine that looks at proteins in the serum. And we were interested whether this technology could be applied to assay biochemical parameters in the frozen specimens and whether these could be used for studies by other investigators.

This study was limited in scope. As I said, 25 samples were selected from five randomly selected veterans who have attended all five examinations between 1982 and 1997. So we wanted to have one sample, so we wanted to look at the sample

throughout the period. And we also wanted to select veterans that had multiple samples so that we do not select veterans that have just one serum sample for the particulates — particular cycle of examination, and that sample is destroyed and cannot be used for further examinations. So all of those veterans had multiple samples.

Multi-analyte profile testing was developed originally by Luminex Technology, which part of that group then became Rules-Based Medicine and Rules-Based Medicine in Austin, Texas now performs those analysis. Those are high-density quantitative immunoassays basically that allowed for identifications of biomarker proteins and can be used for comprehensive evaluations of protein expressions that could be indicative of exposure to disease, drugs, environment and other factors.

I have a list of analytes that I can provide to you. There's 177 analytes; there are 78 specific serum antigens, 43 autoimmune serologies and 56 infection disease serologies that can be tested all in one complex analytical procedure. We were intrigued by that, by the complexity of it and that you can do all those things at once, and also by the fact that you need only 100 microliters of the sera and the samples then can be returned back to Air Force Health Study.

I'm providing just very brief overview; this is not details of the technology of what is involved. But basically what I already mentioned, that the technology basically employs immune bioassays and then they use a very ingenious system of dyeing polystyrene microspheres using high-speed fluidics, and digital signal processing and

sets of lasers that exacts those dyes from the — from the dyes. As I said, there's a set of dyes; there are specific dyes that permeate.

The polystyrene microspheres are coded and create a set that can be specifically recognized, at least 100 different specific dyes. And those microspheres are then covered with capture antibodies that react with the target proteins you want to measure. And then the assay — when the assay's complete, the microspheres pass through a single file through two lasers. The green laser — or the red laser exacts the specific dye that identifies the analyte and then the green laser exacts different dye that enables the quantification of the result.

At this point, all those samples are selected and ready to be shipped to the laboratory and they are very, very close to the completion of the contract activities so that those could be sent to Austin and analyzed. This can be analyzed in a — in a — there's a short turnaround time for the analysis proper. And once the samples are in Austin, we should get results back within about three weeks.

M. STOTO: Okay. Thank you. So I guess a couple of things: one is I hope that if we schedule another meeting to talk about the results from the IOM study that we hear results from this one and ...

M. PAVUK: Well, we were hoping that, you know, that we could have something ...

M. STOTO: Okay.

M. PAVUK: ... because the time — once it's sent out, we could get results pretty quickly.

M. STOTO: Right.

M. PAVUK: But it's — it'd be around April to finish the contracting processing.

M. STOTO: So is — if the IOM finishes in January and we schedule a meeting in February, will this be ready in February?

M. PAVUK: I hope so.

K. FOX: We expect it could be, yes.

M. STOTO: Okay.

M. BLANCAS: The contract has been fully negotiated.

RECORDER: Could you use your microphone, sir? I have to record every word.

M. BLANCAS: Am I on? I spoke to the buyer on the contract and she informed me that the contract had been negotiated as of the day that we left, which was two days ago. All they were waiting was to actually get into the system, electronic system, and go ahead and issue the copies of the contract. So have you heard something similar to that?

M. OWENS: I have not.

M. BLANCAS: But it should be, in fact, maybe as I speak, it's already been issued.

M. STOTO: Okay. We don't need to go into the details. I think it's just clear that it's important that that be ready and it sounds like it could be. There shouldn't be any — now coming back more to the substance, I know enough about the laboratory spheres as I ought to. But I guess the question I would ask is, suppose it turns out that the samples do well in this analysis. How much can we extrapolate from that, you know? What I mean is ...

M. PAVUK: Well ...

M. STOTO: ... is this — is this a narrow or a broad question?

M. PAVUK: ... as I said at the beginning, I think the study is limited in scope and will add some further information to what the sample can be used for. So it will specifically answer that if it turns out good that this particular technology can be used for it. It will not answer the question on the other technologies. But I think more generally, if the samples from '82, '85, '87 turn out well, I think it will suggest that the preservation was good and that the degradation of proteins in stored serum is not so bad. I think it will be positive and it will add a little bit of, you know, let's say, you know, a little bit confidence to the — to the storage process of the samples.

M. STOTO: Okay. Ron, did you have a question? Ron?

R. TREWYN: Why only proteins? Why not look at other ...

M. PAVUK: Well ...

R. TREWYN: ... components?

M. PAVUK: ... that's a very good question. I think we'll get the proteins from the point that I think it's overly, generally accepted that DNA inside the cells preserves better than proteins outside of cells, that they may degrade more. So we opted to look at proteins. We believe that DNA is probably more likely to be well preserved.

K. OSEI: What was the process you used to select this company for this project because obviously, there were some competitors? There has to be a reason why you thought this was a better company or method to accomplish the mission that you wanted, you know, you proposed to solve.

M. PAVUK: I was not involved in detail in the process of selecting the company. But the Rules-Based Medicine did have a presentation at Air Force Research Laboratory at Brooks City-Base, and at that point, not connected to Air Force Health Study. And that's a public presentation that members of the study attended and that's how the Rules-Based Medicine came to their attention. I cannot specifically answer you what are the day-to-day variables how this was decided.

M. STOTO: I think that the question probably is a little more general than the choice of the specific company. It's the choice of the technology ...

M. PAVUK: Oh.

M. STOTO: ... which this company owns, I think. Isn't that ...

K. OSEI: Yeah, that's what ...

M. STOTO: Yeah.

K. OSEI: Yeah, the technology that you're using because this fancy technology is probably not available ...

M. PAVUK: Right.

K. OSEI: ... to a lot of commercial ...

M. PAVUK: Well, from just the technology point of view, when you look at the proteomics, I think we narrowed the — our interest to proteins. And the other technology that we looked at would be based on, you know, high-resolution mass spectrometry, some sort of analysis that you can use of getting protein profiles where we do not exactly know what those profiles mean.

So we opted for this technology, at least provides, you know exactly what you measure. And we can also confirm, we can also compare — although I don't think it's our primary goal — but we can compare the results if there are some results to the previously measured parameters from the Air Force Health Study, which some other technologies would not enable us to do.

M. STOTO: Do you have a — Kwame, is there something else that you would like to suggest or ...

K. OSEI: You know, because I don't know much about the technology, so I think it's coming from my naiveté of knowing what you're getting out of this. And, you know, and the question came, is it simplicity or it's comparable to other laboratory technology? Because at the end of the day when we're going to measure, if you give it to — the

samples to other, you know, investigators, they're not going to use the same technology, so I don't know what they're measuring. It may be viable here, but is it viable to the commercial available assays that we use to analyze the data?

M. PAVUK: Yes. This is commercially available.

K. OSEI: Okay.

M. PAVUK: I mean, this is not some experimental technology.

K. OSEI: Okay.

M. PAVUK: I mean, this is — this is commercially available for several years being tested and the result of the antigen testing, and serum analysis and infectious antigens, those correspond very well or very close to currently gold standard technologies. So that's the advantage; that here you can do it all at once and you get results that are very similar to other standards that are currently used in other laboratories. So that was — that was the advantage.

P. CAMACHO: Just a question, this can be compared and ...

M. PAVUK: Yes. Yes.

P. CAMACHO: ... but with other standards ...

M. PAVUK: Yes.

P. CAMACHO: ... and other people and replicated and so forth?

M. PAVUK: Yes.

D. JOHNSON: I think I'm going to ask the same question a different way.

M. PAVUK: That's why we're here.

D. JOHNSON: Is there any literature that, you know, that shows that this relates to the accuracy of the other parameters that are going to be tested for? I mean, is there something that shows there's enough correlates with ...

M. PAVUK: Yes.

D. JOHNSON: ... the viability of all of the other things that might be — you understand my question?

M. PAVUK: Yes. I think yes; that they did publish studies like that that showed that their technology measures what other ...

D. JOHNSON: I mean ...

M. PAVUK: ... comparable immunoassay measures.

D. JOHNSON: ... in other words, if I say the — if this shows the proteins are all good, does that mean all the other types of tests are — I mean, the other parameters that could be tested in blood are probably also reliable? I mean, does this somehow correlate or has there been any studies to show that this correlates with the other things that you might test for in blood? You understand my question?

M. STOTO: Let me — let me try to ask it this way. I mean, I can imagine that you try to do this and then you find out that the — that the proteins have just degraded ...

M. PAVUK: Right.

M. STOTO: ... which means that nothing else will work in future presumably.

D. JOHNSON: Not necessarily.

M. PAVUK: No. No, not necessarily.

D. JOHNSON: Not necessarily.

M. PAVUK: If this doesn't work ...

D. JOHNSON: And that goes both ways.

M. STOTO: Right.

D. JOHNSON: The proteins might be good, but some tests might not work.

M. STOTO: Right.

D. JOHNSON: The proteins might be bad, but there still might be a lot of useful data there. So I just wondered how much literature there is to correlate those?

M. PAVUK: Oh, now I understand the question. That, I think, is really hard to say specifically. I don't think that if this doesn't fail or even if it is successful, will not tell us how well it correlates with some other things that we could get from those sera, you know. Let me maybe compare, you know, if you do the studies, let's say, on stability of DNA, you know, they've been stored for a long time, it will not answer your question. But if that DNA was irradiated, you know, and — but it degraded too, you know, so I don't know. This — it probably will not.

M. STOTO: Ron, you wanted — oh, Robert?

E. HASSOUN: Is there any way that some of the tests or some of the assays could be repeated and compared to what we previously — what you previously found and confirmed?

M. PAVUK: Yes. Yes, we hope so. Yes, we hope so. That's the — that's the ...

E. HASSOUN: Yeah, that's not confirmed.

M. PAVUK: Because this, for example, you know, measures, you know, levels of some hormones and some of the antigens that were measured in the Air Force Health Study previously. So we can look at the, you know, '87 or '92 results and look or, you know, well is it, you know, in the same range or not? But I don't think that that is the primary focus because, you know, this is different method used for the measurement of the same thing that was done probably in '92.

But yes, we can look at the same analytes and compare the results. As there are 177 analytes, we probably will not look, and look at each of those and compare how the results compares from '82 to '85 to '87. I don't think we have the time or scope to do that at this point of the time. But yes, for some interesting ones, you know, we'll certainly do that and look for more common ones if we do get results.

M. STOTO: Robert?

R. SILLS: So I just want to make a couple of comments. I think this work that you guys are doing is very, very important. The serum samples, you know, are samples which will be very useful in the future. And I think as the Committee is saying, I think

one of the strengths of this is, is you're looking at '82, '85, '87, '92 and '97 and we've got a good idea as to how the samples held up.

But I think as we — as we progress with the study with the short time frame we have, I think it would — I think we need to look broader at not only protein, but a DNA/RNA protein just at all three levels just to — it would be informative for people who are going to use the samples in the future to have that information. I think that will be very informative for additional information about what some of the disease endpoints, you know, this information would be helpful in terms of addressing future disease endpoints.

And so I think as we — as we — as we think about this as Mike said, a meeting to discuss the results would be very, very useful as to how we proceed in understanding, you know, how well these samples held up for future research ...

M. PAVUK: Yes. Well ...

R. SILLS: ... on important — on important health issues to the veterans.

M. PAVUK: ... I have, you know, I have — this effort, you know, have been suggested almost two years ago. And at that time, this discussion that happened, you know, well, why is it only proteins? So let's do DNA; let's do, you know, all sorts of things that you can do with the stored samples. The study as it is, you know, it's not designed to, you know, kind of come up with an idea and well, how much do you need? Well, $150,000 to test, you know, 15 samples for something.

So, you know, we — at least from my point of view and, you know, I cannot talk for everyone what the reasonings were two years ago or a year ago — we didn't, at this point, didn't look at some comprehensive evaluation of the samples. We looked at least a peak to the samples that are stored and doing at least some sort of viability study. As you can see, we are in November, December 2005 and we are still contracting on this one. So that may answer some of the questions.

M. STOTO: Okay. Two comments; you just led into one of them about this is called the "viability study."

M. PAVUK: Right.

M. STOTO: And that it turns out that really is one specific aspect of viability we're looking for. And I guess I wonder if you are drawing samples, you know, these 25 samples, and I imagine that this technology is complex and so on, but there may — there may be some other simple testing that can be done with those same 25 samples that test other aspects of variability — viability.

So that's one question, is whether that might — something along those lines might be feasible and make sense in the same time frame? I don't know what the — I don't know what that might be. The other — the other issue is that you mentioned that there are — there are 177 analytes and you ...

M. PAVUK: Yeah. I have a — I have a list.

M. STOTO: Well, I don't want to see the list. But my — but that — and you couldn't — and I agree that you couldn't afford to all — look at all 177 of them, you know, by January and compare them to the other results. But it probably would make sense to think in advance, you know, what are the five or ten most important ones ...

M. PAVUK: Yes. Yes.

M. STOTO: ... to do and to have — to have a protocol along those lines. I'm not sure if we can contribute to that. If we could, I'd be happy to, but I'm not sure. But I think it's important to have a protocol for that, so ...

M. PAVUK: That's a very good idea and ...

M. STOTO: Okay. Ron?

M. PAVUK: ... we will work on that.

R. TREWYN: Want to follow up on Robert and actually Michael's earlier comment because I think this issue of just picking proteins, if we go back to a — to a comment that Mike made earlier about, "Well what happens if, you know, the proteases have chewed up most of these and so the proteins aren't good?" And one of your initial assumptions was, "Well, but we've figured the nucleic acids are going to be okay."

But if you don't analyze and if you don't look at them, if you don't assess the DNA, the RNA to really know where it is — and this, I mean, I look at it, it isn't that this is a highly, a big broad study. You're doing, you know, some — a snapshot. I think you're using — exactly as you used the term to see do we feel these specimens were

stored in such a way that they will be useful for future studies and people are going to want to look at things other than protein? And so I think that's sort of where a lot of this is and so at least having an idea if you've got some stability there, I think is going to be important.

M. PAVUK: I can't agree more. I mean, that was, you know, that was my first reaction when this whole thing came up. But all of that requires, you know, that requires further funding, you know, or changing what activities being planned. So I don't know. I can't tell you at this point whether there are technologies in other laboratories available or not or how we could proceed on the things. We haven't discussed that with the Air Force.

M. STOTO: Okay. So, Jay?

J. MINER: Yes, finally. I would encourage all of you to go out to the Rules-Based Medicine web site for an overview of their technology and the — and the list of tests that they do because it's a very good presentation, and discusses in great depth and will answer a lot of the questions that you all are asking.

Secondly, on the web site, they also have made some studies on what they describe as a "phenotype of disease;" that a clustering of tests that may show an increase in — I believe the study was done in mice and that's on the web site as well. Depending on what we find on the first 25 samples, we do have some money in the

program to do additional testing for this, but you've got to find out if it's — if it's good first.

M. PAVUK: I didn't get to the — to the opportunities for this technology, which are wide, you know, from the point of diagnostic testing and use for, you know, identification of disease profiles and other things. So I mean, it seems very useful, very broad range of interests that could be covered with this technology. So it's not very specifically focused, a narrow one, but I didn't want to go into ...

M. STOTO: Okay.

M. PAVUK: ... to the overall use of this.

M. STOTO: I think it's important to bear in mind a couple of things, you know. One is that it's possible that you can do this testing. It'll turn out that a lot of the samples just aren't any good at all, which would have very important implications for the disposition of the study, right? I mean, if it turns that the samples weren't good, there's no point in saving them. I'm not saying it's likely. I don't know; I have no idea, but it may well be that we find something that — and that would be an important thing to know.

M. PAVUK: Well, that was the risk, you know, that we are willing to take.

M. STOTO: That's not the risk. That's not — that will be — that will be a success in a sense if we found that. I mean, that was to save somebody a lot of money if that was — that's a ...

M. PAVUK: I think that that is really a small number of samples out of, you know, maybe 50,000 serum samples that there are. I think even if like half of them would be a failure, I think that would still be a success. I mean, and if all of them failed, you know, I would more say, you know, that it would be incompatibility of technology than the failure of the sera, so ...

M. STOTO: The point is that this study has the potential to give us some information that's very important for the question of whether or not these samples should be saved.

M. PAVUK: I agree very much.

M. STOTO: That — I think that's ...

M. PAVUK: Oh yes.

M. STOTO: ... the fundamental thing that we should be focusing on.

K. FOX: That's the purpose of what we're trying to do.

M. STOTO: Right, and that — I just want to make sure that, you know, that wasn't prominent in the discussion. I just want to make sure that everyone really understands what that's about. Now there could be lots of other things that are learned and the possibility that Jay just mentioned about being able to do follow-on studies after this first 25 is an important one too. So I think that that makes it all the more important that we get a good comprehensive report that really addresses all those issues at the next meeting.

R. SILLS: So Mike, that — I suppose that's one of the points I was trying to make; is we're looking at the protein level and, you know, what's your name again, Dr.?

M. PAVUK: Pavuk.

R. SILLS: You know, you indicated that DNA is more stable than proteins and the issue that we're looking at here is the stability of the samples. And so as Mike was saying and the rest of the group was saying is these are just 25 samples; 25 samples are not a lot of samples and it would be useful to get information about the quality of the DNA, the quality of the RNA, the quality of the proteins.

So you're using — you're looking at antibodies here, but you know, there's simple tests that we could just have, you know, that information could be made available. So I don't know what a mechanism is, but I think if we're going to look at the quality of the — or samples, I would like to see not only the protein, but have a comprehensive evaluation of what the samples are.

So for example, the proteins may not be good, but DNA may be good. And DNA could find a lot of information that could translate and you could make extrapolations to what may be happening in the protein level. So the more information we have, I think the better it is going to be for the outcome of the study and how this — how, you know, the next level for this study. So I, you know, mean, I don't know what mechanism is available for us to get these answers as quickly as possible or to — or to include the right analysis.

M. STOTO: I think — I think it's — what we can do is make it clear in, as we've now done and in the minutes that first of all, what the purpose of this study is, and second, that to the extent that we're going to — that 25 samples are going to be drawn, we should get as much information out of those as possible and that we need to have — and I mean, I don't — but I don't want to say how we do that, but I think that that's — that that principle is what ...

K. OSEI: Mike, I think all what we're — everybody is trying to say that you may have proteins, but you may not be able to measure all the, you know, the specific hormones and peptides. You still can measure proteins, but you know, but it has — may have no meaning to the specific assays that we are interested in. Let's say you measure cortisol in 1982. You want to know that 22 years down the road you can still measure cortisol. So you can measure proteins, but it's not necessarily cortisol. So you will have to be able to specifically measure the things that the study was designed to do.

So I think generic measure of protein viability alone probably is not good enough. And I think what we're hearing, if you had shown us a slide where you took '82, '84, '85 just to show that with time it's still viable, these questions would not be coming up at all. But we don't have any, you know, clue what this is about. And I think that's why these questions are coming up because I don't know what you're measuring; viability of proteins doesn't mean much to me. I want to know is, can you measure cortisol consistently in the same sample over 25 years?

M. PAVUK: If I understand you correctly, I think that's what we are trying to do. We'll do the same measurement, you know, in the sample from the same veteran in '82, '85, '87, '92. And I have — I wanted to give you a list of what exactly we're going to measure in there and I believe cortisol is on that list too.

J. MINER: It is.

K. OSEI: Yeah. I mean, using that as an example, but ...

M. PAVUK: Yeah.

K. OSEI: ... we are talking about consistency.

M. PAVUK: Yes. I mean, that's the point. You have the same value from the same veteran from one examination cycle to another examination cycle, so we'll do that repeatedly. Yes.

M. STOTO: Paul?

P. CAMACHO: So in a kind of — for me, a summary would be: you're using these — taking the 25 samples. You're going to — you're thoroughly measuring all of these factors that people want you to measure. You're going to give us — give yourself an estimate of the quality of these things in terms of how long they might last, and then you would really have to go back and get a proper sample size.

If that panned out, then you would have to go back and get a proper sample size to determine the whole — to give yourself a good knowledge base on the viability of the whole set because you just said you have 50,000 of these things. So 25 is far too

small, so you — but the 25 is good that you want to go look at them, right? And you want to find out the viability of all this, but then would you not have to go back and get another sample set to be significant?

M. STOTO: It may well be, but I think that — let's put that on the agenda for when we ...

P. CAMACHO: It's just "n" is — because "n" would be a small number here and I think it's — it might too small.

M. STOTO: Jay?

J. MINER: And as far as the time lag for a second sample set, since it's already on contract, all we have to do is add money. And as Marian said, the process of doing the samples themselves does not take long at all.

M. STOTO: Okay. Well let's — first of all, thank you. Let's wrap this up with the idea that we really think this is important work that's being discussed here, and it has the potential for a lot of valuable information, and that we just need to make sure that we do as much, we learn as much as we can from these 25 samples as possible, and that we want to get this reported back soon so we can think about what might — what might happen — what needs to happen next. Did you — David, did you ...

D. JOHNSON: I think we've covered this pretty thoroughly, but ...

M. STOTO: Yeah.

D. JOHNSON: ... I think we should thank you for looking at viability. It's a critical point; that it's not — that it's not — that you're not overlooking that and we are looking at it very closely. But it seems like this shouldn't be the first time that people have tried to determine the viability of specimens and it — there must be some standards or ways to do this; that it seems like we're sort of breaking totally new ground in our discussion here.

It seems there must be certain methods to try to determine viability for tests that haven't already been checked on the specimens. And I just wonder if that's — if that's out there? And that kind of goes back to my question before; has this protein been correlated with other findings? But I think we've probably talked about it enough for today.

M. PAVUK: Well, you know that some of those samples were viable. You know, some of the stored samples, you know, were sent like, for example, to CDC for dioxin for repeated measured analysis. And they were viable, you know, some of the stored samples. So that was, for example, done. But I agree with you; I'm not aware of it; there is some standardized methods of how you evaluate frozen samples.

There may be and we may look at it, you know, but it — there are some standard procedures like how you evaluate. Probably, you know, NCA has, you know, programs that collect and evaluate stored samples and probably they have some protocols of what samples are, you know, are good, or bad or not good. But a protocol that

somebody else developed for some other purposes is going to serve well for our purpose is another question. I don't know; I'm not a specialist whether there is some golden standard, you know, for evaluating frozen specimens for further viability.

D. JOHNSON: Okay.

M. PAVUK: Thank you very much.

M. STOTO: I think Karen is up next?

E. HASSOUN: Just one ...

R. TREWYN: She has a question.

M. STOTO: Oh, I'm sorry.

E. HASSOUN: I wonder if the samples that were collected from different people were from comparison or from the exposed groups?

M. PAVUK: They were randomly selected. It turned out there were three Ranch Hands and two comparisons.

E. HASSOUN: Yeah, but if you wanted to ...

M. STOTO: You have to go to the mike.

RECORDER: You have to use the mike. Thank you.

