U.S. FOOD AND DRUG ADMINISTRATION

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SCIENCE BOARD TO THE FDA

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ADVISORY COMMITTEE MEETING

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FRIDAY, OCTOBER 31, 2008

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The Advisory Committee convened at 8:00 a.m. at the Hilton Washington, DC North/Gaithersburg, Gaithersburg, Maryland, Barbara McNeil, M.D., Ph.D., Chair, presiding.

PRESENT:

BARBARA J. McNEIL, M.D., Ph.D., Chair
RHONA APPLEBAUM, Ph.D. (morning only)
GARRET FITZGERALD, M.D. (via telephone) (afternoon only)
ERIK HEWLETT, M.D.
LONNIE KING, D.V.M., M.P.A.
JOHN H. LINEHAN, Ph.D.
DAVID R. PARKINSON, M.D.
MARTIN PHILBERT, Ph.D.
LARRY SASICH, Pharm.D., M.P.H., F.A.S.H.P.

BISPHENOL A SUBCOMMITTEE ADVISORS PRESENT:

ANTONIA M. CALAFAT, Ph.D.
JOHN VANDENBERG, Ph.D.

FDA PARTICIPANTS:

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ANDREW VON ESCHENBACH, M.D., Commissioner of Food and Drugs
DAVID W. K. ACHESON, M.D., F.R.C.P., Associate Commissioner for Foods
BERNADETTE DUNHAM, D.V.M., Ph.D., Director, Center for Veterinary Medicine
RANDALL LUTTER, Ph.D., Deputy Commissioner for Policy
STEVEN MUSSER, Ph.D., Director, Office of Regulatory Science, Center for Food Safety and Applied Nutrition
CARLOS PEÑA, Ph.D., M.S., Executive Secretary
WILLIAM SLIKKER, Ph.D., Director, National Center for Toxicological Research
STEPHEN SUNDLOF, D.V.M., Ph.D., Director, Center for Food Safety and Applied Nutrition
DOUGLAS THROCKMORTON, M.D., Deputy Director, Center for Drug Evaluation and Research
FRANK M. TORTI, M.D., M.P.H., Principal Deputy Commissioner and Chief Scientist

OPEN PUBLIC HEARING:

OLGA NAIDENKO, Environmental Working Group
STEVEN G. HENTGES, Polycarbonate/BPA Global Group
STEPHEN MURAKAMI, The Law Offices of Robert H. Weiss, PLLC
DIANA ZUCKERMAN, National Research Center for Women and Families
JENNIFER ROGERS, Reproductive Health Technologies Project
MARDI MOUNTFORD, International Formula Council
JOHN ROST, North American Metal Packaging Alliance, Inc.
URVASHI RANGAN, Consumer Reports
AARON COLANGELO, Natural Resources Defense Council

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TABLE OF CONTENTS

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

INTRODUCTIONS

DR. MCNEIL: Good morning. I'd like to welcome all of you to this meeting of the Science Board. It's a very important meeting, as you can tell from the agenda, and I'm pleased that so many of you have been able to attend, and that we have many guests in the audience.

Since many of the people are here for the first time, what I'd like to do is go around and introduce ourselves to each other, even though many of us know each other. And perhaps we could start with Lonnie -- I'm sorry -- with Martin, and maybe you could say two sentences, Martin, about who you are. Two is the most for each person here.

DR. PHILBERT: Martin Philbert, University of Michigan. I'm a professor of toxicology. My areas of research are mitochondrial encephalopathies due to nitroaromatic compounds, and the development

of nanotechnologies for the early detection and treatment of brain tumors.

DR. LINEHAN: I'm Jack Linehan from Northwestern University. I direct the Center for Translational Innovation. I'm a biomedical engineer, and my area of interest is medical devices.

DR. SASICH: I'm Larry Sasich. I'm the consumer representative. I'm the chairman of the Department of Pharmacy Practice at the School of Pharmacy at LECOM in Erie, Pennsylvania.

DR. KING: Good morning. I'm Lonnie King. I'm the director of the National Center for Zoonotic, Vector-Borne, and Enteric diseases in Atlanta. It's part of CDC. My areas of interest and expertise are veterinary medicine, preventive medicine, epidemiology, and infectious disease.

DR. HEWLETT: Good morning. My name is Erik Hewlett. I'm a professor of medicine and pharmacology at the University of Virginia

Medical School. I'm the associate dean for research, and I do research in bacterial toxins and microbial pathogenesis.

DR. PARKINSON: Good morning. I'm David Parkinson. I'm a medical oncologist. My background -- I've been involved for a long time in therapeutics development in oncology. Right now, I'm CEO of a biotech company in the San Francisco area.

DR. TORTI: I'm Frank Torti. I am the principle deputy commissioner and chief scientist at the FDA. I'm an oncologist, as well, by training.

DR. MCNEIL: I'm Barbara McNeil. I'm currently chairman of the Science Board, as you know. I'm chairman of the Department of Health Policy at Harvard Medical School, and a radiologist at the Brigham and Women's Hospital.

DR. PENA: Carlos Pena, executive secretary and designated federal official to the Science Board.

DR. LUTTER: Randy Lutter, deputy commissioner for policy at FDA.

DR. ACHESON: David Acheson, associate commissioner for foods at FDA.

DR. SALEM: George Salem, Office of Regulatory Affairs, representing FDA field regulatory laboratories.

DR. SLIKKER: Bill Slikker, director of the National Center for Toxicological Research, and my interest is in pharmacology and toxicology.

DR. DUNHAM: Good morning. I'm Bernadette Dunham, director for the Center for Veterinary Medicine.

DR. SUNDLOF: Good morning, I'm Steve Sundlof, director of the Center for Food Safety and Applied Nutrition.

DR. SCHULTZ: Dan Schultz, director of Center for Devices and Radiological Health.

DR. THROCKMORTON: Good morning. I'm Doug Throckmorton. I'm the deputy director in the Center for Drug Evaluation and

Research.

DR. MCNEIL: All right. Thank you all very much. Before we start on the formal agenda, I'd like Carlos to read a statement.

DR. PENA: Good morning to members of the Science Board, members of the public, and FDA staff. Welcome to this meeting.

The following announcement addresses the issue of conflict of interest with respect to this meeting, and is made part of the public record.

The Science Board will hear about and discuss a review of the draft assessment of Bisphenol A for use in food contact applications by the Science Board BPA Sub-committee.

The Science Board will discuss 2009 agenda topics. The Science Board will also hear an overview of current methods for detection of contaminants in FDA-regulated products.

Based on the submitted agenda for

this meeting and all financial interests reported by the committee participants, it has been determined that committee participants do not have financial interests that present a potential for conflict of interest at this meeting.

We would like to note that Dr. Larry Sasich is participating as the consumer representative, who is identified with consumer interests.

Professor Philbert, chair of the sub-committee that issued the report to be discussed by the Science Board later today, has been asked to present the results of the Subcommittee report to the Board, answer questions, but refrain from voting on any matters for the Board related to BPA.

We would also like to note that Dr. Rhona Applebaum, who should be here shortly, will be participating in the morning session only, and Dr. Garret Fitzgerald will be participating in the afternoon session only, by telephone.

In general, the committee participants are aware of the need to exclude themselves from involvement in discussion of topics if their interests would be affected, and their exclusion will be noted for the record.

With respect to all other participants, we ask in the interest of fairness that they address any current or previous financial involvement with any firm relevant to a topic on the agenda, or whose product they may wish to comment upon.

We have one open public comment period scheduled for approximately 1:00 p.m., and I would just remind all to turn on your microphones when you speak so that the transcriber can pick everything up that you state, and turn them off when you are not speaking.

I also request all meeting attendees, including the public, to turn their cell phones and BlackBerrys to silent mode. Thank you.

DR. MCNEIL: Thank you very much, Carlos. Before I introduce Dr. Von Eschenbach, I'd like to remind you that the Science Board has received permission to increase its membership to 21 members. That was mentioned as a possibility at our meeting, and that has been approved. An announcement to this effect has gone into The Federal Register.

The Science Board is hoping to have the additional members in place by our meeting in February. If you have any suggestions for membership on this Board, it would be, of course, wonderful if you could submit that information to Carlos with their names and CVs.

