

1 NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH (NCTR)

2 SCIENCE ADVISORY BOARD (SAB)

3 Minutes of the Meeting held

4 August 30, 2006

5 at

6 University of Arkansas for Medical Sciences

7 Stephens Spine Center, 12th Floor

8 James H. Hamlen II Boardroom

9 501 Jack Stephens Drive

10 Little Rock, Arkansas

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19 REPORTED BY:

20 Susan B. Whitson, CCR

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1 ATTENDEES

2 SAB MEMBERS

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4 University of Cincinnati

5 NANCY GILLET, D.V.M., Ph.D., Sr. Vice President, Charles River

6 Laboratories

7 MICHAEL ASCHNER, Ph.D., ATS, Professor, Department of Pediatrics,

8 Vanderbilt University Medical Center

9 JAMES S. BUS, Ph.D., DABT, Director of External Technology,

10 Toxicology & Environmental Research & Consulting, Dow Chemical

11 Company

12 TIMOTHY P. PASTOOR, Ph.D., DABT, Head, NAFTA Human Safety

13 Department, Syngenta Crop Protection

14 ANTHONY L. POMETTO, Ph.D., Professor, Department of Food Science

15 & Human Nutrition, Iowa State University

16 JAMES A. POPP, D.V.M., Ph.D., ATS, DACVP, Co-founder and

17 Co-owner, Stratoxon LLC

18 STEPHEN M. ROBERTS, Ph.D., Professor & Director, Center for

19 Environmental & Human Toxicology, University of Florida

- 20 LILY JUNG, M.D., M.M.M., Consumer Rep, Medical Director,
- 21 Neurology Clinic, Swedish Neuroscience Institute
- 22 CENTER REPS AND LIAISONS
- 23 CDER
- 24 JOSEPH HANIG, Ph.D., Acting Chief, Deputy Director, Division of
- 25 Applied Pharmacology Research

- 1 SHIRLEY MURPHY, M.D., Acting Deputy Director, Office of
- 2 Translation Sciences
- 3 CDRH
- 4 DANIEL SCHULTZ, M.D., Center Director
- 5 CFSAN
- 6 ROBERT BUCHANAN, Ph.D., Director, Office of Science
- 7 RONALD LORENTZEN, Ph.D., Chemist, Office of Science
- 8 CVM
- 9 KEVIN GREENLEES, Ph.D., Division of Human Food Safety
- 10 FDA SCIENCE BOARD
- 11 JOHN THOMAS, Ph.D., Professor Emeritus of Pharmacology,
- 12 University of Texas Health Science Center
- 13 F. XAVIER PI-SUNYER, M.D., M.P.H., Director, New York Obesity
- 14 Research Center, St. Lukes Roosevelt Hospital Center
- 15 OWH
- 16 KATHLEEN UHL, M.D., Director, Office of Women's Health
- 17 ORA
- 18 PAUL E. NORRIS, D.V.M., M.P.A., Director, Arkansas Regional
- 19 Laboratory

20 UAMS

21 THOMAS G. WELLS, M.D., Professor, Department of Pediatrics,

22 University of Arkansas for Medical Sciences, Arkansas Children's

23 Hospital

24 FRED KADLUBAR, Ph.D.

25

1 DR. PAUL NORRIS, ORA

2 DR. LEONARD SCHECHTMAN, Executive Secretary, SAB

3 NCTR

4 DR. BILL SLIKKER

5 DR. BILL ALLABEN, Office of Scientific Coordination

6 DR. FRED BELAND, Division of Biochemical Toxicology

7 DR. MERLE PAULE, Division of Neurotoxicology

8 DR. MARTHA MOORE, Division of Genetic & Reproductive Toxicology

9 DR. YVONNE DRAGAN, Division of Systems Toxicology

10 DR. LUKE RATNASINGHE, Division of Pharmacogenomics & Molecular
11 Epidemiology

12 DR. RALPH KODELL, Division of Biometry & Risk Assessment

13 DR. JEFF CARRAWAY, Division of Veterinary Services

14 DR. CARL CERNIGLIA, Division of Microbiology

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1 P R O C E E D I N G S

2 DR. ACOSTA: Good morning, everyone.

3 Welcome to the second day of the SAB meeting.

4 It's a great place to have this particular second day.

5 It's a great facility and I thank the individual from

6 Arkansas that assigned us this room. Thank you very

7 much. And I had nothing to do with it.

8 UNIDENTIFIED: Take the credit, Tom.

9 DR. ACOSTA: So we'll call the meeting to order

10 and begin the agenda.

11 The first item on the again is Bill Slikker is

12 going to provide a commentary on strategic focus and

13 realignment.

14 Before we do that, we do have some comments from

15 Leonard.

16 DR. SCHECHTMAN: Okay. A few little housekeeping

17 items. With the exception of those persons staying on

18 in Little Rock, everyone should have been checked out

19 of the hotel by now. If you've had any difficulty

20 doing that, we have noticed there were a couple of
21 snags, please, let us know back in the Washington
22 office and we'll take care of it.

23 The open public portion of the meeting this
24 morning will end at ten o'clock, and this will be
25 followed by a closed executive session of the Science

1 Advisory Board members only.

2 That session will adjourn at 10:30 this morning,
3 after which transportation will be leaving for Little
4 Rock airport. We realize that some of you will be
5 getting there rather early, well before your flight
6 time, but we are just trying to coordinate
7 transportation so that everybody gets at least to the
8 airport certainly on time, and well ahead of time in
9 most cases.

10 As was done yesterday, we will be sending around a
11 sign-up sheet again for you all to indicate your name,
12 the fact that you are here, and the contact
13 information.

14 Okay. Bob?

15 DR. BUCHANAN: I will be leaving at ten o'clock
16 and have a rental car, so if anyone wants to leave a
17 little early, I have room for three.

18 DR. SCHECHTMAN: Thank you.

19 COURT REPORTER: Excuse me.

20 I'm the court reporter back here and I don't know
21 who anybody is. So if you all want to be identified,
22 could I get some names before you speak, please?

23 Thank you.

24 DR. SCHECHTMAN: Okay. I'm Leonard Schechtman.

25 COURT REPORTER: Thank you.

1 DR. SCHECHTMAN: Okay. So, with that, we'll turn
2 the meeting back over to our illustrious chair and
3 we'll go.

4 DR. ACOSTA: Okay. Well, thank you.

5 Bill?

6 DR. SLIKKER: Well, first I want to just open with
7 a few thank yous. I mean, we've had some great support
8 during these meetings, and certainly both Travis and
9 Reginald have been very helpful in not only helping
10 coordinate the thing, but also providing
11 transportation. So thank you very much for that.

12 Vickie --

13 (Applause.)

14 The coordinators for the food activities as well
15 as getting the places ready for us to have our meeting,
16 then, Vickie and Mary Ann were both very helpful with
17 that. Rita Zandoval and Virginia Taylor also was the
18 one that helped decorate and coordinate things at the
19 center, and we appreciate their help very much as well.

20 (Applause.)

21 And then, of course, from our Washington office,
22 most of you are interfacing with Kim Campbell. She is
23 not here, but she was able, of course, to do most of
24 the communication up front and provide the travel
25 opportunities for you, both in Len's office in

1 Washington and our NCTR office there. So I want to
2 thank both Len in his efforts, as well as Kim Campbell
3 for setting this up and organizing things for us.

4 So thank you very much.

5 (Applause.)

6 DR. SCHECHTMAN: Thank you very much.

7 DR. SLIKKER: So let me begin with just a couple
8 of slides, and I want to sort of set the stage for some
9 discussions that I think will help us perhaps move in
10 the direction of even greater coordination and
11 interaction between the various groups within FDA.

12 So, in this regard, I want to take the opportunity
13 to think about the individuals that made the trip here
14 to be part of this activity. I really appreciate those
15 that came from Washington headquarters. We have many
16 different centers represented here, and that was a
17 great effort on your part to be here and take part.

18 We think this was really a first step in trying to
19 get a greater and closer interaction between us and the

20 other centers within FDA.

21 I also appreciate our science -- FDA science board

22 members for being here. Both Xavier and John, we

23 really appreciate you being here and taking part. And

24 I know that it was meaningful for us and I hope for you

25 as well in understanding greater the opportunities for

1 interaction between the various centers.

2 I think that the research strategy for NCTR/FDA
3 really has to be focused and have the resources that we
4 have at our disposal focused on regulatory issues to
5 enhance decision making and many of these kind of
6 opportunities we talked about yesterday. And I think
7 this is one of our main themes.

8 The other focus has to be technical innovations to
9 speed FDA regulated product review and safety
10 assessment. And with some of the products that you saw
11 yesterday that have been developed, both in terms of
12 the bio-chromatic side as well as the omic side, other
13 kinds of imaging technologies, I think you see how
14 we're moving very quickly in that direction. And so
15 these are the two main areas that we want to focus our
16 resources in the future, and have actually been for
17 many years now, in order to enhance the opportunity for
18 us to make a positive difference within the FDA.

19 Now, what are some of the approaches that can be

20 used to focus these resources? We talked about some of
21 these yesterday, and I have some examples up here. But
22 I think you can see that the -- one of these is the
23 product selection board approach, and this is certainly
24 exemplified by the NIEHS at DAIAG that you heard us
25 talking about yesterday. There is other boards that do

1 this kind of thing as well, but we think this is
2 certainly one approach that has worked within the
3 agency. It allows input from the regulators as to what
4 needs they have. They sit at the same table while the
5 protocol is being developed, discuss the data that is
6 being generated on a periodic basis; and, of course,
7 they are involved in the output of that data for useful
8 regulatory purposes. So certainly we think this is
9 certainly one mode that has been working and we want to
10 continue to see that happen.

11 Of course we would like to see this maintained and
12 enhanced. And that is something, of course, that is
13 external to us. That decision is made at least in part
14 by NIEHS, but also by interfacing with FDA and also
15 other -- other agencies. So we hope to see that mode
16 continue moving forward.

17 Another way in which we approach this through
18 focus resources can occur is through the request for a
19 proposal approach. And certainly the Office of Women's

20 Health has been using this approach very successfully
21 over the last several years.

22 In addition to that, as many of you remember, I
23 guess about a year or so ago, there was another
24 approach within FDA, that is the Office of Science also
25 had a request for proposals, and this also encouraged

1 interaction between the various centers to solve
2 particular agency research problems. Those funds are
3 no longer available, as you know, from the Office of
4 Science. So right now as far as the Office of Women's
5 Health offers this only opportunity. We think this is
6 certainly a good example, and we want to see this
7 continued and enhanced in the future.

8 Now, of course, the other way in which we sort of
9 focused resources is based on the regulatory or the
10 regulator initiated approaches. And I think you heard
11 quite a bit about ketamine and the anesthetic agents,
12 certainly is just one example of the many different
13 opportunities that have arisen over the years where
14 their regulatory individuals within FDA have interacted
15 with us in such a way that we developed together a
16 protocol that allows us to solve a particular issue.
17 In this case, even within the area of anesthetic
18 agents, and certainly the area of methylphenidate is
19 another example of that.

20 So, certainly this is going to continue. We hope
21 to find ways to actually enhance this particular mode.
22 And then the last one I can think of just off the
23 top here is research initiated or the researcher
24 initiated. And here what we're talking about are the
25 researchers within NCTR coming up with particular

1 studies that need to be done to move forward to the FDA
2 regulatory responsibility and capability, as well as
3 being able to look at new approaches in particular.
4 And certainly the development of a rate track was
5 something that was done by the researchers and
6 initiated here at the NCTR. The work that we saw that
7 allowed for the rapid identification of terror agents
8 or hosts in making that decision. That was developed
9 here at the NCTR from a researcher's perspective. And
10 oftentimes it meant put together several different
11 aspects of a problem and solving it as a total concept.

12 And this -- this takes a great deal of
13 coordination. But it also takes a great deal of
14 communication, the fact that others within FDA are
15 going to use these techniques. And certainly we've
16 been able to do some of that communication not only
17 through one-on-one contact, but also through press
18 releases and other kinds of presentations. And with
19 the rate track, of course, we've gone the extra mile to

20 actually go and train individual regulators within the
21 various other centers of FDA to use that particular
22 kind of tool, the bio-chromatic tool on the rate track,
23 for example.