K. FOX: It was three Ranch Hands and two comparisons that were randomly selected. It was randomly selected and that's what came out.

M. PAVUK: Two Ranch Hands, three comparisons.

E. HASSOUN: Yeah. I thought that if we want to compare between — I mean, do serial comparisons, it's better that we base that on — or you base that on control or comparison groups because we don't know what the dioxin — if there is — what the dioxin will do to the proteins, you know?

M. PAVUK: Yes. At the same time, you know, you'll get a question, "Well, why didn't you look at the exposed group at all either?" You know, so you can't answer all questions when you get five-people group.

M. STOTO: Okay.

M. PAVUK: Okay.

M. STOTO: Thank you.

M. PAVUK: Thank you.

Air Force Health Study Closure Activities

M. STOTO: So Julie is speaking? Yeah.

J. ROBINSON: It's pretty straightforward. Obviously, we're going to close 30 — sorry — 30 September '06. What has happened so far is all my civilian personnel have been rifted. What that means of the seven, I've lost one coder. She's found a job. I have one statistician that also we hope will be placed soon and the other personnel that are associated with the study have elected to retire. They were in that status; that was an option open to them.

It's interesting when you try to prepare to close for a study that has another committee that is trying to provide recommendations on the disposition of that study. So in essence what I have done, have — I have, with my team, prepared to close the study as though there was not an Air Force disposition committee making some additional recommendation. So we're looking at the proper packaging and archiving of the hard copy records that we have on our participants and where they would go.

We have been making a very conscious effort of digitalizing all the hard copy data and we are also digitalizing the microfiche. If you've ever looked at microfiche, it's extremely hard to read and very tedious as well to look at. So we've been digitalizing those ones that are related to our study participants. Additionally, we have talked with, for instance, Armed Forces Institute of Pathology in regards to storage of specimens and I also have gotten costs on the disposal of those specimens depending on the outcome.

So I have kind of two tracks going along, you know: what is the Institute of Medicine going to recommend and then what would I do as though there was not that committee with additional recommendations? In regards to the two areas that were discussed indeed in relationship to the specimens, we're reorganizing them by individual participant and are well through that process and will have a single database with exactly the individual, how many specimens of each kind do we have there.

We're also seeking to have returned to us adipose tissue that was sent to the University of California at Davis and as well the dioxin specimens that CDC currently has. All those will be returned to us and archived. In relationship to the hard copy materials, the data files, we feel certain that we can definitely take care of the first two items, which is basically a data dictionary. But now with the additional information from Dr. Butler, we may actually be able to do all those recommendations prior to the closure of the study. That's it. Any questions?

M. STOTO: Questions from the — from the Committee?

R. SILLS: In terms of the hard copies, is all this information available in microfiche?

J. ROBINSON: No. The microfiche specifically are the — sorry — are the personnel records that as a military member you originally had on — these real little microfiche shows, you know, where you came into the Air Force, your records of assignments, of probably even your ratings that you got from your performance reports. But the medical records of the participants all have been pdf'ed. Thank you.

M. STOTO: Well, okay. Well, thank you very much. We're scheduled for a break at 9:45 and it's 9:45 more or less. So let's take a 15-minute break; we'll come back at 10:00.

[BREAK 9:48 A.M.-10:02 A.M.]

M. STOTO: We're going to start the meeting everyone. Please take your seats. Okay. Is everyone ready to get started again? Okay. I'd like to get started again. There are two orders of — two items on the — on the agenda right away. First, some people have come in since we started, so I'd like to ask them just to introduce themselves. You want to start? You need the mike. Does someone have the portable mike?

A. O'CONNOR: Hi. Amy — is it on? Hello? Amy O'Connor, IOM.

S. CHERUVILLIL: Sonia Cheruvillil, IOM staff.

J. COHEN: Jennifer Cohen, IOM staff.

M. PAXTON: Mary Paxton, IOM staff.

R. TREWYN: Got a lot of IOM today.

J. COHEN: Yeah.

M. BLANCAS: Manny Blancas, I'm a contractor with the U.S. Air Force working at Brooks City-Base for Project Management.

J. PETRELLO: Jaclyn Petrello, Exponent.

M. STOTO: Okay. Thank you, everyone. We have time scheduled at 11:15 for comments from the public. I just want to ask at this moment if there are people who are hoping to speak at that time? Of course, we'll ask again when the time comes, kind of just for planning purposes. Okay. Thank you.

Review of Previous Meeting Minutes

M. STOTO: And then the other item that I postponed earlier was the review of the minutes. In your — for the Committee members, your blue folder, there is a copy of the minutes. I think they were — they were e-mailed to everybody in the last week or so. And this copy reflects comments and changes that I made and I guess Julie made on behalf of the Air Force, which I also reviewed. And they were appropriate on technical grounds and didn't change the meaning as I remembered it nor do I think my comments changed the meaning. So are there comments on the meeting — on the — on the minutes, any — Ron?

R. TREWYN: I have one other major, major change. On page 11, third line from the top, I believe it's supposed to be "review of medical records or death certificates" not "of death certificates."

M. STOTO: What page?

R. TREWYN: Page 11, minutes. I think it's the minutes, yeah.

M. STOTO: What section?

R. TREWYN: Cancer.

J. ROBINSON: What paragraph?

M. STOTO: Yeah, what paragraph?

R. TREWYN: All right. It's under cancer, second paragraph, it starts with "The time of onset for veterans without cancer."

M. STOTO: Yeah.

R. TREWYN: And it was the sentence that reads “Cancer was determined by a review of medical records” or death certificates.

M. STOTO: Okay. Great. Thank you. Anything more substantial than that? Okay. Would someone like to move and second that we approve these minutes?

S. LEFFINGWELL: Move the minutes be accepted.

M. STOTO: Okay. Thank you, Dr. Leffingwell. A second?

E. HASSOUN: Second.

M. STOTO: Dr. Hassoun. All in favor?

RHAC MEMBERS: Aye.

M. STOTO: I think it seems unanimous. Thank you. Okay. We’ve done that now.

Review of the Air Force Health Study Comprehensive Study Report

M. STOTO: So next I think Dr. — that Colonel Fox is on — up to speak about the history and the — and the comprehensive study?

K. FOX: The Air Force Health Study history, that has just been let by contract. And what that is doing is looking from about the time from Buckingham’s book up to the completion of our study. It, at this time, it will be in an outline form is what’s been let to

contract and we're hoping that will be finished around February, middle of February. And then we'll see if we have enough time to flush out the full history.

M. STOTO: So who — has the contractor been identified for that?

K. FOX: Yes. SAIC has — will be the — Meghan's actually here that will be writing it.

M. STOTO: Okay.

K. FOX: She's been involved with the study for quite a long time.

M. STOTO: Okay. Thank you. Any other comments or questions on that or — go ahead.

K. FOX: The comprehensive study, it's gone through lots of names: longitudinal, summary study. The purpose was to document significant Air Force Health Study findings and we used from the physical examination reports, the technical reports that have been written and then publications — peer reviewed publications. And it was just summarized what we had found and that was given to you to review.

M. STOTO: Okay. So are — I mean, I know some of us have comments on that. Should we just go through that page-by-page?

K. FOX: That's fine.

M. STOTO: And our note taker will take notes on that. And if you feel compelled to respond now or later, you're certainly welcome to do that. So everybody got this a week or two ago and I propose that we just sort of start charging ahead on page 1-1

and see whether people have comments. But I have a number myself on the — on the beginning, but I wanted to give the Committee members a chance to do that. Maybe, I guess, let me add one more thing. I mean, some of my comments are editorial and I think it's probably not worth discussing it, but I could provide them to you afterwards.

K. FOX: Please do.

M. STOTO: More — it's more of the substantive ones I think that we should discuss here. Okay. Anything on page 1?

M. STOTO: One thing that I noticed is that at the — at the end of Section 1.1, line 16 and 17, you talk about the reports from the examinations and journal articles, but then the citations are only the reports from the examinations. And the journal articles come up sporadically throughout the report, but I think it would be important to treat them more systematically. I think we'll hear more about that from Ron later at that point.

I had — I had another comment on — in lines 19 and 20 is that the history about President Diem and President Kennedy. I suspect it's a lot more complicated than that and that the report would be better just leaving those things out rather than trying to sort that all out. I don't think that's necessary for this — for this one here about how we came to be spraying this stuff. Okay.

Page 1-2, any comments? Okay, 1-3 or -4? One of the points I made on page 1-4 I guess in reference to the first paragraph is that the — and this goes back to the previous point — is that these follow-up reports, the five-year follow-up reports should

all use the same statistical models — the same four statistical models, but that the studies in the — in journal articles often use different and sometimes more sophisticated models. And I think that's an important point to make here.

I think — I think there's a tendency for some people to think that these five-year follow-up reports are the study. And they're an important part of the study, but they're really not the whole — the whole study. Okay. Anything else on Section 1 that anybody has? Section 2? Let's start on Section 2. Page -1 or page -2? Maybe I should just ask does anybody have any comments on Section 2?

P. CAMACHO: Was somebody assigned to 2? Nobody did that?

M. STOTO: We were all assigned for these — the first four chapters. Well, I do; some of these things are editorial here. Okay. Let's move on to Section 3, was about interpretation. This is one where I probably have my most important — what I think is the most important point, is the use of statistical significance and so on. I mean, at one point we said that the plan was not to use that word at all, which I think was a bad plan and that — and in fact, it is used now, which I think is good. But I think it really needs — this section really needs to describe that more carefully.

In particular, what got chosen to be discussed in the substantive chapters is based in part on statistical significance, I think, although it's not really clearly stated there. And I think it really needs a good discussion about that. Others agree or disagree or — I mean, in — on page 3-3, line 82 and 83, there's a statement there:

"Some authors suggested that a statistically significant relative risk greater than 2.0 is cause for concern." And does that mean that you didn't discuss anything? That was, you know, 1.5? I don't think that's the case, but you know, that — that's basically the only thing that says what gets attention later on in the report.

And you know, another related area that we've discussed in the past is when there are statistically significant differences in clinical parameters where, you know, the difference is, you know, three parts per trillion or something like that, that doesn't mean it by itself is not clinically significant. And I think there probably needs to be some discussion about this section as well. So I think that's handled later on. Is that — okay. Anything else on Section 3?

Section 4 is "Illnesses Presumptively Recognized as Agent Orange-Connected." And this is the one that begins by having the list that the VA recognizes and then talks about, I think, the — I think the idea is that this talks about the findings from Ranch Hand, from the Air Force — from the Ranch Hand Study about those issues, which I think is a good thing to do.

But some of them, you know, acute peripheral neuropathy, chloracne, porphyria cutanea tarda all are things that are recognized, but have to occur within one year of exposure, which means that you can't possibly have found them in the — in the Ranch Hand Study which started ten or more years after the — after exposure. So I guess I —

I guess my feeling would be that should be noted and there's no point really discussing it here because that's — it's just logically impossible to find that in a — no?

K. FOX: Well, you could've done it with medical records review or for the chloracne if you — we looked at it and saw if they had scars in that distribution. So there are some things that we could've looked — we looked at. But you're right; it's a long time afterwards and we've stated that in the — in the chapters that it's involved with.

M. STOTO: I think it probably — it should be, you know, maybe one way of handling it here is to say, you know, there are — there's this one category of things that really would've had to occur before the examinations began and we looked at the medical records and didn't find anything. That's different from saying that, you know, we did the examination and didn't find it. That's a really, I think, a fundamentally different thing.

Another category is most of the cancers where there really wasn't enough statistical power to find anything in the Ranch Hand Study for these — for relatively rare cancers. So I think, you know, another — that might be another — can be treated as a group that way, you know, than focusing attention here on the things that were found, which were the neural tube defects, spina bifida and the — and the diabetes, I think, were the — I think that you said that you could really focus this on the important stuff,

the better off it would be. I'm seeing people nodding their heads positively. I hope that means — yeah?

D. JOHNSON: On the title of 4, what are you saying there? These are illnesses presumptively recognized as Agent Orange-connected in the study or just in ...

K. FOX: By the Department of the — Affairs — Veterans Affairs; this is what the Department of Veterans Affairs has recognized.

D. JOHNSON: Through the — from the data in this study? No?

K. FOX: From all data.

D. JOHNSON: I think that might be clarified a little bit in that title. Does this — does this almost make you think that ...

P. CAMACHO: It's really a — you might consider it like a quasi-legal definition. This — all this — this presumption comes from as much veterans' activity on Capitol Hill as it did from any study. That's a fact that should not be over- or under-recognized. That's what I've all been saying for years here; that, you know, this is — so much of this is an emotional, political stakeholders' issue and we — and the study should recognize that for the good and the bad sides and the up and the down sides, so ...

M. STOTO: I think that's appropriately handled in the text on page 4-1, but I think I like David's idea about putting that in the title.

D. JOHNSON: I mean, the title — I'm not — by looking at the title, I'm not — is that saying that it's — we've shown that it's associated or is it ...

J. ROBINSON: It's the ...

D. JOHNSON: ... it's recognized as Agent Orange-connected? I'm not sure what that means?

J. ROBINSON: We can change that to reflect that it's the Department of Veterans ...

P. CAMACHO: Affairs.

J. ROBINSON: ... Agent Orange Registry. These are the conditions that as a result of legislation, they are compensating veterans for.

P. CAMACHO: Yes. I mean ...

J. ROBINSON: Vietnam veterans.

P. CAMACHO: ... you don't have to agree or disagree with the decision that they made to recognize this scientifically; is that this has been recognized by the Department of Veterans Affairs as a result of Congressional action and then you're out of it. You're off the hook.

M. STOTO: Sandy?

S. LEFFINGWELL: Wondered whether "presumptively recognized" was the term of art? Is that what the VA calls them?

M. STOTO: Yes. Yes.

P. CAMACHO: Yes. To my — best of my knowledge, that "presumption" is. In other words, I'm a veteran. I'm saying I think this is because of Agent Orange. And

after so much political activity, and lobbying on the Hill and hearings, *et cetera*, *et cetera*, the VA came out and said, "Okay. We're presuming that's what the connection is." So I get treated or I get a disability based on the VA finally coming around and saying, "We presume this is a service-connected illness." But that adjudication came from the committee. That's a political process, not a — not necessarily a medical process at all.

M. STOTO: But it — but it is a term of art, that word.

P. CAMACHO: Yes.

M. STOTO: And it probably — actually it would be better if that word weren't in the — in the title. I think what this really is about is this is the Ranch Hand findings about the things that are on this list; that really is what this is.

P. CAMACHO: Which is a different story.

M. STOTO: Yeah.

P. CAMACHO: And just recognize it. The — you could have a sentence, "The presumption" — word "presumptively recognized" is the phrase utilized by virtually everyone: by the population at large, the stakeholder population at large to acknowledge that this is a Department of Veterans Affairs recognition that the veteran is presumed to have a service-connection illness.

M. STOTO: I wonder if this wouldn't be better actually as part of the conclusions chapter? The conclusions chapter is kind of thin now as it is and then basically, you

know, if you go through these — the chapters one-by-one, and then at the end say here's what we found, and by the way, here's how that relates to the VA list and, you know, you can say that — like I would start out with some of them — we just didn't have a lot of information about things that were on the VA list, but then where we could look at it, we found so-and-so. Ron?

R. TREWYN: I almost think you need it in both places. I think expanded in the conclusions, but it sort of sets context for some of the things that come later. So I think you need something early on so it — so it lays the framework that for the discussions later, but then maybe expanded upon. So it may be able to cut this down a bit, but then — and move some of it to the conclusions section. But I think you almost need this to set the stage for why some of these things were looked at.

M. STOTO: Or maybe it should be in the introduction then.

P. CAMACHO: Yeah. You said here the presumption by the Department of Veterans Affairs. I mean, if you want to put it in parenthesis this is — this is a presumption based on political action.

M. STOTO: Okay.

P. CAMACHO: I mean, I don't know how you say that carefully, but I don't think you have to. Basically, this is all — this was the result of political interest group activity. Am I — am I wrong? I mean, I don't want to ...

M. STOTO: That's not — that's not — it doesn't matter. Yeah.

P. CAMACHO: I'm worried about the "presumptively recognized" and why is that, you know? We're worried about ...

M. STOTO: Sandy?

S. LEFFINGWELL: What concerned me that was just that when someone says "presumptive," by loose association I think "rebuttable" and we're not rebutting that presumption here really. We don't have enough data. We're not supporting it, but ...

P. CAMACHO: When you say "presumption," most people or to me, I — "Oh, it's presumed that there is a connection."

S. LEFFINGWELL: Yeah.

D. JOHNSON: I just — what I thought was the concern was that this title doesn't clarify. You're talking about just those conditions that were identified by the — by the VA or are you talking — or does this report also support that these are all Agent Orange-connected? It's not totally clear in that title. Do you understand what I mean?

J. ROBINSON: We'll make the title descriptive of the chapter content.

D. JOHNSON: Of what it is, just so that it's clear what it is.

J. ROBINSON: Sure will. Thank you.

M. STOTO: Okay.

D. JOHNSON: I had a comment; this is minor. I don't know that you — I don't — this is minor; I don't know that it has to be made. It — but I looked at the chloracne since that was one of the sections that I looked at and it starts off on page 4-3. It says,

"Chloracne is a skin condition that looks like common forms of acne seen in teenagers." But you kind of leave out the fact that it actually has a typical pattern that sets it apart from teenagers.

And then at the end it says and it "usually persists for a maximum of 2 to 3 years." And I think that's after exposure has ceased. In other words, if exposure continues, it would go longer than that, but after two to three years after discontinuation of exposure. And those are minor points; I don't know if you want those or I don't know that those are critical, but ...

J. ROBINSON: We look at all comments.

D. JOHNSON: Okay.

M. STOTO: Yeah. I think that we should definitely communicate anything like that — those things to the — to the Air Force and if we need to ...

J. ROBINSON: If you ...

M. STOTO: If it — if it seems like it might be Committee discussion, we should talk about it now.

D. JOHNSON: Okay.

M. STOTO: How about that as a — as a decision rule?

J. ROBINSON: It's like the chapters that you reviewed for the Cycle 6 report.

D. JOHNSON: Right.

J. ROBINSON: You know, if you have something wasn't stated very clearly, or we need a comma or something like that, go ahead as you have in the past and just hand me ...

M. STOTO: Right.

J. ROBINSON: ... those comments.

M. STOTO: But if I have an idea that I think that Ron may disagree with, you know, I — we should discuss it.

J. ROBINSON: Yes sir, absolutely.

R. TREWYN: But I never disagree.

M. STOTO: Okay. Were there any other comments on Chapter 4?

R. TREWYN: I want to raise one question, but being agreeable while I do it. And it actually — the discussion that went on actually made me think about something that I realized I didn't see in here and I went back to the final report to dig the terminology out. It probably is, in fact, something that should've been in Section 2 or 3. But there is a statement in the final report under "Study Design" that says, "While Ranch Hand veterans spent most of their Southeast Asia service in Vietnam, comparison veterans spent on average less than 30 percent of their Southeast service in Vietnam."

And I think, it would seem to me that from a statistical standpoint for an epidemiological study that is a hugely important factor. That gets back to this "in country, not in country" of the comparison group that may help explain some of the

cancer findings when they're sorted differently. And I'm wondering if that aspect from the final report, "Study Design," should be somewhere in this one to set the context?

M. STOTO: It is somewhere in the beginning.

R. TREWYN: Yes.

M. STOTO: But it could be repeated in this section too, yeah.

S. LEFFINGWELL: In 1.3?

M. STOTO: Yeah.

R. TREWYN: In 1.3, yeah.

M. STOTO: But it may not be — it wouldn't be — hurt to say it here too, yeah. Now here's one of the things where I have an idea that I'm not sure everyone agrees with. In Section 4.9, and .10, and .11 and .13 where there are findings for prostate cancer, respiratory cancer, soft tissue sarcoma, we don't — this thing does not report a relative risk in any — in any sense or any kind of significance findings.

And you know when — basically when a report says there were two in this category, and three in that, and four in the other one and so on, and I don't know what to make of those numbers all by themselves. And I think I would be happier to see, you know, relative risk of this is, you know, 1.03 and the confidence interval is very wide or something like that rather than this.

R. TREWYN: Yeah. It sort of goes away from, again, going back to our earlier discussions. But I think if you don't have some context, some — to put it in, it is a little difficult to follow. I mean, I ...

M. STOTO: To give — to give the ...

R. TREWYN: Something along those lines, I think is a good idea.

M. STOTO: To give the raw numbers here, no one can really make any sense of these numbers just by reading them. You have to do some kind of calculation and you couldn't do the right calculation in your head and — yeah. Okay. And I guess I would — I would say the same thing about the diabetes. Now there's — obviously, there's lots of indicators of diabetes and I think I — for here, I would pick maybe two or three key ones. I don't know what they would be, but I would try to choose a couple ones that kind of made the case as clearly as possible and said that this was supported by other related findings. Okay.

R. SILLS: Only one minor point I would like to make. For example, 4.10 and 4.11 where you talk about respiratory cancers, in terms of a bottom line — bottom line, if it could be a little more consistency. For example, under "Respiratory Cancers," it says, "The evidence of an association, although not a causal relation, between dioxin exposure and the occurrence of respiratory cancers was considered "limited/suggestive" by the IOM Committee." And then they — then they talk about it a little more here, but there's no bottom line.

But in Section 4.11, they do the same thing and then you end with "This conclusion has remained unchanged in *Veterans and Agent Orange* updates." And maybe something like that should be added to 4.10 where you kind of conclude, "The conclusion remains unchanged for all *Veterans and Agent Orange* updates," something like that.

M. STOTO: And there was — there was one, the PCT, Section 4.8 where the point was made that it actually — the evidence level decreased over time and that ...

R. SILLS: Yeah.

M. STOTO: ... that's a — that's a — that was an important point to make, I think. Okay. Other comments on Section 4? How about Section 5? Section 5 is "Reproductive Outcomes" and we actually assigned somebody to that.

R. SILLS: So I was the primary person on that. I thought it was well written; introduction was well stated; the conclusions were pretty clear. The only thing that I would add is like Mike suggested, add a little more references. For example, on page 5-1, line 19 — or 18 and 19 where you say, "A series of journal articles were written based on the 1992 report." I think you should include references there so that one could cite those easily.

And similar on page 5-4, line 128, "The analysis for this report generated a series of journal articles on reproductive outcomes." We need to add the references there so one could easily access that. And I thought it was very clear that there was a lack of

association between dioxin and reproductive effects in males and females based on this write-up.

M. STOTO: Well, there's actually one thing that's missing; is that the results about spina bifida were significant and that's — yes, they are. And that's even noted in Section 4 and that was — that was one of the basis — that was part of the basis on which the IOM concluded there was a relationship with birth defects. It was four neural tube defects in the — in the Ranch Hand group and zero in the — in the control group.