In addition to increasing the membership, the commissioner also mentioned last year that we will be increasing the number of meetings per year from two to four.

There's a lot of work to be done, and it will give us a better chance to get integrated into the activities of the agency,

and to contribute to its successes.

So with that, I'd like to introduce Commissioner von Eschenbach, who's been leading this agency for several years. Commissioner?

COMMISSIONERS'S REPORT

DR. VON ESCHENBACH: Thank you very much, Barbara, and good morning. You know, as you were going around the room introducing ourselves, I really was looking forward to the opportunity of introducing myself to you, because in addition to Barbara's introduction of me as commissioner of the FDA, in view of the outcome of the World Series the other night, I'd also like to say I'm a kid from South Philly.

I really do appreciate the opportunity of greeting you this morning. It is certainly true that this is a much-anticipated meeting. It's one of the many meetings that's essential to the Food and Drug Administration's operations, as we are in an

on-going effort to actively solicit outside expertise to help to inform our work across a broad spectrum of our portfolio.

But this meeting of the Science Board is, for many reasons, of particular significance, and especially for me as commissioner, in part because of my deep conviction that the crucial role that this Science Board must play in the transformation of the Food and Drug Administration, a transformation that we have all together been participating in over these past few years.

Three years ago, when I arrived at the FDA with the opportunity to serve this agency and the American people, as many of you know, I came from the National Cancer Institute, and previously from academia at the University of Texas M.D. Anderson Cancer Center.

And for decades, I had been immersed in the revolution of science and technology in healthcare, where new insights

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and new pathways were being discovered literally every single day. And from that experience, I recognized when I arrived that FDA is an agency that affects the life of every single person in this country, every single American, old, young, and yet-to-born.

Therefore, we would have to address this reality of this new science, and this explosion in science and technology, because between the world of rapid and radical advances in discovery and development, and the delivery of the products of that progress to millions and millions of lives, there is a divide, and that divide is bridged by the FDA.

The FDA for 100 years has been the world's gold standard regulatory agency that assures that those products delivered to those people would, in fact, promote and protect their health.

To address this new reality, on my very first day as acting commissioner, when I addressed the agency, I called upon the FDA to

convert from one that had been a science-based regulatory agency to an agency that would also be science-led.

It sounded very simple. Science-based, science-led. And I think perhaps many assumed that it was just a sound-bite. But today, and over the past three years, many inside and outside the agency have been awakening to the nature of this challenge. And today, those of you in this room will wrestle with issues that underscore just how profound and complex is the requirement for a regulatory agency to be both science-based and science-led.

This is the conundrum that, when I met with Ken Shine, your previous chair, on our very first meeting, I asked him to bring to the Board this challenge and this conundrum. And this is a challenge that must now also consume you and the new Board that will follow you under the leadership of Barbara McNeil. And I'm incredibly grateful to

each and every one of you and to her, in specific, for your willingness to accept and to be immersed in this incredible and difficult challenge.

Although we are a scientific organization, regulatory science has its own nuance. We are not a scientific research organization, so being science-based and science-led in FDA's context has unique meanings.

Some have interpreted that being a science-led organization as being led by any and all new science that's emerging. That's actually an interpretation that conflicts with also being science-based. The conflict emerges because new cutting-edge discovery science is by its very nature in flux, and it requires critical evaluation. Science is always filled with controversy and evaluation, and we want it to be, because the doctrine of today may be refuted tomorrow.

The conundrum is that if FDA's

being science-led is being interpreted as FDA changing decisions with the way this paper, that it=s published, then we, in fact, could rather harm rather than help the American public.

We are a regulatory agency that must make public health decisions that are enforceable, that are based on governing statutes and regulations. We must make public health decisions that are science-based, that must endure, that are based on validated research -- research that has been subjected to the crucible in which data becomes ground into information, and that information results in knowledge upon which life-altering regulatory decisions can be made.

And we know that the decisions that FDA makes must constantly be explored in a scientific and critical way, and explored not only by the agency itself, but by others. Peer review is the cornerstone of scientific exploration and validation, and we're all

raised on our scientific training in this fundamental principle.

So how do we resolve this conundrum? With a better understanding of what it means for a regulatory agency to be both science-based and science-led. Science serves as the core foundation, but science also illuminates the future direction of what our decisions must be.

And perhaps those of you who know me well knew that, within this speech somewhere, there would be a metaphor. It's not a sports metaphor, but perhaps I can best describe my perspective with a metaphor that looks at FDA in terms of what it aspires to be - a bridge and not a barrier between that innovation and that advancement that's emerging from science and technology to the delivery of that promise through Americans in an effort to protect and promote their health.

That FDA bridge affects every American every day, from the moment they brush

their teeth, or put in their contact lenses, through every meal, for them, their family and their pets, for every single medical procedure, prescription, or over-the-counter medication they take. That kind of a bridge must have a structure and a foundation and supports that will and always must be a combination of science, law, and regulation.

The laws and regulations provide the primary frame-work for the bridge, with science providing the necessary support. The support has to be constructed with rigor, precision, discipline, transparency, and validation. The foundation of the bridge must be solid. It must be built from a healthy debate and discussion, and from a preponderance of robust evidence. Regulatory decision-making must be a bridge that is strong and stable and lasting, but that's not to say that it's immutable.

In science-led, a well-constructed bridge also requires sufficient illumination,

if you will, to see the guard rails and the pathway forward. In being science-led, FDA must also use science, not just as a foundation, but also the light the bridge, to help us learn more about the products we regulate and the shape, the development and regulation of products that we will yet see in the future.

We must use science to determine how to improve the quality of our regulatory decisions to see the path forward. We must embrace new science, and stimulate even newer science. New research is essential to showing FDA areas that might require closer scrutiny.

In shining a light, the first images are shadows or signals that always require a closer look, and often require more light. One need not spend much time reflecting on the challenges and the opportunities of post-market surveillance and the detection of signals of adverse events to understand the critical nature of scientific

methodology to separate signal from noise.

And the examples continue throughout the entire portfolio of FDA. To acquire, to achieve those ends, FDA conducts some of that research ourselves, and that must and always continue as a critical core element of the identity and nature of the Food and Drug Administration.

Our laboratories, our scientists, our investigators within the agency are of critical and essential importance, and they provide that light and that scrutiny, but in addition, we also need the scientific community and its opportunity to shed light and its opportunity to continue that critical assessment and scrutiny of data that must be converted to information and then ultimately, knowledge. And we must do this in a crucible that is open and transparent for all to see.

Scientific articles with novel findings are published with the expectation that other scientists will attempt to validate

or to dispute those findings. That evolution of scientific process by independent verification is essential.

Our decisions must endure, but that does not mean they can never change. Just as no bridge can survive for decades without evaluation and repair, our decisions need constant exploration with strong scientific light and illumination.

Our decisions must endure until that constant exploration of science yields new science that meets the appropriate criteria of validation to justify a new regulatory decision or position.

When the exploration indicates that change is needed, then change must be embraced and change will be embraced by FDA. When the science that was illuminating our path is validated and repudiates a previous position, FDA will change that position and embrace a new one -- a new regulation, a new label, a new health advisory, but one that is

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based on the critical and crucial analysis that creates a strong scientific foundation for science-based decision.

It's the conundrum of a rock solid foundation of science that creates a strong regulatory structure that also has the flexibility to change based on a critical assessment of science.

And so now you perceive, not only the complexity of the challenge, but the critical and essential role of the Scientific Advisory Board and the commitment of the agency to that effort and to that process.

Every decision to approve a product creates more work, as we must regulate that product now through its entire life-cycle, from production to consumption. We must commit to explore the science along that entire continuum to call for more illumination, to call for the opportunity to look carefully at those things that come to light as science emerges and the issues come

into focus. We can see more along that pathway, and set a much better agenda to serve the American people.

FDA is striving to be that well-constructed and well-lit bridge to a healthy future for all Americans, where things like our critical path activities help guide us in innovation of medical products. Where we prevent food contamination before it occurs, where we create more nutritious food. But we'll only meet this goal by engaging experts to advise our work.

As you know, we recently asked you for your expertise, and your sub-committee has raised important questions about draft safety statement that you'll be discussing later today.