24 So, just up front, these are some of the
25 approaches that I've seen have been used in the past,

1 and we really want to continue with all of this. But I
2 think there are some ways that we can sort of tweak
3 these to make them a little bit better in some cases.

4 Now, the first one here is, of course, Product
5 Selection Board. We certainly want to see this
6 maintained and we would like to enhance this. It's
7 possible, I guess, that we could have relationships
8 with other government agencies that also want this kind
9 of approach. But we certainly want to see the IAG
10 within NIEHS continue to be enhanced. And over the
11 years we've been able to usually start out with a
12 certain number of support. A good, good strong number
13 for support during that, and oftentimes be able to
14 build on that during the year as important issues come
15 up and become to the point where they have to be
16 funded. So this is a very important interaction for us
17 and we want to see this continue.

18 Again, however, we do not control those particular
19 purse strings. That's something we rely on other

20 agencies to do, and so it has to be a cooperative type
21 of spirit. Of course, FDA headquarters can have a
22 positive influence on that process, because they can
23 certainly let everybody know that these data coming in
24 are important to the agency for decision making. And I
25 think that certainly is done through the CSSRC

1 meetings, at which we usually alternate between the
2 NCTR location and Washington, D.C. location, so that we
3 have plenty of visibility to perform coming out of this
4 particular agreement.

5 Request for proposals, of course, we would like to
6 see this area expanded, not only within the Office of
7 Women's Health, which would be great, and I know that
8 more -- more clients and some support can be needed
9 there. But, again, it could be possible that other
10 kinds of proposals could be made available, other kinds
11 of opportunities. Whether it be ones that enhance the
12 interaction between the various centers or whether it
13 be another sort of special groups of individual
14 classification, whatever. It could be that this kind
15 of thing could be enhanced and that other opportunities
16 for request for proposals can be generated within the
17 agency. This is something that I think certainly
18 provides a focus for research to be accomplished within
19 the agency, and these proposals, of course, are

20 generated around certain themes that are hopefully
21 generated by its regulators that need certain kinds of
22 information, or perhaps new direction for the future in
23 terms of technology assessment and appropriate use.
24 But I think this is something that we can look into and
25 see if there might be other expanded areas in which we

1 can use this principle, as it's been so successful for
2 the Office of Women's Health.

3 Now, in the regulator initiated perspective, we
4 think this benefit could be improved. And one thing
5 that I propose is for the NCTR to create a new position
6 of associate director for regulatory activities. This
7 individual would have support and be able to travel a
8 lot, would be one of the obligations here, to interface
9 between NCTR and the other centers of FDA, with a
10 special focus on the regulatory aspects of the other
11 centers. I would like to see a systematic sort of
12 review and description of all of the regulatory units
13 within the FDA and be able to have this individual
14 interface between them and the folks at NCTR and other
15 researchers within FDA.

16 The idea being that not only the identification of
17 those regulatory groups that may need additional
18 research support, but it would also be an opportunity
19 to let them know what's available, what capabilities

20 that NCTR has, and to hopefully link people up through
21 seminars, through face-to-face interactions, through
22 visits, so that we have the opportunity to interact
23 with these regulatory units within the rest of FDA.

24 I think this is one area where we can certainly
25 improve what we're doing and improve on the idea of

1 research that is initiated from a regulatory
2 perspective.

3 The other area, of course, that we can have an
4 influence on is in researcher initiative. And here I
5 feel like we need to realign the research divisions of
6 NCTR to some extent, and to certainly develop and
7 emphasize that strategic plan.

8 Now, as you know, just recently there has been an
9 FDA strategic plan that is going through a final
10 review. And our strategic plan is being developed from
11 the cascade of that plan at the FDA level. And we will
12 be working on this for the next several months before
13 we have it in draft form where it can be circulated.

14 But I think what we can do right away is to look
15 at the realignment of some of these divisions within
16 the NCTR, to focus on what I think are some of the very
17 important issues associated with regulatory
18 responsibility within the FDA.

19 And I'll get to that example in a moment.

20 But first I would just like to say if people think
21 of other examples or other approaches in which we can
22 use to focus researchers -- research resources within
23 the agency.

24 Is there any ideas out there, other in addition to
25 the ones I mentioned here?

1 UNIDENTIFIED: Bill, will you entertain a question
2 at this point?

3 DR. SLIKKER: Yes.

4 UNIDENTIFIED: With the four approaches you've
5 indicated, what is your current portfolio in regard to
6 those four approaches and what does your ideal
7 portfolio look like if you move and actually implement
8 it down the road?

9 DR. SLIKKER: Well, in terms of percentages, it
10 probably would not change a great deal, but I would
11 like to see all of those just increase in number and
12 support level. That is, you know, we do have a fairly
13 good balance between these approaches right now, but I
14 think that we would probably increase the percentage of
15 the work within that that's initiated by regulators by
16 having this person serve this particular role.

17 I certainly see us -- we're already doing well
18 within this area here in terms of being competitive for
19 the Office of Women's Health grants; however, of

20 course, we could always do better and there could be

21 other opportunities within that area.

22 The -- this group here, the IAG, as you saw

23 yesterday, represents about, you know, 25 to 30 percent

24 of our support at this point in time. And so, you

25 know, that could grow a bit, but I don't see it growing

1 very much beyond that. It just depends on what support
2 the NIH would get.

3 So, you know, I think the ones that may take on a
4 little bit longer significance would be, certainly, the
5 regulator initiated ones; and also I think that we
6 could do a bit more here in this area of researcher
7 initiated ones, making sure that the work that we're
8 doing is consistent with the goals of the others within
9 FDA, especially the regulators.

10 So any other questions or comments?

11 Any other ideas on how one could approach the
12 focus of resources?

13 Okay.

14 (Phone ringing.)

15 UNIDENTIFIED: I apologize.

16 DR. SLIKKER: Okay. If not, I'll move forward to
17 the next one.

18 What I'm interested in here is looking at the
19 opportunity to realign resources so to take advantage

20 of certain very important divisions within our
21 operation currently and actually use their combined
22 resources to create a new division that I think will be
23 even better positioned for the existing ones.

24 Yesterday you heard from both the Division of
25 Biometry and Risk Assessment and the Division of

1 Molecular Epidemiology and Pharmacogenetics. You also
2 heard from the other six centers, but we'll get into a
3 little more detail here today.

4 But these two in particular have certain
5 characteristics and certain capabilities that are
6 really outstanding. And what I would like to do is
7 propose the idea that these two divisions actually be
8 combined as far as their personnel and have a new title
9 that really directs them toward the idea of
10 personalized nutrition and medicine.

11 I think that these form the basis of this
12 particular approach. And the reason is is that you
13 need the bio-statistician working closely with the
14 biologists and the epidemiologists to not only design
15 the proper experiments, but also then utilize that
16 information to have an impact, and that is the idea of
17 being able to select patient groups that are going to
18 benefit from these particular kinds of therapies or
19 these different kinds of nutritional alignments.

20 So this is what we are proposing to do is to use
21 the personnel from these two groups that have been very
22 creative and very capable and to combine them and to
23 make this division, then, to really focus on this
24 issue -- on these issues that we think are so important
25 for the future of FDA and to medicine in general.

1 I don't think anybody can question the fact that
2 we're moving in a direction of individualized,
3 personalized medicine; the idea of giving the right
4 drug to the right person at the right time. And we
5 also feel like nutrition, although not quite developed
6 to the point of the pharmaceutical area right now, is
7 certainly moving in that direction, as well. They can
8 use many of the same tools to accomplish this.

9 So we think this would align us in a better, more
10 productive way for the FDA.

11 Now, what is it that is driving the momentum
12 towards personalized medicine? And I'll just say right
13 up front that I used this slide from Dr. Wheeler from
14 AstraZeneca. It was presented at our FDA Science Forum
15 Symposium that we had on personalized medicine that
16 Dr. Sue-Jane Wang and I chaired. And I think this sort
17 of summarizes some of the reasons why we think that
18 personalized medicine is going to continue to be a big
19 factor within the health care system in the United

20 States.

21 What are some of the expectations? Well,
22 certainly, everyone would like to have safer and more
23 effective drugs. And the idea that one size drug fits
24 all is just not something that's very popular or
25 realistic at this point in time. We can be more

1 specific than that, and we can identify subpopulations,
2 even down to individuals that can be more receptive to
3 certain drug therapies, and also identify those that
4 may have some adverse effect that you want to avoid.
5 So, certainly, this is one of the driving forces.

6 Another one, of course, is the idea that can you
7 move things along more rapidly, using omics, genomics
8 and other information combined with these targets that
9 should allow for speedier clinical trials, you know,
10 based on high responder population. So the idea is
11 that you target your particular trial to include those
12 populations that you feel are going to be responders;
13 and, of course, try to eliminate those who are not
14 going to be responding appropriately or actually will
15 be responding adversely. So we think this is a feature
16 that will drive it.

17 And the last one, of course, is the idea of trying
18 to reduce the cost of health care. I mean the idea
19 here is to avoid those futile treatments and those

20 kinds of technology that aren't going to have an
21 improved outcome.

22 So these are some of the driving forces behind the
23 utilization of this particular approach. But I think
24 it goes really far beyond this with the idea of using
25 the latest technology to help advance both drug

1 development and drug safety, as well as the importance
2 of improving nutritional status across this country.

3 So in this pathway to personalized nutrition and
4 medicine, what are some of the approaches that need to
5 be considered? Well, certainly it's a
6 multidisciplinary type approach. I mean we need the
7 molecular epidemiology and epidemiology in general.
8 Has to be a feature. We have strong people in that
9 area. But what we are going to do is blend them with
10 the bio-statisticians as well.

11 Certainly omics. We're talking about genomics,
12 phobiomics, katalomics. We need all of those to help
13 move this process forward, and these ideas as well.
14 Because what you have to be able to do, of course, is
15 understand more about the individual groups of
16 individuals, to be more effective in utilization of
17 both of the bulk of the medicines.

18 We think imaging can play a role here. Not only
19 in identifying the disposition of food and agents in an

20 automated way, but also using that to look for safety
21 assessment end points that you cannot do, as we say, in
22 many of the human studies that are now going on. We
23 can do that with imaging. We can develop the biobasic
24 techniques and animal models in any given situation.
25 And then, of course, bio-chromatics. You heard a lot

1 about this yesterday. For the rate track and the edit
2 tools, especially the panomics approach, the multiple
3 omics end points that are integrated by the new rate
4 track tools that allow this integration are really key
5 to this whole process. And then, of course, the
6 statistical classification.

7 Certainly the Division of Biometry and Risk
8 Assessment are doing a great job, along with others,
9 and assistant biology developing this technology. We
10 want to see these integrated with the biology up front
11 and to be used in populations that are going to be more
12 sensitive and responsive to these drugs.

13 So this is the kind of resources we have available
14 to us within the NCTR, and what we want to see is the
15 combining of the Molecular Epidemiology Group with the
16 Bio-statistician and Biometry and Risk Assessment Group
17 in a form, a division that we think will be very
18 responsive to FDA needs.

19 The other thing here, of course, you know, why

20 now? Why not later? Why not earlier?

21 Well, we did not have these tools available until

22 just recently. The elevated omics tools, using human

23 approaches, the bio-chromatic tools to do this. And so

24 now we have the tools available to make this

25 transaction.

1 The other thing is that we are experiencing some
2 changes in the personnel at NCTR. And I've been
3 informed that a couple of the leaders in this area are
4 going to retire soon. So, if that happens, that gives
5 you a challenge as well as an opportunity. The
6 opportunity here would be to realign the resources into
7 one division and to build on them via new personnel to
8 reach these goals.

9 So this is the direction we would like to move in.
10 And we think this is overall going to be a great
11 support to FDA. We feel like the research divisions,
12 including our new Division of Personalized Nutrition
13 and Medicine, is going to support the science based
14 NCTR, and therefore the science base of the agency.
15 And this is going to enhance and interact for us with
16 all the other product line centers, including RA
17 within -- within the FDA.