W. GRUBBS: If you look at lines 106 ...

M. STOTO: I'm sorry?

W. GRUBBS: Mike, on line 106 to 110 is the discussion on spina bifida there.

M. STOTO: Right, that's why — and my note is that this is significant and I think that needs to be said. In fact, it is said on page 4-6. Well, maybe the word "significant" isn't.

M. PAVUK: If I may, if you would look at the actual paper, since there is zero and three, there was never really analysis conducted there. So the result was never statistically significant because there were no spina bifida in comparison veterans and the analysis in the paper was comparing Ranch Hands to comparisons.

So in that table in that paper, you know, there are no statistically significant, you know, there's no p value in that table. The numbers are so small throughout the table

and what stands out is that where you expect zero for Ranch Hands, you have three spina bifida. So I'm just trying to clarify what is in the actual paper.

M. STOTO: The fact that the test wasn't done doesn't mean that it's not significant and I believe that we actually looked at those calculations. And there are ways to deal with the zeros there and thought that it was a significant finding when we looked at it. And in fact, that is what is reflected in — on page 4-6. So I mean, maybe at a minimum, you could — you could repeat what's said on 4-6 here on page 5-3.

I mean, that's one of — in my mind, that's one of the most important findings from the Ranch Hand Study after diabetes and it's kind of swallowed up here. It's kind of buried here. Okay. And I mean, I — and I would also put that in the conclusion. I mean, that's not in the — of Section 5. It's — that's missing from the conclusion.

K. FOX: I guess I've got to go back to the "presumptively" word and all. What we found, it didn't meet statistical significance, so it didn't get included. But that's not to say that the — that additional information from other sources could make it that way. But our study did not find it that way.

M. STOTO: Yeah.

K. FOX: Because you ...

M. STOTO: That's a — yeah

P. CAMACHO: Since the test wasn't done, you cannot say that there was no statistical significance; say that the test wasn't done. Then at least you're saying it just

wasn't done. If somebody says why, because according to what I just heard, you felt that the number "n" was too small, and you couldn't get around that and just say what it is. That's there I, you know, because I'm sort — I'm a sociologist.

I'm sort of here in a way to — I'm trying to help you by saying I know what the rock throwers are going to say. And when they see that, that's going to — their eyes are going to open, get very wide and you want to — if you want to — if you say there's no real reason for them to get wide, they're just lay people, they don't understand, well, you better make it understandable to them. I'm just suggesting that because otherwise, people are going to jump on you.

M. STOTO: But this looks like you're burying a finding ...

P. CAMACHO: Yeah.

M. STOTO: ... and which is an important finding.

P. CAMACHO: And that's what you're going to be accused of. And if it isn't — it isn't the case ...

M. STOTO: Yeah.

P. CAMACHO: ... just say so. See, you have to — I would presume a hostile audience in a sense or one that — because there is so much suspect around the whole social science of this stuff, not your medical science, but the whole issue in which this study is always been involved in. So you — prevention here, prevent yourself from getting attacked. Say, you know, just — even if you think it's not worthy of it, prevent

yourself from getting attacked. That's what I would say to do. I mean, as an advisory board person, I feel like I should tell you these things. I'm sorry if you don't like what I say.

K. FOX: No. Thank you.

R. SILLS: So Mike, as you suggested, maybe, you know, after line 110, we could add the statement or modify the statement so it's really clear. From 4.6, line 188, we could say something that, "The result, along with two other epidemiological studies, led the IOM to conclude that there was limited/suggestive evidence of an association between exposure to herbicides and spina bifida in the offspring of exposed individuals, as reported in the 1996 *Veterans and Agent Orange* update. The conclusions remain the same in subsequent *Veterans and Agent Orange* updates," something like that to, you know, fall in line 110 of 5.3 — 5-3.

M. STOTO: Yeah. I think that would make sense to do that.

P. CAMACHO: But tell them that you didn't do the study. But the main point here that you didn't do any — really any testing on the four and zero. Isn't that ...

M. STOTO: No. I don't think that's the main point. I think the main point is that if you had done the test, that would've contributed to this evidence base that said there was — there was a relationship there.

R. SILLS: Yeah.

M. STOTO: I understand why they didn't do that test because the numbers were small and they had to kind of charge it through in a kind of standard way. But, you know, there are ways to say whether that's significant and that's been done. And I think that — I think that the way that Robert said it was a — was a good way.

M. PAVUK: I think I would just want to clarify; what I wanted to say was not that the test was not done. What I was referring to that the table as was presented in the paper that the sentence refer to, that that table didn't include those numbers. That doesn't mean that no testing was done. That's not what I was trying to say.

M. STOTO: Okay. Okay. And again, I would — I would just repeat the suggestion about including something about that in the conclusion of Section 5 too. Other comments on 5? Okay. Section 6 is "Mortality." Paul was the reviewer of that.

P. CAMACHO: And I had to look at it. And it's, again, to me, it's — this is my — I guess my theme song and I have said this at other meetings that we were at. People are going to look at this. Really, as I went through it, well, the first time it really shows up there is on page 6-3 at the bottom when you talk about "an excess of deaths from the digestive and circulatory in the ground crew on the higher dioxin level," but no association in the living. And then you talk about how it gets — but it shows up again: "The increase in deaths in Ranch Hand and from circulatory enlisted did." You know, it increased — 106, 107.

Then you talked about “found no difference in mean levels.” Already, a reader is going to say, “Well, you found a difference; now you don’t find a difference.” Remember who’s reading this thing. I don’t care about the — I know everybody says it’s for the scientific audience, but I’m telling you that a lot of people without any scientific knowledge are going to read this and they’re going to explode on you. And you’re going to have to — it’s this — honestly, I was talking to Dr. Trewyn about this.

Years ago — I’m going to digress here — years ago, a guy named Phil Goulding wrote a book called *Confirm or Deny*. He was an Undersecretary of State for the Far East or for Southeast Asian Affairs and Public Relations. And it was all around the Harrison Salisbury series issue and bombing in Hanoi and Haiphong Harbor. And Lyndon Johnson — the point was that Lyndon Johnson had been out there with his little catechism school pointer and pointing, talking about surgical bombing strikes, and no civilians were ever going to be impacted.

Well, a phantom jet at 600 miles an hour throwing out 500-pound bombs — be brief, continue, all right — but he set up in the public’s head that this was not going to happen; don’t — nothing to worry about. Along comes Harrison Salisbury, the only reporter in there. But he comes out with 22 reports in the *New York Times* saying that the United States and the Air Force are lying, and that they’re dropping bombs, and they’re killing civilians, and they’re blowing up hospitals, *et cetera*, *et cetera*, *et cetera*.

Now later, the government found out through Phil Goulding and other people that he was the only reporter there and he was the only — he never spoke Vietnamese. He didn't really know where he was and he was essentially feeding back press releases from the North Vietnamese Army. But too late; that's the whole point of Phil Goulding's thing. They set themselves up to be shot and they got shot. And then they complained, "This is unfair." But that's what's happening here.

I'm trying to say by analogy that's what's happening here. If I go down the "Mortality Update," no difference, no increase. But increase in digestive and deaths from circulatory among the ground crew, did you — no overall; yes for the ground crew. What was with the — what's the story with the ground crew? Did anyone follow the ground crew? What about at the higher levels for the ground crew? Was there a, you know, a — was there a better body count of how many guys were in this thing on the ground crew?

And when it said later down on the bottom, "no increase in the overall," "an increase in deaths was no longer seen," first thing that popped into my head and I know is going to pop into people's heads, "Oh yeah, of course not. They already died off." That's what people are going to say. Do you understand what I'm getting at? I'm not disputing the science here. It isn't a matter of science. It's what people are going to look at this thing, the way it's — so you have to have something in here about the

ground crew, and what happened to that and why did the numbers at the end — why it wasn't no longer seen?

If it faded out, you know, give an explanation for why this digestive piece faded out from the ground crew. Check all levels on the other there, the — around 137, "increase in deaths from circulatory disease in the enlisted ground crew that was reported in the '91 was still present, although no new circulatory degrees were reported." Check the levels; talk about what — how this is — seems inconsistent.

Somebody reading this is going to say, "Well, what's the story with the ground crew? Did these people follow up the ground crew?" And if you don't have an answer for that, they're going to say you didn't want to follow up on the ground crew. That's the first thing that they're going to say to you. I mean, I ...

M. STOTO: Maybe a way to address it is that there's really no conclusion to this chapter. This chapter — this chapter sort of goes through ...

P. CAMACHO: Yeah. I think you're making a good — the point I kind of wanted to get to. Overall, what about the ground crew? In the end, the diseases and five categories and — but in Ranch Hands was the — not statistically greater. Well, wait a minute. The disease washes out in all Ranch Hands. You can point that out, but you need a statement about the ground crew and something about the circulatory and digestive deaths.

You — I — because somebody's going to say, "Well, what's the story? Didn't you look at this?" I'm not trying to be a — I'm not a medical scientist; I'm a social scientist, in a sense, political scientist. And what I'm going to tell you is taking a look at this and that's what they're going to — first thing they're going to say. If anyone — any — if I showed this to any veteran out on the street who followed — or any member from the American Legion, VFW, *et cetera*, who's following this and is trying to, you know, always trying to get to the Hill on this, just this part, "Well, what about the ground crew?"

M. STOTO: I've got a more technical comment on this. Circulatory system diseases talked about increased and I think that probably means that it's higher; that the relative risk is greater than one compared to whatever the appropriate comparison group is. But I got that — I couldn't sort of rule out the sense that you didn't mean that the relative risk went up over time. Increase suggests time and I think that might be solved by actually using the relative risk in a confidence interval.

That's — you do give one relative risk and a confidence interval on page — on line 158 and line 159, but not for the one that seems important for the overall mortality rather than for the circulatory system. So I think that a more consistent use of, you know, reporting things in terms of relative risks and confidence intervals would help.

P. CAMACHO: Yeah, and again, yes, do that. And by all means please do — I want to say this gracefully — do yourself a favor and put something in this that explains

or shows how this ground crew phenomena is not a concern. Because if it is a concern, people are going to say, “Well, what did you do then?”

M. STOTO: Okay. Thank you, Paul.

K. OSEI: Mike, I think the point we’re making, throughout the whole, you know, document, we have a lot of numbers. I mean, it’s very difficult to follow the exact numbers: 188 people died versus 139. If you can translate that into other relative risk or percent, probably that will help, you know, rather than trying to recollect the numbers. The numbers are very difficult and I saw that more in the diabetes and the other sections. So just a — just a generic comment, but you know, how to really document the risk: low versus high and relative risk, yeah.

M. STOTO: I, you know, I should — I probably should’ve said this at the beginning. I think that writing a report like this is really hard, and I — and I — and I really think you guys should get a lot of credit for having done such a good job, and I’m — and I’m sorry I didn’t say that at the outset. So hopefully this is — these comments are taken constructively. Okay. Section 7 is cardiovascular and that is Kwame. Did you have a chance to look at that — at those? No, Dr. Osei?

RECORDER: Turn your mike on.

K. OSEI: You gave me number 9.

M. STOTO: Oh, I thought I asked you for both. Okay. Did anybody look at 7, cardiovascular? Ron?

R. TREWYN: There's one aspect that starts in — appears to start in Chapter 7 that carries through. I think for most other chapters that I did from doing 14, went back to see where this began. And I think it was in Chapter 7 where Section 7.1.1, "Chapter Structure," there are three paragraphs this chapter is written: the narrative, the results discussed and the '87 follow-up.

Those three paragraphs, any time there is a "Chapter Structure" section from there on, that's just repeated throughout. I would take that back somewhere into one of the early, you know, into the "Study Design" and plug that in or somehow; that restating those three paragraphs chapter after chapter, I think makes it more frustrating or whatever to read. I don't — it doesn't help — necessarily help clarify if somebody's reading multiple chapters, so ...

M. STOTO: And maybe they could be — say "please see so-and-so" for — because I know in every chapter for that ...

K. OSEI: Mike, the only thing I picked up was the — that chapter was supposed to be cardiovascular. But when I look at 7.11, you have kidney, urethra, bladder, x-ray abnormalities, so it doesn't fit. You know, we are looking at cardiovascular. I don't know how it even got there.

M. STOTO: That's a good question. That kind of has changed over the years, right? That probably is what that reflects.

K. OSEI: Yeah.

M. STOTO: But maybe the — maybe the title can be expanded to ...

K. OSEI: Yeah, if we ...

W. GRUBBS: Mike, line 57.

M. STOTO: Line 57.

K. OSEI: 57.

M. STOTO: Bill calls our attention to line 57.

K. OSEI: Okay.

J. ROBINSON: That was a special ...

K. OSEI: 57.

J. ROBINSON: That's the line that starts, "At the 1992 follow-up examination, a KUB x-ray assessment was accomplished." That's on 7-2.

K. OSEI: 7-2, but then we need to think about it, you know, "Cardiovascular Assessment," and I mean, then you have — you — genital, inclusion cardiovascular assessment and that's — it's page 7-11, 238, that's to 240, unless I'm missing something because you're talking ...

M. STOTO: I guess — is the point is that this KUB and any ...

K. OSEI: It's not a cardiovascular disease.

M. STOTO: ... and any other — so this is stuck here because it has no other home?

K. FOX: Right.

J. ROBINSON: Because it was only used to detect hardening of the arteries.

K. FOX: Detect hardening of the arteries, that's what it was used for. It didn't have anything to ...

M. STOTO: Oh, I see. Okay.

K. FOX: That's the whole — so we had to explain ...

M. STOTO: Yeah.

K. FOX: ... why are you — I have the same question. Why is KUB in this? And then we looked back at what they were using the KUB for and it was for the arteries, so that's the reason why it's there.

K. OSEI: Okay. Then, you know, I think we may have to rephrase that.

K. FOX: But we're looking at the hardening of the arteries ...

K. OSEI: That's what I'm saying.

K. FOX: ... for the KUB, which is part of the circulatory system.

K. OSEI: Yeah.

M. STOTO: Maybe ...

K. OSEI: You may have to explain that a little bit or retitle "classification" of whatever deaths that you're looking at and not get into the bladder and all that because it's out of place.

K. FOX: But that's what a K — we're just saying that KUB stands for what it stands for. And that x-ray that was done, what we were looking at for the circulatory

system was the hardening of the arteries that you can see on a KUB, nothing else. That's just what they were using it for.

R. TREWYN: Couldn't you have then just retitle that though as a — as that other analyses for hardening of the arteries and then put in your statement that this was a ...

J. ROBINSON: Sure.

R. TREWYN: Okay. So that way it ...

K. FOX: Okay.

R. TREWYN: You don't have the title looking way out of place.

K. FOX: Okay.

R. TREWYN: Okay.

K. FOX: We can do — we can change a title.

K. OSEI: Yeah. The title is off, yeah.

R. TREWYN: And then just a little — just a little bit of explanation ...

K. FOX: Explanation.

R. TREWYN: ... in there as to why it's done.

K. FOX: Okay.

R. TREWYN: Then it's very clear.

K. FOX: Okay.

M. STOTO: Okay. Any other comments on 7? Seven is the first place where the — this kind of standard table shows up too. On page 7-3, where you have basically

all the variables that you ever looked at, and then which the examination it was looked at in with a — with an X, and then the ones that were significant or something are bolded. And does that mean that if it were done six times that it was significant once, or all six, or enough to make someone think about it more or ...

K. FOX: It had it at least once.

M. STOTO: At least once.

R. TREWYN: Could the X, where it was significant, be bolded? Would that help? I mean, so at least you know if you've got one that goes every analysis across there for whatever ...

M. STOTO: And it would be a little bit more information there, yeah.

R. TREWYN: ... myocardial infarction, that if that was — just the X was bolded wherever it was significant, that at least would then give people an idea where to go back to.

M. STOTO: Yeah, or you might have like a, you know ...

K. OSEI: Asterisk or something.

P. CAMACHO: Or a new index.

M. STOTO: You might have a dot if it was tested and a — and a plus if it were positive, or significantly positive or something like that then. David?

D. JOHNSON: This was not — this was not my chapter to review, but I just — when I look at the conclusion, it's — I just wonder if I can ask somebody to clarify it. It

says, “After 25 years of observation, the prevalence of cardiovascular disease did not appear to be associated with dioxin exposure. Abnormal pulses,” *et cetera*, *et cetera*. “The increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand non-flying enlisted personnel, however, does point to the possibility of an association with dioxin.” And I just don’t — I — what does that mean?

R. TREWYN: It did, but it didn’t. No, it didn’t, but it did.

D. JOHNSON: I mean, was there a statistical association? Was there not one? What does it mean that it “points to the possibility of an association?” I — it’s not a very clear conclusion. Does anybody else know what that mean?

M. STOTO: That’s a good question. I — the other thing I notice is that there’s lots of bold things in this list of variables too for ...

P. CAMACHO: I don’t want to jump the gun, but when you — you’re going to have to have some explanation of that because that came up in a — in a later chapter I had to review. You have — if I look back at the table, I see bold. Immediately, I’m saying — and right above it on line 98 in the chapter because they showed a statistically significant result adverse to Ranch Hands.

Then I look at the table; I see all this. I see all bold, two non-bold. Immediately, if I’m a — if I’m a veteran or I’m a staff person on the Veterans Affairs Committee, I’m going to tell you what I’m going to do. I’m going to say, “holy expletive.” That’s what I’m going to say, right? I look at — just think about it; you said above it “statistically

significant results adverse to Ranch Hands." What the heck? That's all I'm going to say.

These guys aren't going to be going — I'm telling you, they're going to look at that and they're going to — all these things are significant and then they're going to go to that conclusion, but they're saying things aren't significant. They're going to go back to the table and they're going to go, "But you said you bolded these because they were." They're going to go back to the conclusion and they're going to go back and forth. I'm sorry if I'm not being helpful. I'm not trying to really be smart — "smarty pants" here. I'm just telling you that that's the kind of thing that ...

M. STOTO: Yeah.

P. CAMACHO: It's ...

M. STOTO: Is there a diabetes — potentially a diabetes connection here?

K. OSEI: Possibly, you know. If we get to the diabetes, we'll maybe talk about that. So there's the possibility of other things: hypertension, diabetes as a confounding variable. But I think this — what the argument is on this — the statement itself, you know, where they seem to go both ways.

And I think we need to clarify and if we show a significant increase, say so. It doesn't have to be dioxin-related, you know. They had to be in the war, you know. The process of going to war and being for 25 years probably could do that, so you don't have to necessarily tie dioxin to this. If it's not related, it's not related, you know. Yeah.

P. CAMACHO: Let me — let me put it another way to show you how serious I am about this Phil Goulding effect. If I was on the committee — somebody's got theirs on or should shut theirs off.

L. SCHECHTMAN: Can everybody shut their microphones on who's not speaking?

P. CAMACHO: Off.

L. SCHECHTMAN: Off.

P. CAMACHO: Off.

L. SCHECHTMAN: Not on.

P. CAMACHO: They're not on. All right. If I — if I'm on the committee — if I'm a staff person on that committee, I'm going to whisper into my member's ear to say something and it's going to be something like this. "Are these tests, carotid" — excuse me; I can't pronounce this — "diastolic, are these all health tests? Can you give me a simple answer?" I assume you're going to say yes.

"They all showed significance according to" — yes. "So there's a connection?" "Well, we don't want to say that." "Well, are they significant or not? If they're significant, tell me why there is not a connection that you say doesn't exist in the conclusion." Do you — do you understand what I'm getting at?

K. FOX: I do. And I think what would help is if we bold the X and you see that it's — only one thing is one — significant for one test and not any other time that you're

looking at it. Would that help? Because that's a lot of — unfortunately, that's a lot of what's going on here is when you look at the — when you look at the — we're only talking most of the time, except for diabetes where you then can continue to show '92, '97, 2002 were it. But a lot of these are just one-time examinations. It showed it was significant there, but didn't continue through and it was one time.

P. CAMACHO: Say that. Say that.

K. FOX: Okay.

P. CAMACHO: Say that.

M. STOTO: I think that would help a lot.

K. FOX: Okay.

M. STOTO: And I think that to support that what you need is in the chapter, what it is earlier where you — I was suggesting you talk about statistically significance, you have a discussion about 5 percent alpha levels means that when you do 1,000 tests like you've done here ...

K. FOX: Okay.

M. STOTO: ... you expect 5 percent of them to be positive even when there's nothing going on. That's an important point to make.

K. FOX: Okay.

M. STOTO: Yeah.

D. JOHNSON: And I just want to agree if you — to say that it was significant at one of the — one of the seven findings, but not in any of the others and so there was a lack of consistency to support an association, that is — it means a whole more than not saying it and ...

K. FOX: Okay. We'll — and that's really — that's where we came — that's what we were trying to say, but we'll put it in words.

M. STOTO: Okay.

R. TREWYN: One other thing though in the conclusion section — and I get back to the point that was made earlier — don't necessarily tie everything to a dioxin effect. And if you have an increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand non-flying enlisted personnel, nobody is going to look at that as being insignificant. These people died.

Okay, and so whether or not it's correlated to something else, if the Ranch Hand non-flying enlisted personnel, if there were more of those folks dying than the other of cardiovascular or whatever, I mean, that's something — you make that point. Okay. If you aren't certain of the cause, but I think it's critical so you don't — you get to this effect; that you are pointing this out very clearly that was a finding of our study; that in this group and whether you've nailed the cause or not, at least you've reported that there is a, you know, an increase in deaths and that's a concern.

D. JOHNSON: If I can follow up on that, see, I didn't know what this means when it says, "however, it does" — there's an "increase in the number of deaths." So are you saying there that there was — there was a — there's ...

K. FOX: Where are you?

D. JOHNSON: In the conclusion again — there was some excessive deaths, however, it did not reach the level of significance? Is that what is being — is meant to be said there or is it one of the situations where it just occurred one of the seven examinations? It's not really clear.

K. FOX: Okay.

D. JOHNSON: It'd be easier — it'd be better to state it just as it is.

K. OSEI: The other point, Mike, actually just to follow up on that, they have one-time abnormality, myocardial infarction. The question that comes up is what will the co-morbidity and mortality associated with that event, the MI? When they had it, did it make it or did not make it because that may change your conclusion that — and so that maybe explains some of the numbers, the confusion that we have here. And I think it's something you can look at, you know, whether they made it or not.

M. STOTO: I want to add another point. When you think about cardiovascular disease, you realize it's really a lot of risk factors, known risk factors for cardiovascular disease other than dioxin or service in Vietnam. And in fact, the statistical models that are used were primarily adjusted for those things. And I don't think — I'm not sure if

that point is made at all, but it certainly isn't made prominently. I think this is — that's an important point to make; is that you're really talking about results, I think, that are adjusted for known risk factors to the extent possible.