Let me be clear. There's no shame in having one's hypothesis or previous tenets questioned or disproved. That's the purpose of science - to test hypotheses and theses appropriately, and have a healthy debate about

where the data do and do not lead us in seeking to validate or disprove a position.

The shame is not having the curiosity and the courage to generate the hypothesis in the first place, and to not put it out there for a community to debate and to validate. For without thought, without our ability to create well-framed hypotheses in the first place, learning is not possible.

For FDA to fail to catalyze scientific debate on important public issues by asking for that deliberation would, in fact, be a failure of our commitment to protecting and promoting the public health.

Over a year ago, I asked this Board to evaluate the scientific needs of the agency. Unfortunately, the agency's lack of resources and infrastructure eclipsed the core important work in that effort to critically assess how to optimally align FDA's research portfolio of regulatory science in a world of explosive progress in discovery,

translational, and clinical science.

The resource and IT infrastructures were and continue to be addressed, and much progress has been made, but much more continues to need to be done, and that progress must be sustained. But we also need this Board to focus on the fundamental questions that we face regarding the alignment of our regulatory science and our portfolio with our need to serve the American people in the context of rapid and radical changes in the world of science and technology around us.

How we can use science to illuminate our path and lead us to a future, not as a research institution, but as a regulatory agency, is the fundamental core question that this Science Board and the community must struggle with, and that the agency must resolve.

The discussion today calls into sharp focus the need for insight into

processes and technology that are on the horizon, and to direct that technology development in a way that it creates, in the future, a strong foundation for regulatory decisions. As you proceed through today's agenda, please consider how FDA can gather more light, and convert that light into validated research that can reinforce the foundation of our regulatory bridge.

I can't end by not emphasizing the deep gratitude that not only I, but every single member of the Food and Drug Administration has for all of you being willing to give of your time, your effort, your talent, and to make the commitment to take these positions, as visible as they are, and as subjective as there are, to the same stresses and pressures that those within the agency face, to engage in a struggle, and to do it in an open and transparent forum for all the world to see in terms of the need to engage in a quest -- a quest that requires, at

times, controversy, difference of opinion, and self-critical analysis, but a quest that always is intended to protect and promote the health of every single American.

Thank you for that commitment. Now I'll take questions.

Q AND A AND DISCUSSION

DR. MCNEIL: Thank you very much, Commissioner. Are you able to stay for a few questions?

DR. VON ESCHENBACH: Sure.

DR. MCNEIL: Are there questions of the Commissioner?

DR. VON ESCHENBACH: Dave Parkinson, you've never not had a question.

DR. MCNEIL: Alright.

DR. VON ESCHENBACH: We go way back to M.D. Anderson when we were trying to cure kidney cancer, and you always had questions.

DR. PARKINSON: You always had answers.

DR. HEWLETT: I'm very supportive

of the idea of continued research by the investigators and scientists and regulators at the FDA. I'm interested in your thoughts about what the objectives are of those individuals continuing to do research, because I realize that's been a controversial issue. I've done some lab reviews in the past. That's always an item that's greatly discussed.

DR. VON ESCHENBACH: Yes. Thank you for bringing that forward, because I think that is really one of the exciting opportunities for the dialogue between the Board, advisors to the Board, and the agency itself.

And I've asked Frank Torti, as chief scientist, to really kind of help catalyze that continued dialogue. We've made some internal changes within the agency to align our regulatory research agenda with the larger agenda that's occurring in the context of basic all the way through to clinical research.

Some of the things that we've done is, for example, to ask Bill Slikker and NCTR to take on a core role, as a core resource, within the entire agency so that the effort that is going on in research at NCTR is really what we would consider to be developmental regulatory science that's asking questions to focus research initiatives, research projects, on specific areas that we are anticipating will become the next generation of regulatory decisions, for example, in nanotechnology.

And to be able to start that research agenda so that we will build that foundation, since science has already illuminated the fact that this will be an important part of the kinds of products that will be emanating out of discovery and development that's occurring in the world around us.

The developmental science that's occurring as a core resource at NCTR is then complemented by and integrated with what I

would describe as the applied regulatory science that's occurring within the centers, where they are engaged in specific research activities that are focused on much more proximate questions about specific products or issues, such as the research that perhaps is going on, as an example, in CDRH under Dan Schultz, where we're looking at actual specific devices that are currently now within our purview, but for which there are important research questions that have to be asked, everything from what happens to a product when you take it from a macrosize and you miniaturize it in terms of its internal circuitry and software changes that occur. Those are important research questions, just as a device, and it flows through there.

And then finally, the third level is to re-position our entire scientific portfolio in the field, and in the laboratories of the field, which is much more analytical science, but brings into that

analytical component more modern technologies and techniques that have emerged from science -- everything from high throughput to moving into more elegant methodologies of the scientific analysis.

And that gives us the opportunity to make decisions about actual products in context of regulation, whether it's determining the components of baby food or baby formula, or determining unsuspected contamination of heparin, and being able to develop the scientific validated methodologies that would enable us to address that public health threat.

And in fact, that real world example occurred where we were then able to disseminate that methodology to the rest of the world, and immediately give them the opportunity to address a world-wide public threat from the contaminated heparin.

So there is a body of research that must continue to occur within the agency

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across that spectrum. And my constant message is that, within the agency, that research now must be much more integrated and collaborative across the various components, with vertical as well as horizontal integration. And that is a major focus of our development of our scientific infrastructure at White Oak, for example. And it must also be constantly immersed and integrated with the science that's developing around us in terms of what's occurring in other fields of endeavor.

And I think your discussions later today will truly focus on some of the issues having to do with that interface between what's occurring in that space. But all of that is built on the fact that, one, we move to regulatory decision-making, the foundation upon which the decision is made must meet another level of rigor and criteria for decision-making because of the very nature of the infrastructure of it being a regulation -- a regulatory process that must endure and has

far-reaching implications and impact.

So that's, in a nutshell, kind of the broad -- the capture of the broad perspective of what we're trying to continuously improve and evolve to.

Is that helpful? Lonnie?

DR. KING: Commissioner, I really applaud your vision of being science-based and science-led. You know, part of that is the culture of FDA, and what's your plan and vision to be able to retain and especially recruit, you know, the bright minds in science and research that are going to not only maintain this vision of strong science, but flourish in it?

DR. VON ESCHENBACH: Well I think, Lonnie, one of the greatest -- I would say, one of the most gratifying moments that I think I'll reflect on in my tenure at FDA was just a few days ago, when we welcomed our first class of FDA fellows.

The fellowship program is now

underway. It is a curriculum-driven two year program that incorporates regulatory science, regulatory policy, regulatory law, and regulatory practice. It is a mentored program and curriculum-driven, and it really encompasses a broad spectrum of disciplines across scientific disciplines and medical disciplines, but also is embracing emerging and new disciplines, including computational biologists and computational scientists and engineers, physicists, et cetera.

What I am extremely excited about is what that creates for FDA, and our ultimate goal over the next three to five years, as we hope the Reagan-Udall Foundation is able to be fully established and creates an opportunity for additional support of the fellowship, our expectation and goal is to ramp up to 2,000 fellows. One thousand a year for a two year program. That brings into the agency the best and brightest of the newest generation of investigators and scientists who have grown up

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in these emerging new disciplines and fields and opportunities who have been part of that world of discovery and development.

In the process, our expectation is we will retain the top 20 percent of each graduating class, which means an infusion of 200 individuals with career paths that have been defined and outlined within the agency, so it becomes a source of constant replenishment of our intellectual capital, and 800 sons and daughters of FDA will go back to academia and to industry and to other endeavors with a very in-depth understanding of the very nature of regulatory science and regulatory function within the FDA. And I believe that will catalyze this ability to bridge between those two emerging realities. They will, in fact, be the living bridges, both inside and outside the agency. So one strategy to address that challenge of where will we continue to replenish the brilliant minds that you see sitting on the other side

of the table. I believe it's primarily through the fellowship.

In addition to that, we've also implemented very specific measures towards career development for those individuals who are already a part of the agency, because it is absolutely essential that everyone in the agency grow in terms of their continued ability to grow and adapt to the incredible progress and changes that are occurring around us.

And so Frank also is charged, as chief scientist, with also looking at our current staff, and to create enrichment with regard to their career development, and to vitalize the intellectual life of the agency as a learning organization.