18 As you saw yesterday, we do have a lot of
19 interaction with the academic area, with industry

20 through CRADAs and interagency dealing with other
21 government agencies. And I think what's critical here
22 is that this interaction continue to be improved with
23 the rest of FDA. You can do this through CRADA
24 opportunities, you can do this through situations where
25 you are forming alliances. And I think that we can see

1 more of this opportunity as with the CBAC Institute to
2 develop these interfaces. And all of those, of course,
3 working together is going to produce these
4 collaborations to protect public health.

5 So this is the direction that we have configured
6 ourselves in and what we're going to move to, and we
7 think that adding this new division will really help
8 this process and move us forward to be more effective
9 in interacting with the rest of FDA and improve health
10 care for America.

11 So I will open it up for questions and discussions
12 at this time.

13 Yes. Bob?

14 DR. BUCHANAN: In putting together the two
15 divisions into a group consolidated form, based on what
16 you would put out, if there being -- would there be a
17 de-emphasis in the risk assessment area?

18 DR. SLIKKER: Well, you know, the thing is is that
19 we're going to maintain the same scientists and even

20 grow the number of statisticians within this group.

21 One of the moves that we're working on now is

22 actually moving some of our contract statisticians into

23 the Biometry and Risk Assessment Group, and this will

24 likely give us greater capacity in this area.

25 So, no, I don't see us de-emphasizing that.

1 Matter of fact, what we're going to have is, like right
2 now, is probably a branch structure which will still
3 maintain the importance of biometry and risk assessment
4 in the process, to allow these individuals to work more
5 closely with the biologists where we need that
6 interface to grow and be extended. Not only on
7 interpreting the data that comes up with biology, but
8 building the experimental plan for the rights of
9 statistical design so it can be useful, and then
10 developing those, those bio markers and influence where
11 they can be classified using the new statistical
12 alternatives that have been developed.

13 Are there any additional comments or suggestions?

14 Yes.

15 DR. THOMAS: Thomas.

16 How do you propose to enhance your IAG
17 collaborative activities?

18 DR. SLIKKER: Well, one thing that we've tried to
19 do and have been successful at is to produce quality

20 work, quality data that can be used in the regulatory
21 arena. And I'm very proud of the staff at NCTR, in
22 cooperation with the other centers, in generating these
23 data. And I think the idea that you move beyond sort
24 of the cookie cutter approach of doing a two-year
25 bioassay to really examining what the problem is,

1 understanding what end points need to be evaluated and
2 doing it in a systematic way, including
3 pharmacogenetics, oftentimes blood levels, and certain
4 existing information, that that model has proven very
5 successful and was actually picked up by NTP in general
6 in many cases.

7 But I think, you know, Fred Beland and his group
8 and all the other divisions that contribute to the data
9 generation, the quality data that is used by FDA to
10 make critical decisions, that really is the first thing
11 that we have to continue to do, because with that, we
12 have a good history to say that we can do this and we
13 can do it right.

14 The second thing, of course, is that we have been
15 very successful, thanks to Bill Allaben, in working
16 with the NTP administrators and NIEHS to keep this core
17 level up. And we have been able to grow it a little
18 bit over the years, as you saw, from '93 down to --
19 less than a million to somewhere around 13 or

20 14 million.

21 So we want to continue that feat; but, of course,
22 that is dependent upon the administrators within NIEHS.

23 It's not solely dependent upon us.

24 The other way, of course, is to enhance the
25 understanding within FDA that this is important to FDA

1 and that FDA can have a role from the top down in this
2 regard, interacting with the other agents and the other
3 centers. So we're hoping for that kind of support, as
4 well.

5 And then, you know, we have been able also to work
6 with other government agencies. And I think this is
7 the key. NTP, NIEHS is obviously kind of the big kid
8 in the block. However, you know, this last year, for
9 example, the IAG support from NICHD has been close to
10 two million. Okay. We have other interagency
11 agreements with EPA, with NIDA. We have various groups
12 over the years that have helped support this effort.

13 So we want to diversify our portfolio a little bit
14 and see if we can reach out to other governmental
15 agencies that are also eager to have our support. But
16 it all has to be within the mission of FDA, and that's
17 one thing that's been very strong about the NTP and
18 NIEHS relationship, because it's driven by FDA
19 regulatory issues.

20 Of course, NICHD is right in there, too, with
21 methylphenidate, ketamine, and anesthetic agents, of
22 course, that fits in with what we're doing. So we want
23 to continue that interaction.

24 Does that answer your question?

25 DR. THOMAS: Yes.

1 Thank you.

2 DR. SLIKKER: Okay. Yes?

3 DR. HANIG: Kind of a very general question,

4 but --

5 DR. ACOSTA: Please identify yourself.

6 DR. HANIG: Oh, Joe Hanig.

7 I was wondering what the status of the statutory
8 authority of NCTR really is. One of the -- one of the
9 problems we've always faced over the years is when it
10 came to the research areas, we didn't have that much
11 statutory authority, but we were able to relate to the
12 regulatory needs of our center and others. And I'm
13 just wondering whether there are -- there are any
14 interpretations of the statutory authority or the
15 regulations that would allow a -- a, you know, greater
16 participation on the part of NCTR in the actual
17 statutory activities of the various centers.

18 Is there any -- is there any legal interpretation
19 that you might be able to get that would extend or help

20 you to share the regulatory activities of the other
21 centers without infuriating them? Let me add that.

22 (Laughter.)

23 DR. SLIKKER: I'm not sure we need to even answer
24 that question.

25 It seems to me that that is based on the laws as

1 written by Congress as who has authority to regulate
2 certain areas, and that is given and picked up by one
3 particular group within FDA, whether it be, you know,
4 veterinary medicine or whether it be foods or
5 biologics.

6 And so, you know, I don't -- I don't really know
7 if there needs to be additional categories of that, I
8 think is a little of what you're asking, is additional
9 categories.

10 But, you know, I think that the framework that we
11 have currently can certainly, you know, handle this
12 particular kind of interface. It's -- I don't think we
13 really need anything more in terms of laws to make this
14 happen. I think we just need to make sure people
15 understand what the capabilities and opportunities are
16 and to enhance those interactions.

17 DR. HANIG: Well, I -- I really wasn't thinking in
18 terms of new laws. I was just really thinking in terms
19 of the interpretation of the existing laws as they are

20 articulated by the various regulations of the project

21 area. Because the spirit of the whole thing, I -- is

22 really the law, but the letter of it through the regs.

23 So anyway, just --

24 DR. SLIKKER: Yeah. I appreciate you.

25 Yes?

1 DR. LORENTZEN: Ronald Lorentzen.

2 I do have a related question, I think. I think

3 what Joe is referring to is creative interpretation.

4 But it seems to me that --

5 DR. HANIG: Much appreciate it.

6 DR. LORENTZEN: -- the four categories -- I

7 believe there are four -- that you have, that you --

8 you don't have direct control over any of them. And,

9 you know, that may be part of the problem. I mean,

10 I -- and this is sort of a rhetorical question. Is

11 there some way that you can shore up the agency's

12 commitment to NCTR in a more general -- to give us some

13 stability?

14 You know, I notice those four and I said, you

15 know, the -- doing creative things in all four of those

16 continually, and you've not going to have a base.

17 I don't mean to sound pessimistic, but it seems to

18 me that that's missing in the -- in the structure of

19 things.

20 I know it's not a question, I'm sorry, but it's a

21 general observation.

22 DR. SLIKKER: Well, I mean, I think we do have

23 control over some of those categories. Not complete

24 control. I don't think anybody has complete control.

25 DR. LORENTZEN: Direct. Not direct control.

1 DR. SLIKKER: Yeah.

2 I mean, we can certainly align some of things we
3 do have within NCTR to be more effectively interfacing
4 with other than FDA. But we can certainly provide a
5 way, a conduit for greater interaction between us and
6 the regulatory division and agents -- divisions and
7 staff within the rest of FDA.

8 But you're obviously right. We do need a base in
9 terms of a support base, and we do have a line item
10 that says NCTR on it and it has funds associated with
11 that. And so that -- that does need to be maintained,
12 because all these activities are based on the idea that
13 you have a facility that's capable of doing the work,
14 which means that it has to be maintained and it has to
15 have maintenance and it has to have, you know, natural
16 gas and water and electricity. You have to have
17 personnel to do this work and they have to be, of
18 course, funded and supported. And then you have to
19 have supplies and equipment to get this work done, as

20 well. So you do need this base funding. It can be, of
21 course, supplemented by outreach to other groups and by
22 bringing in special interactions with Office of Women's
23 Health, for example. But you're assuming you're sort
24 of working with a base that's already there. I think
25 that's what you're speaking to. And, yes, we do need

1 to maintain that base and it needs to be actually
2 enhanced of where it is now.

3 You've already seen the Senate mark up and the
4 House mark up and how the Senate mark up will allow us
5 to be productive next year. But as you also saw, it's
6 not increasing over the last five years, and so, we've
7 been hopefully stable. And that base can be maintained
8 and needs to be enhanced. You're absolutely right
9 about that.

10 DR. ACOSTA: Let's see. John and Nancy.

11 DR. THOMAS: John Thomas.

12 I know it's preliminary with respect to your
13 discussions about realign, but if one of your goals is
14 to enhance your interagency agreements, rather than to
15 look towards an appointment of another associate
16 director, which you entitled regulatory -- what was it?

17 DR. SLIKKER: Activity.

18 DR. THOMAS: Regulatory affairs. If I were
19 sitting in another federal agency, I guess I would be

20 more impressed with associate director for -- and I'll
21 just pick a name out of the air -- external scientific
22 affairs. I would be more inclined to deal with you if
23 I had a scientific problem unresolved, particularly if
24 you're dealing with someone out of NIH. Why am I
25 dealing with someone who is regulatory affairs, we

1 don't do any regulatory things at NIH. So just a
2 thought.

3 DR. SLIKKER: Right.

4 DR. THOMAS: As you consider, you know,
5 realignment nomenclatures.

6 DR. SLIKKER: Yeah. Well, John, you have a good
7 point there. I think that, certainly, you know,
8 science and research are the core of NCTR. The idea of
9 reaching out to the regulatory divisions and staff
10 within FDA is to enhance that force that will drive us
11 to be more interactive and provide more guidance to the
12 regulatory divisions, so that's why I move in that
13 direction. But I understand what you're saying, in
14 that we're going to be obviously reaching out to other
15 government agencies, and they will be more science
16 based.

17 So we're not scheduled right now to change the --
18 the name of our organization, which is the National
19 Center of Toxicology Research.

20 DR. THOMAS: Well, your question you have research
21 in your title. There is a lot of groups within FDA
22 that would love to have part of their nomenclature.

23 DR. SLIKKER: Right. So I don't think there is
24 any requesting we change that. But, I mean, I think
25 that you're absolutely right in terms of visibility.

1 It's nice having that as your title of your
2 institution.

3 DR. THOMAS: Just something to think about as you
4 move forward.

5 DR. SLIKKER: Thank you.

6 DR. ACOSTA: Nancy?

7 DR. GILLETT: Nancy Gillett.

8 Bill, what I liked about what you presented was
9 the first part, where you talked about focusing
10 research centers and helping to define critical
11 decisions for regulatory and innovative technology for
12 critical path. And then the next part was to take --
13 was more expanding where your proposal can work where
14 it comes from, which is actually with the mixing of
15 issues. So you may want to be expanding proposals, but
16 I think that bringing it back into focus around those
17 two points and really making sure that that mission is
18 very visible on everything that you do, both internally
19 and externally, I think with the strength of the NCTR,

20 in the years that I've been associated with NCTR, I've
21 been impressed that there is more focus now on critical
22 FDA issues than before, particularly in a time with
23 limited resources, that have been decreased. And I
24 think that the team as you go through your strategic
25 plan in the next few months and in focusing on those

1 points has every project, same thing, Bob's point,
2 about where is the portfolio sitting today. Where is
3 the portfolio going. How do these new proposals fit in
4 to those two main points, I think would be a good
5 approach.

6 DR. SLIKKER: Right. Well, that's a very good
7 point. I mean, the idea that we want to provide data
8 for decision making and that we want to develop new
9 technologies that advance decision making, that really
10 has to be the core, and that's what you're saying, so I
11 appreciate that.