P. CAMACHO: So that you can refer to potentially confounding variables that are out there and make that, you know, make that as a part of your claim. And for me, it's like you've got to make it as part of your defense because when you point these things out, this is — this is through a number of chapters. I know it's — I'm going to say much the same things we've already said here about Chapter 16.

M. STOTO: Can we go on to Chapter 8 on dermatology? David? Oh, Sandy, did you have something else on this?

S. LEFFINGWELL: One more thought on this. If there's a need to prepare this for a non-technical audience as well, I wonder if a brief discussion of Phil's postulate somewhere in the first part would help explain why consistency is important?

M. STOTO: Yes. Okay. David, on Chapter 8, "Dermatology."

D. JOHNSON: I just noted on line 7, again, that chloracne may persist for almost — for most — for at most two to three years after discontinuation of exposure. I thought it was written — I thought they did a pretty good job here and I really didn't have any major changes with this.

M. STOTO: Okay. Other comments on Chapter 8? Great. Thank you. Chapter 9. Kwame?

K. OSEI: Yeah. Chapter 9 was very well done. Actually, the only suggestion I want to make would be on the diabetes part, which I — so far, seem to be the highlight of the day. If you could put this in a — even a bar graph to show the, you know, incremental prevalence from '82, '80, you know, '85, it would actually, you know, display precisely what you are trying to write in words, just add one figure to it.

I had a couple of questions about fasting urine glucose; 2 — 9.2.6 and 9.2.7, and I don't know what that means actually. At the baseline, it seems that dioxin — people with higher dioxin levels initially also had glucosuria. They have high prevalence of ...

M. STOTO: What lines are you referring to?

K. OSEI: 9.2.6, line 215, 216, 217, 218. Is that true that when they came in, if you had higher dioxin at initial period, you had a higher chance of having glucosuria?. Is that true even they didn't have diabetes or they had diabetes then? Yeah, and the same thing apply to 9.2.7. Yeah, because if they did — didn't have diabetes, it means the dioxin could be, you know, actually nephrotoxic; that they have glucosuria. It's a poison to the tubules, the reabsorption mechanism of the kidney.

And it's very interesting because that also relate to some of the high rate of diabetes as you move forward, so if you could clarify that. Yeah, and the only thing I would add again, we look at percentages of people who had developed diabetes rather than just the numbers. If we could translate that to the risk, relative risk, and percent of people over time who developed diabetes that will also help. Yeah.

And in conclusion, I think under the diabetes, I would suggest that we link that to the cardiovascular and that may help, you know, that the CVD increase may be related to other core associated conditions, such as diabetes. So you can, you know, you can put that in; that probably will help you, yeah, and sort of tie into dioxin.

K. FOX: Cardiovascular was controlled for diabetes.

M. STOTO: Turn your microphone on.

K. OSEI: Oh, it's controlled for diabetes?

K. FOX: Yes. Cardiovascular was controlled for diabetes.

K. OSEI: All right. Okay.

M. STOTO: Okay. So well, that's a point that needs to be made in the cardiovascular chapter.

K. OSEI: Yeah. Yeah.

K. FOX: It — the extensive control that we did for confounding factors needs to be pointed out.

K. OSEI: Right.

M. STOTO: Over and over again, you know, it's relevant. I had a — on line 489 and 90 in the conclusions there, it talks about they "showed a consistent and potentially meaningful adverse relation." I don't — I don't think there's any question about whether it's potentially meaningful. I would just say "consistent adverse relationship."

K. OSEI: And to kind of — the last conclusion, I think, 499, "Sporadic associations between dioxin levels and thyroid or gonadal hormone abnormalities appeared unlikely to be clinically important," I don't know what you meant by that.

K. FOX: Then when you look at FSH, and LH and that kind of stuff, it was — it was maybe one year and then it skipped a couple of years. Maybe in another year, it's again, it wasn't — the diabetes you can see it: '92, '97 ...

K. OSEI: Exactly.

K. FOX: ... and all, but you can't — you don't see it.

K. OSEI: Yeah. I would — I would not be — I would take it out.

K. FOX: Okay.

K. OSEI: Yeah.

M. STOTO: Of the conclusions?

K. OSEI: The last sentence.

K. FOX: Okay.

K. OSEI: It's not — the conclusion is good and you're going to modify it a little bit, but the last sentence is ...

K. FOX: Just take it out?

K. OSEI: Yeah. Yeah.

M. STOTO: Okay. Other comments on ...

K. OSEI: And the only other thing I want to say, you know, you've done a — the team has done a phenomenal job. Again, I agree with you, Mike, but when you try to explain everything and I think that's where you're getting into trouble. You cannot explain everything and this is a report.

It's a report of, you know, significant positives, significant negatives. And I think that's what you should be — not trying to explain every deviation, every fluctuation because it's just a biology, so you can't do all that. And I think if you can streamline what you want to say and, you know, so sometimes the strong, you know, weak; that's it.

M. STOTO: Yeah. This is an important principle, I think, really — that really goes beyond this one chapter.

K. OSEI: Yeah.

M. STOTO: And sometimes I think that you set yourself up for a harder job than you needed to by having a rule that says we're going to discuss anything where there's — that's been significant even once.

K. OSEI: Yeah.

M. STOTO: Because most of those things turn out not to be very meaningful and you kind of lose the real meaningful things in there. And so I guess I would think about moving in the direction where you say we looked at this, that and the other thing and we got some occasional positive things, but they looked — but it was only occasional and

we're really going to focus our attention on diabetes and a couple of other things. That's a — okay.

K. FOX: Well, we don't want to be also complained that we didn't address everything either.

P. CAMACHO: You will be. You will be.

K. FOX: So I'm damned if I do and damned if I don't.

P. CAMACHO: Yes.

M. STOTO: Well ...

K. FOX: Sorry.

M. STOTO: ... what you have to — but of course ...

K. OSEI: Give them the source, yeah.

M. STOTO: Those ...

K. OSEI: You can refer them to the source, you know.

M. STOTO: Yeah.

K. OSEI: But in the report — yeah.

M. STOTO: Everything — all these things have been published before. This is only a summary of the things that have been published before and the idea is to make a summary that focuses on the things that we think are meaningful and reports that other things were looked at.

K. OSEI: Yeah.

P. CAMACHO: Or you could divide it in — divide that, sort of talk about the things that showed up significance. Everybody's got their "back to the mike disease" again; you should shut those off if you're not talking because otherwise, it's ringing. But it — the point is if you put — if you put in one side, okay, these were the significant things, but we want to be able to say that we covered everything, but they weren't consistent and the real focus is on — so you have the significant, but lack of a better word "trivial" here. And then a section, significant and not so — not trivial at all here.

Then you might've covered your — but I feel like a referee in a boxing match and I feel like telling the Air Force, "Protect yourself at all times. Don't drop your guard down." That's really — that's what I'm going to come up to when I get my shot at this and throughout this thing. And — but I — and also I feel like I'm a little — I've been saying this for about several — couple of years now, you know, with this thing.

But no matter what happens, no matter what you think, people are going to take this thing and they're going to just go through it like Sherman through Georgia with whatever knowledge base they have. And it's probably not going to be a very big knowledge base, so you have to protect yourself. The Air Force has to protect itself at all time. Am I right, Dr. Stoto, on this thing?

M. STOTO: I don't think anybody's disagreeing with you.

K. OSEI: Mike, also the — probably I don't know whether you can do it or not. There has to be a disclaimer in this report; that this report is from 1982 forward and had

no bearing because you did not study them prior to ‘82 so that there may be other events that’ll come before ‘82 that could have, you know, impacted on some of the results that you’re looking at. And get that out of the way so nobody comes to you and say, “What happened to ‘81 and ‘80, those who died?” So they don’t use this document to support that finding, yeah, and it needs that disclaimer in here. I don’t know whether it’s legal or not, yeah.

M. STOTO: Okay. David told me he’d like to go back to one of the earlier chapters.

D. JOHNSON: Could I ask ...

K. OSEI: Yeah.

D. JOHNSON: Could I ask a question about the conclusion on the dermatology? Eight-four, the last line it says, “The interpretation of the increased frequency of reported acne after service in Southeast Asia in Ranch Hand enlisted ground crew was observed, but is of uncertain meeting because secondary lesions that were observed” — meaning scars, *et cetera*, correct? — “revealed no association with herbicide or dioxin exposure.” What does that — you mean the distribution was not ...

K. FOX: That people that had secondary lesions did not — were not — it wasn’t associated with Ranch Hands or with the dioxin level.

J. ROBINSON: Here in background or both.

K. FOX: Yeah.

D. JOHNSON: So you're saying that those that had secondary lesions were not — they were not in the categories of exposure to dioxin?

K. FOX: That is correct.

D. JOHNSON: Okay. Okay. All right, thanks. So, okay.

M. STOTO: Okay. Now we'll jump ahead to Chapter 10. Dr. Hassoun? Oh, it's time for public comment. It's 11:15 now and this is the time when we announced there would be a public — opportunity for public comment. So I need to ask whether there's someone would like to comment? Okay. Thank you. Now, please go ahead.

E. HASSOUN: Yeah. The gastrointestinal is a well written chapter. I have a few comments or questions. If you look at the chart, you said that "variables appearing in bold type are discussed." The GG or the gamma glutamyltransferase has been discussed, but I couldn't find it on the chart. At the same time, the ...

K. OSEI: It's in there.

E. HASSOUN: Oh, 10- ...

K. OSEI: Yes, it's in there.

E. HASSOUN: ... 3, the one that I have — I mean, that I received, it seems like, yeah, it's different from the one that we received in the electronic form. That's the one that I received. It's not there.

J. ROBINSON: GGT?

E. HASSOUN: GGT.

K. OSEI: GGT.

J. ROBINSON: I'm looking at the one you ...

E. HASSOUN: Oh.

J. ROBINSON: ... received and it's right under "direct bilirubin."

E. HASSOUN: Okay.

K. OSEI: Yeah.

E. HASSOUN: Okay. I'm sorry. Yeah. Then for "prior hepatitis B," you discussed that and it's not in bold on the chart. "Prothrombin time" should be also bold because it's been discussed. And my other question would be about — would be the conclusion. Although the enzymes, there was not — the enzymes were significantly, or have been significantly changed, or ALT, AST, GGT.

Let me see which page is that; conclusion, liver enzymes, yeah, 10-11. "Analysis of" — lines 363, 364 — "Analysis of laboratory data indicated that dioxin was associated with hepatic enzymes such as AST, ALT and GGT, and with lipid" so-and-so. "Although hepatic enzymes showed" no — "an association with dioxin, there was no evidence of an increase in overt liver disease."

But if we look at the chart to other liver disorders, these are significant. The — what — first of all, I mean, what these disorders include? The chart in 10-3, there are other liver disorders and there is a discussion about other liver disorders, but I didn't know what these disorders are.

K. FOX: So we need a description of what we're talking about?

E. HASSOUN: Yes.

K. FOX: Okay.

E. HASSOUN: And if there is — if there are some disorders, there might be an association with the enzymes. I mean, you know what I mean? In the conclusion, there is no association. "There was no evidence of an increase in" the overt — "in overt liver disease." But if you define these disorders, there might be an association with the enzymes and the disease.

K. FOX: Okay. We'll add those.

E. HASSOUN: Okay.

M. STOTO: One thing that strikes me just now looking at these tables is that they're listed in alphabetical order, which I guess — I guess that makes sense for people who are trying to look things up.

K. FOX: We had arguments. You can dice and slice these tables any which way, and how we did it, and eventually we just decided we weren't going to win any way so we went alphabetical.

M. STOTO: I withdraw ...

K. FOX: But I agree with you.

M. STOTO: I withdraw that comment.

K. FOX: We — it had some lengthy discussions on how we were going to order this and it just decided that it was easier in the table just to go alphabetical. Then we tried to discuss areas that were similar in the chapter.

M. STOTO: Now shouldn't "alpha" be with the "AL's" or — okay. Dr. Hassoun was that ...

E. HASSOUN: That's all.

M. STOTO: Okay. Thank you.

E. HASSOUN: That's all that I had for this chapter.

M. STOTO: Let's turn now to, let's see, "General Health." Dr. Johnson? That's Chapter 11.

D. JOHNSON: I'll have to say that I reviewed this prior, but on this particular document, I haven't gone over that in detail. Can I — can I take a quick look at it here, the conclusion? I did skim this, I believe, sorry.

M. STOTO: Let me — I'll ask a question here about the body mass index in this one. I mean, obviously that's related to dioxin, but that's almost surely because dioxin depends on body mass index rather than the other way around.

D. JOHNSON: Right.

M. STOTO: Right.

D. JOHNSON: I believe that I recall that to be the only finding, but let — can — do you mind if we come back to this one and give me a chance to ...

M. STOTO: Okay.

D. JOHNSON: Can I briefly ...

M. STOTO: Okay. That's fine. So Chapter 12, Dr. Hassoun, "Hematology."

E. HASSOUN: Let me see. Again, it's a well written chapter except for the minor correction for absolute neutrophil. Neutrophils should be in bold and absolute, they're — both of them: the bands and the segs in the chart. But if you — if you — if we come to the discussion of that, I mean, you talk about absolute neutrophils. You didn't talk about the segs and bands. Can you have — I mean, it's either that you have both of them as one absolute neutrophils in the chart or you discuss them separately. That's all what I have with regard to this chapter.

M. STOTO: Okay. Other comments on Chapter 12? David, are you ...

D. JOHNSON: For 11?

M. STOTO: Are you ready to do 11 now or ...

D. JOHNSON: No. No, let me come back to this; just give me a few more minutes.

M. STOTO: Okay. You had your — you had your hand up. So let's move to Chapter 13, Dr. Leffingwell, "Immunology."

S. LEFFINGWELL: I didn't have any very profound comments on — I didn't have any very profound comments on that, which makes me wonder if I was just numb when I was reading it. On 308 — line 308 and 309, the phrasing of that confused me a

bit. I'm not quite sure what it's saying. I suspect there were no consistent findings to support the presence of an autoimmune disorder. The number of those tests don't have anything to do with ANA.

M. STOTO: Okay. Other comments from anyone else? Moving right along, we then go to Chapter 14, "Neoplasia." Ron?

R. TREWYN: Okay. I just have some comments on the first two pages and then toward the end. A few of these are essentially editorial, but I think it's just quicker to just get through them now rather than send them. There's some, in my view, some strange use of terminology in here and so I've tried to — tried to work on that. In the line 3, "Many types of cancer are thought to be related to," I'll give you three options other than "related to:" "caused by," "induced by" or "initiated and/or promoted by." Pick; "related to" doesn't tell me, you know, that studies have shown that they've been — they cause cancer or whatever.

So the next line, take out "exposure to" and then, "Although herbicides have been determined to be carcinogenic in animal studies," I think that will read much better. In the next paragraph ...

M. STOTO: It's "exposure." It's singular, so it should be "has."

R. TREWYN: You're taking "exposure to" out.

S. LEFFINGWELL: "Although herbicides have been determined ..."

R. TREWYN: "Although herbicides have been ..."

M. STOTO: Oh, I see. Okay.

R. TREWYN: Okay. Yes, that's ...

M. STOTO: Okay.

R. TREWYN: That was the point. It isn't the exposure that's carcinogenic. It's the herbicides that are carcinogenic, so that was — that was my point.

M. STOTO: Okay.

R. TREWYN: In the next paragraph, the first sentence, "Many studies," that makes it sounds like people have used humans as in the — as an experimental animal in these studies the way that's written. I think that first sentence in that paragraph could be taken out and modified to then just start with, "While the cumulative epidemiological data from human studies" and go on from there. I think that makes the point a little better.

Dropping down to line 26, the use of "behavior" in a few places here, I don't think it's behavior that's being described. So "In the Air Force Health Study examination reports, skin neoplasms were analyzed by diagnosis as malignant or benign. In particular" — then the rest is, at the end of this next one, "following four categories: all of them malignant, benign or skin neoplasms of uncertain or unspecified nature." Take out "behavior."

And on the next page, line 41, 42 — 41, change "behavior" to, for example," "characteristics were analyzed by" — oh, I — oops, my notes don't make any sense.

Okay. We're back to, again, the same breakdown of malignant or benign and then you've got these four categories again, so the same changes.

And then going over to 14 — page 14-10 or section whatever because on the bottom, it says 14-10. Line 309 to 311, it just seems to me that last sentence in from that publication, the point was made that they — by the authors — and I agree that the — one should approach this cautiously. But I think the importance was by doing the study in a different way, doing a different sort, they found some significant results.

I think just taking that last sentence, "The authors of the journal noted this," a lot of things are noted in the journal articles. I don't — I think that just says to a reader that you're trying to downplay that this was not a — an important study and I don't think it helps you to do that, so I would leave that out going back to my sociology colleague over here.

And I think, again, the conclusions could be strengthened a bit. If I go back to in the final report, a problem I had with the things that were put in the preface where it talks about the limitations, but it talks about that it did not account for potentially important risk factors. I think if one were to just structure this that "other potentially risk factors were analyzed in the publications, finding, you know, cancer effects," you know, something that leaves it. You've just talked about these three papers, two of which have some — show some cancer effects. So I just think it's the wording of that to make

it appear that you aren't trying to downplay or just making a broader statement about those publications. And that's it.

M. STOTO: I've got a comment on this cancer one. A number of the things on the VA presumed list, whatever that's called, are cancers. And I think that many of them, in fact, are too rare to really have a good enough power to detect in this study size. And that may be — it probably would make sense to measure that — mention that here in this chapter even in — even in the conclusion.

R. TREWYN: Good point.

M. STOTO: I don't know whether that's true with respect to prostate cancer though. It's not true?

K. FOX: That's not rare.

M. STOTO: I know it's not rare; that's why I'm asking the question.

K. FOX: Yeah.

M. STOTO: I mean, has any — has anyone looked at a — is there a ...

R. TREWYN: The 2004, I think, one of the two papers.

K. FOX: Yeah.

R. TREWYN: The most recent one showed the ...

K. FOX: Showed prostate.

R. TREWYN: ... statistically significant increase in prostate.

M. STOTO: Oh, it does? Okay.

K. FOX: Yes.

R. TREWYN: Yes.

M. STOTO: Great.

K. FOX: Yes.

R. TREWYN: That and melanoma.

M. STOTO: Fine. Paul, you — turn on your mike.

P. CAMACHO: The paper — when you — what did you just say? A paper from this — one of the findings from this study that shows it is significant, but it's not in this — it's not in this chapter? Is that what you just said?

R. TREWYN: No.

P. CAMACHO: Okay. Okay.

M. STOTO: Actually, Section 14.5 talks about high PSA levels, significant and so on. And then Section 14.3.2.6 on the top of page 14-8 is about prostate cancer.

R. TREWYN: No, it's in the publications.

K. FOX: It's 14.6.1, 6.2 and 6.3.

P. CAMACHO: If I could, you know, again, but it's not in the conclusion? I mean, you don't make a definitive statement in the conclusion that there is some connection?

M. STOTO: I mean, I think — I think this really does need to be in the conclusion.

P. CAMACHO: Yeah, and you got that pesky ground crew again. They show up all over the place.

M. STOTO: But I think that the point for the conclusion is that there really are a couple of cancers that are raised to a level of suspicion because of the VA presumption and that and you ought to say what you found about them, you know. Some of them you — the sample size just wasn't big enough to say anything and say that.

P. CAMACHO: Yeah.

M. STOTO: And some of them you actually found positive results and I think that's important to say too. That's what conclusions are all about really is ...

R. TREWYN: Well, and it's going to get back to the point of when we were discussing the final report; of the issue of by not including the most recent 2004 and now 2005 publications, the information in those where by doing spraying days, whatever, various other parameters that you wind up finding significant elevation in cancers.

And I think this gives you an opportunity, especially since you had just cited those 2004, 2005 articles here, to at least make the point in the conclusions because here is your opportunity to say it's a reason why this data needs to be maintained. So then by looking at other diseases with these sorts — by sorting somewhat differently, not necessarily the parameters that have been used throughout, but it gives you the

opportunity to find some significantly increased changes. And so I think this is the place to make that point.

M. STOTO: Okay. Thank you. Other comments on Chapter 14? How about if we turn to Chapter 15 now? Dr. Sills and "Neurology."

R. SILLS: I thought — I thought this section was well written. I think one of the things we need to add to this section in the introduction is a statement that "there were adjustments for other known causes of peripheral neuropathy, such as diabetes." And I appreciate the staff adding a point in the conclusion on page 15-11 where they said, "The authors stressed that cautious interpretation of these results was appropriate until the relationship between pre-clinical diabetes mellitus and peripheral neuropathy has been further evaluated."

One of the things that I worry about is, I think as Mike has alluded to this, is capturing the major issues in the study, so peripheral neuropathy is a big issue in terms of dioxin exposure. And I think it's captured, for example, in the section on — Section 4 where you talk about "illnesses presumptively recognized as Agent Orange-connected." Now when you come to the conclusion of this paper, we make statements like, for example, "Increased risk of peripheral neuropathy has been somewhat indicated in the — in those personnel with the highest levels of dioxin." This is conclusion statement, page 15-11, lines 363 to 364, 365.

And then you went — you went on to say, “Some indication for an association with probable peripheral neuropathy was found in the 1985, 1992 and 1997 follow-up experiments.” The problem I’m having here is we’re saying it in the conclusions, but when you look at Table 15-4 and you look on the “possible peripheral neuropathy” which is at the bottom, there’s no data that show — that matches with what were you saying in the conclusions. So there are no X’s here and this is — this is an important finding in the study.

And so here under, you know, I mean, it’s just “polyneuropathy severity index,” maybe you don’t have that data. But somewhere along the line, we need to say that, you know, you know, here, this is an indication of peripheral neuropathy. We’re saying that, you know, in the conclusion, “Some indication of an association with probable peripheral neuropathy was found in the 1985, 1992 and 1997 follow-up experiments.” But when I look in this table, I see no data in those brackets where you talk about peripheral neuropathy.

And so maybe you should explain that. It’s — this is on 15-4 at the bottom. And so I, you know, I mean, that’ll be helpful that somewhere or another we emphasize the major points in the study because here’s this table right here with all these X’s. And so my question is why isn’t there more information on the peripheral neuropathy, which is the most important finding in terms of neurological diseases? And so I don’t know if the staff could help us a little bit with that?

And then the conclusions, one of the things in terms of editorial — in terms of editorial — in terms of editorial comments of how you — how you conclude statements or how you talk about journal articles versus the reports, I'm not too sure you need to say — you need to say this: "In a" — "In a 2001 journal article, Michalek, *et al.* and colleagues performed additional analysis." I think you can just say "Michalek, *et al.* and colleagues performed initial analysis" and just cite it. I don't think you always need to write, "In a" — "In a 2001 journal article," this is what it performed. You can just go ahead and say that "Michalek and colleagues performed additional analysis" and this is what was found.

So I looked at the Section 4 where we talk about the diseases associated with dioxin. Then I read the section on peripheral neuropathy and which is an important issue in the study. And then when I came to the conclusions, there was nothing on — conclusions which is Chapter 19 — there was no discussion on peripheral neuropathy.