DR. MCNEIL: David? No?

DR. PARKINSON: No, maybe more a reflection than anything else, because I'm very sympathetic to the goals you've talked about.

I've had the opportunity in the last few weeks to be both in China and the Middle East, and in both places, people were talking about the new FDA offices being opened up. So everything you've said about what is being driven within the United States actually carries over to other places, and the consequences of a lack of regulation in those places is part of what we'll be talking about here today.

So it's the right direction. And the change you talk about within this agency is reflected in the change that's actually happening in the industry, all being driven by new science, and I think the brilliant minds on the other side of the table are seeing that also.

It's a time of great change, and it's good to see the agency adapting to that. So more a reflection than a question.

DR. VON ESCHENBACH: Thanks.

DR. MCNEIL: Questions from this

side of the table? No?

DR. VON ESCHENBACH: They actually don't have the questions. They have the answers.

DR. MCNEIL: Well, I knew that. I was just trying to be polite.

DR. VON ESCHENBACH: That's where I got all this.

DR. MCNEIL: Are there any further questions? All right, if not, I'd like to thank the commissioner very much for his time, and his very thoughtful remarks.

DR. VON ESCHENBACH: Thanks, Barbara.

DR. MCNEIL: I think they fit in very well with some of the discussion that we had at our last meeting.

So, let's see. We're going to have Frank Torti now, who is going to talk somewhat about science at the FDA, an update. We heard a very interesting presentation last time in which he gave his vision in part of what

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science should be, and at that time, introduced the concept of the FDA fellows that the commissioner just talked about. So Frank, you're on.

SCIENCE AT THE FDA: UPDATE

DR. TORTI: Thanks, Barbara. Well, we've got it all solved now, so we can just -- but actually, thanks for this opportunity, and thanks to Andy for sort of setting the stage for a lot of the issues which now I can bring to you, I think, as examples of some of the themes that were brought up in the first discussion, but also in the questions.

So let me begin, and let me see if I can figure out how to -- so I hope that this statement, which I showed you when I first came here, captures for you how science at the FDA relates to its regulatory mission. And it's that top quality regulatory science will actually improve regulatory decisions, regulatory consistency, which I think is very important, and eventually will lead to

speeding new products to the marketplace.

So I tried to distill in this next slide the entire Science Board report to the FDA into three bullets, which is a challenge, but I wanted to do that so I could begin to reflect today on some of the issues that were raised by the Science Board, and I'm not going to hit every bullet in detail in that Science Board report today, because I can't, but what I will tell you is hopefully by the end of the year, I will deliver to the Science Board a full response to your suggestions and where we're going in that regard, so you have something to look forward to there.

The three issues around which the Science Board report was based were sort of scientific leadership, scientific investment, partnerships both within the agency and partnerships outside the agency, and priorities and priority settings in science.

So that was sort of one group of themes, and of course you scrape the bottom of

the barrel and got yourself a chief scientist, so you have some aspect of leadership there. But a lot of this I'm going to talk about and show you where we've gone.

The other issue, and Andy has addressed this because it's essential, is scientific recruitment and retention. And I'm going to show you some of that. And then the issue of IT infrastructure and its relationship to science and how it supports the scientific mission of the agency, and I'm going to bring you up to date a little bit about that, as well.

I tried to -- in order to get there, you know, having read that Science Board report, one of the issues was what are the principles that would drive my sort of leadership, my decision-making, in that regard. And there were three, and I mentioned them the last time, and I'm going to sort of start to fill those out now.

The first was that the FDA cannot

do it alone, that is has to partner more, and it has to partner smarter if its going to leverage its assets to the fullest extent. So that was principle number 1.

Principle number 2 was that the FDA must enhance its own core scientific expertise, and principle number 3, which I think drives the rest of this, is that the scientific strategy of the FDA must, in fact, be pre-emptive, not reactive, and I'm going to touch on some of those points, as well.

So now in order to develop that, I'm going to show you a series of tasks that we've undertaken, some finished and some in progress, and show you where we are.

And the first task, which of course is the task that the legislation that created the office of chief scientist gave to me, was to develop a scientific strategy for the agency. And we've done this in a very exciting way with the center directors, and I just wanted to describe for a minute the

process, and then tell you about some of the implementation of that process.

So we've met with the center directors and asked the question, "What are the critical priorities in science that will need to be addressed to solve the regulatory issues?" Let's start again. Let's start fresh in thinking about this, and let's lay those out in detail, but let's only pick the absolute top priorities in each center.

And then let's begin to instantiate those in a way by saying, what are the projects that actually need to be developed and tackled in order to get to moving these priorities forward in order to solve regulatory problems?

And let's not do this in a philosophical sense, but let's say, for those priorities and the those projects, what are the time-tables? What are the deliverables? And in fact, this won't be for free. This will cost something. What is it going to cost each

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of the centers to do that?

And we've made some progress in this and it's actually been a lot of fun. So here are some of the absolute top priorities that the center directors have addressed. Now I'm not going to go over them in detail, but I want to give you a flavor of them. And of course, these are just sort of key words, and there's a lot around these. But rapid detection technologies, and you're going to hear something about that later today. Bio-markers to predict both safety and efficacy of products. Adverse event detection, both before and after a product is marketed. How to use clinical trial designs to enhance and speed and improve the ability to get new products to the marketplace. Personalized therapy and personalized nutrition. Understanding microbial contamination in a deep and lucid sense that will help regulatory decisions. And technologies and manufacturing science, and I'm going to come at the end to show you how I

think that relates to our mission, as well.

So those were what the center directors who are driving this process have identified as some of the absolutely top scientific priorities. So how do you take that and start to develop that?

For each of these priorities, we've asked the center directors to develop a number of projects to tackle these. And the point here is to make is that for some of the top priorities, there are projects that go across a number of the centers, and we're not done with this. A couple of centers are still giving us their projects.

But the point is that there's going to be enormous opportunity for integration along some of these issues because these projects by their very nature -- I mean, it's remarkable how much consistency there is in the identification of top priority areas.

So that's good. So where are we going? Assess integration and collaboration

among center priorities in order to complete the plan, complete the identification of projects that will move forward on these scientific priorities, and yes, you do have some more work, Science Board, so one of the things we're going to ask you today is, as we develop this plan, to engage with us and review the scientific plan, just in the spirit that Andy has developed in his presentation. So that's task one, and where we are.

So task two is to develop a workforce to implement that strategy. And Andy stole a lot of my thunder here, but I also have to say that one of the best moments I've had in the FDA was meeting our new commissioner's fellows.

And I want to thank many of the people on the Science Board who have actually gone out and helped me in many ways recruit some of these people and have been involved in helping me think about how to get them here, because, of course, we did this on a short

time frame.

But we had over 1,000 applicants for a small number of slots. They're incredibly talented people. They're just highly selective, and this program really is unique at the FDA, and maybe just unique period, in that it actually exposes these fellows, not to the science in one center, not to the regulatory process in one center, but regardless of where their mentor is, regardless of where their project is, they get exposed to the entire spectrum of FDA science. So they're going to know a lot when they leave, and I've given you examples of some of the kinds of courses that they'll be taking and be involved with.

And here's just some of the kinds of projects. I just have to go over this, so you know, anti-cytokine therapeutics, how cytokine signals affect FDA regulatory decisions. They actually do. Bioequivalence of generic and innovator drugs, drug and hormone

residues in animals, cardiac electrophysiology in device regulation, regenerative medicine issues that relate to the FDA. Aqua-cultured fish diseases, which is an important issue, actually, for all of us. MedWatch issues, risk assessment and communication, ethical issues in pediatric studies.

So you just get a flavor of the range of projects that these folks are engaging in.

And the other thing that Andy said is besides the fellowship program, we're trying to drive an improvement in the experience for people who are scientists and regulators at the FDA, and part of that is just sort of practical little things that need to be done, but they're important and I want to show them to you.

One, for example, is we've now developed and have approved quarterly FDA-wide science symposia. There's one in November on bioinformatics. I'll have a discussion, and

the one in April is actually going to be on nanotechnology, but actually will involve an international effort to define regulatory issues of nanotechnology because, actually, the regions of the world have gotten together, talked about regulatory issues and nanotechnology, and have actually divvied up some of the science. So EU, Asia, et cetera, and we're going to bring that together in a dialogue in the spring.

