Science Board to the FDA Committee Roster

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Dr. McNeil: Today we're going to dive into a number of very important issues we talked about addressing at our last meeting.

Before we do that, though, I'd like to introduce several new members of the Science Board. As you know, earlier -- at the end of last -- I guess it was in the middle of last year -- Dr. von Eschenbach indicated that he was increasing both the size of the Science Board, and the frequency of our meetings, and we are benefiting enormously from several individuals who have joined the Science Board.

So, what I'd like to do is tell you each a little bit about them, and I'll go through their names in alphabetical order. And then for those of you whom -- who are old, I'm going to ask you -- I'm just -- old -- that's not quite the right word. For those of you who are more seasoned in terms of your membership on this Board, I'd like you to say a word about who you are.

But let me just start with the new members. So, alphabetical order: Dr. James Broach,

he's currently Associate Chair of the Department of Molecular Biology at Princeton. Background includes service on the Executive Committee of the Cancer Biology Training Consortium, and the New Jersey Commission on Cancer Research, and he's published extensively in his field. So, Dr. Broach.

Dr. John Floros, is not here. Is a Professor and head of the Department of Food Sciences at Penn State, immediate past president of Institute of Food Technologists, and a member of the Board of Directors of the Council of Food Science Administrators. And we'll be looking forward to his input into a number of areas related to some of the food issues that we've started to deal with -- or, that we started to deal with last year.

Dr. Sangtae Kim, there he is, is Executive Director of the Morgridge Institute for Research at the -- in Madison, Wisconsin, and distinguished Professor of Mechanical and Chemical Engineering at Purdue. Expertise includes the role of cyber infrastructure at the intersection of the biological, computational, and mathematical

sciences, and the link between informatics and data-intensive processes in FDA-regulated industries.

Dr. Kushner, Frederick Kushner, is a consultant, and he currently serves as the Medical Director in the Heart Clinic of Louisiana in Marrero, and has academic appointments as Clinical Professor of Medicine, and Associate Clinical Professor of Community Medicine at Tulane. He will bring a number of insights to us from his role as a practicing physician. As you know, we frequently bump into areas where we really want to know more about what is happening in medicine, and the intersection between that and the practice of -- practices of the FDA will be important.

Dr. Russell Pagano is a Lineberger Professor of Cancer Research, and Director Emeritus at the University of North Carolina's Lineberger Comprehensive Care Center. And he's had extensive experience in infectious diseases, microbiology, oncology and virology, as well as genetics and microbiology. Not much missing.

So, Alan Russell is a Director of the

McGowan Institute for Regenerative Medicine at the University of Pittsburgh. And he's an expert in the field of regenerative medicine, and that was an area -- you may recall -- was one of the issues that was highlighted by the review of the FDA Science a couple of years ago.

And Dr. Stephen Spielberg is the Marion Merrell Dow Chair in Pediatric in Pharmacogenomics and Director of the Center for Personalized Medicine and Therapeutic Innovation at Children's Mercy Hospital in Kansas City. And he will bring an expertise in both pediatrics and toxicology -- both are areas that we have been, and will continue to deal with, in this Science Board.

Now, I wonder having introduced the new members, if we could just say a couple of words about ourselves among the more established members, so I no longer say "older" members.

So, Cathy, why don't you start?

Dr. Woteki: My name is Cathy Woteki, I'm currently the director, globally, for Scientific and Regulatory Affairs for Mars, Inc. My background is

in human nutrition and food safety, and epidemiology, and in the past I served as the Undersecretary for Food Safety.

Dr. Parkinson: I'm David Parkinson, my background is medical oncology, and I've spent many years in therapeutics development in cancer medicine.

Currently I'm CEO of a small start-up bio-tech in the San Francisco area, focused on personalized medicine.

Dr. McNeil: Dr. Russell, do you want to say anything to expand? Okay.

Dr. Pagano, we introduced you, okay.

Jack, you want to -- ? Okay.

Dr. Linehan: I'm Jack Linehan, and I'm a Professor of Bioengineering and Medicine at Northwestern University, and Director of the Center for Translational Innovation there, and I'm also a Professor of Bioengineering at Stanford in the area of bio-design. And my area of interest, relative to the Board, is biomedical engineering and medical devices.

Dr. King: Yes, good morning. I'm Lonnie King, I'm currently Director of the National Center for Zoonotic, Vectorborne and Enteric Diseases at CDC in Atlanta. In the past, I've been a Dean of the College of Veterinary Medicine at State, and Administrator of Animal Plant Health Inspection Service of USDA. My interests are in epidemiology, preventative medicine at CDC, working in the areas of food safety, emerging infectious diseases and cellanosis.

Dr. Hewlett: My name is Erik Hewlett, I'm a Professor of Medicine and Pharmacology at the University of Virginia. I'm the Chairman of the Board of the University of Virginia Patent Foundation. I have a research program in bacterial toxin pertussis, anthrax, and most recently C. difficile and, that's all.

Dr. FitzGerald: I'm Garrett FitzGerald, my name is thus, and I'm a Professor of Medicine, Pharmacology at the University of Pennsylvania, where I direct the Institute for Translational Medicine and Therapeutics, and Chair of the

Department of Pharmacology.