12 DR. ACOSTA: Ralph?

13 DR. KODELL: Okay. Ralph Kodell.

14 I would like to go back to Joe Hanig's comment and
15 I think a little bit to John Thomas', as well.

16 I think you hit a critical point about we need to
17 be critical to FDA. And I think if I could speak
18 freely, I think over the years we've -- some of us or
19 maybe we -- we've had lots of interactions with other

20 scientists in the regulatory center, and I think we've
21 made lots of contribution. But I think there has also
22 been an attitude that we're different from the
23 regulatory center, we don't have a regulatory mission,
24 so we should be looked upon different. And I think
25 that was okay when money was free flowing, but now, in

1 kind of hard times funding wise, I think that was a
2 mistake, because we're not receiving the credit. And
3 so now, you know, the last few years, we've tried to
4 change that approach and that attitude and find a way
5 to be critical so that, you know, something has to go
6 through NCTR as well as it has to go through some of
7 these other agencies. And so I think that's a key
8 point, we need to really pursue that and that's, I
9 think, why, you know, Bill is talking about the
10 associate for regulatory activities, so that we can
11 really engage, you know, fully and try to find out what
12 the issues are and be sort of critical to address
13 those.

14 And I would also like to, if I could, speak a
15 little bit to Ronald Lorentzen's comment, and I think
16 this to Nancy, as well. Bill's proposal to reorganize,
17 realign, and personalize the nutrition and medicine
18 idea, you know, that's not your traditional toxicology
19 at all. But the fact that resources are limited, you

20 maybe can't feed every research program to the level
21 you would like to, I think he's trying to do some
22 consolidation and put some emphasis in an area that
23 really is high on the priority list of the acting
24 commissioner, the EPI commissioner, and the secretary,
25 and the Secretary of Health. At least personalize

1 medicine. And we feel that we do have a contribution
2 to make there.

3 And so, Ron, I mean, I guess that's like, well,
4 not just going to the center, but going to the agency
5 for funding, but I think that's an overall sort of a
6 broader goal, and that's why Bill is doing that. So I
7 think sort of both, I mean, kind of sort of attack both
8 areas. Go to the regulatory centers, be critical, do
9 something overall that's really important to the powers
10 that be at FDA and NHHS.

11 And so, I mean, I think that pretty much sums up
12 why you're proposing what you're proposing, at least in
13 my opinion.

14 DR. BUCHANAN: Yeah. I have --

15 DR. ACOSTA: Bob, if you'll identify yourself.

16 DR. BUCHANAN: Bob Buchanan.

17 I have -- one is a question in terms of my role as
18 a liaison back at my center. And then I have a second
19 comment on your reorganization.

20 But the first one is, this is a public meeting,
21 and normally I would feel that anything that can be
22 said in a public meeting is for public dissemination.
23 Has this reorganization been announced to all of your
24 staff and has the union been notified and can I go back
25 and say that this reorganization is in the process of

1 taking place? Or if I preempt this, am I going to get
2 you in trouble with all of those people involved?

3 DR. SLIKKER: Well, what I presented to you was a
4 proposal that's been headed with the senior staff of
5 NCTR, with my immediate supervisors in Washington.

6 DR. BUCHANAN: Okay. So it has not been
7 announced --

8 DR. SLIKKER: This is a proposal.

9 DR. BUCHANAN: Okay. It has not been announced to
10 nonmanagement personnel?

11 DR. SLIKKER: That is correct.

12 DR. BUCHANAN: Because I need to know that because
13 if I go back and it's for general dissemination, it
14 will get back to all of your --

15 DR. SLIKKER: Right. I mean, there is probably no
16 doubt that since we've been discussing this for over
17 four months, that probably everyone already knows. But
18 what I wanted to use this opportunity to do was to make
19 this proposal so I can get discussion from individuals

20 that are within the rest of FDA, our science board
21 members, and members of the senior staff. And we've
22 been having these discussions at that level for some
23 time, but I wanted to extend that opportunity for a
24 greater discussion here. So that's where it is right
25 now. Yes.

1 DR. BUCHANAN: And then the only other
2 recommendation I would have is, before you use the
3 name, as you've so indicated, which includes the phrase
4 personalized nutrition, that you talk to the applied
5 nutritionists within the center, our center. That is a
6 very controversial approach to nutrition, and it sets
7 up all kinds of red flags to people within the
8 nutrition community. And so, before you invest in that
9 name, you need to get some buy-in from the nutrition
10 community.

11 DR. SLIKKER: I think that's a very good idea, and
12 we have floated it out there, so some people that are
13 strong in nutrition -- but I need to talk with more of
14 the folks within your organization that deal with
15 nutrition on a daily basis, as well.

16 So that's a good comment. I appreciate that.

17 DR. ALLABEN: So, Bob, do I detect a turf issue
18 here?

19 DR. BUCHANAN: No. You have a -- well, you have a

20 turf issue in the entire field of nutrition. You have
21 people who buy into a medical/drug paradigm approach to
22 nutrition, and then you have the other side of the
23 community which is the food/dietetics paradigm of
24 nutrition, and they are literally -- they, I'm not
25 going to say at war with each other, but tremendous

1 debate when you get down to coming up with daily
2 requirements and things like that. It's just a huge
3 Academy of Science which report on these kind of
4 things. And it's something that you need to be aware
5 of before you put your feet in the water in nutrition.
6 I mean, these are very definitive camps within that
7 discipline, and --

8 DR. SLIKKER: I appreciate that.

9 But, I mean, I also appreciate the fact that we're
10 talking about using new technology to try to solve some
11 of the issues within nutrition, and it may not fit into
12 either one of these existing camps that, as you've
13 said, are at war with each other. So I do want to get
14 their input, but our approach is really not a
15 traditional one. It seems the new kind of omics, the
16 new approaches that help deal with the issues other
17 than using traditional older methods.

18 Yes, Joe.

19 DR. HANIG: Joe Hanig.

20 Well, I think the issues that were brought up
21 about names are very -- are very important. I mean,
22 it's almost a semantic issue. When you go ahead and
23 you name something and that name is already known for
24 certain things, you also have the disadvantage of all
25 the associations that go along with the name. You have

1 to live with it.

2 The thing is, the NCTR has a tremendous reputation
3 that's associated with the title. But I've always
4 felt, despite the fact that toxicology is near and dear
5 to all of our hearts, that the term toxicology is
6 somewhat isolating in a sense. I wouldn't go as far as
7 to say consider renaming, but there are a lot of people
8 who say, well, we're not in the business of toxicology
9 or preventable type stuff, we're more interested in
10 efficacy and clinical stuff. And you all seem to be
11 doing that, but I think a lot of times you get isolated
12 by the names that you choose and what people associate
13 it with.

14 I've always felt that NCTR was at the forefront of
15 a lot of strategic planning and science, whereas a lot
16 of the things that were in the various centers were in
17 certain ways more tactical because they address the
18 very specific regulatory needs that we have.

19 So, we've never, in recent times, had any sort of

20 organizational or discipline lines. I remember very
21 clearly when we broke out of all product lines, and
22 that had some tremendous, you know, duplicative
23 implications right there.

24 So I think an awful lot of thought ought to be
25 given to the ramifications of the whole organization

1 and how -- and how research responsibilities are parsed
2 out. And I really think the new -- that the acting
3 commissioner and possibly the new commissioner is
4 somebody who might appreciate all of the subtleties and
5 help you with this problem which I seem to be having
6 trouble, you know, really articulating, but I think you
7 know what I'm -- what I'm driving at.

8 The issue that was brought up earlier about not
9 having statutory authority, those of us who do research
10 in SEDA, we really don't have statutory authority
11 either. We -- we try to elicit a consensus as to what
12 is important. But a lot of times looking at -- you
13 know, for love in all the wrong places, and it's very
14 hard for us to identify our constituencies. I think we
15 started out doing it by group and by individuals. I
16 find it's much better to look at the regs and see
17 what -- what they demand. For instance, with
18 pediatrics, there is a tremendous need there and then
19 you go to the people who -- who have that interest and

20 whatever.

21 So, anyway, I've rambled on long enough. But I
22 think there are certain things that could be explored
23 in order to strengthen a lot of the things that it
24 looks like you want to accomplish.

25 DR. ACOSTA: Xavier.

1 DR. PI-SUNYER: Yeah. Xavier Pi-Sunyer.

2 I wanted to ask you if you could clarify a little
3 bit your ideas about molecular epidemiology. Do you
4 see your center collaborating in large clinical trials
5 and getting involved in omics and imaging and so forth?
6 Do you see yourself setting up your own cohorts? Do
7 you see yourself using existing data sets or -- I mean,
8 you know, this is an extremely complicated area, and a
9 very expensive area to get involved in. And the
10 question is how will you approach the molecular
11 epidemiology market?

12 DR. SLIKKER: Right. It really is a multiple
13 level kind of situation and answer.

14 There are certainly some situations where we would
15 either hope to come or already are placed with the data
16 being stored and analyzed and manipulated. And those
17 kinds of cases where we have interfaces with, whether
18 it be the CPAP Institute or whether it be CDISK, which
19 is a census building group that has certain standards

20 they want to see for data set storage and analysis, we
21 are interfacing with them and, of course, with the
22 other centers at FDA to make these opportunities
23 happen, where the data would be stored and manipulated
24 and analyzed at NCTR in conjunction with other centers.
25 So that's a partial answer.

1 In the case of data sets for -- and in the data
2 sets for those would come, oftentimes, from industry.
3 They would make them available through CDISK and
4 through CPAP and other organizations where they can
5 come in and they can then be gathered by researchers at
6 NCTR and other centers and brought in.

7 So, yes, those are very expensive data sets to
8 generate, and in that case we would be using other
9 people's data, and knowing that they would be able to
10 have access to that data and be able to benefit from
11 the options of those analysis. So that is ongoing.

12 The other things are using data sets that are
13 available through other government agencies, such as
14 NCI and the VA and some of those movements that we
15 talked about yesterday. So there we're sort of sharing
16 data with already existing sources of data.

17 So those will be two ways.

18 Now, also, because of our interaction with the
19 university here, Arkansas Children's Hospital, and

20 others, we do see the opportunity to also grow data
21 sets that are more specific and do it in conjunction
22 with other clinical facilities, and those kind of
23 interfaces are going on as well.

24 So, at three different levels we see ourself
25 interacting. And the more fundamental one, though, is

1 to share data with others and then to store it, analyze
2 it, and use it for decision making in conjunction with
3 the other centers of FDA.

4 Bob?

5 DR. BUCHANAN: Bob Buchanan.

6 Just to follow up a little bit more on molecular
7 epidemiology. And, again, that comment about, you
8 know, what's in a name.

9 You use the phrase molecular epidemiology, but
10 you're using it in conjunction with adverse event
11 reporting. You have to be careful about building a big
12 infrastructure and have it removed if we go to a
13 centralized adverse event reporting system. And having
14 a center that devoted millions of dollars to developing
15 an adverse event reporting system, we're now in the
16 throes of having it try to get everybody to join in
17 together for a central big investment that you could
18 just have it disappear overnight.

19 The second one is as soon as you get into

20 molecular epidemiology in a regulatory -- as part of a
21 regulatory agency, okay, and you have to put your
22 activities in that context, you do need to reach out to
23 the Centers for Disease Control. They do not like
24 people meddling in molecular epidemiology that are not
25 professional epidemiologists and they react badly.

1 DR. SLIKKER: Well, Bob, I appreciate you pointing
2 out all these battle fields that are out there.

3 (Laughter.)

4 I have to say that we already have a division of
5 molecular epidemiology of pharmacogenomics, and so that
6 is something that we cannot change at this point in
7 time. But I understand the sensitivities. When you
8 mention warring camps within nutrition, there is also
9 those within that area.

10 And certainly Luke and Fred is also here, too, can
11 talk to some of these issues. But I understand that
12 there are sensitivities that we've got to be aware of.

13 And that perhaps a more general topic or title of
14 epidemiology to be more holistic may be a safer course
15 in this particular situation. But that division
16 already exists. I'm talking about moving it into a
17 division that would combine it and focus on these other
18 issues on this mission. But certainly that's
19 important. Our part of it would not go away. You're

20 absolutely right.