There was no — there was — there was no discussion about, you know, these are early onset. These were — this, you know, these, you know, in terms of dioxin's a peripheral neuropathy. And I think we really need to pull out the major things in the study. And I know we haven't come to the conclusions, but in the conclusions, we need to pull out the most critical aspects of the study. And there's nothing written on peripheral neuropathy in the conclusion and it's an important finding in Vietnam veterans.

M. STOTO: Yeah. I want to support that. I mean, that's the first of the things on the VA presumed list, except that it's acute, and so that needs to be explained.

R. SILLS: Right, and so I — I'm like you, Mike. You know, I mean, and that's where we need the staff to help us to help interpret that ...

M. STOTO: Yeah.

R. SILLS: ... in terms of the audiences; is peripheral neuropathy is something that's well known in terms of dioxin. And so in terms of — in terms of the conclusion, there needs to be a paragraph discussing that, you know, this is an acute effect. We didn't see it in this study or, you know, because, you know, the studies were conducted later. But there's all this presumptive evidence and have a discussion about that.

M. STOTO: Yeah, and probably also the relationship to diabetes too needs to be ...

R. SILLS: Has ...

M. STOTO: It needs to be reminded about that and how that was controlled for or not ...

R. SILLS: Precisely.

M. STOTO: ... or whatever.

R. SILLS: And see, we ...

M. STOTO: Yeah.

R. SILLS: ... also need to add in the conclusion.

K. OSEI: Also, maybe Bob, you can help us out. The last sentence, "The composite indices for assessing neuropathy, however, were weak and did not show the same association that were present in the analysis of 1997 follow-up examination data." What were you trying to say?

The last — 378 and 77 to 379 because you have a — 375, you made a bold statement that you have "increased risk of abnormal pinprick examination absent patellar reflex," which are, you know, evidence of some neuropathy. Then the next sentence, you know, talk about the fact that there was no consistent association. And I think this is what we see throughout the whole write-up, trying to explain each one and each event rather than focus on what you found at the end of the day. Yeah.

M. STOTO: Okay. Other comments on this chapter? I'm just looking at the time and the agenda. And it turns out we do have a public comment, so what I would like to do is to finish up this — reviewing this and then break for lunch.

K. OSEI: Okay.

M. STOTO: And then come back, and do the comment and the other things ...

K. OSEI: Okay.

M. STOTO: ... after lunch with, you know, a working lunch if that's okay? Okay. So then now let's move to Chapter 16, "Psychology." Yeah.

P. CAMACHO: I — well, we'll go — we'll do it. I'll try to do it fast. This thing is, again, this thing is — you're in trouble. If I look at the — let's — I'm going to try to go to

the bottom line and then I'll go back. And I really, I'm pointing this out to you because I'm going to give you my reaction exactly what the community's reaction is going to be.

If I get to the very bottom line of 437, "In summary, there does not appear to be any clear evidence of disorders or syndromes that can be associated with exposure to herbicides and dioxin." My — when they get to that conclusion after reading this, their jaw is going to drop. I ...

RECORDER: I'm sorry. Where are you?

P. CAMACHO: No, I'm talking about conclusion.

M. STOTO: The conclusion.

P. CAMACHO: 16-12, I have here.

M. STOTO: Section 12 on page 13.

P. CAMACHO: Oh yes, page 13, Section 12. All right. You see the conclusion? The last — basically the last two sentences or the last sentence: "In summary, there does not appear to be any clear evidence of disorders or syndromes that can be associated with exposures to herbicide and dioxin." All right. May — can I — should I go? Okay.

I cannot see how — see, first of all, I just wrote the stuff down. I can't see how you get to this conclusion given the prevalence of higher scores in the majority of all the scale measures, particularly when in the introduction you say only — you only discuss the pertinent findings. You realize how many of these things — and it's a scale. You

might want to say where on the scale: low on the scale so you wanted to dismiss it or high on the scale.

Do you know how many times you're saying the word "greater prevalence," or "higher scores" or "higher than average scores?" You use that in all these tests. It's throughout the entire chapter. People read — if it's — it frankly, reading the thing, you'd say, "My God, these guys are in serious trouble." Look at — just look — grab some of these and then notice you got — then is — I — here's another question. I'm trying to get rid of this stuff and to get to the main stuff.

Is education being used here as a confounding variable or is — do you think it's — is it being — I get the sense that it's put out there and it's left for the reader to decide whether this is a confounding variable or an implied factor in saying why some are showing more symptoms than others. So that's one piece; then there's another one, but let me — let's go down.

The "Chapter Structure" stuff, the Cornell Index, ten scales; the medical index, three scales; alcohol dependence, well, I mean, that's the other thing. Is alcohol — are you saying that's a confounding variable, or you're trying to — are you implying or is just left up to — for anybody to guess, or you're saying that this is possibly an outcome of the exposure? I wouldn't — I would think you're saying it's a confounding variable. I mean, alcohol dependency has plenty of things to bring that up besides exposure.

And MCMI, 20 scales; MMPI, 14 scales; others; question; these are the bolds. You get to the sleep disorder, and you have a couple and then you have the unbolded sleep disorder. So you have — like that's opened up, but the scale measures, what were these scales? That's collapsed into just those scales.

Ranch Handers showed higher things. All right. Let's go through the — I said the education with that pesky enlisted ground crew shows up again and nobody explains that piece. I mean, I'm being — I guess I — and I'm not trying to be too — but I'm a — I'm a former enlisted man; that's why I'm bringing this up that ground crew shows a higher prevalence of things.

Now is the education thing the lower thing? What about higher levels? Did the high levels did not — low dioxin category implies that there was a high dioxin category and those guys washed out? What happened to the guys on the high? The sleep problems, then we get to the Cornell Medical Index: "scatter of complaints, the A-H subscore" — 127 — "a measure of scatter complaints indicating a diffuse medical problem, although other interpretations were possible."

Was this significant and do we list them? If so, are you obligated? And if other interpretations are possible and that negates the significance, are you obligated to discuss those? That's just a question. And then I said, "Ranch Hands" — I look at this, 131, "had a higher (adverse) average." Mike, I put notes, but the M-R score was normal? Did that — I don't get that; 135, 136, 137, the "20 scales was constructed as

an operational measure derived from a theory of personality and psychopathology." What theory? There's a gazillion theories out there. I'm a sociologist, not a psychologist, but what theory? Do you have an obligation to at least name it?

You know, and so you had six moderate down at the bottom: "Nine of the MCMI measures precipitated," *et cetera* and three other scales of severe disorder. So let's go through this. No ...

M. STOTO: Just a second, I mean, you've got lots of specific things and I don't know whether — I suspect you're not prepared to respond to these?

P. CAMACHO: I don't know. I'm just pointing them out. I mean, I don't — I just — I just want to point them out.

M. STOTO: No, I'm — I'd like to ask them a question.

P. CAMACHO: Okay.

M. STOTO: I presume you're not prepared to respond to them one-by-one right now?

K. FOX: Correct.

M. STOTO: Right, so the goal here is just to list these things for you to have a chance to respond to later.

P. CAMACHO: So to get through this more quickly then.

M. STOTO: Okay.

P. CAMACHO: Well, let's underline every — look at — look at the places. Avoidance scores, where did I — I'm almost — put on the avoidance other confounding variables in all of this: the dependent, a passive-aggressive, lifetime drink years earliest. The real part gets on page 16-7: "MCI borderline increased as the dioxin increased;" next, "higher average;" the next one, "increased;" the next one, "higher than average;" the next one — I'm now looking at line 206 — increased, "Ranch Hands increased;" score was also "increased in black Ranch Hands;" "increased as '87;" back to the next one on 217, "one of the three scales increased."

So in 18 scales of 20, there was an increase. But the conclusion said there's no — nothing to worry about. I'm just — let me go through it. I'm trying to save the Air Force here in a way; 18 — look at the Minnesota one. The same kind of thing: eight of 14 show an impact and high scores, high scores, high scores on almost all of these things; then back to that educational piece.

If I go to the next one, the serum and the MMPI stuff, I get confused around 273, 4, 5 and 6: "No positive associations between level and clinical elevations were observed based on the '85 follow-up. No association between dioxin and post-traumatic stress disorder, as measured from the MMPI." Well, you say that there, but we're back to the previous ones. I'm telling you that the reader is already predisposed to say, "What the heck's going on?" I'm just going to tell you that.

M. STOTO: Okay.

P. CAMACHO: All right, so that — I would go through this whole thing and be able to — I know you want me to end this as — be quickly.

M. STOTO: No, what I'd like you to do is to go through that in writing.

P. CAMACHO: You want me to get back and produce ...

M. STOTO: I mean, I don't think that — I think we can use our time more productively.

P. CAMACHO: All right. Fine, but my bottom line is if you walk through this and look how many — just count how many times "higher," and "increased" and "greater than average" is used. You — the average — the layperson coming to the conclusion says, "How can you say that there's no impact?" That's the first thing they're going to come to. It's impossible for them not to come to this conclusion because the conclusion on the last sentence does — makes no sense compared to what I just read. And that's what they're going to say to you.

M. STOTO: That's an important review and I think it really needs to be addressed very carefully.

P. CAMACHO: But I'll — yeah, I'll try to put it in writing. But I'm giving you the heads — the — I'm trying to do my job and help the ...

M. STOTO: No, I think that's — it's appreciated. I had one thing about this chapter. I noted that you often look at blacks and non-blacks here, which is unusual and they were in the report. I'm not sure if it appears in any other chapter.

K. FOX: It's that particular year. When you look at what part of it is that this is very limited, the values are only from, what, 1987. So you don't — there's a lot of these that aren't carried throughout and all, so it's only one time. And I'll have to tell you, that report looked at it a lot of different ways that we didn't continue on looking at it. So that's part of the problem; is that it's — we're citing a lot of stuff from 1987 that really did some subdividing of things. And when you lumped them more together, they weren't — it wasn't positive; it was only this. If you sort of ...

M. STOTO: Why ...

K. FOX: ... didn't look at this one thing ...

M. STOTO: Why does this ...

K. FOX: ... that's all we saw.

M. STOTO: ... not show up in cardiovascular? Did they look, or they didn't — they didn't find anything or ...

W. GRUBBS: It does for some.

K. FOX: On some, but unfortunately, when you look at what we looked at psychology and all, most of the ones that had all these things is 1987, which is the one that looked at it in a different — and subdivided it so much. And unfortunately, you don't — when you stop subdividing it and you go to the bigger group, then you're not seeing anything; that's the problem. So I think I have to explain that is what you're telling me.

Here is a unique study group that it's all positive because it's 1987 and we divided it up into small groups, but when you put them together and you — and all, it disappears.

P. CAMACHO: And then they're going to go, "You're damned if you do, damned if you don't." I know that.

K. FOX: Well, I already know that.

P. CAMACHO: I already said so they're going to say to you why wasn't it looked at ...

M. STOTO: No, that's not what I'm saying.

P. CAMACHO: ... in other — why wasn't the breakdown ...

M. STOTO: No, that's not what I'm — what I'm — what I'm saying is that, I mean, if it's — if it's there in the 1987 analysis and it's there kind of consistently across a number of different measures, that may be something worth thinking about. But I think you need to think about it in a different way and maybe you should, rather than sort of pull it out, you know, one place at a time and maybe you should say that, you know, in 1987, it was looked at. In addition, it was looked at, you know, broken up by race, and they found some interesting things, and here's kind of the general finding there, and then refer back to the 1987 report.

K. FOX: Okay.

M. STOTO: Because I think this here, this makes it seem more complex and more than it — than it is.

K. FOX: And I think that's what — yes.

M. STOTO: Yeah.

K. FOX: It's the way the 1987 came out.

M. STOTO: And that may or may not be meaningful, but that was presumably handled in 1987 and you can ...

K. FOX: Yes.

M. STOTO: ... go back to those conclusions.

K. FOX: And it kind of — some of the things that they pulled are risk factors that you would think about that increases some of the stuff so ...

M. STOTO: But race ...

K. FOX: ... social, economic, type of education all have some — are known to confound these things and so they subdivided it.

M. STOTO: Well, but this class of stuff is treacherous and I think you need to be careful in how you deal with that.

K. FOX: We'll try to explain it a little bit better.

M. STOTO: Sandy?

S. LEFFINGWELL: In the 1987 analyses, were there significantly more than five percent of the tests done positive?

K. FOX: I don't know. And I'm looking at the statistician and he's not sure either, so the answer is I don't know.

K. OSEI: The — Mike, the — I think the whole issue of race and ethnicity is critical, especially cardiovascular and diabetes, so we need to tease that out.

K. FOX: That ...

K. OSEI: You know ...

K. FOX: For those ...

K. OSEI: Yeah.

K. FOX: For those things, those are usually our confounding factors and so we do control for those.

K. OSEI: Okay, and I don't know how you can, you know, we say we can — do control for it. But did you really separate how many blacks were in the group that you analyzed versus non-blacks and asked that fundamental question instead of saying you "controlled" by what that specific analysis between blacks and non-blacks because of the ethnic and the genetic predisposition to the disease?

I don't know how you can control, you know, the genetic predisposition in the — in the — in, you know, statistically. And so the question will be blacks versus non-blacks, how many people had diabetes? How many had cardiovascular endpoints? And just look at that unless you say you don't have enough statistical power to look at that. And I guess that's the same here, so what did they look at?

M. STOTO: I think that when you say they're "controlled," that means that race was a factor entered into the ...

K. FOX: Yes.

M. STOTO: ... regression equation.

W. GRUBBS: Correct.

K. FOX: Correct.

M. STOTO: Simple as that, which is a — that, you know, that is one meaning of the word "controlled," but that's not ...

K. OSEI: But that doesn't ...

M. STOTO: Yeah.

K. FOX: I'm not a statistician. I can't definitely ...

M. STOTO: I mean, I think that's an appropriate use. But I think it's important to recognize the limitations of that and it's probably as much as you can do given — I'm sure that the number of blacks was relatively small in the — in the sample. Okay. Anything else on psychology? Okay, so Paul, really I think that writing that stuff out would be really very helpful. Yeah. Yeah.

P. CAMACHO: A one- or two-pager?

M. STOTO: Yeah. Whatever — however it is convenient. I don't know.

P. CAMACHO: Send it to you?

M. STOTO: Yeah, probably send it to Kim and then who'll distribute it. Yeah, maybe send copies to the Committee too. Okay. Yeah. Okay. It's almost 12:00, but I think that the next three chapters are relatively — are going to be brief. So let's go

ahead and do “Pulmonary.” David, you can also, if you want, also go back to the other one at the same time too.

D. JOHNSON: Okay. I noticed on — this is a minor thing on line 35, page 17-1. It says, “The IOM report consistently concluded there was inadequate or insufficient evidence to determine the existence of an association between exposure to certain herbicides used in the Vietnam War and non-malignant respiratory disorders.” Now when I read that, I’m going to — I’m right away I think that, well this — were there malignant disorders? Were there?

M. STOTO: Yes.

D. JOHNSON: There were malignant disorders, respiratory?

M. STOTO: Respiratory cancers.

D. JOHNSON: Significant respiratory malignant disorders? Because I didn’t ...

M. STOTO: I think it was limited suggestive for that.

D. JOHNSON: There was?

M. STOTO: Yeah.

D. JOHNSON: Okay. Otherwise throughout this, you know, for the different things assessed — asthma, bronchitis, pleurisy, pneumonia, hyperresonance, rales, wheezes, FEV, FVC, *et cetera* — there was a sporadic finding here and there. But I think in the conclusion in this case, it’s written in a way that explains that.

It says, the "Patterns that might be expected if there were dioxin or herbicide effects on the pulmonary function, namely consistent results across examinations, an adverse health effect for Ranch Hands or Ranch Hand enlisted crew, and adverse effects to Ranch Hands in the high dioxin category, were not evident. Sporadic and isolated effects were present in many of the endpoints examined, but there was no consistent evidence to suggest that herbicide or dioxin exposure was associated with ill effects on respiratory health." So that's what we've been ...

K. FOX: We'll try to repeat that.

D. JOHNSON: I think that needs to be — that needs to be used and hopefully, the layperson will understand that. It's clear to us and hopefully, that's understandable. For the "General Health Assessment," as you mentioned, the body fat was associated with high dioxin and that's thought to be not the dioxin cause in the ...

M. STOTO: So go back to Chapter 11 now.

R. TREWYN: Yeah.

D. JOHNSON: Go back in Chapter 11.

M. STOTO: Were there any other comments on the pulmonary ...

D. JOHNSON: Not from me.

M. STOTO: ... before we go on? Okay. Let's go back to 11.

D. JOHNSON: Okay. Again, like you were saying that the association with obesity, however, it was thought that the dioxin, not causing obesity, but the obesity

causing a retention of dioxin. And the conclusion, I think, states pretty much — this is pretty straightforward there. I mean, we found this; we found that. And in the conclusion, it brings out and restates the findings that weren't consistent. They weren't — where they were not consistent though.

But now on page — on line 83 it says, "At the 1992" — this was a good example of why you can't take an inconsistent finding and go make too much out of it. It says, "At the 1992 follow-up examination, the percentage of Ranch Hand officers who appeared older relative to his age decreased as the dioxin levels increased." So I would hope that people wouldn't take that to mean they should consume dioxin to maintain their youth — youthful appearance. But that, I mean ...

R. TREWYN: That guy in, yeah, in Europe, who — yeah, they've got — it didn't help his appearance.

D. JOHNSON: I didn't have any other comments.

M. STOTO: Yeah.

K. OSEI: Mike, the only comment ...

D. JOHNSON: My comments were pretty straightforward.

M. STOTO: Okay.

K. OSEI: ... Dave, was even the location where this "General Health" is placed, you know, when you talk about all the diseases. And then all of a sudden we get here and we have "General Health Assessment."

D. JOHNSON: Was that alphabetical?

K. OSEI: It's Chapter 11.

D. JOHNSON: Alphabetical.

K. OSEI: Alphabetical, okay.

K. FOX: Yeah, alphabetically.

K. OSEI: All right, because it just threw me off. I would ...

K. FOX: We could — when you think about this, again, multiple discussions as to how to organize this and we just decided the chapters would go alphabetical when we got into the organ systems.

D. JOHNSON: You could consider, make an exception for "General Health."

K. OSEI: Yeah, "General Health" ...

R. TREWYN: Yes.

K. OSEI: ... and everything else.

D. JOHNSON: You know.

K. OSEI: Yeah.

J. ROBINSON: We can put them anywhere you want.

K. FOX: If you want it in the front, that's fine.

D. JOHNSON: No, not necessarily, but that's so — it is kind of unique. "General Health" is just such a general thing that ...

K. FOX: Okay.

D. JOHNSON: And then you could — but ...

K. OSEI: Yeah.

D. JOHNSON: Okay.

M. STOTO: Okay. Thank you. And Sandy for "Renal," Chapter 18.

S. LEFFINGWELL: Yes. I think I had only two problems with that on lines ...

RECORDER: Microphone.

S. LEFFINGWELL: I had only two problems with that on lines 32 through 36. I just came away not quite understanding what I was being told and I can't offer any suggestions for fixing that paragraph. Even looking through the chapter later, I'm not quite clear what I was being told.

M. STOTO: Julie, you want to speak to the mike?

J. ROBINSON: In some of the chapters, there was, you know, people who were younger; people were older and it wasn't defined. And I don't believe anywhere in this chapter age is an issue, so it wouldn't be ...

W. GRUBBS: Line 63.

J. ROBINSON: Oh, is it? Okay. Yeah, younger non-black Ranch Hands, so that just explains to you who the younger Ranch Hand would be.

K. FOX: And the problem was the definitions changed due to the different examinations. And when there's a positive one, we thought you — we should explain what we meant by "younger" and so that's where that was coming from.

S. LEFFINGWELL: And then the only other area I had was in line 54. "More Ranch Hands had a higher average" seems repetitively redundant or something like that.

M. STOTO: Okay. I think what I'd like to do is break for lunch now, and come back and just spend a little bit of time looking at this globally, and in terms of the conclusion after we do lunch. We also will hear from Rick, want to speak on behalf of the — in the — in the public session. So why don't we try to pick up our lunches, and come back to the table maybe in 15 minutes and then we'll get started? Is that okay with people that we work over while we eat our lunch? Okay. So at 20 after 12:00, we'll get ready; we'll get started again. Thank you, everybody.

[LUNCH 12:05 P.M.-12:22 P.M.]

Public Comment Period

M. STOTO: I'd like to call the meeting to order.

R. WEIDMAN: Am I on? Hello?

M. STOTO: Yeah.

R. WEIDMAN: Madame Recorder, I left my card with you for the spelling. My name is Rick Weidman, Director of Government Relations with Vietnam Veterans of America. I've spoken to this Committee on behalf of Vietnam Veterans of America

many times, so I won't be redundant in most of what I've had to say before having to do with the design of the study itself. The — there are significant problems with that.

Having said that, I would draw your attention and perhaps the most important thing that can be done now and that this Advisory Committee can do and the Air Force can do is to follow the recommendation of the Institute of Medicine panel that in their most recent review that was an interim letter report that was delivered just recently.

In terms of translating the data now into a standard format in order to preserve that data for the future, number one, and number two, is to ensure that the samples, the integrity of the samples, chain of custody and the physical custody in the sense of freezer maintained, *et cetera*, are maintained while the Congress makes its decision and IOM finishes up their recommendations, this panel of scientists, in terms of making a recommendation to the Congress about the disposition of the study from this point forward.

I cannot stress to you strongly the obligation that the Air Force has to do this. It's — we have spent over $140 million on this. The public has invested this money — wisely or not, one can argue — but the point is the data belongs to the people of the United States and to be made available to reputable scientists, and scientific institutions and academic institutions across this country in the — in the future for further analysis and mining, if you will, of the data sets that exist.

The general comment — first a question I would ask and something that came out of the last Ranch Hand Advisory Committee was that there is an additional study being planned that would be a comprehensive look at the entire study, not just the segments, but the entire study. And let me ask you, is this going to then be that? But then it's my understanding the gentleman from SAIC who spoke up said that there was going to be an additional protocol developed. Colonel, can — or anybody from the Air Force, can you answer that question?

K. FOX: The comprehensive is the one that's in the — in your hand.

R. WEIDMAN: In my hand? Okay.

K. FOX: Yes.

R. WEIDMAN: Thank you.

K. FOX: And it's just, again, it's not — it's summarizing the — what we found in our portions of the study.

R. WEIDMAN: Okay. Thank you, ma'am. I would then follow through with a — with a general comment; is that the conclusions are not supported by the data presented. That is not the first time that's happened in the past 20 years in the interim reports and the — and the periodic reports issued by Ranch Hand. It, unfortunately, has been a pattern that VA has existed and all comments on Ranch Hand of conclusions are not supported by the data. And if you go back and analyze the data and what was actually there, the conclusions ...