Dr. Applebaum: Thank you. Rhona Applebaum with The Coca-Cola Company. I'm the Chief Scientific and Regulatory Officer, my background is nutrition, food micro, and food safety.

Dr. McNeil: Well, thank you all, very much. I think you can see, since our last meeting, we've expanded the expertise on this Board significantly, and at the same time, as you'll learn from Dr. Torti, and from the discussions of several of the presenters today, we're expanding considerably, the areas that we're diving into. And we can expect, as we said yesterday, much, much more involvement from this Board in the work of the Agency.

So, I think with that, I'd like to turn it over to Dr. Torti.

Oh, I'm sorry, okay. Doug, do you want to introduce yourselves? I'm sorry, we'll go down this side of the room, as well, I'm sorry about that.

Dr. Throckmorton: Good morning, I'm Doug Throckmorton, I'm the Deputy Center Director in the

Center for Drug Evaluation and Research.

Dr. Sackner-Bernstein: Hello, I'm Jonathan Sackner-Bernstein, Associate Director, Center for Devices and Radiologic Health.

Dr. Sundlof: Good morning, I'm Steve Sundlof, Director of the Center for Food Safety and Applied Nutrition.

Dr. White: Good morning, I'm David White, I'm the Director of the Office of Research at the Center for Veterinary Medicine.

Dr. Slikker: Good morning, I'm Bill Slikker, Director of the National Center for Toxicological Research, FDA.

Mr. Chappell: Good morning, I'm Mike Chappell, Acting Associate Commissioner for Regulatory Affairs.

Dr. Acheson: Good morning, David Acheson, Associate Commissioner for Foods.

Dr. Lutter: Good morning. Randy Lutter, Deputy Commissioner for Policy.

Dr. Alderson: Norris Alderson, Associate Commissioner for Science.

Dr. Pena: Carlos Pena, Executive Secretary of the Science Board.

Good morning, some 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, as being part of the public record.

The Science Board will hear about and discuss updates from the Agency on the continued assessment of the updating of FDA regulated products. The Science Board will hear about the plans for the following: The review of FDA Center Science Programs, the review of each Center's projects within science and priority areas, and the handling of biospecimens used for genomic and proteomic analyses.

The Science Board will also hear updates from two working groups on economic and motivated adulteration of FDA-regulated products, and rapid detection of salmonella in foods.

Based on the submitted agenda for the

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

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 would be noted for the record. With respect to all other participants, we asked 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. I would just remind all to turn on your microphones when you speak, so that the transcriber can pick up all that you state, and turn them off when you're not

speaking.

I would also request all meeting attendees, including the public, to turn their cell phones and Blackberries to silent mode.

Thank you.

Dr. McNeil: Thank you very much, Carlos, I apologize for forgetting that important announcement.

Okay, Dr. Torti, you're on.

ACTING COMMISSIONER'S REPORT, DR. FRANK M. TORTI, M.D., M.P.H., FOOD AND DRUG ADMINISTRATION ACTING COMMISIONER

Dr. Torti: Good morning. Thank you all for attending this meeting of the Food and Drug Administration Science Board.

I hope all of you here today will welcome our members of the Science Board and especially those new members who don't yet know what they're getting themselves into, so we welcome them.

As you know, the Science Board is our advisory group on emerging scientific issues. They keep us abreast of the latest scientific

developments in the academic community and in industry.

This meeting, I think, represents a completely unheralded, but nonetheless important, juncture in our Agency. Today we've initiated a new schedule under which the new Science Board will meet four times per year -- twice as often as it has in the past.

Today is also the first meeting of the Science Board since the revision of our charter to enlarge the membership. Dr. McNeil introduced our new members, and I want to welcome these new members to our FDA family.

I want to tell you that not all of the slots in the Science Board membership have been filled, and we have left a number of slots open for the new Commissioner to appoint, as well.

I want to thank the nominations from industry, from the public, and especially from the deans of more than 100 medical schools, to whom I wrote for help in identifying Board members, and who have provided me with many more qualified names than

we can appoint. I want to assure them, and others, that these names will be reviewed for vacancies on our many expert panels. We intend to put everybody to work.

So, let me get back to the reason why this is an important juncture for the FDA. It's not because of the number of meetings that has increased, nor the size of the Board. But rather, I think it's our deliberate strategy to engage the external scientific community in helping us approach some of the most vexing problems we face at the FDA; strategy that I've crafted, along with Dr. McNeil. And we began this process -- as many of you know -- in October, and it's fully operational today, at today's meeting.

Today I'm here not in one, but in two capacities, reporting as FDA Chief Scientist, and also as FDA Acting Commissioner, so I have the opportunity to give two talks. Mercifully, I've chosen the single, rather brief introduction here, this morning.

So, I want to begin the morning by making

good on a pledge that I made last May at a Science Board meeting, by presenting to members of the Board my report, which is entitled, "Status of FDA Regulatory Science, Progress, Plans, and Challenges." It provides a roadmap for FDA science, and responds to many of the concerns raised by the GAO, the Science Board report of 2007, the reports of the National Academy of Sciences, a number of them, and others. It's my hope that this report will become an annual event for future Chief Scientists.

This morning, I want to begin by taking a minute to review the challenges and opportunities we face. The FDA has lost some credibility in recent years. This should come as no surprise to anyone in this room.