21 DR. BUCHANAN: And you still need to reach out to
22 these organizations.

23 DR. SLIKKER: Yes.

24 DR. BUCHANAN: Particularly if you're going to
25 build a very large infrastructure and then starting to

1 put out press releases about these new systems and then
2 CDC says, why didn't we know about it and why aren't we
3 involved.

4 DR. SLIKKER: Correct. But a lot of these now are
5 focused on issues that are regulatory issues within
6 FDA. And so that is a consideration.

7 And, Yvonne, maybe you would like to make a few
8 comments along this line just to sort of strengthen or
9 think about as far as interaction with these various
10 groups.

11 DR. DRAGAN: Hello. I think that it --

12 DR. ACOSTA: Will you identify yourself?

13 DR. DRAGAN: I think that -- Yvonne Dragan -- in
14 part we need a presence to move more towards
15 translation in science, as opposed to being complete
16 just realign to personalized medicine. It's that
17 transition in between. We've had multiple interactions
18 with other agencies, obviously. Again, you're starting
19 with a base of NCTR and building it in a certain

20 fraction. Again you have components of this already in
21 place.

22 The systems cost division, for example, is doing
23 things way personalized medicine. That in conjunction
24 with what molecular epi and statistics group is doing
25 makes a very strong movement towards translation of

1 science, builds on the preclinical to clinical
2 opportunities that are both necessary for growth in
3 this area and in any area of toxicology, and
4 specifically a safer assessment.

5 DR. GREENLEES: I'm Kevin Greenlees.

6 I wanted to actually add on to something that Bob
7 mentioned and maybe a little -- at least from my
8 perspective, I think it's a little closer to what he
9 was getting at.

10 Coming from a center that was built some years --
11 some years ago, and it may not help you with this, the
12 strong interaction of medical for CDC, I understand
13 exactly what you were striving, in terms of how this --
14 what you're doing is FDA mission related. That does
15 not in any way address the need or increase the --
16 moving into this area for the FDA lead, increase
17 communications with folks like CDC so that they can
18 stand the fact that you're not creeping into their
19 turf -- their turf here, or that they have a role to

20 play, perhaps, in adjusting the realignment of where
21 you're going or feeding into what you're doing could be
22 important, or having what you're doing contribute to
23 their need. It's communication if you wanted this a --
24 a reality of the substance of what you're actually
25 doing.

1 So I would really concur with them and emphasize
2 the need to reach out to these other groups,
3 particularly folks like the Centers for Disease Control
4 and arbitrary, so that you need to feed that
5 opportunity very, very highly.

6 DR. SLIKKER: Okay.

7 DR. BUCHANAN: If you're on the premarket side,
8 that's one thing. As soon as you move over to the
9 post-market side, you really have to have lines of
10 communication.

11 DR. SLIKKER: And I would say that USDA, as well,
12 because there is a large interest in the nutritional
13 side of things there.

14 DR. KADLUBAR: I think I can address the CDC
15 issue.

16 DR. ACOSTA: Can you identify yourself?

17 DR. KADLUBAR: Yeah. Fred Kadlubar.

18 I'm expecting to become chair of epidemiology at
19 UAMS about October 1. And I am charged with recruiting

20 about 20 to 25 faculty, all of whom will have partial
21 appointments in the health department. And in doing
22 so, they will be supported in large part by grants
23 through CDC, using population that currently exists or
24 data sets that exist in the health department. And,
25 you know, we'll be collaborating heavily with NCTR in

1 all of the molecular epidemiology efforts that we do.

2 So that tie in should satisfy any concerns about
3 turf issues with CDC, I would think.

4 DR. BUCHANAN: They don't really care about turf
5 issues. They just don't like being surprised.

6 DR. SLIKKER: Yes.

7 Luke?

8 DR. ACOSTA: Will you identify yourself?

9 DR. RATNASINGHE: I'm Luke Ratnasinghe.

10 The VA across the street has an initiative
11 underfoot to develop pharmacogenomics lab in molecular
12 epidemiology, pharmacogenomics lab. Fred Kadlubar and
13 myself and others have written a proposal. And I think
14 we're one of two now competing to build this lab in our
15 VA across the street. And NCTR is going to be a
16 central component of it.

17 So molecular epidemiology post-market in clinical
18 trial setting and our contribution to it is well
19 underway. Turf ballots aside, public health

20 contributions is kind of where we're hoping to set our
21 focus.

22 And I don't think there is a battle, really,
23 because it's a young field.

24 DR. BUCHANAN: There is nothing -- this is Bob
25 Buchanan.

1 There is nothing here about a battle. But when it
2 comes to epidemiology, the federal agency that has
3 primary -- primary responsibility for epidemiology is
4 CDC, and you need to keep them informed and involved in
5 your plan from the very beginning, so that they have
6 the opportunity to interact with you so that you find
7 out what they are doing. Because you don't want to
8 develop a system -- develop a lot of time and effort
9 without them knowing about it and find out that they
10 are not going to use it. They are going to be your
11 primary client in this, and so you need to talk to your
12 client.

13 DR. SLIKKER: And certainly one of the clients,
14 and I agree with you, we need to keep them in the loop.

15 Any other comments?

16 Yes, please.

17 DR. UHL: Kathleen Uhl.

18 Bill, actually I applaud you. You know, I mean,
19 you laid out a plan here that a lot of people hadn't

20 heard about in advance, so basically you are standing
21 naked in front of the group, so to speak, and letting
22 the other centers attack you. And so, I mean, I -- I
23 applaud the fortitude of doing that, you know, and
24 getting comments and feedback.

25 I do have a comment, though, about what Bob is

1 saying with the CDC, you know. And in the Washington
2 area, there are so many times that one agency has no
3 clue what the other agency is doing. And -- and I see
4 it all the time between FDA and NIH, because I now have
5 a lot more relationship, you know, and a larger
6 relationship, a stronger relationship with NIH. And
7 although part of it does come down to turf battles, it
8 really comes down to communication. And I -- I echo
9 your concerns there, Bob.

10 But I think that what you're doing and what you're
11 proposing to do and the collaborations that NCTR has
12 vocally with this medical center is laudable,
13 absolutely. Because in Washington it's impossible to
14 establish some of these collaborations. And I think
15 that realignment and restructuring is always received
16 either with total agreement of, you know, bringing new
17 ideas, or what I tend to see more in government is, oh,
18 my god, we don't want to change. Nobody wants to
19 change. But you have to have to restructure to really

20 meet your mission, and it seems like what you're really
21 trying hard to do is maximize the limited resources
22 that you have and that NCTR has and to leverage that to
23 get the optimal amount of science out that really meets
24 the FDA mission, which is very different from the CDC's
25 mission.

1 And CDC may think that they are the
2 epidemiologists, but I will venture to say that they
3 are wrong and that there are as good if not better
4 epidemiologists within the agency with the focus on
5 what are the agency's needs, which CDC doesn't know.

6 Thank you.

7 DR. SLIKKER: Well, thank you.

8 And I think you're absolutely right.

9 I mean, what we want to do here is to get the view
10 and the comment and the suggestions from this very
11 esteemed group, and then at that point in time, we can
12 take it based on that outcome to more levels of
13 communication, which would certainly include some of
14 the other agencies. But we use, of course, the
15 interface with the acting commissioner and others to
16 help do that.

17 Steve?

18 DR. ROBERTS: Steve Roberts.

19 I don't know if the FDA threat is played out or

20 not. I have another comment about the organization.

21 Okay. Bill, the question is, is with the

22 reorganization plan, this clearly gives you a division.

23 If someone asks what is NCTR doing, I mean, the

24 actually critical data, how does it fit in, point to

25 the organization chart, point, especially with this

1 division, contends that during the presentations
2 yesterday, it seems like a lot of things, systems, tox
3 very well, certainly the agency critical path. And I
4 was wondering if there had been any discussion about
5 whether or not, you know, that division might fit into
6 this or how those, how systems tox will relate to this
7 organization. Is this an overlap or --

8 DR. SLIKKER: Right. Well, it would be a very
9 strong sister division with this one. Okay?

10 All of our divisions, as I think you probably
11 noticed in the presentations, work well together.
12 There is a lot of people in one division working with
13 another to solve problems. That's already going on
14 between individuals within the systems tox, which is a
15 strong division in its own right, and others within
16 either Biometry & Risk Assessment or within
17 pharmacogenomics. So we see that just being enhanced.

18 But certainly systems site is going to remain
19 strong and very cooperative and interactive with the

20 other divisions of NCTR, and their outreach to other
21 centers has been very, very positive. So, you know, we
22 want to keep that going.

23 What we're trying to do here is -- is bring
24 together two other divisions that are relatively
25 smaller in nature and with very commensurate goals and

1 bring them together to be even more effective than they
2 are currently. But this would not have any negative
3 impact on systems sites. In fact, we're trying, I
4 think, this is another opportunity for them to work
5 more closely together.

6 DR. LORENTZEN: Ron Lorentzen.

7 This is not a simple question. Have you -- have
8 you made this proposal to the acting commissioner or
9 this, you know, what should -- you know, the program
10 you have here, have you --

11 DR. SLIKKER: Yes. Both to the acting
12 commissioner and to the deputy commissioner of
13 operations.

14 And, in fact, the name of personalized nutrition
15 and medicine was Dr. Ron Chibock's (phonetic) idea.

16 So, yes.

17 DR. LORENTZEN: And -- and further from that,
18 there was support for it or --

19 DR. SLIKKER: I would think so.

20 (Laughter.)

21 DR. ACOSTA: John.

22 DR. THOMAS: John Thomas.

23 I'm a little bit skeptical about terminologies

24 that relate to personalized medicine and personalized

25 nutrition.

1 And just to share my view with you, jaundiced as
2 it may be, there is no question but safer and more
3 specific drugs is the goal for all of us. I mean,
4 that's certainly my goal. But now you start
5 translating that into the industry, and suddenly you
6 have a group of responders that has lessened your
7 amount of people that are going to buy that drug.
8 That's where the rubber is going to hit the road. And
9 the amount of efficacy is still going to be related to
10 some extent of that bell shape curved. Certainly you
11 can pick out the ones that are on top of it and be more
12 focused and more specific, and that's good. But I
13 think thereafter is where I'm having trouble with
14 personalized medicine.

15 We've tried that for a long time in oncology, I
16 mean, so it's not really a new concept. And it hasn't
17 really worked all that effectively there.

18 DR. SLIKKER: Well, you know, every approach has
19 its limitations.

20 I would say two things. I would say that the
21 tools that we have available now to make these
22 selections and to probe this process are far better
23 than what we had ten years ago.

24 I would also say that the risk to pharmaceutical
25 development of having adverse effects is perhaps more

1 visible and are more tenable than before.

2 And so I think the downside of not making this
3 move is quite large. Really large. So I think there
4 is different forces in front of us now than there were
5 ten years ago.

6 There is a long ways to go. This is still an
7 experiment. We don't know if this is going to fully
8 work. We know it's not going to be applicable to all
9 agents. But the hope, of course, is that it would
10 allow for faster drug development and some drugs to
11 move through the system more rapidly and some to be
12 used in populations that are going to benefit more from
13 them and not have so many adverse effects. But we
14 still have a long ways to go to make sure this whole
15 process is going to work. And it will take years at
16 this point for this to play out, and it's not going to
17 be for every agent.

18 But I think that the writing on the wall is very
19 clear. This is something that the American public

20 wants and it's something that we're moving toward. We
21 don't know yet just how successful it's going to be, I
22 agree with that.

23 DR. BUCHANAN: Bob Buchanan.

24 And I just have to ask Ron, and this is no
25 reflection on your program or anything like that.

1 I had got an offhand comment from a friend of mine
2 who is a world class nutritionist, made the comment
3 that the greatest tool you have -- have right now for
4 personalized nutrition is your bathroom scale.

5 (Laughter.)

6 DR. SLIKKER: Well, you know, I would argue that
7 that's -- that that's part of the attitude. Okay.

8 However, I think that there are the possibility of
9 using these newer technologies to try to understand
10 what are some of the sensitivities within
11 subpopulations that are going to have more difficulty
12 keeping that bathroom scale as a good buy marker for
13 them, and that we could help improve that process by
14 learning more about their particular make up.