M. STOTO: If you have specifics ...

R. WEIDMAN: ... are not supported. I under — I understand that, Michael, and I'm just adding to it and ...

M. STOTO: And if you have specifics — if you have specifics along those lines, I think that you should submit them to the Air Force with a copy to us and we can see whether we want to support them or not.

R. WEIDMAN: Michael, I will do just that and that length if that's okay with you, not only in terms of specifics, but in terms of general conclusions. The problem is from our point of view is that the press is going to read that bottom line. And it's very hard to convince our guys that it's the Air Force has not set out, and DOD has not set out and SAIC has not set out in order to deceive by the conclusions. Whether that's true or not, I make no judgment and VVA makes no judgment.

I'm just telling you that that's the perception that's going to be among our members and it is something — a real problem. Paul pointed it out a little bit before. I — but I'll strengthen that because I've got to go back and deal with my members and lay leadership. And they are going to say they're not telling the truth and that whether I don't — I personally make no judgment on that and our organization doesn't, but I will tell you that that's going to be the general perception in there.

There should be time now to correct that if, in fact, you put your mind to it in the last year, year and a half of the study. That's really all I have. I will follow up with that

written report as suggested by the Chairman and I thank you for the opportunity to present.

M. STOTO: Okay. Thank you, Rick. The first point about going back to the IOM report — which we heard discussed earlier, actually discussed a lot this morning — I think that what I heard was that our Committee supporting of it, being very supportive of it. And I think I heard the Air Force suggesting they were already moving to do many of the things that were suggested in that interim report. But maybe it would help actually to be formal and then just to indicate our Committee's endorsement of that — of that report. Is that — do you think that would make — how do people feel about that?

P. CAMACHO: I don't know if they came to a conclusion really. They came — they said that the Air Force should prepare the data ...

M. STOTO: But they came to ...

P. CAMACHO: ... and that they're looking at it.

M. STOTO: They came to a very specific conclusion on one of the five charges.

P. CAMACHO: Yeah, and that I'll agree with.

M. STOTO: Yeah. I mean, I'm obviously can't pre-agree to the other four. But for that one specific thing that we spoke about this morning and, you know, and we had the written report. How do others — how do others feel about that?

R. TREWYN: Well, I guess we've certainly made the point in the past that we support the retention of the data and the specimens for future use. And I certainly don't think, you know, so that would be ...

M. STOTO: It's consistent with what we ...

R. TREWYN: It's consistent with that, absolutely.

M. STOTO: Yeah. Okay. We probably should actually vote on this.

D. JOHNSON: Could you just state it once more clearly what we're voting on?

M. STOTO: I think that we would like to — the Committee would — endorses the findings from the Institute of Medicine's interim report and give the title and so on. Yeah, and I mean, that way we — we're not — I think it's important that we're — that we're saying it's their report and we're endorsing it. We're basically adding on to it rather than try to say we came up to those same conclusions ourselves. I don't — I think ...

R. TREWYN: I mean, perhaps we could say, I mean, most of us have not had a chance to read through the material that was left, but we heard the presentation. And I think the — that we could certainly be supportive of this effort by the Air Force to continue, you know, to follow through with what's been asked; that this is consistent with the long-standing stance of this Committee of the importance of retention and those sorts of things. So it just sort of maybe blessing, endorsing, whatever, this approach; that we are — we are appreciative of it.

K. OSEI: Mike, can I add? The other alternative would be to actually support the objectives, the five objectives that have been presented here for us and also the spirit of doing this. This is what we — where we — because we don't have the final, so the intent and the spirit we can ...

M. STOTO: Well, we've already — I think we already have done that.

K. OSEI: Right. Okay.

M. STOTO: But the issue is whether we want to endorse the specific conclusions with respect to one of the points.

P. CAMACHO: Like this conclusion ...

RECORDER: Turn your mike on, Dr. Camacho.

P. CAMACHO: Like this, see, we've got to be careful, I guess. Like this conclusion in bold on page 6, the Committee concludes that "the present state of the documentation or organization of the AFH medical records and other study data and laboratory specimens is an obstacle to retaining and maintaining these materials after the currently scheduled termination date." I — but that contradicts the notion of let's try to get these things in shape. I mean, I'm sure there might be an answer.

M. STOTO: No. No, it doesn't.

P. CAMACHO: I don't know. It's an obstacle.

M. STOTO: An obstacle, so something needs to be done.

P. CAMACHO: Something needs to be done about the obstacle. Somebody worried could say, "Well, the obstacle becomes a reason to jettison." I — I'm just — Rick just got up there and told you nobody's — trusts anything.

M. STOTO: Okay.

P. CAMACHO: So I — I'm happy to — I want to see the — I think all of us have gone on record individually and in the Committee, we gone on individually. We want to see everything done that can be done to make the study data available to independent researchers.

M. STOTO: That's different from endorsing the report. That is not what the report says. I mean, that doesn't — they're not — I don't think they're inconsistent with one another, but that's, I guess, I would prefer not to call the question if it's not going to be unanimous. Right.

R. TREWYN: Can I suggest something here? I believe because, as I recall, we were going to have some additional follow-up on what the Air Force is planning to do and we're going to get into an issue related to the very last point that was made; that additional funds separate from existing may need to be allocated to this so ongoing studies can continue. If that — and I don't know where that's going to wind up.

So maybe we could defer until the end of the meeting to see where — because I don't know what they're going to say. Whether they're going to cancel all the ongoing studies and put all that money into meeting the tasks that are laid out in this or are they

going to say yes, we're going to continue the studies that we've talked about already, *et cetera*? So ...

M. STOTO: Okay. So that's a — that's a fair point. So let's defer that until we hear the other reports on — from the Air Force.

Report on the *Nightline* Interview

M. STOTO: Ron, you're next on the agenda to tell us about your experience of being on TV.

R. TREWYN: I will make this very quick, very fast since I did stay up last night to find out what they actually did out of the — out of the material they filmed, how much actually got incorporated. And probably if any of the Air Force Study team viewed that, that they may have noted that I didn't have an awful lot of favorable things to say. I will say I did say a few favorable things, but those didn't make it into the edited version.

But a couple of points; one is, and I will go back to the — I have this down here — the "KGC" approach; that's the "kinder, gentler Camacho" approach that we've seen thus far today. Going back to our November meeting a year ago, clearly I had some specific recommendations on the cancer chapter. The Committee had some specific recommendations overall. In particular, I focused in on some of those in the conclusions.

We were told at the June meeting that most the suggestions were incorporated. That certainly was not true in the cancer chapter; editorial changes were made. It was also not true in the conclusions overall. A fair number of changes were made in the introduction.

But the arguments I think we were coming up with a year ago, had a lot of that information been put into that final report, we could've then — I could've then very legitimately taken the stance that yes, they've got new information by resorting, by analyzing the data in a different format than they had been up to this point. They are finding now new things and utilizing that as an argument to move forward.

As it was, I have to say that the — I've been very disappointed in the stance that was taken in this and I expressed it, so it was on last night.

M. STOTO: Any other — any response to that or other comments on this? Any other — either response to Ron or other comments about the show?

K. OSEI: I don't know anything at all on this. I don't understand what you're talking about. What was this about?

M. STOTO: Last night — last night, *Nightline* ...

K. OSEI: Oh, okay.

M. STOTO: ... did a show about the Ranch Hand Study.

K. OSEI: Oh, okay.

M. STOTO: Yeah.

K. OSEI: Okay.

J. ROBINSON: We did include your statement in the introduction in regards to the journal articles. The report itself was specifically on Cycle 6 examinations. We're writing the summary report to include a comprehensive view of what you're particularly interested in — cancer.

M. STOTO: Okay. Thank you.

Program Management Update

M. STOTO: Mr. Ogershok? Is there ...

K. FOX: It's Lieutenant Levy.

M. STOTO: Lieutenant Levy?

S. LEVY: I don't look like Mr. Ogershok. Okay, John? Mr. Ogershok can't be here today. He's the Program Manager for Ranch Hand down at Brooks City-Base, the Human Systems Group in Texas. He's unable to be here today for medical reasons, but he wanted to extend his greetings to everyone here, all the — yes, and the Committee.

I'm Lieutenant Susan Levy. I'm the Deputy Program Manager for Ranch Hand; I'll be briefing you today. I'd like to start by saying that the system — the Program Office, our Human System Program Office, we provide the financial and acquisition

support to enable the Air Force scientists and technical team to accomplish the protocol requirements and activities.

We've got three topics today to discuss: total costs for the Ranch Hand project, also the FY'06 budget, and FY'06 contracts. The total project Ranch Hand epidemiology study costs starting in 1981 were, including our estimated budget through the 30th of September 2006, is $139.5 million. This includes the 13,177 physical examinations that have been given, including all the participant travel, lodging, meals. It also includes all the data collection, storage, analyses, report writing and journal articles. So that's a lot of work for $139 million.

The FY'06 budget, it's going to include all kinds of intramural or in-house activities and also some extramural activities: our in-house activities, the routine activities, the data retrieval, storage, coding, scanning, analyses, medical records maintenance, writing, editing, not to be forgotten, Program Management.

And this also includes some other intramural activities: the mortality analysis and reports; the Congressional reports and briefings; final articles and technical reports; disposition of medical records, data and specimens; also the disposition of the equipment, the computers. Hard drives have to have Privacy Act, HIPAA data. And then there's also our extramural activities and which includes the tasks that we're placing on contract.

So for FY'06 contract efforts, we have our SAIC plan modifications. Those modifications include the longitudinal summary for Cycles 1 through 6; the study history; multiple analyte profile testing for specimen viability and relational information warehouse. We also have the CDC serum sample testing for dioxin congeners and other chemical measurements. So that's what we're doing.

The Ranch Hand Program Management, you know, is trying to do everything they can for the Institute of Medicine as far as our budget, finance and time constraints will allow us to.

M. STOTO: Can I ask what the relational database is?

S. LEVY: Do you want to ...

K. FOX: We'll be discussing that later on and ...

M. STOTO: Okay.

K. FOX: ... and the — what we're planning to do in the future.

M. STOTO: And the congeners is going to be discussed later on too, right?

K. FOX: Yes.

S. LEVY: Right.

M. STOTO: Okay. Any questions or comments from the Committee? So what about are we going to discuss the response to the IOM's suggestion that more money be added to do this thing?

K. FOX: That will come up when I — we tell you what we're planning to do.

M. STOTO: Okay.

S. LEVY: And we'll be talking about it.

M. STOTO: Ron?

R. TREWYN: I can at least say one thing, nice thing that I did on *Nightline* then because I was convinced by their crew that it was a $120 million study even though I had said up front it was $140. So I referred to it as a $120 million study, so I just knocked off $20 million.

S. LEVY: Even more work ...

M. STOTO: You saved the government $20 million.

S. LEVY: ... for $20 million less. Good job. That it?

M. STOTO: Okay. Thank you very much.

S. LEVY: Okay.

M. STOTO: Okay. So the next thing we have on the agenda is Karen to speak about the — Karen, the two things that I have left here don't sound like it's what you — what you just mentioned you're going to talk about.

K. FOX: No, because I have other things at the other end. I have some more stuff at the last — the latter part, the future ...

M. STOTO: Okay.

K. FOX: ... collaborations and all that. Yeah.

M. STOTO: Okay. I thought that we were — we were going to do that this morning when David was still here. But anyway, let's — we didn't, so let's move ahead.

Air Force Health Study FY'06 Activities

K. FOX: Okay. All right. On 6 October '05, I briefed the House and Senate Veterans Affairs Subcommittee. And the topics that I covered were the results of the 2002 follow-up examination results; the publications that we had done since the last time we briefed them, which was in January '04.

I talked about five publications, and then what we presented at scientific meetings, and how we were involved with this Committee, and then what we had been working with with the Institute of Medicine concerning the disposition of the study. And then I briefed them on planned research activities that we were having in the future. And it seemed — the presentation seemed to be well received and they invited us to come back at the end of the study next year. Any questions on that?

M. STOTO: Questions?

K. FOX: And then on 8 October '05 that same week, the Ranch Hand organization had a reunion down at Fort Walton Beach. They had about 50 participants — 50 Ranch Hand members and their family members present. And during their dinner, I briefed them also on what I had briefed — the same topics that I had briefed at the Congress and all. And I believe — what year is it that their reunion — next year —

next year is the 40th. Next year is the big time period for their reunion — the reunion. And I can't remember which year it was, but they're hoping to have a large turnout then.

M. STOTO: Okay. That's 40 years after 1966.

K. FOX: Yeah.

M. STOTO: Yeah.

K. FOX: Yes?

R. WEIDMAN: If it's okay with the Chairman, I'd just like to ask one question about their reunion, ma'am.

RECORDER: Please use a mike, sir. I've got to record every single word.

R. WEIDMAN: Thank you. Of those 50 participants who were at the reunion with their spouses and others, how many of those would be, in your estimation, enlisted versus officers, in other words, crew versus pilots and copilots?

K. FOX: I — I'm sorry; I really do not have an idea of that number in all.

R. WEIDMAN: Was it sponsored by the Ranch Hand Association?

K. FOX: Yes. It's the Ranch Hand Association's reunion that they have every year and down at Fort Walton, except when there's a hurricane that kind of takes care of a hotel.

R. WEIDMAN: But it — but it's always at Fort Walton Beach and in the same time period?

K. FOX: Yes. It usually is. It's always on that weekend.

R. WEIDMAN: Thank you, ma'am.

M. STOTO: Okay.

K. FOX: And the follow-up on the 2002 follow-up physical examination, it was officially result — released on 8 July 2005. We've responded to some numerous e-mail inquiries about it and it's available at this web site.

M. STOTO: Okay.

K. FOX: Okay, and I think that was — and do I keep on going? I'll keep on going. Okay. I keep on going. Some of the activities that we've got scheduled or that we've contracted, one is the Air Force history study and I've talked about that. It's looking at from basically when Buckingham's — from where Buckingham's book ended and two, concerning about the — how we formed the Ranch — Air Force Health Study and the history on that. And at this time, it's only on contract for outline. It is — does not have for it to be fully written so, and it's — the outline, we're hoping to be ready by the end of — the middle of February.

M. STOTO: So what does that mean? That the — that SAIC will prepare an outline and then what happens to the outline?

K. FOX: Now it's going to be a balancing of all the other things that we've got going on to try to see if we can make it happen. It's — the contract does have an option to go and complete the history. It's just that are we going to have enough money?

M. STOTO: I see.

K. FOX: So it hasn't been let out on contract, but it is a possibility and one that we would like to see done.

M. STOTO: Okay. Comments or — maybe we should hear about the whole range of these things and then see if there are ...

K. FOX: Okay. All right.

M. STOTO: ... more comments about the priorities among them.

K. FOX: And you've already seen the comprehensive study, which has had other words of "longitudinal" and all that. But the ...

M. STOTO: Right.

K. FOX: That is — you can see where that is at this time and we're still obviously going to take your comments. Collaborations: we've developed some new guidelines for collaborations, past and present, due to the fact that we're about to — the study is ending. And so we've put some time-lines down for our collaborators as to when we expect the paper, and results from our information and the stuff that they have to take.

We're getting — we're working with CDC in the dioxin congeners and Dr. Pavuk will give a lecture on that afterwards to show you the preliminary — what we have of 106 samples on that. UC-Davis was the adipose tissue and that has basically ended. We've gotten the last information from that. Texas Tech with Dr. Lynne Frame is

submitted three papers too concerning dioxin and insomnia, sleep disorders. And that's what's listed and that should be submitted shortly for publication.

We also have on contract a compliance study looking to see the factors that impacted study participation in the six-month — six follow-up examinations, and to analyze what made them come or not to come, and to see and maybe have an idea whether or not it would be feasible next to continue on to have another examination.

M. STOTO: Is that based on existing information or is it ...

K. FOX: It's based on existing information only. We are not going out and polling the members. It's just on what we've seen what's happened over time.

M. STOTO: Is that being done in-house or ...

K. FOX: SAIC has been contracted and we've been working — I — we — he's — Mr. Bill — Dr. Bill Grubbs will be visiting us next — not next week, but the week after to work some stuff out on that one.

M. STOTO: One thing that you might think about at some point is that the kind of analysis that you would do for this might also be useful to help you to adjust for the results for non-response. And if you could predict who comes — who comes and who didn't come, there are — there are methods called "propensity score" methods that actually allow you to say something about whether or not if the folks who came, who didn't come actually came, whether they — you would've gotten different results in the

end. Now that's further down the line, but I think that these — this could — this could be important for other reasons too is to — I guess the main point I'm saying.

K. FOX: And we're trying to. I think it's, again, trying to support what things can be done in the — in the future with the study.

K. OSEI: How long is that going to be, the follow-up? How long?

K. FOX: How long for ...

K. OSEI: The six follow-up visits, the physical examinations.

K. FOX: Together — when the report is due ...

W. GRUBBS: It should be done by February.

K. FOX: I believe we'll have it by — we'll get it by February.

M. STOTO: This is just a statistical analysis of existing data?

K. FOX: That is correct. That's all it is.

M. STOTO: All, yeah.

K. FOX: Analyzing what's happened over the last ...

M. STOTO: Okay.

K. FOX: ... the six cycles. Relational database: it hasn't been put on contract and with the IOM's report — let's go ahead and go into that. As Julie mentioned, we've had this report for about a week or so and we've looked at it. And we had a discussion with the technical staff and we think that for the most part, we can do almost everything that they've asked for and all.

Part of it is that the part that we're not positive about is when you put the whole code book that the big part, how they divided it up in the report, they said you need step one to be done, and then step two to be done, and then maybe you can get step three. Well, we can do — we're — we think we can do step one. We can do step two. Step three was a little bit this thought of this relational database.

What we're — it hasn't been put on contract, but it — what it was was going to be done in a step-wise fashion. We're now going to have to go back and look at this with the intent that I'm not sure that — we're not really positive that a step-wise method is appropriate and maybe trying to put more assets to making it all happen at once. And so that part is not — we're not positive. Trying to develop a database that has one, two — Cycles 1, 2, 3, and 4, 5 and 6 all together and that you can relationalize it. That ...

M. STOTO: So if I — if I — let me just make sure I understand. I mean, and you and the IOM agree that you need to find a way to make these data more accessible?

K. FOX: Yes.

M. STOTO: And that the relational database was your original idea, and they have — they have a new idea which may be overlapping with this or may not, and you're trying to think through how to achieve the goal?

K. FOX: Yes, and I — and I — so this — the relational database has not been put on contract yet. And now with the IOM, we're going to — we're going to have to go back into some discussion to see, but we're going to ...

M. STOTO: If there's a — if there's a different way of doing the same thing ...

K. FOX: Yes.

M. STOTO: ... essentially?

K. FOX: We think.

M. STOTO: Yeah.

K. FOX: So we need — we probably need to discuss with IOM a little bit more on if this would have met what they were talking about. But of all the things, the labs, we're already doing. Our plan was we were doing it already and we're going to continue on with it. And the parts that they said we were lacking, we think we've got the expertise now who know the history and will put it down in writing so that it can be used by other people.

M. STOTO: So maybe it would make sense to take this up again if we have another meeting ...

K. FOX: Yes.

M. STOTO: ... after the ...

K. FOX: Because ...

M. STOTO: ... full IOM report comes out and we can discuss it.

K. FOX: Yes.

M. STOTO: Yeah. Okay.

K. FOX: I'm just not ...

M. STOTO: Is that okay with everybody?

K. FOX: I'm not sure where this is going to go yet.

M. STOTO: Yeah. That's — so that makes sense to put it off a little bit, not too long, but ...

K. FOX: Yes.

M. STOTO: ... so people have had time to think it through.

K. FOX: Publication support: we were looking at these three. The — we did 16 nerve conduction studies on 30 Ranch Hand — well, 60 of the participants and we were just planning to do a short analysis of those in response to a previous paper that had been written.

"Dioxin and memory" and "dioxin and hepatic function," those again were — they're about to be put on contract. But it does bring to the point where we're going to be doing this database whether or not we can get to those at this time. And I can't tell you if we can do everything and all, so those are up for discussion right now. If I hadn't had the IOM, we would've been telling you that it would've been on contract, but the IOM has changed some of our thoughts.

M. STOTO: Can I ask about these things? Do any of these include contracting with Joel Michalek to help finish up?

K. FOX: No.

M. STOTO: Is that contemplated separately or ...

K. FOX: Things were contemplated at one time and it didn't work out.

M. STOTO: Okay.

K. FOX: But these are our — the nerve velocity conduction is with Dr. Alberts, who was on the previous paper. And the other two were on papers and they're going to follow the same gist of the previous papers and all to try to look at it with the new data that we have. In-house research, we have the mortality. We'll go through 31 December 2003 and all; is — we should be able to start that shortly with that data. We also have some collaborations with other researchers out there that we're working on. Yes?

D. JOHNSON: Could you go back to the previous slide?

K. FOX: Yeah.

D. JOHNSON: Can you go back a slide? Why did you — these are things — three different topics you're going to write papers on? I'm just curious. Did you pick those for a particular reason? Were there findings? Were there significant findings in those?

K. FOX: It was carrying on from previous reports that we had done and just to try to add, to complete the topic with the newest, the latest data that we had.

D. JOHNSON: Okay, so there — if I recall — I don't recall hearing any significant findings in these areas, associations here. There was?

K. FOX: I believe there was. And again, it's not — it's not from the report, but from the papers and all. And so we look at a little bit different, and therefore, there was some suggestions and that we thought to complete the study.

D. JOHNSON: Okay.

M. STOTO: It's based on part on things in the — in the literature from other authors as well then that you think that the Ranch Hand Study might contribute to?

K. FOX: I'm — I ...

M. STOTO: I mean, is it — is it because someone else has found something about dioxin and memory and you're — and there's an idea that the Ranch Hand Study might be a way to replicate that and ...

K. FOX: No, it was more from the fact that we had done a previous paper on it that gave some suggestions to it, and therefore, we were trying to complete the ...

M. STOTO: So it was ...

K. FOX: And because ...

M. STOTO: ... internally?

K. FOX: Well again, the dioxin, the memory wasn't done consistently over the study, so we have a — here's a time where we redid it again and we would like to analyze and compare. We have now two points to compare.

M. STOTO: Okay.

K. FOX: Mortality, we're doing that; and then we have some collaborations from other that are doing it; and then the viability study that we're — we've already just — we've discussed as some of the things that we'll be doing in-house. And then it leads to Dr. Pavuk talking about the congeners and what we've seen with the 106 preliminaries.

M. STOTO: Before you go away, let's see if there's any more comments on this '06 activities. Robert?

R. SILLS: Could you tell us a little bit more about the collaborations and what are some of the outstanding collaborations? I think in earlier slides, you talked about you had given colleagues or collaborators deadlines in terms of completing studies and I ...