So, how do we regain this credibility? To the public, we owe a clear, timely, accurate information on the risks and benefits of the products we regulate. For many issues of risk, science does not have all of the answers, and the FDA must be honest and forthcoming about our

uncertainty. Sometimes hard for a regulatory agency to do.

When the science is complex, and can not be encapsulated in a sound bite, we must recognize that oversimplification becomes a kind of demagoguery in its own right.

To members of Congress, and others who oversee the Agency, we need to rebuild our partnership through engaging in collaborative efforts to reshape the FDA.

To the academic community, and others, we propose a much closer, and broader engagement in tackling scientific issues that underlie FDA regulation. Some of these collaborative plans will be evident this morning, and the rest of the day.

To the companies we regulate -- and I know some of them are in this audience -- we acknowledge their creativity, and imagination in developing new products. We need new products, and we need safe products. The issues of detection of adverse events -- particularly rare events -- is a scientific challenge. It involves informatics, personalized

health records, mechanisms for coding and tracking devices and drugs, interrogation of complex data sets with a high signal to noise ratio. This is regulatory science, and we must tackle these issues.

For my own family of FDA colleagues, we must create an environment where politics has no standing in regulatory decisions. Where scientific discourse and reasoned disagreements are accepted and respected, and we need to reward excellence more and better.

Even in this transition, when we're awaiting a new Secretary of Health, and a new FDA Commissioner, there is a great deal that we should do, and must do, to drive these processes forward. And we have begun, and you'll hear more throughout the course of the day, about some of the initiatives we have engaged.

Can I have the first slide, please? Okay.

So, I want to just highlight, now, a few of the areas where I think we've made some progress. And it's not that in any of these areas there's not a whole lot more that we need to do. But I want to

start with this idea of defining some overarching scientific priorities for the Agency, how we've engaged that, and where we need to go.

So, it began with meetings, and a number of meetings that I had over the course of the -- this last fall -- with the Center directors. We sat around a table and began to develop and identify the top priorities for science -- for regulatory science, and their Centers.

We then said to ourselves, "Well, it's one thing to identify those overarching priorities, but now, how are we going to tackle those issues that are raised by those priorities?" So, for each of the priorities that we identified, we then said, "Let's develop some projects that will tackle those. What is the hypothesis? What are the methods? What are the deliverables? What is the timetable? And, yes, how much is it going to cost?" And so we've done that.

And then we asked that this be, not a process that occur only within the confines of the FDA, but we're going to bring these projects to the

Science Board to review, so that there can be an interaction between the FDA and the Science Board, regarding these projects. And as some of you know, David Parkinson has been appointed to head a subcommittee, and he'll report on this later today, to engage the Center Directors on this issue.

What are those priorities? It's remarkable that, as we asked each Center for three, we would have had well over 20 priorities, but because there's so much overlap among the Centers, there are only 7 priorities, and they're shown here. The rapid sensitive high through-put detection of contaminants, so rapid detection being one. Biomarkers for safety and efficacy, adverse event detection, and analysis, clinical trial design and analysis, personalized medicine and nutrition, microbial ecology and contamination, mitigation strategies, and manufacturing science.

So, the other thing that was clear to us is that these kind of projects can not be tackled, sort of, on a year-to-year, or a one-year basis. That a good scientific project of the dimension that

we're asking for is going to have to spread over a number of years. And so, we're trying to plan for a multi-year attack at these issues.

One of the things we haven't done, yet, and I just wanted to acknowledge it, is tackle these problems from the outside. So, as many of you recall when I first came here, we proposed Centers of Excellence with academia, where the FDA could reach out to academia to approach these problems.

So, we're not there yet, we'd like to get there, we've got to put resources on the table in order to do this, and I hope in the coming weeks and months, we're going to be able to look at that, and perhaps begin that project, as well. We'd like to take two approaches to this issue, if we can.

So, let me turn now to career development and training, and essential -- an essential -- piece of our strategy at the FDA.

And I want to take just a few minutes to go over the fellowship program, which I think is the -- what we call the Commissioner's Fellowship Program, which is an extraordinary opportunity for

the FDA, and for others to engage with the FDA.

And one of the handout on the table, and I hope you have a chance to look at it, are the -- the first-year fellows, actually, projects -- the titles of their projects -- if you ever wanted to understand the relationship between what we're doing and regulatory science, you need only take a look at the titles of some of those projects. Better still, would be to meet the fellows themselves, and perhaps at some point we can arrange for you to do that.

So, the vision for the program was to bring the best and brightest folks to the FDA and new science, and new scientists. We wanted them to challenge convention, and we would develop a plan where they would be exposed to all of the FDA centers, not just one center, regardless of where their preceptor was located. And, clearly this was a program that would serve not only the fellow, but the preceptor.

So, the class of 2008, the first class of fellows, we recruited 50 fellow, we're in the process of recruiting another 50 for 2009. I point

out to you that this number is actually -- although it seems large, is relatively small. And we wish it could grow, in future years.

If we have a steady state of 100 fellows, and we divide those among the Centers, that only means that we'll have 14 or 15 fellows per Center. And if we hope, say, that half of them will stay at the Agency, that's a relatively small number within the context of the FDA. And yet, these are extraordinary people who will change the face of the FDA over time.