So in order to be scientists, you've got to have the right tools. We increased this one subscription from 150 journals to 2,000. Overall, we've gone from about 2,000 journals to 4,000. We're now at a level of information that's comparable to the NIH in terms of its capacity, and I think that's absolutely essential for a scientist to have rapid and complete access to the literature. We're now going to fund a quarterly symposia driven by the young scientists at the FDA on distinguished

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speakers.

The only thing I've asked is that the speakers and the symposia reflect back directly on the priorities that the center directors have said, so that this is actually a self-feeding process where we emphasize, in everything we do, those priorities of the centers.

We are in the middle of the challenge, which I think we're going to succeed this spring or early summer in establishing a journal of regulatory science so that regulatory scientists actually have a forum for this. If any of you are around on November 10, we will have the first annual science writers symposia, so that we actually bring science writers to the FDA to understand some of the cutting-edge science that's done here, which often is not exposed. That is already over-subscribed, and I'm delighted at the opportunity there.

And I've worked specifically,

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because of my background with the oncology program, to develop a career development plan with Rick Padzur and others in the agency. And that will be announced very shortly, so these are the kind of things that need to be done to drive this process forward.

So IT, Sangtae Kim, and Barbara is going to relate to this in a few minutes, was the advisor to the Science Board, I believe was on the Science Board, and dealt with the infrastructure issues. In the Science Board report, I asked him to come back to the FDA, spend a couple of days, review where we were going in terms of our IT decisions and investments, and he's come back - he can't be here today, he's in Asia - but he has sent a report to Barbara, and he is going to continue to engage with the FDA to be sure, from the standpoint of the Science Board and science, that we're on target in our investments in informatics and bioinformatics.

Task four. So we've chosen a few

problems to drill down and to actually try and use modern science to help the regulatory process, and you're going to hear about two of those in just a few minutes, so I won't go over them in detail.

Both of these you asked for. If you remember what you asked for at the last Science Board, you wanted us to address the issue of rapid detection. Well circumstances have evolved that these have become not only theoretical issues but issues of great currency.

So we're going to address issues of the science of rapid detection, and we're going to look at economically motivated adulteration. Again, this all day is about foods in one sense or another, which I like to call economic bioterrorism, in a sense, and how we can use science to think prospectively about those.

And of course, that issue that Andy brought up, we're talking about BPA today

because we have asked the external community, specifically you, the Science Board, to help us in this decision. And so we're going to hear from Dr. Philbert and his sub-committee in just a few minutes.

So those are some of the agenda items for today. And I won't go over this because you'll hear about this, but we hope to engage the Science Board in an ongoing way for each of these topics that we're going to lay out today. So this is not going to be a one-time gee-whiz kind of session.

Today, in terms of both the rapid detection issue and economically motivated adulteration, we're going to present the problem, and then as we drive toward solutions, we're going to come back to you and show you where we are and continue to seek your advice.

So I want to turn now to -- a lot of what I've talked about is sort of classic science in a way, and I've put together, as

you must do in this job, a series of talks about the FDA more generally. And I came to my own sort of, just sort of private independent sort of conclusion is that, right around the turn of the century, right around the turn of the millennium, you can almost target a change in the FDA that has changed the FDA drastically and permanently.

And I think there are three ways that has occurred, and then I'm going to take that back and show you how science relates to those changes.

But first is the overseas production of drugs, devices, and foods. Second is the issue of bioterrorism and how that affects the FDA. I'm not going to talk about that in detail, but clearly that has, as of September 11, 2001, has had an impact on everything we do, and presented new and different challenges to us in a scientific sense.

And the third and perhaps most

important is the rate of change of science itself, which is extraordinary increasing logarithmically or faster, and is a challenge that we have in this agency, and Andy addressed that.

So I'll give you a few slides that actually show this, and I apologize for starting to get into data here. But I think this is worth just -- and would interest you.

So here are the FDA-registered domestic and foreign manufacturing sites tracked by calendar year from '91 to 2007, and the dark blue are the foreign sites, and what used to be green but is now white are the domestic sites, and what you can see is that, in 2007 -- first you can see the shape of these curves in terms of what's happening, the foreign sites are increasing dramatically.

And I can tell you that, in 2008, this line is actually crossed. So there are more FDA-registered foreign manufacturing sites than there are domestic manufacturing

sites. And if you look at 2000, to make my point, you see that wasn't such an issue back then, although it was becoming an issue.

And this is my favorite slide. This is the actual lines of import that the FDA deals with, and a line in the customs regulations can be everything from a box to a whole ship, but if you look at the numbers here, you're looking at devices over 4 million. If you're looking at foods, over 6 million events of import.

And if you look at where they're coming in, to 295 active sites in the United States, without saying anything, that should, for you, capture the essence of an incredible challenge.

So how does regulatory science contribute to protecting people in the face of this increased foreign production of foods and medical products? So Andy alluded to this as well, that one must evaluate the entire life-cycle of the drug, device, or food, thereby

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identifying the problem at the source, not at the border.

But that relates specifically, as you recall back to one of the top priorities that the center directors have identified in terms of manufacturing science, because knowing where the fragile points are in manufacture, or the fragile points are in the field, in a farm, et cetera, in ecology, are essential to protecting public health. That's a science.

And you can't inspect everything. I've pretty well convinced you that that's true. The algorithms for risk-based inspection are complicated, biostatistically-based algorithms that require scientific input.

We've already talked about field-ready enhanced techniques for rapid identification of contaminants. You're going to hear about that science, as well.

And then, to track all of this, of course, informatics. Informatics for the

supply chain is absolutely essential. The science of doing that is quite clear and needs to be enhanced, as well.

So science touches on a lot of the broadly-based, the point I want to make, mission of the FDA, as well as some of the things we think about in the more classic sense of science.

So there's a lot to do and there's a lot, I think, we've already done, and we're going to need your help and support. We're going to have to get science in the forefront of peoples' minds, understand regulatory science, have a substantial and real budget for regulatory science, which I know you've supported on the Science Board, if we're going to achieve success.

Science can't be hidden in the agency. It has to be very visible and at the forefront of all of the decisions we make. So thanks for your attention.

Q AND A AND DISCUSSION

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DR. MCNEIL: Thank you very much, Frank. That was a very nice presentation.

Are there questions for Dr. Torti? Yes, Jack?

DR. LINEHAN: That was a great presentation, Frank. Thank you.

One question about the fellows. I know it's sort of -- they've just gotten here, but it would be interesting to know a little bit about them, where they come from, what their fields are, and so forth.

DR. TORTI: We'll get you some demographics. They come from all over the country. There is a slight preponderance, as you might expect, from the DC regional area, but not -- certainly not all of them don't come from there.

The fields are just enormous, and we'll give you that. There are MDs, there are PhDs, there are PharmDs, there are engineers, there are people who have worked in policy and biostatistics, and in other aspects of public

health.

So that's one of the gratifying things is the way we designed this on sort of a preceptor-based sort of selection process has given us an opportunity, one, to tackle real problems that the FDA has since the problems, although will be defined and refined by the fellow and the preceptor, began with the preceptor identifying on a web-site what the FDA problem that needs to be solved was.

So broad demographics, wide area of interest. We can actually get you all that data, and we have it collected, so we'll bring it to you.

And Jack, thanks for your help with getting us some engineers in this. So Appreciate it.

DR. MCNEIL: Frank, I had one question I'd like to ask while others are thinking. You mentioned understanding better the life-cycle for devices, in particular, as a way of understanding how you could identify

problems at the source rather than at the point of use.

Can you give an example of -- a couple of examples of what you were thinking about in that area?

DR. TORTI: Absolutely. So let me take food first, which is perhaps the least intuitive, but I think is actually interesting to me, and Steve and Bernadette can chime in and amplify what I say.

But I, for example, am very interested in the reasons for contamination of food supplies, whether it be domestic or foreign. And we all know that it relates to sort of ecosystems in and around the farm. And those can be studied in a scientific way. I mean, there are aspects of topology, of geology, et cetera, that actually can help us predict where the likely sources of problems will arise there, again so that we can have a science-based inspection strategy that's based on high-risk areas, so science can contribute

to that.