15 DR. BUCHANAN: And I agree totally with you, but I
16 just had to add that.

17 DR. SLIKKER: Right.

18 DR. ACOSTA: Great.

19 Thanks so much for that overview and some of the

20 exciting developments of NCTR.

21 We are ahead of schedule somewhat.

22 Do you want to just continue on?

23 DR. SLIKKER: Yeah.

24 DR. ACOSTA: Unless someone wants to take a five

25 minute break.

1 DR. SLIKKER: Yeah. Maybe we should take a break.

2 There are still some things outside to snack on, and
3 certainly I think some coffee.

4 DR. ACOSTA: Five or seven minute break. That
5 would be good.

6 (WHEREUPON, a brief break was held at this time.)

7 DR. ACOSTA: If everybody would take their seats.

8 Yes.

9 DR. GREENLEES: I would like to just make a couple
10 of comments.

11 DR. ACOSTA: Do you want to identify yourself?

12 DR. GREENLEES: I'm sorry. Kevin Greenlees.

13 This is a very general comment. I didn't want to
14 make it during the session before, because that was
15 really talking about a real specific realignment that's
16 being proposed for the center.

17 But yesterday there was a brief discussion. We
18 were talking a little bit about the things that NCTR
19 could not do and a discussion in genders where an

20 example was given where the request from the Centers
21 for Veterinary Medicine had to do with chloroethylene
22 toxicity of cats. And I want to give you a slightly
23 different take on that.

24 This was a question that came up in part of our
25 product evaluation groups or preapproval groups for

1 chloroethylene for use in cats. These have been -- in
2 fact, there are some approvals for these compounds, and
3 there continue to be products that are coming out for
4 this kind of use. And it's incumbent to question by
5 the review scientists because of some interaction we've
6 had with NC Journal, and what are some of the expertise
7 over there, we were able to ask some questions that
8 came back down, said, is this even doable? Can you
9 even design a study that would allow you to look at
10 this.

11 What we got back was the answer that, yeah, we can
12 do this. And it allows us to actually get a handle on
13 what would be the scope of trying to address this
14 problem. Well, the answer came back then, well, the
15 scope is actually maybe bigger than the problem that
16 you want to go after, and you have to decide if you
17 want to commit those resources or not. That was an
18 extremely valuable dialogue. And the fact that we did
19 not come back with a, here is a research question. Go

20 do it and here was the answer to that, to the question

21 as part of a research program. That's not the issue.

22 The issue, from the regulatory center was, they

23 allowed us to make some decisions about whether or not

24 we wanted to still pursue that -- we're still making

25 that decision -- whether we want to pursue it as an

1 agency or whether it's something we want to put back on
2 the firm, or how we're going to deal with that. That
3 kind of interaction is an incredibly valuable tool.

4 And it also is an interaction that tie in closer
5 to product centers. Having done that once, you're more
6 likely to get that kind of question again, because it
7 was so productive. And I don't want that to get lost
8 because it's -- that ad hoc interaction is very
9 valuable to the product center. I recognize it's also
10 very difficult to deal with and goes into a program,
11 Bob, on your side, but I don't want that to get lost as
12 you're going through these discussions.

13 DR. SLIKKER: Well, I appreciate those comments,
14 because I think that oftentimes the consultation that's
15 done can be helpful to all parties concerned, and
16 certainly that's one example of this particular study
17 that was mentioned in the cat. But also it goes into
18 other areas as well. And certainly the interest in
19 mercury and other areas is along that same way, which

20 consults are being conducted between SAB here at NCTR
21 and those of the other centers. And I think that is
22 important in some of our important interaction in terms
23 of those kind of interfaces.

24 But thank you.

25 DR. ACOSTA: Yes?

1 Identify yourself.

2 DR. MOORE: I'm Martha Moore.

3 I just wanted to add to this, and this is
4 something that builds on what Ralph said. Is this
5 issue as to whether main as the center are different
6 than the other centers, because we don't have a
7 regulatory mission. I think these are all examples
8 where we really do participate in the regulatory
9 affairs of the agency. And I think -- I mean, I've
10 been here for six years, so my history is not as long
11 as some of the rest of you, and I gather that the
12 situation has changed somewhat, the pendulum has moved
13 over time. But it seems to me that the pendulum is
14 moving more and more over to where we participate more.
15 And I think that that's really quite a good thing. And
16 I just wanted to emphasize that we do do that and I
17 consider that to be important.

18 DR. ACOSTA: Okay. Thank you.

19 The next item on the agenda is to look at one of

20 the responsibilities of the Science Advisory Board.

21 And for our new members they have experienced for the

22 first time the discussion of the review of the

23 neurotoxicology from yesterday.

24 Historically there has been a cycle in which the

25 various groups within NCTR have been reviewed on a

1 periodic basis. Ideally it should be about every four
2 years. Probably is happening every five or six years.
3 And so, the process will be that the -- there will be
4 two or more, most likely two members of the SAB that
5 will serve as a subcommittee of the SAB to conduct the
6 peer review of the science of the individual division
7 that has been selected for the next review. It will be
8 a very critical review of the -- of the program.

9 Will -- will -- not all of our SAB members have
10 that expertise of that particular division. So we will
11 select ad hoc reviewers. And the best approach will be
12 to seek out the colleagues or experts that you're
13 familiar with, provide the names to Bill or me in terms
14 of the review. I'm assuming the director of the
15 division that's selected can also suggest names of
16 individuals who are experts in the field.

17 So we will then collect the information, decide on
18 the chair or co-chair of the review group for SAB.

19 Then you will have to determine a time to come and do a

20 site visit. Most likely about two days, a day and a
21 half for that particular site visit. Documents will
22 have to be prepared. Some type of a self study will be
23 done by the division to provide to the review team and
24 then the review will take place.

25 Then, once that's been conducted, there will be a

1 report generated by the subcommittee and we'll have and
2 discuss it at the next, I won't say annual SAB meeting,
3 but, as Bill said, it will probably be every 12 to 18
4 months, and we'll try to get on a schedule. That way
5 we don't have the same thing that happened at the last
6 time, where we didn't meet for over two years.

7 So that's what we're going to be doing now.

8 I would like Bill to discuss the -- since he has
9 the records of the historical review of all the
10 divisions, to provide us with the information on the
11 divisions that should be next in line for review.

12 DR. SLIKKER: All right. Thank you, Dan.

13 And this is really an important process where we
14 get in-depth reviews of the individual research
15 divisions by this site visit group. There are two that
16 have been reviewed about an equal amount of time in the
17 past, and that is biochemical products and
18 microbiology. And I think at this point in time then
19 we're going to move forward with microbiology as the

20 one that we review next in the spring time. They will
21 prepare a nice report that will be provided to the site
22 visit team. And we have a format that this follows,
23 and it provides information that the site visit team
24 needs in advance. And then we will have this day and a
25 half or so interaction on site at NCTR, and that will

1 provide the opportunity for review. And then there
2 will be a report that comes from that.

3 So this is moving forward with Dr. Carl Cerniglia
4 in the microbiology branch for spring time. And then
5 after that we will follow with another review or two
6 within the next year or so following that. So we'll
7 keep moving through the divisions in a systematic
8 fashion.

9 DR. ACOSTA: Are there any questions from the SAB
10 members or the other members of the audience?

11 Yes?

12 Please identify yourself.

13 DR. BELAND: Yes. I'm Fred Beland.

14 Carl graciously agreed to go ahead of me in the
15 review.

16 I would just like to bring up a couple of concerns
17 and then maybe you can provide us with advice as to how
18 we proceed.

19 You know, as Bill pointed out, there is two

20 possible budgets next year. There is the Senate budget
21 and then there is the House budget. If we have the
22 House budget, we will have no research. That's pretty
23 clear. I mean, no FDA set forth research.

24 If I'm going to do -- you know, if I'm going to
25 do, have a site visit review, the way I look at a site

1 visit review is the people come in and we present where
2 we're going to go. Well, if we don't have any money,
3 you know, where are we going to do? Where are we going
4 to go?

5 And the last, you know, four or five years, the
6 amount of money that biochemical toxicology has
7 received from the FDA has not been very substantial.
8 Other divisions, you know, have been the same way.

9 So I wonder -- I guess I would like to know, you
10 know, we can talk about -- within our division, we can
11 talk about what we do for the next toxicology program.

12 If the site visit, that committee doesn't like it, I'm
13 not sure what difference that makes. We have a
14 contractual obligation to do this work. So they can
15 say they hate it, but I have to do the work because
16 I've been paid a great deal of money to get it done.

17 And so I'm trying to -- you know, when we were
18 last reviewed, we had a decent amount of money and we
19 could say this is where we want to go, and then some of

20 the direction we wanted to go the committee liked very
21 much, others said they -- we don't like it, we altered
22 things accordingly. In this climate we have right now,
23 where we don't know how much money we're going to have,
24 there is a chance we're going to have very little
25 money, I'm not quite sure what I'm going to tell the

1 site visit committee, you know, other than very
2 general. You know, I can tell them what we are doing,
3 what we would like to do, but it's going to be very
4 dependent upon the amount of money that we're sent.

5 DR. ACOSTA: Is that a comment or a question?

6 DR. BELAND: I think it's a comment. Or a
7 question. A question as to what we expect we need to
8 tell or what -- and Carl is in the same situation. I
9 mean, he's far more dependent upon receiving funds from
10 the FDA in what he's experiencing. What are we
11 supposed to tell the site visit? Where we are going?
12 Is it what we're doing?

13 DR. ACOSTA: I can -- I'll let Nancy talk first on
14 it.

15 Identify yourself.

16 DR. GILLETT: Yeah. This is Nancy Gillett.

17 I still think, even with the limited resources,
18 and maybe even more so with the limited resources,
19 these reviews are very important. And, again, I would

20 go back to the point I made earlier about the focus of
21 the mission on NCTR and how these individual centers --
22 centers and divisions play into that. So I still think
23 it's worthwhile to step through each individual
24 scientists' effort, what's the direction of the
25 productivity science to date, how does it fit in the

1 broader scheme of the NCTR's mission, and focus on the
2 critical path of the decision making. What are the
3 outreach and the collective energies of the different
4 agencies. How is their collaborative effort, where we
5 don't have this silence, because I think we certainly
6 recognize on the NCT the challenges of the resource --
7 shrinking resources that we've had -- the resources
8 have had.

9 I guess what I'm looking for is how are we
10 leveraging, how are we asking and getting beyond the
11 silence we've had. So that's what I would see.

12 DR. ACOSTA: And just to maybe give you an example
13 from the academic side. At our institution, we're
14 experiencing a fairly severe budget crisis. And at the
15 same time we're going through a series of evaluations
16 of all of our programs, academic programs, and doing
17 the strategic planning.

18 And some people may say, well, we don't have the
19 money. Why are we doing all this other extra work and

20 proposing ideas and initiatives that may not have the

21 necessary resources to do them, to start them up.

22 However, we are finding it very important to really

23 look at those programs that are productive, those

24 programs that are not as productive, gives us a way of

25 setting the goals and objectives for the future, even

1 though our budget is cloudy and confused in terms of
2 what amount of money we're going to get.

3 And, essentially, I think what happens, if I
4 understand your budget, your -- you're going to
5 continue to have the salaries for your staff. Can they
6 fire -- can they fire -- if you don't get your budget
7 approved at the level you would like, then you will
8 have to let go scientists that have been working for
9 20, 25 years. They will not have jobs. It's still not
10 clear to me how you're going to match your budget.
11 You're probably going to reduce your operating
12 expenses, if you don't have the money that Congress --
13 that you feel Congress should give you.

14 So you're still going to have a good number of
15 your personnel being paid their salaries. Where you're
16 not going to have flexibility is, I think, you know, in
17 buying supplies, equipment, other things like that.

18 And I -- that's where you get into what is known as
19 reallocation. You then do a critical analysis. If

20 that House budget is approved, then NCTR will have to
21 look very carefully at all of their programs and decide
22 which ones are going to have higher priority than
23 others.