So, let me give you just a quick -- and I'm not going to go over this in detail, but you have to have the context of what we're trying to do here.

So, in the -- this is just the didactic coursework. In the first semester we have courses in FDA law and public policy, negotiation and influencing, ethics, decision making, international issues, conflict management, presentation skills, decision making, et cetera, so they get a broad sense of the issues broadly related to FDA law,

policy, leadership.

Then in the second semester, they drill down into some of the sciences which are absolutely essential to the FDA -- statistical methods and applications, a course taught by the University of Maryland School of Public Health. A course in population science and epidemiology, another course taught by Maryland. Clinical trial design, and evaluation, a course taught by Johns Hopkins School of Public Health. And in the summer they have a course in drug development, sort of an MBA view of drug development taught by the Duke Business School. So, sort of a very intensive background in the -- in these areas.

In the third semester, the second year, now they are exposed in detail, and each of the Centers takes on the responsibility of teaching them the science -- regulatory science -- of FDA regulation, for each of the Centers. Regardless of where the fellow is, they are exposed to all of this information.

And then in the fourth semester, they

tackle such issues as process control engineering and chemistry, risk assessment, risk management, et cetera.

That's a part of their program. The largest part of their program is to develop a hypothesis-driven project with their preceptor. A detailed research proposal, oral presentation, final report, which is going to engage 60 to 70 percent of their time.

And I go over this in some detail, because I know this is important to the Science Board, and we've talked about how this would be framed, so now you have an opportunity to see how it actually is framed. It's going quite well.

But career development is more than just the fellow. So, we're trying to do a number of other things. Career development also involves the preceptors in the fellowship program, as I've mentioned. We've begun to develop a cross-Center sabbatical, so FDA scientists can actually have an opportunity -- someone in the food agency, for example, can have a sabbatical in drugs, and vice

versa. Relatively low-cost, but high-yield, in terms of interactions. We want to increase the number of sabbaticals in academia, and we're working on projects to do that.

We've established a distinguished lecture series, now, that are FDA-wide, six times a year. And the only thing I've asked is of this lecture series is that they -- it reflect back on the over-arching priorities that the Center Directors have identified. So, it sort of targets back to those issues.

So, Shawn Kennedy, from the University of Minnesota, is one of the world's experts on economically motivated adulteration. You'll hear about that today from Randy Lutter, so we're bringing in outside people to approach these issues, as well.

We have also engaged a four times per year, FDA-wide symposium, called the Science First Symposium. And again, the symposia will reflect back on the overarching priorities of the Center Directors -- the first one is in April of 2009, and

will involve nanotechnology, and it will actually be an international symposium, there.

We want to try and increase funds for workshop attendance of FDA scientists. We have these FDA Chief Science Challenge Grants that we've just initiated.

And I just have to say a word about this, because -- just so you don't think it's all rosy, for example. I was able to sort of dig up $500,000 for these projects -- that's about 100 -- and then we're going to fund about four of them, about $100,000 to $125,000 per project. And we thought we'd have a handful of applications. We had, actually, 88 applications for what is, essentially, four -- what will be -- four awards. We'll be funding that at a 5 percent level.

So, there's a part of me that says out of those 88 applications, 80 of them are meritorious and worthy of funding. So, we still have some jobs to do there, in bringing this kind of, really, innovative regulatory science to our own scientists.

And we've worked with the oncology group,

in particular, to develop a very detailed professional development plan, that I hope can be used by others, as well.

So, this gives you a little sense of the career development approaches we've taken.

I want to talk about, next, about the genomics initiative, something that was dear to the heart of the FDA Science Board Report in 2007. So, based on the Science Board recommendations -- but also based on an internal retreat of the FDA on genomics -- we decided to appoint, in the Office of the Chief Scientist, a Genomics Coordinator for the FDA, Dr. Elizabeth Mansfield, who was to speak to you today, but I've just been told, actually injured her back last night and will not be here.

But Liz is great, and she is going to take on some very important tasks that you have recommended, to integrate that various "omics" -- not only genomics, but proteomics, and metabalomics -- across the FDA, and to be sure it's well-integrated in regulatory decisions; to coordinate genomic research and data analysis, to develop for

us some enhanced informatics, analytic capability, so that we can actually share this across Centers.

It exists in many of the Centers. We're not going to duplicate what exists in the Centers, Liz's job is to make sure it's coordinated so everybody at the FDA can accept the capabilities. And, in doing so, create a very small, but functional core facility, to coordinate these efforts. So, I think that's a move in the right direction, and we're really pleased to have appointed Dr. Mansfield.

The fourth area of progress that -- in regulatory science that I want to speak to, is just the importance of actually communicating that science.

So, in November of 2008, we held our first-ever Science Writers Symposium -- extraordinarily well-attended, we actually had to limit the attendance of science writers -- where they were able to hear, in detail, about some of the extraordinarily innovative science that is done at the FDA and how it relates to public health, and the

FDA mission.

I think we plan now to do this, at least as an annual event, and to bring writers here so that they can begin to understand better, and in more depth, the quality and the importance of regulatory science to the FDA. I'm not sure that that message is always well communicated, so I think this is a good way to do it.