K. FOX: To be honest with you, there's, that I know of, we only have about two. Well, Dr. Goff has expressed an interest in collaborating with us and also Dr. Boyle, so it's more people coming to us and all. And I'm not sure with our new time-line people are going to be willing to be able to work with us on this because we've asked for it to be done by the time we leave, we close the door.

R. SILLS: And then, you know, another point I want to make is, for example, the nerve velocity conduction studies. When we get that data, when it's published or, you know, when we have data from these types of studies, are we including that in our bottom line in terms of what it means in terms of health effects?

K. FOX: The comprehensive study is what it has in it and then we will continue to add data. But it will not be — there won't be another report trying to summarize that at the end, no. So the comprehensive study is what we've produced up to now and all. And if there's anything else published, it won't be in that and there's not a way to make that happen.

R. SILLS: Thank you.

K. FOX: But we'd like to get it published. And if we don't have enough time to get it in a peer review journal, we will at least have it done as a technical report so that it is available to people to look at.

K. OSEI: Do you have a publication coming to you that decides who your collaborators and potential coauthors would be?

K. FOX: Do ...

K. OSEI: Or do you have a publication coming to you for an — a — for the study where ...

K. FOX: No, we don't have any other than what I have told you about at this time.

M. STOTO: David?

K. FOX: Yes?

D. JOHNSON: It sounds — it sounds as if the Air Force Study we reviewed today is just — is not a final. It's a draft that you're going to be adding to it?

J. ROBINSON: It is a draft.

D. JOHNSON: And it doesn't ...

K. FOX: It's a draft.

D. JOHNSON: And there's really nothing on this report. It says a "November 2nd" report and there's nothing on it to indicate that it's a draft.

M. STOTO: It says "November 2nd," yeah.

K. FOX: Yes. We've noticed that it's been passed out, yes.

D. JOHNSON: Pardon?

K. FOX: We've noticed it's been passed out. It's a draft; it is not — no. It's — that's — it's for your — to get your input.

D. JOHNSON: Because you indicate you're actually going to add more information to it as well. No?

K. FOX: No, we won't.

D. JOHNSON: No?

K. FOX: It's what's covered now. It will be that's all. We will not add in any more so, but we will take your comments to change it, to modify it to try to reflect your concerns. And so I'm hoping that in the next couple of months, it will be published.

D. JOHNSON: Yes, the comprehensive report.

K. FOX: Yes.

M. STOTO: Okay. Ron?

R. TREWYN: I, at least since 1999, have at least once during every meeting had to point out the in country, not in country problems with the comparison group. And I understood from the last meeting that there are problems cleaning that up and sorting as to who was in country in the comparison group and who wasn't. But I think an important — we did talk at the last meeting about, oh, days of spraying, the time that they were in country, the period of service and those sorts of things.

When those analyses were done, we finally got to some significant cancer effects. Prior to that, there really had been none. We had talked about maybe utilizing that sort to then go in and look at birth defects, reproductive outcomes, whatever, and some other parameters. And I didn't see anything suggesting that was going to be done, and yet, that may be a way of sorting and getting, teasing out whether there really are some significant effects in other areas other than just cancer in this population. Is there any thought to move forward with those or ...

K. FOX: At this time, no. We're — it's not that we're closed off to any new suggestions or looking at it, but at this time, no. There wasn't — we don't have any other plans at this time. We are going to — we are in discussion to try to get the — some of that written up that we briefed last time. That is one of the things that is currently still in discussion, but hasn't been finalized yet.

R. TREWYN: And I guess not being an epidemiologist, biostatistician or whatnot here, the way the data — as you're going to be pulling this stuff together to hold it, I

would assume these sorts that gave rise to days of spraying, and the calendar period of service and whatnot, that is information that's there? So if later on if somebody wanted to go in, they wouldn't have to start from scratch to be able to do that?

K. FOX: Yes.

R. TREWYN: That they could pull that out and re-analyze?

K. FOX: Yes.

R. TREWYN: Okay.

P. CAMACHO: When we clean up the databases for the relational properties, we're not going to dump fields?

K. FOX: No. What we — but we've got to explain some of the nuances of the fields, like we know that one person wasn't there because of this and this. So we need to — that's the part; to give the exceptions and so, no, it's not to eliminate any field. It's to explain all fields and that makes it a very difficult task and all.

It would be very easy to just to eliminate some of them, but no, we have to explain these. What they wanted also was the exceptions to be explained and all and that's the time consuming part. And the study sure has changed over the years and physical — Phase I first physical is not — is going to take a lot of inventive — creating from scratch on a lot of stuff.

M. STOTO: Okay. Other questions or comments?

Update on the Dioxin Congeners Study

M. STOTO: Well, then maybe we can move to the congeners then. Dr. Pavuk? Thank you, Karen.

M. PAVUK: So this presentation will address results on measurements of dioxin, dibenzofuran and polychlorinated biphenyls in a sample of 106 participants of Air Force Health Study that didn't have any previous valid TCDD measurements and before. It is also here we present for the first time values of those congeners for any veterans in the Air Force Health Study. As you all know, in 1987 and then later in the study, only TCDD, one dioxin — one of many dioxin congeners was measured as recommended by CDC.

Originally, we thought that all those veterans were comparison veterans, but there were 12 Ranch Hands in this group of 106 people. As you can see, some of those comparison veterans didn't attend any previous physical examination so that was the reason why didn't have previous TCDD measurements. Some didn't have a valid measurement; that could have meant that there was a problem with the sample, or with the analysis or with the quality control. And there were 12 Ranch Hand veterans that also didn't have measurements.

CDC uses high-resolution gas chromatography, high-resolution mass spectrometry to analyze dioxin-like compounds. The levels of these compounds in human samples are reported in picograms per gram of lipid for dioxin, dibenzofurans

and non-ortho substituted polychlorinated biphenyls. Mono-ortho substituted polychlorinated biphenyls are in so — are in higher levels of — the measurements are presented in monograms per gram of lipid.

Two measurements of ten, seven dibenzodioxin congeners — so-called “2,3,7,8 substituted” — that is the substitution on — in the tetrachloride dibenzodioxin molecule. And so seven dibenzodioxin congeners, ten dibenzofuran congeners, three or four non-ortho polychlorinated congeners, and five or six mono-ortho PCB congeners became over the years the standard in exposure assessment of dioxin-like compounds in humans.

That concept also takes into account something what we call “toxic equivalency factors;” you can see on the last line there. And what that means is that the toxic potency of other congeners, dibenzodioxin and dibenzofurans, have assigned values relative to the toxic potency of TCDD. TCDD potency is one and all the other congeners are then related to TCDD having the TEF, toxic equivalency factors, of one or smaller than one.

Most of the congeners, TCDD being the most potent congeners, have smaller potencies than TCDD. And basically, you can then calculate what is called “TEQ,” toxic equivalency, summing up the TEQs of all different congeners and come up with the total toxic equivalency of dioxin-like compounds in a given sample.

These are just demographic characteristics of the veterans. I would just like to note that this was not a random samples. These are basically veterans, as I said before, who either didn't participate or for different reasons didn't have the measurements. But the — they are very similar in the sense of their age, their BMI, not so different on alcohol, pack years of smoking. As you can see, there was slightly different distributions given their military occupation. It's a high proportion of officers in the small Ranch Hand group.

So this presents the results for Ranch Hands and for comparisons for dioxin congeners. As you can see, the only congener that was measured previously, 2,3,7,8-TCDD, and there are six other dioxin congeners. If you look at the numbers, you see the ranges and the mean values there are similar in both groups for those veterans. For those of you familiar with the background level and populations, these numbers are similar to other levels found in general population in the United States or other industrialized countries.

These are the results for dibenzofurans. Again, the levels are fairly similar in both groups and we do not see any indication of some other occupational exposure in these veterans. These are the level for non-ortho PCBs. There are many other PCB congeners — PCB congeners being measured or these congeners are measured here. These are non-ortho substituted and these are mono-ortho substituted. And those are

those congeners that do have dioxin-like toxicities as based on laboratory animal testing or testing *in vitro*.

M. STOTO: You've got a — you've got a question here.

D. JOHNSON: For the PCDDs, the PCDFs, *et cetera*, that you've chosen to measure in addition to TCDD, why did you pick those? Are those also all ...

M. PAVUK: Are those ...

D. JOHNSON: Are — those are all contaminants of the herbicides as well or they're just ...

M. PAVUK: No. These are — these are the 2,3,7,8 substituted congeners, dibenzofurans and dibenzodioxin, that have toxicity similar if you test them in animals as TCDD. So these are the ones that are measured in human populations in epidemiologic studies; then you measure exposure to organochlorine compounds.

D. JOHNSON: So why are we looking — I mean, pardon me for asking, but why are we looking at that? What is the purpose of looking at these? Are they potentially exposed in Vietnam to these as well or not or why are we comparing those? What is our interest there?

M. PAVUK: Basically, interest there is that all of us are exposed to all these compounds throughout our lives. The thinking behind this, and if you remember some of the critiques of the study — well, of this study — was that only TCDD congener was measured. What we're talking about here is that throughout your life and through some

of the occupations that people may have, you can be exposed to other dioxin congeners than TCDD. For example, people working with chlorophenyls or working in different occupations where there's exposure to chlorines can have higher levels of some of the dibenzofuran or dibenzodioxin congeners. And that would be detected if you measure all of those congeners.

But let me maybe get back to your question. Originally when people analyzed Agent Orange and other pesticides that have been used in Vietnam, it was found that those pesticides were only contaminated by TCDD. That's why it was decided that only TCDD should be measured in Air Force Health Study veterans since that was the only contaminant.

Throughout 1980s and 1990s, it was found that populations have been exposed to this; that everybody has a measurable levels of this compounds and that they can be detected many years after your exposure; and that we can tell from the patterns of the levels of this compounds to what you could have been exposed many years ago.

So technically speaking, you can have low TCDD. But if you, for example, work in a plant that produce chlorophenyls, you would also have increased — you would also have increased pentachlorophenyls and hexachlorophenyls and we would see a different pattern of your exposure through those congeners. And we could say that, well, you were a Vietnam veteran and you were exposed to TCDD in Vietnam, but there

is a suggestion and a pattern of the congeners in your blood; that over your career, through your profession, you have been exposed to other dioxin congeners.

D. JOHNSON: We are fairly sure that these other ...

RECORDER: Microphone.

D. JOHNSON: So you're saying we're fairly sure that these other congeners are not present in herbicides in Vietnam? So ...

M. PAVUK: Yes, we are.

D. JOHNSON: we're fairly — pretty certain of that?

M. PAVUK: Yes.

D. JOHNSON: So that if they're elevated, they would indicate that the person has some exposures to ...

M. PAVUK: To other things ...

D. JOHNSON: ... other things ...

M. PAVUK: ... than herbicides in Vietnam.

D. JOHNSON: ... in Vietnam, or prior to Vietnam or at any time?

M. PAVUK: After — at any other time.

D. JOHNSON: Okay. So ...

M. PAVUK: So basically what we're looking at here, what we wanted to — we wanted to test here our assumption basically. That's what CDC outlined and why original decision was to measure only TCDD congeners, but that would be the only

difference. We would expect that this two group of veterans were similar in respect to exposure to all these other congeners that have toxic properties of dioxins and can cause potentially ...

D. JOHNSON: Similar.

M. PAVUK: ... similar health effects.

D. JOHNSON: Okay, so you just — you just wanted it to have — also have elevated — these other elevations might not have been due to the herbicides could be confounding the results of the study.

M. PAVUK: Could be confound results of the study or be a cause for misclassification of the exposure.

D. JOHNSON: But it's not to say that if my TCDD is high and one of these others are high, that doesn't mean that I was or was not exposed in Vietnam? We're not looking at that; we're just looking if there's other confounders that could be causing illness ...

M. PAVUK: That's like the other question.

D. JOHNSON: ... other than TCDD.

M. PAVUK: Yeah.

K. FOX: What happened was CDC, when we asked for dioxin now gave us all this. It's all on — all on a battery, so we're getting more information than what we've ever gotten before. We would've — we would've asked for dioxin levels on the people

that we didn't have dioxin levels. And what they've given now is that they're not only doing the dioxin, but they're also doing all this.

And so now we have more data that we've never had before because they hadn't done it before and all. So we're now just showing you that, hey, they've given us some more data, and now we get to look at it again and let's just muddy up some more, but we're going to look at it to see if we can see if there's any kind of anything breaking out.

D. JOHNSON: Well, that's helpful because you didn't actually set out to study this.

K. FOX: Absolutely not. This ...

D. JOHNSON: It's just you had the data ...

K. FOX: This came ...

D. JOHNSON: ... and now you're looking at it.

K. FOX: That's right. The data was given to us and so we felt obligated to look at it. So we don't know what this is going to show and because of it — well, I'll let you continue and we'll — he'll give a punch line.

M. STOTO: Ron?

R. TREWYN: Well, I mean, I — as I look at, for example, this slide, I mean, it really looks to me like ...

M. PAVUK: I'm sorry. I did not ...

R. TREWYN: That slide. No.

M. PAVUK: This one?

R. TREWYN: Go back. This one, yes. I mean, it's okay; leave it. As I look at this one, I mean, it really does appear that it's just TCDD that differs. So in fact, all of these others help confirm that the lifetime exposure, as least as I would look at those, has been relatively consistent to the other aspects, the other potential toxins that you could get with this group. Now two slides down, you're going to see some where, in fact, it looks to me like the Ranch Hand are lower very substantially, which could create certain interesting questions.

K. FOX: Which is why the punch line is we're — we've got about 600 more things being — 600 more people being looked at because this is not — this isn't randomly selected by any means. And so ...

R. TREWYN: Okay. Okay.

K. FOX: ... now you've got to — now you've opened that up. And so we're going to go — they're looking at some more randomly selected Ranch Hand and comparison so that it can be looked at.

R. TREWYN: Okay.

K. FOX: Sorry, I ...

K. OSEI: How about the biological activity of these congeners and these, I mean, in terms of if you took the first potency as one, what would be the relative potency of the metabolites or are these — are these metabolites potency?

M. PAVUK: Which one were you asking about?

K. OSEI: All of them.

M. PAVUK: Well, they ...

K. OSEI: Yeah, I know, the metabolites.

M. PAVUK: The ...

K. OSEI: Okay.

M. PAVUK: ... potencies of these congeners differ. For example, penta-TCDDs has the same toxic equivalency factor as TCDD, 1; the first hexachlorinated is 0.1; all hexachlorinated is 0.1; heptachlorinated dioxin is 0.01.

K. OSEI: Okay. Okay.

M. PAVUK: And all the substituted is 0.0001.

K. OSEI: Okay.

M. PAVUK: So the potencies differ widely among the congeners and the point there is that when you multiply — when you multiply the measured values with the toxic equivalency factor, then you get your ...

K. OSEI: Overall.

M. PAVUK: ... TEQ level. And you can add up all those potencies through dioxin, dibenzofurans and PCBs and get a total cumulative exposure to all these compounds.

K. OSEI: Right.

M. PAVUK: So while here, the difference may be three times for three TCDD and the overall TEQ in the small sample is not really different, you know, or not that much. And, you know, some of that may explain why we don't see that many differences in some of those between Ranch and the comparisons because the overall exposure to dioxin-like compounds may not have been different.

K. OSEI: So you have to rewrite your report?

M. PAVUK: Right.

R. TREWYN: Start over.

M. PAVUK: Start over. Well, in ...

D. JOHNSON: And you — and the — and ...

M. PAVUK: ... effect since we already jumped ahead — since we already jumped ahead, I can also jump ahead here. And this is the preliminary results on 300 and 300; I thought you would be interested. We're still finishing the data set with the CDC and still kind of recalculating the TEQs, and non-detectables and other things that you need to do in data set before you can start analyzing anything.

But this is on 300 and 300, and this provides a little better picture and illustrates the point a little bit better in the — between TCDD and total TEQ. See the difference here? This is 3.2 and 10.2, difference about seven parts per trillion: this 37, 38 and 42.5. So the difference is about five in there, so it's close to that difference in the TCDD. So you can say here that, yes, the exposures overall were similar, but the

difference is really caused by the exposure that they were — they experienced in Vietnam because the only difference we see is only in TCDD and in none of the other congeners.

D. JOHNSON: The TEQ includes ...

M. PAVUK: So it gives you more information to confirm your assumptions; that their exposure, the difference in the exposure was in TCDD that may have been in Vietnam.

M. STOTO: I can ...

D. JOHNSON: Just to be completely clear that TE — the TCDD is included in the TEQ?

M. PAVUK: Correct. Yes. Here, maybe I should note, I mean, this should not really be here because this one is part of this one. I was asked to show this one, but really TCDD is part of this column. But only this column here add up.

K. OSEI: Use a pointer.

M. STOTO: I'm going to ask about the relevance of this given all the other things that could be done with the amount of time that's left and so on. I mean, you know, the Ranch Hand Study started out comparing people who were exposed to herbicides to controls.

M. PAVUK: Well, I thought that ...

M. STOTO: Let me finish, please.

M. PAVUK: Sorry. Sorry, I thought you were finished.

M. STOTO: And, you know, 20 years ago, CDC figured out how to measure serum dioxin and then that turned out to be a good — a better measure of exposure than just being in the cohort was and so we kind of have been focusing on that. And then over time, there's been more and more of a shift toward thinking this was a study about the effects of dioxin, which was a big shift.

And now this is kind of saying, "Oh no, we're — this is a study about the congeners of dioxin." And I guess I'm not, I mean, to the — to the extent that this tells us yes, it does look like that the difference between the TCDD levels between the Ranch Hands and the controls is due to their exposure to Agent — to herbicides, that's nice to know. But I guess I can't — I don't understand why it would make sense to put a lot more effort into this beyond this. Ron?

R. TREWYN: Can I follow up with one other thing because then I'm going to go back to my other point? Because when one looks at things like days of spraying, calendar period served, there were — there were cancer health effects teased out. Might it be possible other health effects could be teased out by doing those analyses with other parameters? And yet, we're focused on what are probably fairly expensive studies.

I don't know what the cost is, but I — any time you're going to do a laboratory analysis versus crunching numbers, just re-analyzing data sorted somewhat differently,

I would think the cost would be — would be substantially higher. So I guess going back again to my social science colleague over here and the fact that, you know, the issues are were there adverse health outcomes due to some of these exposures? If there's an opportunity to pull out potentially more health parameters or not versus interesting stuff, I mean, this is — this poses some interesting scientific questions, but I don't know that it gets to the bottom line as much as some of the other things could.

M. PAVUK: Well, if I may address some of your points, if you would have asked Dr. Schechter about this, whether this would be important to pursue, you would probably got a slightly different answer. This was one of the ...

M. STOTO: He's been saying this for years that we — that we should do this, yeah. True.

M. PAVUK: And I agree. I am not trying to make a joke here about this because from the point of view that if you measure only TCDD in these veterans, your exposure assessment to organochlorine compounds is incomplete. It has been one of the — I was — I'm a little surprised by the reaction of the Committee because I thought that was one of the major criticism of the study; that the exposure assessment was incomplete here and that, you know, this technology has been available since about '85, '87. In '87, they could have measured all the congeners too, you know, and ...

M. STOTO: This has — this has been Dr. Schechter's criticism for ...

M. PAVUK: Well, it's not only Dr. Schechter's. I mean, many other study that is compared to Air Force Health Study is the OSHA study of chemical workers that have been exposed. And, you know, they did some analysis of sub-samples of the — of the — of the workers there and ...

M. STOTO: I mean, I guess I don't — I don't find this convincing that this should be a high priority thing given the amount of time and money that's left. I mean, I'm open to hearing ...

R. TREWYN: I'll take — I'll just take the other side just for the heck of it just to show I can argue both sides. I do think there is some interesting data coming out of this. And if the bottom line is and some stuff where there really have been questions for a number of years on what would this show and whatnot, so I think that is valuable.

If it turns out that the recommendation of the IOM is continuation and even a bigger if, if then that's approved, blessed, whatever and by Congress or whoever's going to move this forward so additional studies will be done, I think then having some of this analytical data perhaps may make it more attractive for even more researchers to want to pursue it. So who knows?

K. OSEI: And Mike, I think this is also very important because you — the assumption has always been that TCDD was the primary culprit and that it may not be. It may be that there are other congeners that are even more toxic, so now you're looking at the total exposure burden in the — that individual rather than one entity.

And so having this kind of information gives you an idea where to focus your energy. If you didn't have this, you would be, you know — just focus on one thing and it may be a mistake. I think this gives you some insight into what the culprit is. And it's good to exclude that and say this is not what the issue is so we can spend our money on something else.

M. PAVUK: I mean, our problem really — probably more important problem than the congeners was the fact that the samples are collected so many years after exposure in Vietnam. So when this is also then many years after exposure in Vietnam so, but ...

K. OSEI: Is one more stable than the other?

M. PAVUK: Pardon me?

K. OSEI: Is one of these congeners more stable than the other? If you say five, years, ten years, 20 years, would one ...

M. PAVUK: Well, some ...

K. OSEI: ... decay faster?

M. PAVUK: Some of them — some of them decay faster than the others; that's true that their half lives do vary. Some are shorter than dioxin, which is about seven, eight years; some are quite longer.

R. TREWYN: And these specimens were collected when?

M. PAVUK: 2002.

R. TREWYN: Then so all of these — the 300, now the 600 ...

M. PAVUK: Right.

R. TREWYN: ... these are all 2002?

M. PAVUK: This is all 2002.

R. TREWYN: Okay.

M. STOTO: Now go back to the, you know, page 1 of the comprehensive report. The purpose of the study: "The objective of the Air Force Health Study was to determine whether the long-term health effects exist and can be attributed to occupational exposure to herbicides with specific emphasis on Agent Orange." This may be an interesting scientific question, but it's a very different scientific question.

M. PAVUK: It is, but at the same time, you know, the — I think the — how this adds to those questionnaires, that you may have people who have low TCDD, and have been classified as having being in a low TCDD category ...

M. STOTO: I under — I understand that point.

M. PAVUK: ... and they may be in high TEQ category. So that introduce, you know, the problem that you can then address from the other perspective.

M. STOTO: Well, but it — but ...

M. PAVUK: And we have that problem because we have 40 percent of Ranch Hands that have TCDD levels same as comparisons, you know. And we can't deny them that ...

M. STOTO: Okay.

M. PAVUK: ... they were in Vietnam and that they were exposed probably more than comparisons.

M. STOTO: I understand that point.

M. PAVUK: Sure.

M. STOTO: And I'm saying that but to do the — to redo all the analysis using this kind of information, plus get it on a couple thousand more people ...

R. TREWYN: Six hundred.

M. STOTO: Well, it's not just the — it's the Ranch Hands, and the controls and so on. And so I don't know; it's a lot of — a lot of effort to get ...

M. PAVUK: Right, I ...

M. STOTO: ... to get these things.

M. PAVUK: I agree.

M. STOTO: And a lot of money.

M. PAVUK: I agree.

M. STOTO: And that may be an important question, but there's lots of other questions that could be asked. And I have to say I personally don't feel that given the amount of time and the amount of money that's left in the current project, which is the one that we're advising about, that this is a good investment.