24 DR. BELAND: Well, if the House budget is
25 approved, you will have salaries. You will not have

1 any money to produce the --

2 DR. ACOSTA: You mean to buy animals? To buy
3 supplies?

4 DR. BELAND: I mean, that's -- isn't that correct,
5 Bill? I mean, we would be --

6 DR. ACOSTA: Then FDA as a whole will have to come
7 and do reallocation within the whole agency or
8 administration to decide. If FDA says we really need
9 some research to be done in this particular area, then
10 FDA on the commissioner level is going to have to say,
11 well, we'll have to give you some money for that. I
12 don't know.

13 You're really pointing at a scenario that no one
14 knows if it's really going to happen. Has it ever
15 happened before?

16 DR. BUCHANAN: Not with FDA. But it happens in
17 the government.

18 DR. ACOSTA: Identify yourself.

19 DR. BUCHANAN: Bob Buchanan.

20 To understand where you -- I've lived through it
21 in other agencies, where you get in the situation where
22 your budget cannot support your salary, you then go
23 into a reduction in force mode. That happens commonly
24 within the military. It's happened within the FDA.

25 And, basically, there is all kinds of federal

1 rules for how you go through a reduction in force.

2 Last in is the first out.

3 DR. ACOSTA: Right.

4 DR. BUCHANAN: Then you get to the bumping rights.

5 It's a highly destructive process.

6 DR. ACOSTA: Yeah.

7 DR. YOUNG: That's exactly right.

8 DR. ACOSTA: Okay. Go ahead. Identify yourself.

9 DR. GREENLEES: Kevin Greenlees.

10 I actually have a question on that. Because more
11 than half of the NCTR work force is actually out in the
12 field working, that would seem to me like you might
13 have a more severe impact on your program than perhaps
14 some other -- other groups, where that the bulk of your
15 employee is based on normal GS salary force.

16 DR. CERNIGLIA: Carl. I had had a comment about
17 that.

18 DR. ACOSTA: Identify yourself.

19 DR. CERNIGLIA: Carl Cerniglia.

20 My only comment, Dr. Acosta, is this: You know,
21 Fred and I, and it's not a problem, I've been through
22 these twice before. So in terms of the nuts and bolts
23 of a review, it's not an issue for me and we've agreed
24 to that, so that's fine. But what I was thinking in
25 terms of the better use of the board initially might

1 be, because as Bill, when he gave his presentation,
2 talked about, you know, he gave the division directors
3 a draft of the strategic plan, which at least some of
4 those have commented, given comments on. We've heard
5 today about the proposed realignment, which from the
6 discussion it appeared to me needs to be thoroughly
7 reevaluated or reconsidered, in terms of the people, et
8 cetera, and even the mission and all of that, and maybe
9 even the names.

10 So -- so my sense is that the next time this body
11 gets together, to me it might be more value to the NCTR
12 to really flesh out the bigger picture first and then
13 obviously have this order of review, just like in my
14 case and then maybe Fred's case and then the next case,
15 our staff.

16 So my -- my sense is that maybe the spring meeting
17 or whenever people's schedules can come together, to me
18 it might be better for us, at least the way I look at
19 it, would be to kind of get the bigger picture first

20 and then, you know, get the schedules set up.

21 Again, if we want to go with it in the spring or

22 whatever is convenient for getting these committees

23 together, it's fine, you know, we'll do it. But at the

24 same time, I would think my own personal opinion would

25 be to get the bigger picture, get it discussed

1 thoroughly, internal in our own management team,
2 division directors, get some critical discussions on
3 these issues, and then -- and then kind of come up with
4 a well thought out plan and then propose it to our --
5 our SAB and the FDA liaisons, because they are our
6 chief clients, and certainly the members of the science
7 board if they have time to come back here again. To me
8 I think that would be a more logical way of providing
9 that. That's an alternative that might be open for
10 discussion.

11 DR. BUCHANAN: Bob Buchanan.

12 I heard some comments here about contractual
13 agreements, and you have to do them, et cetera, and
14 what role would the SAB play on that.

15 On the other hand, if we have most of our programs
16 reviews done by the science board, or respective groups
17 of it, and the science board came back to us and said
18 we don't think that you being involved in contractual
19 agreements in the following areas is in keeping with

20 the mission of FDA and probably is not appropriate, the
21 likelihood that those contractual agreements would ever
22 be renewed or will be pursued again would disappear.
23 So that the board actually does have a very important
24 role in helping us decide what additional outside
25 sources of funding we should be seeking and what are

1 appropriate in conjunction with our overall mission.

2 DR. ACOSTA: You used the term science board, or
3 you said the science board you're talking about. Are
4 you talking about this SAB board?

5 DR. BUCHANAN: No. We use the FDA Science Board
6 to do our external review.

7 DR. ACOSTA: Okay.

8 DR. BUCHANAN: Which I -- can --

9 DR. YOUNG: So what are you saying, Bob?

10 Let's get down to the brass tacks.

11 DR. BUCHANAN: That something like the SAB, as you
12 spend more and more time going out seeking outside
13 funding, the SAB I think can provide you with some
14 appropriate advice on what is outside the bounds of
15 what is appropriate for NCTR in keeping with its FDA
16 mission.

17 I've -- just to be blunt, I've seen research
18 organizations that become so in -- are required to go
19 seek outside sources of fundings, that go so far or are

20 given their researcher's permission to seek funding

21 that are so far afield from their core mission, that

22 they lose their identity and they lose their purpose.

23 It becomes simply a matter of getting funds for

24 individual researchers.

25 And, from my standpoint, that could be the kiss of

1 death for NCTR, if everybody went off in another
2 direction and had no real theme about what they're
3 doing and how that fits into the FDA mission.

4 DR. YOUNG: Okay. I understand that, and I agree
5 with that. But what about, you said, how does the SAB
6 reflect our outside contracts and how will we manage
7 those?

8 You've mentioned that. What are you saying
9 exactly about that?

10 DR. BUCHANAN: Well, are they -- it might not be a
11 good -- it might not be a bad idea to have an outside
12 pair of eyes go out and look at them and say, you know,
13 is this really appropriate.

14 DR. YOUNG: Like our animal care staff and our
15 pathology staff and our library staff?

16 DR. BUCHANAN: No. Not that.

17 DR. YOUNG: Okay. Well, that's what our outside
18 contractors are.

19 DR. BUCHANAN: Okay.

20 DR. SLIKKER: And I would like to address your
21 other issue.

22 I mean, the work done with NIEHS/NCT/FDA
23 relationship is driven by FDA regulators. They
24 nominate the compounds, they review the information,
25 they devise the protocols, and they see the work being

1 produced. Okay. So I don't see how that is any way
2 can be construed with the problem with not having input
3 from FDA and being part of that.

4 The other protocols where we interact with others,
5 such as NICHD and that sort of thing, they go to
6 support projects that are definitely within the FDA
7 mission, such as ketamine, methylphenidate, et cetera.

8 So, you know, I don't really understand that
9 comment, and it's not within the way in which we do
10 research at NCTR.

11 DR. BUCHANAN: What percentage -- the team that we
12 heard yesterday as we took the tour, that we heard in
13 the meeting, is the need for individual investigators
14 and groups to be seeking new opportunities for outside
15 funding. Okay?

16 A lot of this is driven from the PI generated
17 research.

18 Do you have -- and I think it would be good to get
19 an input from the SAB and your other centers on what

20 is -- what's out of bounds for PIs to be going out and
21 seeking external funds. What projects -- where is the
22 boundary between when it is no longer appropriate to
23 the mission of FDA, and do you have good guidance for
24 them, or do you exercise that in your review process
25 when people go out and seek external funding. I

1 don't -- and I don't know.

2 DR. SLIKKER: Yeah. There is an extensive review
3 process, including, as I mentioned, the concept paper
4 has to be reviewed internally and also that's fed into
5 other centers within the FDA, and then there is also
6 the protocol that goes along with that. And for any of
7 the tralines, of course, it has to go through a review
8 process at multiple levels within the FDA organization.

9 So all these proposals are -- are certainly
10 embedded and reviewed at multiple levels within the
11 agency. And I think that is important. I think that
12 is important, too, because our work needs to be
13 supporting the FDA regulatory mission. I don't think
14 there is any doubt about that.

15 So, now, in terms of encouraging investigators to
16 look for opportunities, we do that, and I would expect
17 everyone to have an opportunity to look. But those
18 opportunities have to be consistent with the FDA
19 mission.

20 DR. BUCHANAN: And that -- and partially that's
21 reflecting my own experience, because we have to go
22 through the same process, and that is the most
23 difficult process, particularly when you have people
24 trying to make deadlines which are always very short in
25 terms of submitting proposals. So it helps to have, we

1 find, some clear guidance to say, you know, these
2 projects are just out of bounds, don't pursue that.
3 Because if not, they all come through in a rush and
4 they may only have ten days to get a proposal, and
5 through the rather complicated bureaucracy.

6 DR. ACOSTA: Joe?

7 DR. HANIG: Yeah, I was just going to make --

8 DR. ACOSTA: Identify yourself.

9 DR. HANIG: Joe Hanig. Excuse me.

10 I think the point that Bob makes is really very
11 important. I would think the response from you is very
12 appropriate. But those raise a much larger issue, I
13 think, than the specifics of the SAB review. And
14 namely that is, whether or not most research being done
15 should be done with appropriated funds that represents
16 the will of Congress. I mean, we're operating in SEDA
17 with a tremendous amount of DUFA money. It's coming
18 from industry. It has helped us tremendously, but it's
19 not appropriated money. CRADA money is not

20 appropriated money.

21 So you can ask very, very general questions about
22 the appropriateness of peer reviewing these other
23 sources of funds. But in my mind there is absolutely
24 no doubt about the appropriateness of the utilization
25 of the funds that NCTR has been able to leverage. So

1 what I'm saying is, is the issue you've raised is very,
2 very big.

3 One of the interesting things that we ran into was
4 trying to use money from another agency without a very
5 big IAG or something. The IAG is an instrument that
6 allows GAO to audit and to look exactly -- because the
7 intention of Congress, when it gives one agency money,
8 is not that that agency should go ahead and give it to
9 another group to do something, if that is not
10 necessarily the will of Congress and so on.

11 So these are very broad issues and I'm just making
12 a comment on it. I still feel, though, that the money
13 that's been leveraged by NCTR to do the research is
14 definitely within the mission and so on. But I
15 certainly think the thing that you raise -- I mean,
16 when you have a division that's operating on 15 percent
17 appropriated funds, you've got to wonder what the
18 intention of Congress really is, in terms of what they
19 think is important.

20 Yeah?

21 DR. ALLABEN: Allaben.

22 Let me just correct you on that. That was a
23 misunderstanding, I think, of what was discussed
24 yesterday.

25 The IAG moneys coming into NCTR are appropriated

1 funds, and neurotox has a significant portion of those
2 IAG funds in support of their neurotox studies with a
3 chromane.

4 So that was not necessarily -- I think there was a
5 misunderstanding of what was said.

6 DR. HANIG: No, I --

7 DR. ALLABEN: And the CRADA -- the CRADA money
8 that the neurotox has is a small portion that they
9 operate, outside of appropriated funds.

10 DR. HANIG: Believe me, I understand.

11 DR. ALLABEN: So it's not 15 percent, Joe.

12 DR. HANIG: No. No. No. I understand and I
13 fully appreciate what you're saying. And as I said
14 earlier, I think it's highly appropriate that that
15 money is being used, and it's well within the mission.
16 But I do think that more attention ought to be paid to
17 providing appropriated funds to FDA to do things so
18 that we don't have to explain these ratios the way we
19 do.

20 Okay? That's -- that's the only point that I'm

21 making.

22 DR. LORENTZEN: If you know how --

23 DR. ACOSTA: You have to identify yourself, if you

24 want to make a comment.

25 Do you want to make a further comment?

1 Ron?

2 DR. LORENTZEN: No. I was going to make a wise
3 crack.

4 DR. BUCHANAN: Okay.

5 DR. HANIG: Off the record. Off the record.

6 DR. ACOSTA: All right. All right.

7 Well, I think these are all very good points that
8 have been raised, and really Fred and Carl are in the
9 limelight right now, because you are the next two
10 groups that will be reviewed.