We are also, now, quite a way along to developing this FDA Journal of Regulatory Science. It's not so different than the kind of journals that the NCI has, or the CDC has, that will allow our scientists to report on issues of regulatory science in a peer-reviewed journal, but allow others, as well, outside the Agency to publish these more specific regulatory issues. So, we're excited about that, and we hope to have it up and running, and to announce a editor-in-chief by July.

Next is an area of informatics. And here is an area that we want to engage the Science Board even more. The FDA is -- and again, highlighted in the Science Board Report of 2007 -- was the need to

modernize our informatics structure. And this is a major effort that is ongoing at the FDA right now. We've had Dr. Sangtae Kim, who is on the Science Board, come and review this fall, the progress of our informatics initiative, to make sure it's on-target from an FDA scientific standpoint. And I'm going to ask today, Dr. McNeil, to consider appointing a subcommittee of the Science Board on informatics to advise us, as we engage this endeavor.

I think this is the kind of thing where you can't do too much thinking, inside the Agency, and outside the Agency -- you've got to get it right. There's a long history of big informatics initiatives in other places where it was it was not right the first time, and that is very costly. So, we want to get everyone's input into what we're doing, make that as transparent as possible, and be sure that this informatics initiative -- which is absolutely essential to the FDA -- is done correctly.

So, I think in some ways, one of the major

areas of progress which sort of gets missed sometimes is our partnership with the Science Board. And really, that relates to the agenda of the Science Board today. Because if you take a look at it today, and the pieces of it, it really does represent a new way of engaging the external community, our scientific community with the FDA.

So, you're going to hear this morning, about an update of an adventure we began this fall, to begin to bring modern science to the issue of rapid detection, in general, and salmonella, specifically. And this is an important area, and one where science can contribute substantially, to these issues.

You're going to hear about our approach to a proactive look at economically motivated adulteration. When one looks at melamine, when one looks at heparin, and other contaminants, there's an economic basis to those adulterants. If one can anticipate those, then one can do a much better job at screening and anticipating future economic adulterants, instead of just waiting until one

appears. So, this is an important strategy, Dr. Lutter is going to address where we are and where we're going.

We are also going to hear from Dr. Parkinson about the peer review of the FDA projects, which I've mentioned; Dr. Alderson on the broader and different kind of review, now not on the overarching priorities of FDA science, but looking at each Center from the totality of its science, and how that meshes with its regulatory mission.

You were to hear today, and I may just take a few minutes in Dr. Mansfield's place, to talk about one very specific and important issue that relates to genomics and the FDA, and that is how we manage biospecimens. You might not think that those two are related, but they're absolutely essentially related, and I'll bring that to you today, and we're going to give you an update on where we stand on BPA and where we're going in that area, as well.

So, the partnership with the Science Board, the BPA plan. And I want to go over this in just a little detail, so I'm going to go back to my

notes. So, here is where we are with BPA.

We've opened the -- as you know -- our assessment to external scrutiny and advice. We've developed a draft assessment of BPA exposure from food contaminant contact substances. We opened the draft assessment to the public for comment. We engaged an expert subcommittee of the Science Board for their review, which we have received at the last Science Board meeting.

I hope it's clear that we are not required, nor have we traditionally opened such assessments to public scrutiny. It was our choice to reach out to the broader community for their input. This appears to be, sometimes, forgotten, and I think is worthy of mention.

Further, as we reported at the Science Board meeting in October, any decision should be informed by an evaluation of the risk of all forms of exposure. To that end, we have begun to develop and implement our approach to the assessment of BPA levels in devices and other medical products, and you'll hear about that today, as well.

It's important to note that we have made no final decision about the safety of BPA. Our recommendations are in draft form. We could take regulatory action tomorrow, based on new scientific evidence, or based on the reevaluation of current evidence, such as that requested by the Science Board.

However, we continue to take a number of approaches to the problem. First, we asked ourselves what we could do in the meantime, while we were reviewing the situation. We have convened with Health Canada a meeting with industry to see to what extent voluntary efforts could be made to reduce BPA exposure to infants.

Second, we are working to address the Science Board's comments and suggestions, and today you will hear and learn of our substantial progress in that area.

Third, we have asked ourselves, "If the final assessment is that there is currently insufficient or inadequate evidence to make a definitive conclusion about BPA at this time, then

what evidence would it take for us to make such a definitive determination?

I personally believe that -- to the extent possible -- we should design these experiments ourselves. To this end, we have partnered with the National Toxicology Program of the NIEHS to develop experimental protocols, each designed so that it could substantially influence FDA regulatory decisions. If we can tackle these four protocols, we will have assured the public that we will not be in the same position a number of years hence.

You will hear about these protocols briefly today, and it is our intent to provide them in much more detail to the Science Board for review in the coming weeks and months.

Fourth, and finally, we have also asked what human, epidemiological evidence might inform our decisions? And I am very gratified with the partnership with Dr. Ray Kingston at the NIH, the help of Dr. Nieder-Ugar, the team at the NHLBI, and many others at the NIH, the CDC, and the FDA, who are working on this issue, as well. We are not yet

ready to describe this approach in detail, but we should be able to do so soon, and we will provide this to the Science Board, as well.