R. SILLS: And that's my concern too. I think we need to have the most consistent data set, which is what we have right now. And we need — and we're

drawing conclusions and so we need to be careful. I think this information is important. It's important, which will — it's information which will add to the exposures.

But in terms of making correlations or making sense of the data we have right now, we really need to go with our solid data and use that data to help explain the effects that we see in the study. And the study ends in September 2006 and I'm very worried that if we're, you know, if we — if we don't have consistent data that we know about is solid, then we could run into, you know, I mean, we, you know, it could — it could cause — it could bring up some issues. And I would prefer to go with consistency over not being consistent.

And because once you get the data set, then you have to analyze it. You have to do all — you have to do — you have to do — you have to have — make sure your controls and everything is — you really have to have confidence in the data. I support this data 100 percent. This is the data I, you know, in terms of future studies, I see — I see, you know, there's a lot of strength for this. But as I — as I ...

M. PAVUK: It's a little — too little, too late.

R. SILLS: Right, it's a little too — well, all I'm saying is that we really have to have confidence in the data. And in order to have confidence, you have to look at the data. You have to analyze it. You have to do a number of internal studies or — there have to be a lot of discussion back and forth.

And so I like the idea that Mike is proposing that, you know, we go with the most consistent data, which is the data we have right now that we have in our hands. And we have analyzed it; we have discussed it. And these type of studies, I think, would be studies for the future. I mean, I think, you know, I've been sitting here and I've been — I've been worried about it.

M. PAVUK: Well, I agree with you that, you know, at this point, we are — we'll have data on 600 veterans and we are not going to have the results for the rest of the study, so our analysis ...

M. STOTO: Okay.

M. PAVUK: ... of health outcome is limited.

D. JOHNSON: Can I ask a question?

M. PAVUK: So we're not going to pursue this.

M. STOTO: Marian, this is the Advisory Committee and we're giving advice to you. So I'd like you to answer our questions, but not argue back against them. Sandy, go ahead.

S. LEFFINGWELL: Another illustration, I guess, of this axiom: "If you don't know what you're going to do with the answer, don't ask the question." But you didn't ask the question; you just got the answer, which raises another question. The extra — presumed extra cost of doing these analysis comes out of whose pockets? Is this now

done because that's the standard way CDC does it and they can't give you a cut rate if they analyzed for less?

M. PAVUK: Pardon me? What was the question?

S. LEFFINGWELL: Well, the analogy is to a hospital laboratory.

M. PAVUK: Yes.

S. LEFFINGWELL: You don't any more order a blood urea nitrogen. You order a SMA-20 or something because it's more expensive to do a bench analysis for a single analyte. I'm wondering whose pocket these extra analyses came out of? Did the Air Force have to pay for it or was this just CDC's flat rate and way of doing things and ...

M. PAVUK: I think Dr. Miner can answer that question.

J. MINER: Flat rate.

D. JOHNSON: I have ...

J. MINER: What — it was their way of doing things and there was no price reduction for doing less. It's just that was the panel — boom.

M. STOTO: Okay. David?

J. MINER: And it comes out of our pocket.

D. JOHNSON: I have three questions, but then I don't mean to argue. Well first of all, I wanted to say that's one of my original questions. I didn't mean to jump ahead of you, but I was trying to figure out why you were doing it and so — and it — and it was interesting to find that out. But is it — is — are we assuming that the toxicology is the

same in all these congeners? They all cause the same — do we have laboratory studies to show that they actually cause the same illnesses? I know that ...

M. PAVUK: There've been quite a bit of studies, but I wouldn't classify it as a — as a uniform outcome for every congeners.

D. JOHNSON: I mean ...

M. PAVUK: There have been — different congeners may have different ...

D. JOHNSON: Outcomes.

M. PAVUK: ... outcomes.

M. STOTO: And they're based on animal studies, I believe. Is that correct?

M. PAVUK: Yes. The testing, yes.

D. JOHNSON: The other thing I'm assuming then, you read the study — this is my second question — that the study reads that this is a study of exposure to herbicides. So we're assuming that, because we've been talking about dioxin in here, we're saying that dioxin then is a surrogate for herbicides? Is that what we're assuming?

M. STOTO: Yeah.

D. JOHNSON: I guess we've kind of brought this up before.

M. STOTO: No, we have and that has problems, I mean, because some of the herbicides don't have — didn't have dioxin. And I forget which ones, but some of them didn't. So I think that's part of the reason.

D. JOHNSON: But that's — but that's what we're doing then, I mean?

M. STOTO: Yeah, that's part of the reason why we, I think, Model 1 has always been carried along, which is the one that just compares the Ranch Hand the controls.

D. JOHNSON: It has limitations, but that's what we're — that's why this study reads this way and you can ...

M. STOTO: Well, the study, you know, this is what was authorized at 25 years ago.

D. JOHNSON: Right.

M. STOTO: Jay?

J. MINER: Yes. I would like to, again, I do this almost every time, but I'll ...

D. JOHNSON: Right, I know. I know.

J. MINER: ... read from the protocol, page 1, "Purpose of the Investigation: The purpose of this epidemiologic investigation is to determine whether long-term health effects exist and can be attributed to occupational exposure to Herbicide Orange."

D. JOHNSON: Right.

M. STOTO: That's essentially what it says here in the comprehensive report.

D. JOHNSON: Right, but I'm trying to remember now. I know we've asked this before. I was trying to put it back to what he was saying about this is a study — why are we looking at congeners ...

M. PAVUK: Because ...

D. JOHNSON: ... because we were looking at herbicides.

M. PAVUK: Right.

D. JOHNSON: But we're — we've really been talking about dioxin the whole time. So I guess my final question is, is there a chance by studying this it would show more of an effect on behalf of the people exposed? Because if there is, then we have to be careful about not doing it now that we started on it.

M. PAVUK: This, as I mentioned before, this gives you a more detailed assessment of personal exposure in a sense that we are all exposed to this compounds. And it's true that the herbicides had only — the only contaminant was TCDD there, but all human beings, whether comparisons or Ranch Hands, whether living in United States or being in Southeast Asia, have been over the course of their life exposed to all the other compounds. So that's the idea behind the exposure assessment and analyzing so many different compounds.

D. JOHNSON: So the analysis is more likely to show less of an effect?

M. STOTO: Yes, because somebody with diabetes, it might turn out that he has a higher level of something or other and it can only take away from that, the fact that it's there. Jay, one more — one more point?

J. MINER: One more comment: as far as the use of the money to do any more of these, Program Management has been talking about that. And since the IOM report has come out, this has moved further down on our — in our priorities.

M. STOTO: Yeah. I mean, from what I have understood now is that, you know, we, as I said at the outset, it started out to be a study of herbicides. Dioxin was thought to be a good proxy for herbicides, a good biomarker for herbicide exposure.

J. MINER: Herbicide Orange.

M. STOTO: And then CDC decided that it's going to just give the whole panel of results rather than just the TCDD results and we kind of got it. We kind of got this data and now we're thinking about what to do with it. And that's not a, to my mind, a good sound scientific reason for focusing on these — on these data.

J. MINER: Well, as I remember though from years past, and it might've been a little before your time, this Committee did heavily criticize us for only looking at TCDD and recommended that we would look at the congeners.

M. STOTO: I know that people — I do recall people saying that.

J. MINER: Yes.

M. STOTO: I was not one of them.

J. MINER: No, you were not.

M. STOTO: Okay. Ron?

M. BLANCAS: And if I might add, this probably would've been already completed a couple of years ago except that we had problems getting money to CDC to accept the particular money that we had. They didn't like the color of money, so it wasn't done. So that's why we're completing it now.

M. STOTO: Ron, turn your ...

R. TREWYN: Well, I — yeah, and I will wrap up because it does — because something was dictated 25 years ago, we're going to do it same way since confirms in my mind that that is bad science. The issue here is, I guess, it can be then blamed on Congress. But this is, you know, you go where the — where the science leads you and this is — yeah.

M. STOTO: Well, okay. I think what I'd like, I just want to wrap this up. I think that we don't need to make a — I'm sorry. I do — I do want to wrap this up now unless there's — and I don't think we need to make a recommendation here. I think — I think that the point that Jay made about the IOM's going to make a lot of recommendations about all this and I think this needs to be reconsidered in light of all those is a good one. So, you know, I think we should just stop for now. Okay. Thank you. Okay.

Review of the Air Force Health Study Comprehensive Study Report [continued]

M. STOTO: We have remaining on the — on the agenda Committee discussion. This is the stuff that's for 3:30. I would like to do a couple things: one is come back to the conclusions of the comprehensive report and talk about that now a little bit more, and two, I raised the idea about whether we want to endorse the IOM report.

But I think that probably that it's not going to make much of a difference one way or the other and we're going to have a — I think have an opportunity to talk about it in more depth at our next meeting. So I think I'll — unless someone really wants to push that, I'll — I think we'll drop that for now. And I'm sorry?

D. JOHNSON: It's kind of one of the reasons we had a separate group look at — they chose for a separate ...

M. STOTO: Yeah.

D. JOHNSON: ... group to look at it, so we can let — yeah.

M. STOTO: Okay, and then — and then we need to think about setting a date for a new meeting, for the next meeting. So on the — on the comprehensive report, one thing that struck me is about the need to balance honestly reporting everything that was done and not leaving things out, which Paul rightly tells us would be — could be trouble, versus focusing attention on what's important and telling a good story.

And that's a hard compromise and I think a lot of what we were discussing, you know, had to do with how do we come down on that and, you know, I — and I don't want to pretend that that's easy. But I would propose, just to put on the table this idea that one way to do that is to bring the VA list of presumed diseases that are — that are related to herbicide exposure and Agent Orange up to the front of the report. And say that, you know, there's been a lot of work in this in the scientific community in general,

in the IOM's reviews, and in the Ranch Hand Study and use that as a framework for presenting the results.

And then you could say, you know, some of the things the Ranch Hand Study is consistent with the VA findings and, in fact, are the leader or the main — like diabetes — are the main thing that's led to that finding. In some cases, the Ranch Hand Study is not really able to address the issue because the sample size is small, or because it's chloracne that happened long before the study or something like that.

And then in other cases, that there were these other things that the Ranch Hand looked at that aren't on the list that the VA has and that we didn't find anything either on those lists. So kind of frame it that way and then, you know, describe the study and all that that's there. And then go through each of the outcomes and describe, you know, what was done and what was — what was — what was found, more or less like it's there.

But have the — have the conclusions of each chapter come back to that framework so that, you know, the endocrine chapter will talk about diabetes and the cancer chapter will talk about how it could — it did find some things in prostate, but couldn't find anything for soft tissue sarcoma because the sample size was small and so on. And then the overall conclusion would basically just sort of pull, wrap together those — the conclusions of each of those individual chapters.

And I think that way we, you know, that the — each chapter does have what was done, and what was found and what not found, but it puts it in the context of this bigger framework.

R. TREWYN: And that would include then publications done by the Ranch Hand team?

M. STOTO: Absolutely.

R. TREWYN: Okay, and not just — yeah.

M. STOTO: Yeah.

R. TREWYN: Yeah.

K. OSEI: Mike, and another way to look at it is, you know, as you pointed out, there should be a whole section on limitations with the study, I think, so that we don't have to revisit everything. So the limitation — and we put only one paragraph in here, but you should really write the whole issues so that you can put the whole thing in a better context than what we are trying, you know, what we're talking about. So you lay out what are the limitations of the study so that we can now have a better view of what the study can do and what it's expected to do, not what it cannot do.

M. STOTO: Okay. Yeah. David?

D. JOHNSON: Yes, I mean, I want to bring this up. But this discussion has come up, I guess, almost every meeting as indicated back there about is it herbicides or

is it dioxin that we're studying? And you've sort of — the last few comments you've made, you've talked about it being herbicide exposure.

But if you look in the — if you look in this text, repeatedly it talks about increasing dioxin or decreasing dioxin and it talks about the associations with dioxin throughout this report. Now it seems like I don't know if there's a place where that's — if this is explained in a — in a paragraph, an introductory paragraph that explains why we talk about dioxin. But what we're really doing ...

M. STOTO: Yeah. I think it may be in there, but it probably needs to be in Chapter 2. I think it may be needs to be clarified, strengthened.

D. JOHNSON: It's not just one chapter though. It's the entire report ...

M. STOTO: Well, chapter ...

D. JOHNSON: ... refers to dioxin, whereas ...

M. STOTO: Well, Chapter 2 is "Measures of Exposure."

D. JOHNSON: Oh, okay.

M. STOTO: So that — I think that ...

D. JOHNSON: Do you think it explains the fact that the original study was for herbicides, but yet, this report refers almost entirely to dioxins and why that occurs?

M. STOTO: Not as well as it might.

D. JOHNSON: Pardon?

M. STOTO: Not as well as it might. I mean, I think it can be — no, I think this is the place where it belongs. I'm not saying that it's done well now. I agree with you that it needs to be strengthened.

D. JOHNSON: It's a fairly broad and important point.

M. STOTO: Yeah.

D. JOHNSON: To be clear or at least ...

M. STOTO: It's a fundamental point.

D. JOHNSON: ... as clear as possible or at least attempted to be explained.

M. STOTO: Yeah. It's a fundamental point.

K. OSEI: But another way to look at it is we say dioxin is a surrogate. We use that as a surrogate of — no, so that — so people don't get the idea that what you're looking at is just dioxin association and diseases, but as a surrogate of, you know ...

J. ROBINSON: Agent Orange.

K. OSEI: ... Agent Orange, yeah.

D. JOHNSON: And, you know, and when you spend the time in here discussing this with this group, you start thinking you're talking about dioxin because that's what we talk about all, you know, for hours. And you're not thinking that we're — that we're really thinking in terms of herbicides in general and I don't know if that's made — so it's not always that clear when we're talking about it. I don't know if it's made clear in the document and it seems to be an important point.

M. STOTO: Well, some of the findings are stated in terms of the Ranch Hands versus the controls, which is — gets us back to the original purpose. So, but I think that your fundamental point is right; is that this really needs to be clarified.

P. CAMACHO: You're back to the history again and dioxin is what captured the imagination of all the stakeholders. Had this exotic chemical; they heard about Times Beach.

M. STOTO: Yeah.

P. CAMACHO: I mean, over the years, this is the surrogate, if you will, or the term, the concept that captured the political awareness of all the stakeholders and then all the responders to the stakeholders. I mean, all you have to do is say that. I don't think there's a big mystery here, I mean, or a big tension. You say it and then you say what that means to us in terms of the study and that, you know, you get back to what you've been saying.

M. STOTO: No, I think that's a slightly different point and, but an important one to say. Ron?

R. TREWYN: And I was just trying to dig through the 2004, 2005 papers to find where it is. And it may just be something I was remembering from a presentation at the last meeting where the time that the individual served in Vietnam, there was a correlation to the early years there when the — when the lots that were utilized of

Orange and the others were more contaminated with dioxin; that there really seemed to be a much higher correlation, I believe, in the — in the cancers from that group.

M. STOTO: There's something in Section 2 about that.

R. TREWYN: Yeah, and I think, again, it's not that dioxin is always the bad thing to be looking at. It is — it is really an indicator of exposure to Orange and two or three of the other — four total? Okay. But it isn't for Blue, I know, and there's one or two others that were — White? Purple? Okay. Pink? All right. Green? Okay. Anyhow, but yet it does serve as a measure for some.

But again, I think there are useful — there are ways in which it can be used in a very positive way for analyzing the data and showing certainly exposure, potential exposure to those — a particular group — and those were the ones that were sprayed. No, it's clearly Orange, what, 11 million gallons out of the 19 was Orange, I believe. And you add in the other dioxin containing, it goes even higher. So, I mean, it is a substantial amount.

M. STOTO: Okay. Jay, one more comment.

J. MINER: On the time frame of those early and late that was talked about the last — at the last meeting and I went back and I looked. The assumption was that somewhere in 1968 was one cut point, I think, or 1969. In fact, Purple was stopped being used in December of '64 and Agent Orange started in January of '65.

So if you were wanting to see a difference in the cut point, then that was the event. And that should've been the cut point that came out, which kind of goes then to when you just slice and dice the data and, "Oh that's suggested," and see how, you know, sometimes you've got to watch that.

M. STOTO: Okay. I don't want get into the details of that — of that now. I mean, I think the question on the table really is about this organization of the report and the conclusions, particularly, and I think we had a good discussion about that. Anything else to add about that? Sandy?

S. LEFFINGWELL: Kind of wondering if what you're describing is more a newspaper style of writing where you lead with the hot items and then fill in the data instead of the scientific thing where you plow through it all and then give your conclusions?

M. STOTO: It is to some degree. It is to some degree. And I think that's because I'm trying to balance those two things that I mentioned at the beginning. And I think as long as we have the body of the report in these chapters that really deals with everything in a systematic way, I feel much more comfortable with that than — and then, of course, we will — we have the six cycle reports too. I feel much more comfortable with that. Do you?

S. LEFFINGWELL: I don't have a problem.

M. STOTO: Okay. Right. Yes, I think that helps. Yeah.

S. LEFFINGWELL: A stylistic thing might be helpful.

M. STOTO: Yeah. Okay.

RHAC Business

M. STOTO: Okay. So we come down to now to the next meeting. And I guess it was two questions: one is how many more meetings do we need to have?

R. TREWYN: How many can they afford?

M. STOTO: Yeah.

L. SCHECHTMAN: Money is never an issue in the federal government — off the record.

R. TREWYN: Yeah. Yeah, your mike was on; too late.

L. SCHECHTMAN: So the big issue is based upon what took place today, what do we consider in terms of numbers of meetings that would be required before the closure of this entire effort, September 30th, 2006? If we wanted to hold one around late February, for example, to allow for the information that would be gathered that we would want to consider at that point in time, then we might be thinking about, say, two more meetings during the year: the late February meeting and then one perhaps around, yeah, late summer, early — late summer.

M. STOTO: Yeah.

L. SCHECHTMAN: Yeah, perhaps in August or something of that nature and then September 30th is only a few weeks beyond that.

M. STOTO: Well, I think that we almost surely need the one in February; that we almost surely need the one in February. And I think that there's a quite good chance that we'll need another one later in the summer. And I guess ...

L. SCHECHTMAN: Something else occurred to me; that if Air Force does get an extension on funding to carry out some of the activities, there may be additional activities that this Committee would be involved in after that date of September 30th and it may not involve meetings of this nature. It may be just online/off-line activities, exchanges of information or maybe there will be another gathering; that — that'll be yet to be determined.

But I think we'll just have to take it a step at a time because we, at the same time, would need additional funding to carry out such an activity beyond September 30th. So we'll see how that goes. Right now, the funding agencies that have been furnishing the funds for these kinds of meetings have said, "That's it. Drop dead date is September 30th." They're finished with the funding.

But we will need to know as soon as possibly, obviously, if there will be an extension of Air Force funding. And there's no way, of course, to predict that based upon the IOM report, Congress and their conclusions, and so on as to whether or not we will have to go forward at the same time to request additional funds for this purpose.

M. STOTO: Did you know that at the beginning of the Carter — of the Clinton Administration in '92, they were looking at federal advisory committees? And there was this article in the *New York Times* saying that, "Look at all these dumb advisory committees." And this was given as the prime example, but it lasted for 13 years after that.

R. TREWYN: I would assume we, members of the Committee, will get the final IOM report as soon as it's available? I, you know, one — and that is going to be before the very end of February, right? That's ...

M. STOTO: Right.

R. TREWYN: And so I think we clearly then, based on the recommendations in there, I mean, we clearly then have to meet soon after that because that's going to then tell us an awful lot about what we need to be doing, what our recommendations, what our advice will be for ...

M. STOTO: Some decisions are going to have to be made quickly, so we want ...

R. TREWYN: Yeah.

M. STOTO: ... that to be as soon — as soon as possible after the last possible date they can deliver their report.

R. TREWYN: Did we get a drop dead date?

M. STOTO: Yeah, we did get a — no, David gave me a drop dead date.

R. TREWYN: Okay.

M. STOTO: January 31st.

R. TREWYN: Okay. January 31st?

L. SCHECHTMAN: And the additional information that we've been discussing here out of Air Force I heard was around mid-February that that could happen?

K. FOX: Having the meeting at the end of February would be a better thing to do ...

L. SCHECHTMAN: Right.

K. FOX: ... because it would take some time before we can figure out what we can do versus what and all so that, you know, we could say, "Yeah, we're looking at it." And we wouldn't be able to tell you anything either, so it's a catch-22 if you do it too early.

L. SCHECHTMAN: Right.

K. FOX: We haven't had any time to see if it even can be done, what the recommendations are. So ...

L. SCHECHTMAN: Well ...

K. FOX: ... the first part of March, end of February.

L. SCHECHTMAN: Well, the very end of February would be around March — sorry, February 27th, 28th: 27th is a Monday; the 28th is a Tuesday. The week before that would be February 22, 23, 24: Wednesday, Thursday, Friday, something like that.

So it might be difficult to nail down the exact date now, but we might be wanting to think about if we're talking about the end of February, the block of time between February 22 and 28, which it brackets a two-week span.

M. STOTO: Okay.

L. SCHECHTMAN: It's not a whole two weeks; it's days within those two weeks.

R. TREWYN: We understand.

L. SCHECHTMAN: Okay. All right. Other than that ...

R. TREWYN: This is federal government calculations.

L. SCHECHTMAN: Right. Other than that, we're talking, because of other scheduling conflicts, probably the end of March. We're going to be losing all of March — the beginning of March, so it's best to get it in at the end of February if at all possible. And then we'll, at that time, we'll look at the following meeting slot.

M. STOTO: Okay.

L. SCHECHTMAN: We will canvass — I'm sorry — we will canvass everyone involved: the members of the Committee, Air Force and try and — try and nail down that date as soon as possible. Okay.

M. STOTO: That sounds good. Thank you. Any other items for our agenda?

Closing Session

M. STOTO: Well, let me thank everybody on the Committee for your participation, the Air Force and all — and all the staff for your presentations and working with us. And I look forward to seeing everybody again in the cold of the winter.

RECORDER: Dr. Stoto, you have to formally adjourn us.

M. STOTO: Okay. The meeting is adjourned.

[ADJOURN 2:01 P.M.]

CERTIFICATION

State of Georgia)
)
County of DeKalb)

I, Nadine Rivera, do hereby certify that the foregoing transcript, consisting of pages 1 – 196 in total, was personally typewritten by me and is a true, complete and accurate transcript of the proceedings recorded by me.

I further certify that I am not related to, employed by, or attorney of record for any parties or attorneys involved herein. I further certify that I have no financial interest in this matter.

WITNESS MY HAND AND OFFICIAL SEAL BELOW.

This 30th day of December, 2005.

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Nadine Rivera

[Seal]