The other area that I know CFSAN is quite interested in, which I think is extraordinarily important in this regard, is we don't actually understand the actual pathway by which a contaminant, a bacteria or other contaminant, actually gets and maintains itself in even the simplest sort of ecosystems and areas. And Lonnie, you're an expert at this. But that's a science, and that has to be driven. So that's the food area.

You turn to products, and it=s absolutely intriguing. I mean, if you accept the fact, and Andy has made the statement, that you can't build quality in at the border, you have to build quality in from its origin and production, then you need to understand scientifically where actually the fragile sites are in the production process so that those fragile sites can actually be identified and targeted in the inspection review process. There's a whole science to

sort of what I would call fragile sites, because I'm interested in fragile sites and chromosomes, but it may have a different name in food and product science.

But the idea is you can identify, if you actually study it very carefully, what that whole process is. And you can identify where contaminants are likely to be interjected into that process, and you can inspect those. And that's an essential part of manufacturing science. So Barbara, those are just some examples.

DR. MCNEIL: Bernadette?

DR. DUNHAM: I'm just going to reiterate what you just heard from Frank. I mean, it's very exciting, the opportunity to participate in all of this, and we really do need to fill these gaps, because they're very important as to how we're going to be able to modulate further our regulatory processes that are so important to protect public health.

So I think these are exciting

opportunities, and we look forward to your comments once you see the whole package that we're going to pull together for our proposed studies. Thanks.

DR. MCNEIL: Lonnie?

DR. KING: Frank, we're really excited that you're on board and leading this charge.

One of the questions, and it doesn't probably have a specific answer, but you talked about a rapid change in acceleration in science and technology, and the same thing is happening in the world of commerce.

So I saw the write-up, there's $12 trillion in global commerce. It's probably less in the last month, but it's $12 trillion. You know, so how do you actually take science and leverage it to get ahead of this?

So somebody pointed out to me there's no Health Committee in the WTO. It's about the deal. It's about getting things

done. It's about moving product, creating wealth.

So how do you actually try to get ahead of this curve, because it's increasing as rapidly as the science, and realizing that's somewhat philosophical, but it also talks to the tension between globalization and what's happening in your agency.

DR. TORTI: Yes. That's a great question, Lonnie, and others may want to chime in, as well. I'll give you one thought that I have based again on just sort of food supply, and that is, you know, how technology and science enrichment through scientific advances, including genetic engineering, actually target and improve human health by providing food and opportunities where those might not have existed before. And that becomes an issue for the FDA because we regulate that, and we have to do that in a way that's thorough and careful, but the opportunity there for human health and human

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survival, in a sense, is absolutely profound if it's done right, because there are opportunities that science brings to the table to bring food to the table, for example.

So I think that's one example of how commerce and science touch, and how the FDA regulation, you know, appropriately applied, will actually facilitate and help that process.

DR. VON ESCHENBACH: Lonnie, can I pick up on that, as well, because I think you just put your finger on what is an unbelievably profound challenge, but also an unbelievably exciting opportunity for FDA to play in this global space of world-wide trade and the world-wide marketplace.

It's really an opportunity for FDA's leadership in the context that there are certain things about this new reality that we will directly control, and there are other things that we have the opportunity to directly influence.

The private sector is stepping into this space in a very explicit way in terms of trying to assure the integrity of the supply chain of their products because of the downstream risks that are associated, not only from the point of view of liability, but also, importantly, from the point of view of brand equity.

When I visit a Wal-Mart, you know, Wal-Mart says it doesn't matter where the product comes from. Once we put it on our shelves, it's ours, we own it. And if there's an adverse outcome that comes from that, it's now our problem.

So they're moving up in the supply chain to start to look at establishing standards for those products. And we have to play in that space from the perspective of taking the leadership in establishing those standards based on science, because if they're not science-based standards, then we're going to have chaos with regard to what's occurring

in terms of our ability to have harmonization in this global marketplace.

And as I've travelled around the world, and I'll be in Singapore next month for a meeting of the heads of global regulatory agencies coming together for the third time around this issue of how can we harmonize our own regulatory processes, because we are governing these products, and do that in a way that we have harmonization.

And I think FDA's leadership is going to be critical, working government to government, so in those regulatory agencies that need to evolve and mature, that they're doing it in a way that's profiting from and benefiting from FDA's experience and FDA's capacity in those that are mature, that we're getting greater integration of our approach to standards upon which we will demand and expect compliance as it relates to our ability to accept those products coming into our marketplace and to our citizens.

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And three, to work directly with the private sector so that we really can affect what will essentially be a systems approach to a systems problem. And if we don't do it based on science, then there really will be downstream consequences of what I just described as chaos, because it won't improve public health necessarily, predictably, and it can create all kinds of problems with regard to the interruption of the global flow of products across borders, which is now the reality of this maturing global marketplace.

Does that help?

DR. PARKINSON: My question follows up on some of your comments, Frank. Very nice.

And it relates to scientific strategy. Do you expect that the - maybe it's for you, Andy - that the agency will have a scientific strategy that somehow relates to the recommendation, in a document or a working plan? How will that relate to the response to the Science Board recommendations that you

made, and will that come from center up?

I'm closest to ORA because I was involved in looking at their sort of strategic plan, prioritization of what they wanted to do. Will there be an attempt to integrate those across centers, because your comments about opportunities for cross-center science I think are great. I'd be interested in how you see all this fits together so that it can be associated with budget time-lines and resource allocation together with prioritization.

DR. TORTI: Great question. And let me address it in a couple of ways.

So we have a very explicit idea of both the process and the product here. So this will be written down, and this will be a document, you know, a document that will be mutable and changeable as science changes. However, one has to be careful about that, and sometimes when one writes things down, they take a permanency that's inappropriate given the rapid change of science.

But I just want to go over in a little bit more detail, to answer your question, the process, because I think the process is very important to the outcome.

The first thing we asked the center directors is -- we didn't ask them what science is, cross-center science, because I do believe that there are certain profound scientific questions, in devices, for example, that might not be sort of co-held by CFSAN, by the food agency. So in order to really bubble up what the key science that we need to address is, we first have to understand what the key issues of each of the centers are, including ORA, which we've done.

Now the process by which the center used to do that, of course, is then they ask their constituencies and develop this bottom-up, back-up. But at the end of the day, it has to be bought in by each of the center directors, and has been so that there is a leadership buy-in as to what the priorities

are, and not, you know -- not 90 of them, but just a handful of them so that you have few enough of them that you can actually tackle. So that's part one.

As we do that, then we're seeing these areas where, clearly, we're going to have opportunities to take mutual and collaborative approaches to that science. And that will be round two is to say how can we integrate, and therefore more efficiently target those approaches. I think the economy is there, both economies financially and opportunities intellectually for cross-fertilization.

So then when we target those down to the level of what kinds of projects would you need to do to be able to solve that problem or move that priority to the next level, or maybe knock that priority off our list, what are you going to do, what are the specific aims, what's the hypothesis, what are the deliverables, what's the time-table?

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We're already into that, so we've gotten this pretty far along, although we're not done with that. That's hard, and that involves making some choices in terms of how to approach these problems.

So that is the process. The product, then, will be a written document which we'll be able to use, we'll show to you, but we also want you to be engaged in a discussion about this, not just the review of the document.

So that's the process. There are issues here related to the finances of this and the budget. It has been difficult in the past, and Andy addressed this, for the FDA to advocate for a regulatory science, sort of line-item budget that puts science right up there, and not something that the center directors sort of have to pull out of the hat each year, out of a line-item that sounds like it has nothing to do with budget.

I don't think this agency will

ever be completely successful in its scientific mission unless that rises to a level of visibility in the budgetary process, and in the overall process of people understanding about people like the members of the Science Board who can endorse that. Otherwise, we're going to have trouble getting there.

But we do this, we asked them the question. You know, I proposed last time and we're still working on these ideas of Centers of Excellence with academia. How do we then engage the scientific questions? Part of it has to be within our own centers, and part of it has to be to reach out to the best people to help us answer the problems efficiently.

So that's yet another round of drilling down once we get those priorities. But before we reach out, we have to be absolutely clear, absolutely clear about what we want to achieve.