So, let me end this presentation by turning, again, to the issue of public trust. I spoke at the celebration of the 100th anniversary of the American Association of Cancer Research this fall in Roswell Park, where the Association was founded, and said that the future of the FDA will be written in its science and its scientists. It is through the application of science -- and only science -- that through our regulatory decisions that we can regain the full public trust.

So, thank you for your attention this morning, I think we have a great agenda.

Dr. McNeil: Thank you very much, Dr. Torti.

Are there questions? It's a long -- there's a lot of events going -- a lot of things going on, here, so I'm sure that there may be some -- yes, Rhona? Rhona, and then Erik?

Dr. Applebaum: Dr. Torti, an excellent

presentation. But, I'm still troubled by the fact that there's not as much emphasis being given on the importance of communication. And I understand you have to fix your house, first, absolutely. But in the period of time that it takes to make sure -- and, again, sound public policy is based on sound science, so I support that 100 percent.

But, in the interim, in the absence of proactive communication with the public, it's very worrisome to me to see the declining -- the data, in terms of consumer confidence in FDA going down. That is -- that is -- it's bad for a regulated industry, like mine, it's bad for the public, me, to have that type of confidence continually being eroded.

And I don't have an answer, I'm just sharing a concern. But I think it would be in the best interest -- if I could be so bold -- to really focus in on, and do what you can -- I know with limited resources, especially in this challenging economic environment, it's not easy -- but the importance of behavior. The importance of how to

communicate to audiences. I think it's wonderful in terms of the outreach to the media, but having these types of workshops once a year, in the face of crises that are happening almost on a daily basis, I think there's a key role, an opportunity for FDA, in terms of proactivity in that area.

And, again, no answers here, I'm just sharing with you a very, very sad, and a very worrisome concern that I have as it relates to FDA's credibility continuing to be eroded.

Dr. Torti: Thanks, Rhona.

So, I'll give you two reflections, not really answers to your question.

First of all, I agree with what you say. I mean, we need to communicate more frequently, and better. I think there is two sides to communication. First of all, we have not presented a communication plan to you, I mean, this is not part, primarily, of the Science Board issue, although communicating science certainly would be one of them. So, when I was talking about communication, I was talking about a very small

slice of our efforts, here.

I think it's fair to say, though, that communication has two pieces. People have to speak, but then people also have to listen. And, you know, to the extent that the FDA does have a continuing and large outreach, I think it's also important that there be some receptivity to the messages that we're trying to bring to the community. Perhaps we don't do them as well as we should, but we have a, you know, a real commitment to try and communicate fully and completely to the public, and we will continue to attempt to do that.

Now, we're open to suggestions and ideas about how to do that better, and you say you don't have any, but I want to engage you, and others in the room, to tell us how we can do that better.

The other reflection, in any way, is the idea here is not to drive first, in my mind, toward public relations, but to actually get things the way we are -- that we want them, working just the way that they should be, and then to some extent -- because this is the way you would respect, and I

would respect -- have them speak for themselves.

Now, there have been resource issues that have limited our ability to do that, but now things are improving. And we are going, therefore, to make major investments in various aspects of the FDA -- not only in FDA science, but in many other aspects. And we want to certainly communicate those, but we want to build that strength of the FDA, so that it is completely apparent to anyone who chooses to look.

So, those are just two reflections on your comment.

Dr. Hewlett: I would like to understand better the fellowship program, I think that's a great idea. The topics that are listed here for the projects -- are these the projects that are being done? Are these proposals for projects? Some of them are -- sounds very ambitious for a two-year program.

Dr. Torti: Well, each -- so, the way we do it is, these are the proposals -- the titles of the project -- that are reviewed, then, by -- first

by the preceptor, so this is a document that is being, now, vetted with the preceptor, then by a committee of senior FDA scientists to make sure that it's doable, that it is reasonable, achievable, et cetera. So, we have, you know, we have much more details about these, we have abstracts, we have little books that will provide much more detail to you.

But this was just to give you a flavor of how diversified, how interesting, how much they're focused on regulatory issues. This is just one piece of that story.

Dr. Linehan: Just as a short follow-up to that comment, about the excellent fellows program, which I really am excited about -- I understand that one of the reasons for the program is to train young men and women in regulatory science, the purpose of which is to recruit some of the best of them to the FDA.

Dr. Torti: Yes.

Dr. Linehan: On the other hand, it's an opportunity to -- to the public relations aspect --

to get the word out about the excellent science going on at the FDA. I'm hoping that these young men and women will get the opportunity to present the findings of their science to the relevant professional societies, so that it becomes part of the community.

Dr. Torti: Yeah. So, Jack, we actually have a specifically, sort of, earmarked funds for them to travel and do that, and it's an expectation that they do that. So, that's a very important part of their training.

You know, I just want to mention one other thing about the program. You know, although primarily these are young folks, they're all folks who have, you know, who are professionals. They've finished their M.D., usually a fellowship, as well. They've completed a Ph.D., so they are substantial folks in their own right.

Many of them are young, but some of them are mid-career people, who've decided they want to change and move their career into a more regulatory focus.