11 I appreciate the fact that we don't know what
12 Congress is going to do with the House budget versus
13 the Senate budget. And as an SAB member, and being a
14 member of an advisory committee for other groups within
15 the government, I've always found it difficult to
16 understand the true role of a science advisory
17 committee.

18 I'll give you an example. I won't mention the
19 names. But I'm on one -- on another one in which

20 really the advisory committee is -- our advice is not
21 being sought. We meet, they tell us things, and that's
22 it, and there has not much opportunity for our
23 committee to provide advice and input.

24 This particular SAB for NCTR is -- is more
25 involved than I've seen in other committees. We do the

1 reviews, we're trying to provide science review, peer
2 review of your science. We're trying to give you
3 information that we see in our own expertise to help
4 you do better science and to do your job at NCTR.
5 We're advisory in nature. We cannot -- as citizens we
6 can individually talk to our own Congress people, our
7 Senators, and indicate we think it's important that
8 NCTR be funded. As an SAB, we cannot formally lobby
9 Congress.

10 However we can make recommendations within our
11 group to say we believe that the mission of the NCTR is
12 important. We believe that it should be fully
13 supported in terms of funds. We can put into the
14 minutes certain comments, and I would like to do that
15 before we end, so that it is in the minutes. And then
16 I would like the SAB members to see if they agree with
17 that. We can do those types of things.

18 We don't know what the budget is going to be, so
19 it's hard to respond to Fred, your comment about if

20 you're going to have the money and how you're going to
21 respond to a site visit team if you don't have the
22 money. We don't know if that's the case.

23 We'll be working closely with Bill. And you're
24 also in a delicate situation. We have an acting FDA
25 commissioner, we have an acting director of NCTR.

1 In a separate session I think we can ask some
2 other questions, as well.

3 So, at this point, I just -- I would like to say
4 that, first of all, we want to thank all of you, the
5 scientists, the staff, the administration of NCTR for
6 this visit. You've been very helpful to -- especially
7 to the new members of the SAB. This is a learning
8 process for a number of these individuals here. A
9 couple of us have heard this before and are aware of
10 the situation. But for the new members, I hope you
11 realize they are learning and they are learning what
12 their roles should be. So we thank you, all of you,
13 for all of your help, that's been very important and
14 been very stimulating.

15 We also like to -- as I said, I would like to
16 place in the minutes as a chair, and I'll let any SAB
17 members, if they would like to make further statements,
18 we feel that -- at least I feel that the dedication and
19 the efforts of the scientists of the NCTR are very

20 commendable. They are meeting the mission of the FDA,
21 especially on the note that, if you look at the overall
22 budget of the NCTR, it's a very small percentage of the
23 overall FDA budget. And that being the case, any
24 reductions in your budget has a very dramatic effect on
25 what you can do in terms of the mission and goals of

1 NCTR.

2 So I would like to state very specifically to --
3 to the administration of FDA that we feel -- I feel
4 very strongly as a chair that there should be a very
5 careful review and analysis of the mission of NCTR and
6 how it applies to the overall FDA mission, and to be
7 certain that its budget reflects that mission. And if
8 there are cuts to be made, there should be a very -- a
9 thorough analysis how those cuts may affect the overall
10 mission and activities of NCTR.

11 Further, we believe that this should be forwarded
12 to the commissioner, acting commissioner and deputy
13 commissioners, to say that as a chair of SAB I feel
14 very strongly they have to look very carefully at that.

15 I would like the SAB members, when they do their
16 review -- and actually I made this same statement two
17 and a half years ago, so I'm really reading from my
18 notes from that time. So I just want to repeat those
19 that were agreed upon by the last SAB, but I would like

20 my SAB members to make any comments if they so wish.

21 DR. JUNG: As a consumer member --

22 DR. ACOSTA: Identify yourself.

23 DR. JUNG: Lily Jung.

24 I would like to second your comments.

25 DR. GILLETT: Nancy Gillett.

1 I would recommend them to go in as an entire
2 committee, as opposed to just individual comments by
3 the chairman.

4 DR. ACOSTA: So we have -- so move?

5 DR. POPP: Yeah. Jim Popp.

6 I mean, I certainly agree with the comments you
7 made. I think it could be embellished or enhanced by
8 putting it in the context, that is the review of the
9 budget and so on and the mission, in the context of the
10 opportunity that the research and the research results
11 will have for impacting decision making, rather than
12 coming across -- I guess it came across to me a little
13 bit, Dan, as sort of a straight, well, it would be good
14 if they had more money, then they would do better
15 things. But I think to somehow get it more in the
16 context of contributing to the overall mission, and if
17 that money is not there, that contribution will not
18 occur.

19 DR. ACOSTA: You said it much better than me. I

20 think that it's now reflected in the minutes.

21 DR. POPP: Okay. But it's the same thing, it's

22 just a slightly different perspective.

23 DR. ROBERTS: Steve Roberts.

24 And I certainly concur with the sentiment.

25 I wonder if putting it in the minutes would be the

1 best way to get it to the commissioners, whether it
2 would be appropriate to write a letter to the
3 commission.

4 DR. ACOSTA: That's a good point.

5 I'm not sure if that's ever been done.

6 DR. SCHECHTMAN: Can I speak to that?

7 DR. BUCHANAN: Yes.

8 DR. SCHECHTMAN: Leonard Schechtman from NCTR.

9 I also sit on another advisory committee. The
10 name is not important. And that committee also ran
11 into difficulties with support for its activities. And
12 what they decided to do was generate a letter on agency
13 letterhead at that time that was directed to the
14 Secretary of HHS. So, in that case, the committee was
15 an HHS committee. In this case, the committee being an
16 FDA advisory committee, basically, it would seem that
17 if that precedent is in place at that level, that there
18 is no reason why in this science advisory board
19 couldn't generate such a letter directed specifically

20 to the commissioner of the agency with their insight or
21 recommendations.

22 DR. SLIKKER: And just to comment about that.

23 If I remember correctly, our regulation states
24 this is an FDA/NCTR advisory committee, I believe. So
25 just to clarify that, that I think that we certainly

1 first respond to the NCTR and the NCTR director.

2 Now, we have two representatives here from the FDA
3 science board, and they may have comments on this,
4 about how this information may be moved forward. But I
5 think the way it's written right now, I'm not sure --
6 this is not an FDA committee, per se, it's a NCTR/FDA
7 committee, and I think they need to respond to the
8 director.

9 Not that I'm discouraging the idea of putting this
10 information forward, but I think it has to be proper
11 channels. And maybe our FDA science board members
12 could clarify that for us.

13 DR. THOMAS: I'm not that sage at interpreting --

14 DR. ACOSTA: Identify yourself.

15 DR. THOMAS: John Thomas.

16 Just an observation, and it's not an original one.

17 You've still got an acting commissioner and you have an
18 interim director. I would suggest, just as my
19 administrative experiences, is just have a verbal

20 post-meeting follow up and express the concerns of
21 the -- of your science board at this point in time,
22 rather than to get yourself put in writing for
23 something that might be turned upside down a week from
24 now.

25 DR. BUCHANAN: Bob Buchanan.

1 You can write that letter. The commissioner does
2 not -- or the past commissioners I've interacted with,
3 don't like to get letters from committees saying you
4 ought to give this group more money. It puts them in a
5 very awkward situation.

6 You can write the same letter saying that you were
7 impressed over the last two years of the change in the
8 direction, so that NCTR is much more directly involved
9 in pursuing the mission of FDA and its significant
10 contributions it's made. You can get the same point
11 across and never once ask for more money. And I would
12 recommend you do the latter.

13 DR. THOMAS: I would -- John Thomas.

14 I would -- yeah, I would reinforce that. An SAB
15 doesn't function -- certainly they are advocacy, but
16 they don't micromanage. And we make great -- go at
17 great lengths to stay out of budgetary considerations.

18 DR. ACOSTA: Well, we -- again, the minutes may
19 not be the best place, but at least it makes the

20 opportunity to say that the group as a whole was very
21 pleased and excited about the developments that are
22 occurring in the organization and would truly support
23 the need for support of their activities. That's fine
24 to say it in that way.

25 DR. BUCHANAN: And you can say that by directing

1 it to Bill.

2 DR. ACOSTA: Bill?

3 DR. BUCHANAN: And cc the commissioner.

4 DR. YOUNG: Absolutely.

5 DR. ACOSTA: Yeah. Okay. I think it would work

6 that way.

7 So I think maybe the solution would be that I
8 would like to draft a letter for the SAB members to
9 review, and then once we agree to the language, we'll
10 submit it to Bill and cc at the bottom the
11 commissioner. And I think do it in the way that you've
12 suggested, Bob, to really indicate how pleased we are
13 with the progress and the new exciting developments
14 that are occurring, and that we don't have to mention
15 the budget.

16 Okay. Excuse me. Any more items before we go
17 into executive session?

18 I, again, want to thank everyone for their
19 participation. It was very informative and, again,

20 thank everyone here.

21 I know I'm very bad with names, but I definitely
22 wanted to say to Dr. Wells, thank you so much. You had
23 to be somewhat involved. This was a great place to
24 have the second day of our meeting. We all obviously
25 appreciate the fact that you were here yesterday also,

1 and I know there is a strong relationship between NCTR
2 and UAMS. So I think that's good to see that that's
3 continuing.

4 Thank you so much.

5 And, again, thank the scientists, the staff,
6 everyone here at the NCTR for all of your information
7 and what we've learned so far.

8 So I would like to -- do we have another comment
9 before we break?

10 DR. SCHECHTMAN: Sure. I just wanted to say, on
11 behalf of NCTR, Bill Slikker and myself, a special
12 thanks to all of the SAB members, our SAB leadership,
13 and our FDA science board liaisons for all of their
14 efforts and their valuable counsel, their insight, and
15 sharing their experience with us.

16 We also want to thank all of the FDA center and
17 office representatives for their contributions to this
18 SAB meeting, their ongoing support of NCTR, spiritual
19 and otherwise, and their strong collaborations and

20 interactions with the NCTR. We would also like to
21 thank all of the NCTR division directors and directors
22 of the NCTR centers of excellence, as well as their
23 respective staffs for their dedication and hard work
24 that makes NCTR FDA's primary research project.

25 Finally I also want to extend NCTR's and my

1 personal gratitude to Dan Acosta, our chair, and Nancy
2 Gillett. Both of them who have provided service to our
3 SAB over the last several years and who, unfortunately,
4 whose terms are coming to a close. We're hopeful that
5 following the required break in service, as is
6 necessary in this type of committee, we can look
7 forward to both of you to the possibility of signing on
8 again, so that NCTR can then gain your valuable
9 experience and counsel.

10 Thank you.

11 DR. ACOSTA: Thank you.

12 Well, we officially end in June 2007, so we're
13 still on a little bit longer.

14 DR. GILLETT: At least I have a date now.

15 DR. ACOSTA: All right. Well, thank everyone. So
16 officially we adjourn.

17 We'll go into executive session.

18 (WHEREUPON, the above-entitled proceedings were
19 concluded.)

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1 CERTIFICATE

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3 STATE OF ARKANSAS)

4 COUNTY OF PULASKI)

5

6 I, SUSAN B. WHITSON, Certified Court Reporter and
7 notary public in and for Pulaski County, State of Arkansas, do
8 hereby certify that the NCTR SAB Meeting, held August 30, 2006,
9 was taken by me in Stenotype and reduced to computer-generated
10 typewritten form by me or under my direction and supervision; and
11 that the same is a true and correct reflection of the proceeding
12 that occurred, to the best of my knowledge and ability.

13 I FURTHER CERTIFY that I am neither counsel for,
14 related to, nor employed by any of the parties to the action in
15 which this proceeding was taken; and, further that I am not a
16 relative or employee of any attorney or counsel employed by the
17 parties hereto, nor financially interested, or otherwise, in the
18 outcome of this action; and that I have no contract with the
19 parties, attorneys, or persons with an interest in the action

20 that affects or has a substantial tendency to affect
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22 original transcript or copies of the transcript before it is
23 certified and delivered to the custodial attorney, or that
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2 _____.

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5 SUSAN B. WHITSON, CCR, #158

6 NOTARY PUBLIC IN AND FOR

7 PULASKI COUNTY, ARKANSAS

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9 My Commission Expires: June 4, 2012.

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