DR. VON ESCHENBACH: Let me take

your question, David, in a slightly direction, because I didn't use examples in my presentation to illuminate this conundrum between science-based and science-led for lots of reasons.

But let me pick one based on your question that I think you and I both can relate to in terms of our background in oncology, but that really kind of crystallizes a lot of the concerns, a lot of the issues, and a lot of the challenges.

In the beginning, when I talked about the need to support a strong science base within the agency, a science portfolio within the agency, I would often get the question, what do you need science at FDA for? You've got all the science at NIH, and all the science going on all over the place, and why don't you just use that, so to speak?

And your question really then gets to focus on the fact that, within the regulatory processes that are being carried

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out in the various centers, there is this need for this foundation of science to be established within the agency upon which we can build and base regulatory decisions.

And yet, that's illuminated by the kind of evolution that's occurring in science around us. So the story that's familiar to the two of us is, you know, our understanding of HER2/neu may point us in a therapeutic direction with regard to the treatment of breast cancer, but there has to be a science that brings that observation to a level of validation that then enables it to become a part of an enduring regulatory decision about the product that will be used on that basis to treat women with breast cancer.

You and I both know, from an exploratory point of view, BCR-ABL has been around for a long time, and as an interesting, important part of the pathogenic cascade of the outcome of cancer. And yet, as we were talking earlier this week, we haven't moved to

the point in our understanding of that where we have that validated in a way that we have a way of applying that across an entire terrain as a standard upon which this regulatory decisions, or the use of products could be obtained.

So what you're alluding to, what you're calling to, is this has to be, first of all, a process that begins with the centers identifying where those critical issues are that need scientific rigor and further understanding.

And at Frank's level, across the entire agency, we recognize that once we move it to that point, as a biomarker, if you will, it has implications that can go across the wide spectrum of the agency. So we're doing this almost in a bottom-up, top-down integrated fashion because the end point of all of this is that it enhances the ability of FDA to carry out its primary mission of regulation to protect and promote the public

health.

And there's a complexity in that that I have been alluding to which requires us to struggle with this, to continue to work with this, to continue to evolve this. It's not a magic wand simple solution. It's a constant ongoing effort to create the science within the agency that fulfills that kind of expectation, and does it in the context of it being ongoing and constant in its search for new knowledge and new information.

Does that help you get the sense of it?

DR. PARKINSON: No, it does. I actually talked on this yesterday in a different context at a different meeting, and I listened to Doug a week or so ago talk about some of the critical path initiatives.

And I think a shared responsibility that regulators have and the NIH, NCI, from my perspective, but this is across-disease, and industry and the academic

community have are, to pick up on your point, develop tools. It's what's missing in a lot of the diseases we're working with. You can call them biomarkers if you want, the tools to get further insight into the disease. So we get the read-outs that are more accurate so regulators can look at data and understand what it means, so drug developers or device developers can more efficiently go about what it is they're trying to achieve.

And it's amazing to me that, as we watch the concept of human disease evolve in front of our eyes, as it's happening, we, and I say we as the community, not just the agency, have not as a strategic sort of goal taken on the challenge of developing tools to more efficiently go about this business.

Dan, I see you nodding your head. You live with this, right?

DR. SCHULTZ: Yes, I mean, taking this from sort of a philosophical to a very practical level, I mean, we need to develop

the science to be able to take an article that says, this is an interesting clinical finding, more research is indicated, to a guidance document that says, we now understand enough about this for this to go to public, and to be part of the armamentarium of physicians treating patients at the bedside.

They=re two very, very different, and yet in some ways, integrated and connected questions. But the first question is the one that, essentially NIH's task with doing, developing interesting findings, developing things that are potentially, you know, but more research indicated. We have to make decisions, concrete decisions, every single day about, you know, there's a product, and is that product ready to go from, you know, having been used in 100 patients to being ready to be used in 100 million patients? And those are the tough decisions.

And if you look at Frank's list, there are a lot of things up there where I

think there are cross-cutting opportunities for dissenters. Clinical trial design. We all know, and we're not supposed to look at cost, but we all know that clinical trials are becoming more and more expensive, people are demanding clinical trials for more and more different kinds of products, even in devices, which traditionally has not been, in many cases, clinical-trials based, but we have to figure out smarter ways to do those trials.

I mean, if we're going to try to upgrade the clinical data, we can't use the old models and say that that's going to help us five years from now, ten years from now, to get these products on the market. We have to do smarter kinds of clinical trials. We have to engage statisticians and clinical trials, both inside and outside the agency, to figure out how to do this.

In modeling, in device modeling -- again, we've used very, very primitive types of tools in doing our device development. And

there are other tools out there that are used in other industries that we haven't even scratched the surface. We have to be able to develop those tools so that we can get these products and understand how they're going to work, and be able to take them from a good idea to a product that can be used.

DR. PARKINSON: I think that's really well-stated and what I liked in Frank's answer was, as he worked through the steps, you got to external interactions because I really think this is shared responsibility, and the critical path philosophy incorporates that.

We on the industry side have to work actively to develop tools so we and you can be more accurate as well as efficient. And I just think that that cannot be emphasized enough, and as you move to develop your strategy, I would look for opportunities to engage -- you've already talked about it -- engage the external environment.

DR. MCNEIL: Frank, could I just follow up on that for a second? I think it was implied or maybe even explicit in your remarks about the NIH.

To what extent will your tasks involve discussions with the NIH, following up on the comments that we just made. It sounds as if there's a potential gap or way to get a synergistic response.

DR. TORTI: Well, you'll see today lots of synergies already. I'll give you one example of a meeting we had just yesterday with the NIAID and their food and water borne disease network and Steve and Bernadette were in that discussion with me to try and engage the NIAID as the develop their new RFP for this very successful and very important area, you know, to touch areas of zoonoses, and to anti-microbial resistance, etcetera, that really target issues that are mutual interests to NIH and to the FDA.

And the remarkable meeting we had

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-- yesterday was a busy day with the senior representatives, past presidents of the AACR to bring to us their recommendations on a number of issues related to biomarkers, etcetera that will eventually be incorporated into our guidance as well.

So, I mean, we do this every day, and we need to continue to do that, and we need to do more of it. That's my thinking.

DR. MCNEIL: We have time for one more question. Rhona, I thought you had your hand up?

DR. APPLEBAUM: Thank you and I apologize for being late and missing your commissioner's presentation and just coming in late, Dr. Torti, on yours.

But, going back to the life-cycle management of food and products, which is very important right now to the industry, one of the things -- and I really applaud the way you're going about it from a global systems approach, looking at it, if you will, as a

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global HASSOP system, for the world.

Earlier, I think in the summer or late in the spring, there was mention about having global field offices for FDA. India was mentioned. Even the EU was mentioned. I was wondering if you can just give an update on where those offices are? Did you say that? Did you talk about it?

DR. TORTI: Yes, Andy. Do you want to do it? Go ahead, Andy.

DR. VON ESCHENBACH: I'll be leaving in a few days to open our offices in China -- in Beijing, Shanghai, and in Guangzhou. Our offices in India will open in the first part of December, as will our office in Europe -- in London and in Brussels with the EU and EC.

We will -- Latin America, we'll open before the end of the calendar year. Presumably, we'll cut the ribbons in December as we're trying to work out the schedule between the Secretary and myself to go down.

The principle office there is in Costa Rica, but we have multiple satellite offices through many of the countries in Central, and will ultimately be in South America, as well as in Mexico.

And then, finally, next year, the plans are underway and the discussions are taking place for offices in the Middle East.

So, FDA beyond our borders is up and running and being implemented as we speak. All the groundwork has been laid. Our people have been selected. We have nationals in all those areas that are being selected, and the strategy of course, is multi-layered. There are a number of components to what the people will be doing. We've created the IT systems infrastructure so that there will be seamless communications and interactions between those offices and our field and our centers here. And the centers integration and interaction with those processes that are occurring over there is underway and a work in progress.

So, it's no longer a concept or an ideal. It's real, and it will be unfolding within a matter of days.

DR. MCNEIL: Well, Thank you very much, Commissioner and Frank, for your remarks.

I think it would be good now to take a brief break, 10 minutes, and we'll start again at 9:45. And I'd encourage you all to be here because we have a really tight schedule today, and it would be good to be on time. Thank you.