If you think about the enormously limited number of opportunities to actually do that, this program represents a -- almost unique -- opportunity for someone to say, "You know, I've had a career doing X, Y, Z, you know, now I'd like to really explore, you know, a different career." And these more senior people actually bring an enormous amount to the table, as well. Something a little different than someone that's just starting out their career. And there are many fewer options to do that then there are to get a fellowship right out of your training program. So, this fellowship program has a lot of dimensions that people don't recognize.

Dr. McNeil: Could I just follow-up quickly on that? Are most of these people coming from academic centers, or are some coming from industry, as well?

Dr. Torti: Well, you know, all of them -- I would say the majority of them come from academic centers. If you come from industry, of course, you have to resign that industry appointment, and you are actually hired by the FDA, so you have to go

through all of the vetting, divestitures, confidentiality issues that any FDA employee would. But they come from a variety of past experiences.

Dr. Pagano: This is my first look at this program, and what I see in it is something quite different from the other part of what you're trying to do. You're trying to come in from above, and bring in advice at the top level. This is potentially a very powerful networking, science base that's created at the bottom, and then at the bottom up, because it's going to have big influence. Because it's based on science, and energy and young people, or people who want to change their career.

And they also -- and I particularly think is very important -- is the networking that you -- that is built into this, across these very divergent areas of science -- it's very unusual for people to come together in that way. And I think there's going to be completely unanticipated benefits from this, and insights that nobody at the top who have thought it. Wait and see.

Dr. Torti: Yeah, thank you.

Lonnie?

Dr. King: Dr. Torti, thanks very much, great comments.

One of the things I was wondering -- I really believe in the fellowship program and what's happening and the excitement around that, but what's happening to the rest of the employees? In terms of their own personal development -- how are they keeping up with science? Is that funded within FDA? It seems like, you know, really great organizations have a percentage, just used for training and human resource development --

Dr. Torti: Yeah.

Dr. King: -- keeping up with science no matter what the budget is. And, so what's going to happen with the rest of the folks? And, is that kind of budget going to be sustained?

Dr. Torti: Well, that's a great question, Lonnie, it's equally important. And, if not more so. And we have taken the steps that we could afford at the current time to do that, and I've outlined some of those, such as the sabbatical

program, building career development pathways.

One of the things that we're all committed to, but we need to build more, is that, you know, there needs to be two routes to promotion in any agency, such as the FDA. There's an administrative route, which is the traditional route. But many people who come to the FDA, that's not where they want to grow. They want to grow in their own specialty, in their own skills as a reviewer, in their own, sort of, academic areas of excellence.

So that, they need a pathway toward growth that is very much that they can see, they can understand, that is tied to remuneration and dollars for a non-administrative pathway, as well.

Now, some of this exists. Nothing that you've heard today is an invention, right? But we need to do better at that, and we need to build that more. And we need to get more people out into the academic community for sabbaticals, for meetings, then we have been able to do in the past.

Now, we're starting to make improvements of that, but we have been limited, as you know.

Steve?

Dr. Spielberg: Frank, just one comment to that -- as past President for the American Society for Clinical Pharmacology and Therapeutics, one of the strengths of that society has always been participation by FDA colleagues. And it's a great environment to bring together academic, industry and FDA, tackling real issues. And many of our past award recipients from this society -- most recently, Larry Lesko, indeed, came from the Agency.

And I know that we've been having more and more difficulty having people being able to attend the meeting, because of financial limitations.

This year we're doing it in Washington, specifically for that, to get more FDA participation. But then we get calls from our colleagues in Asia, they want to have a meeting in California, and it's harder for you folks.

Is there any prospect of having additional travels funds, so that people who do want to attend scientific meetings have the way to do it?

Dr. Torti: Yeah, I think, you know, this

is a -- a turning point. We have a President who has identified science as a major initiative -- that's very exciting, and very exciting to the folks at FDA. And, you know, with that, I am sure, will come some additional resources to do that. I'm very positive about that. You know the problems we've had in the past, but I think we -- we're going to fix them.

Dr. Russell: Yeah, I really enjoyed your presentation, it's also my first meeting. It sounds like what you've recognized is that you need to enhance the culture of creativity amongst many interdisciplinary people. And it sounds like you've realized that that's not a natural behavior for scientists; that although they should collaborate and communicate across disciplines, you have to stimulate it in some way.

How do you make sure this goes FDA-wide? I mean, I heard some really interesting, nice nuggets that, perhaps, could be catalysts, but how do you make sure that the whole of FDA, that all of the various silos truly begin to communicate with

each other?

Dr. Torti: Well, we're taking a number of steps to do that, which I haven't presented this morning, but it is very important.

For example, I'm now -- one of the things I've learned, actually, is I've brought together small groups of FDA scientists, across disciplines. So, for example, we brought together, last week, groups of people who are interested in cardio renal issues, from across the -- all of the -- centers, including foods, which has -- actually ha a substantial component of people interested in that because of the nutritional aspects of that.

And one of the things that they continue to teach me is just what you say. Is that sometimes there are -- there is a lack of interaction that, if it could be facilitated, could really help them in their regulatory decisions, and in their growth, and in this sort of -- this fermentive kind of interposition of different kinds of science.

So, we want to -- and, so, we want to begin to bring people together across Centers, in

some of these different kinds of strata.

Now, they all may not be disease based. I mean, you might have some that are cardio renal, that's already done, of course, in oncology, you might do it in neuro, where there are a lot of cross-cutting issues.