STRATEGY FOR 2009 SCIENCE BOARD TOPICS

DR. MCNEIL: All right. Why don't we start. Thank you all. I hope you've had a nice break. So, what I want to do for the next few minutes only because we really have a lot to talk about at the end of the morning, is say a little bit about what our strategy should be, or might be, for the coming year.

And for those of us in an academic setting, this is the beginning of the school

year. We plan ahead. Actually, we're a little bit late, if it's the beginning of the school year, but we'll take the analogy in that way.

And I had four or five thoughts that I wanted to present to you and ask your thoughts about them, and I've gone over these already with Frank and with Carlos, and others, and would welcome additional points.

So, there are several things that link together with what we talked about at our meeting this summer as potential follow-on activities. And Frank, actually mentioned some of them already. As a matter of fact, while the commissioner stole some of his thunder, you did steal some of mine, but I won't hold it against you.

So, there are several things that we really should plan for February, and hopefully by February, we will have been able to recruit some of the additional slots that have been added to this Board, which would help us with our work load.

The first one will be the task force -- a task force that the agency will be implementing for the rapid detection of food contaminants, intentional food contaminants, like melamine. And the thought there would be that -- correct me if I'm wrong here, Frank. You will be working on that in the agency -- you are already working on it and would be presenting your findings to us probably in February?

DR. TORTI: That's right. At least an interim update.

DR. MCNEIL: An interim update, and at that point, we could take a look at them and decide whether you just move on as you are doing at that point, or whether there would be further immediate activities for the Science Board. Is that right?

DR. TORTI: That's right.

DR. MCNEIL: Okay. Second possibility, also mentioned, would be the rapid detection of contaminants in food, like

the salmonella and the putative tomatoes turning out to be peppers that we read about. And you're looking at that as well in the interim?

And I thought that you talked about presenting some of those findings in February, but is that going to be a little too soon?

DR. TORTI: No, I think, again, and Dave Acheson and Lonnie, will both be involved in that, can help me on the timing. But we'd like to bring to you at least an update of where we are there and what we've already looked at -- the agencies that we've brought together to help tackle this problem, etcetera, so I think, again, an interim kind of update would be appropriate.

Lonnie, does that sound reasonable? And Dave?

DR. KING: Yes.

DR. PARKINSON: Yes.

DR. MCNEIL: Okay, great. So, we'll

do that. And then, if you recall -- I guess it was all of last year, we've taken on the job of reviewing centers, each of the centers, periodically. And we reviewed ORA and NCTR last year. And the question is, do we think that we would like to go forward and review another center in the coming year?

So I guess we could take thoughts in that from both the staff and the Science Board staff, meaning this side of the table. Any thoughts?

Larry?

Q AND A AND DISCUSSION:

DR. SASICH: How, in previous reviews -- in previous center reviews -- did FDA staff find those helpful?

DR. MCNEIL: So ORA and NCTR -- Bill?

DR. SLIKKER: Well, I think that indeed it was a great opportunity for us to be able to describe the research that we're doing at NCTR in conjunction with the other centers

to from a basis for regulatory decision-making, and it was an opportunity to describe some of the cutting edge technologies that we're validating for use and safety assessment issues.

So, I think in that sense it was very valuable. And also, express the importance of the holistic approach of leveraging resources and working with others within other government agencies, within the academic community, within the industrial community to build consensus on areas of importance to FDA. And this process is continuing on, and I think something that you certainly reinforce with our activities.

DR. MCNEIL: Steve?

DR. SASICH: You were of super value to us. I think I can speak for myself and my colleagues, but I think the thing that we want to know, does this actually help you in your operations or moving forward with planning in the future -- those kinds of

things?

DR. SLIKKER: Well, Larry, I think that's a very good point. And certainly, as we go through the planning process, and each year NCTR develops a strategic plan in conjunction with the other centers and under the guidance of Dr. Frank Torti. And certainly you'll see that with that plan, there are many of the kinds of issues that your committee brought up, and so these are reinforced by those kinds of reviews and issues that you bring up as something that needs to be looked into and certainly are, so we do appreciate that input and it does become part of our plan for the next year. Actually, we do a five year plan, and update it annually.

DR. MCNEIL: How about Steve, ORA, because that was one of the ones we did last year as well.

DR. SOLOMON: Sure, Thank you. This is Steve Solomon, Office of Regulatory Affairs.

The review that was done was very valuable to us. It was very timely in that we were in the midst of what we call "ORA revitalization exercise" and getting the Science Board's review of that and feedback to us has helped validate the direction we were heading and help us prioritize the actions that we're taking, so that was very valuable feedback to us. We appreciated that.

DR. MCNEIL: Okay. Well, if the Science Board -- it sounds like the centers think it's a good idea. So if that's the case, and if the Science Board concurs, what probably we should do is have Frank and his staff think about what would be the appropriate next center to review, and come back with suggestions or an actual decision to us.

You don't have to raise you hand now. You can do that quietly. So, that's number three.

Number four -- we're going to hear

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about BPA today in terms of the direct food contact application. And then, of course, as you all read in the documents and Martin and his committee's report, as well as in the FDA report, there's a whole issue of BPA in technologies, like IV tubing and blood containers and other such things. And the question is, should that not be a follow-on project to complement the exposure risks that are already known from Martin's well-done report. So, that would be a fourth.

Probably, rapid -- we want to make a decision on doing that relatively soon, is my guess. Is that correct? Frank, do you want to comment on that?

DR. TORTI: Our plan was when we looked at the entire complexity of the science behind BPA, we knew we couldn't do it justice in one block, and that our plan was to do this in pieces so that we could appropriately apply the science to those issues. So we certainly would endorse and be enthusiastic in our

planning to move ahead with this review, and would like to engage the Science Board.

So, Dan will be heavily involved in that. Do you have anything more to say?

DR. ROST: Yes, we're actually -- I mean, we've contemplated this and we're actually already moving ahead trying to do inventory -- our portfolio, in terms of understanding which products.

One of the things about devices is that we have a large inventory of different kinds of products and the question is: how do you try to address this single issue as it relates to all these products?

Can we look for some worst case scenarios where we can do some experimentation because there's obviously some missing information in terms of how much is in the product, how much comes off the product, how much exposure there is, who are the target populations that are affected by these various different products. So there is a lot of

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questions that need to be addressed.

And then the sort of penultimate question is, how do you do this as efficiently as possible in a reasonable period of time to try to come up with an answer that would be scientifically credible and allow us to make some decisions. And that's where -- and I think we would certainly be very, very happy to try to get some input into that so that we don't go off in a direction that people think is inappropriate.

And I'd rather, frankly, I'd rather see some of that work get done up front. We'll provide an outline of where we think we ought to go, but if we can get some feedback earlier on in the process so that we all agree that we're moving in the right direction, I think that would be extremely helpful.

DR. MCNEIL: I think that's a good point. One of the things I hope we don't have is a dead four month period between now and

February on the part of the activities of the Science Board itself, so to the extent that you can help us figure out how we can help you with specific tasks during this next four month period, I think it will be more valuable than our just coming together in February and hearing all of your hard work. So I'm not sure how we should do that, but maybe we can either think about it by the end of the day or think about it over the next week or so and have some e-mail communication.

And the last thing is really an FYI, and Frank mentioned this -- part of Gail Cassell's committee's report on the agency in general had a section on IT and the infrastructure needs of the agency for IT.

One of the members of that committee was Sangtae Kim, who Frank mentioned in his remarks. He's moved on to the University of Wisconsin, but the agency had a two day retreat a month or so ago that looked at what its priorities should be in terms of

revitalizing the information technology components of the agency, and they want to move forward with implementing those priorities. So Dr. Kim, who as I say, had been on the original Science Board review last year, has moved on, but is willing to participate in that pro-bono, which is always good, and we'll figure out exactly how that will work out and should be hearing from that group sometime in February as well, in terms of their progress.

So, the bottom line on this is there are four things for sure -- that is the salmonella, the adulterated foods, the center review, and BPA two, BPA part two, that potentially have a active role from this Science Board. We'll have to figure out -- I think those are "givens,: aren't they? Does anybody think we want to eliminate any of those from the list?

So, assume those are givens, and our job will be to figure out how we implement