But then we might want to do it in other ways, as well. We may want to do it across epidemiologists, or statisticians from different agencies who could bring things together.

So, we're going to formalize all of that into working groups that actually have a real role in the FDA, and we're just beginning that. But that's a great thought.

Dr. Linehan: Just one more short comment. In terms of an organization like the FDA that's spread around the world, interconnectivity is really important in getting to know people in the silos -- demonstrating the side roads is important, and it can be done.

General Electric, as an example, has software that's sort of like Facebook on steroids

for the company. It's called, I think, Source General, it connects all 350,000 employees very well, in interest groups that are somewhat personal, but generally technical and scientific.

And I dive down deeply into that because I was interested in seeing if that could be transferred to universities, and it is, imported to that.

But something like that would be critically essential when you have scientists around the world who have problems but don't know their colleagues.

So, I would suggest, again, that the FDA look into that.

Dr. Torti: Jack, let me just -- so, almost for your entertainment, I had exactly the same thought. So, jut about a week and a half ago, I actually called Jimmy Wales, who was the founder of Wikipedia, one of the founders of Wikipedia, just to talk about the issues of how to interact.

And as I always do, every time I come up with a good idea, I learn that the FDA folks already

had these good ideas, and I jut didn't know about them, so there was a fair amount going on at the FDA in this regard, as well.

But we need to do more of that, that kind of connectivity and the, sort of, the electronic and internet-based capabilities are something that, you know, as we build, of course, our informatics programs, are going to be essential. Communication, in that way, is essential.

Dr. Linehan: Just as a real quick follow-up on that, the fellow that runs things at GD is a former student of mine, this is available for purchase now, commercially. I think, out of India, Sal said, it's ready to go, it'll be done tomorrow.

Dr. Torti: Well, you get us the appropriate discount.

[Laughter.]

Dr. Kushner: Thank you, Frank, that was a wonderful presentation.

I'd like to just amplify that being new on the Board and listening to this, I think that the ability to integrate vertically from the bottom up,

and the top down is very important, but especially horizontally across, not only the FDA itself, and through the science interaction between your fellows and the scientists and the greater scientific community, but especially echoing Rhona Applebaum's comment -- it's very important to get the process and the message about what happens here out to the public, and interact with the public.

And I think your idea about the writer's conference is an excellent idea, and I think in general, there's a lack of clear communication of what happens in science to the general public. And I think this is especially important when it comes to regulatory issues, for instance, regarding the FDA, because I think many people in the lay public don't understand the science, and don't understand how it applies to these issues and to their own personal lives, and I think there's a lot of work to be done in that vein.

Dr. Torti: Thanks.

Dr. King: Just one other thing on partnerships. I think what you have in terms of

identifying regulatory science is kind of the new entrée, it has a lot of power. And I don't see that happening in the academic world yet. It looks like this is actually a leadership program for government agencies. And I think that matching, if you will, with academic worlds in kind of defining regulatory science and developing programs, could be another pathway to create these strategic partnerships.

Dr. Torti: Thanks, Lonnie.

Dr. McNeil: I suspect there are more questions, Frank, but I think we're going to leave them to the coffee break, and thank you for your -- I think that was actually a spellbinding talk, there was a tremendous amount of enthusiasm, at least as I sensed it from the questions. So we congratulate you on all of your progress, and the staff's, of course, in les than the year.

So, let's go on to David Acheson, who's going to talk about contaminants in food, and give us an update. We've talked about this several times, but this will be an important update.

Thank you, David.

RAPID DETECTION OF CONTAMINANTS IN FOOD: UPDATE BY DAVID ACHESON, M.D., ASSISTANT COMMISSIONER FOR FOOD PROTECTION, OFFICE OF THE COMMISSIONER

Dr. Acheson: Okay, well good morning, it's a pleasure to be here. What I'm going to do is to give you a very brief update on what we've been doing on the rapid detection tool side of the house.

If you recall, in October we presented this idea to you all as a way to move forward, and I recognize that there are many people at the table today who weren't with us in October as part of that initiation discussion.

So, I want to kick off, essentially, to try to put this in perspective, and to address the question of why do we need rapid detection tools? And it certainly goes way beyond FDA requirements, but essentially, what we're trying to do here is simply to move faster. So, rapid detection sort of falls into a number of areas, but from our perspective at FDA, it's during those formative stages of an outbreak where rapid detection can be

really critical. I think we're repeatedly seeing examples of outbreaks of food borne illness, where you are starting to get one or two people sick, and gradually we're pulling the story together, and it's several months -- or certainly many weeks -- before ultimately a food vehicle is identified, and then we're actually able to move forward, and shut this thing down.

When I gave the introductory talk in October, obviously we were just coming out of salmonella, St. Paul outbreak, which was all about detecting salmonella on tomatoes and peppers.

Now, of course, we're moving into a whole different salmonella arena, and we're all stuck up with peanut butter, but the concept is the same. In both of those situations, we were dealing with several weeks, or months, of not being sure, "What's the vehicle, here?" And until we know whether the vehicle is an FDA-regulated product, a USDA-regulated project, or a person-to-person issue, or what it is, it's very difficult to be able to focus in, and narrow it, and thereby protect public

health, which is the goal. So, obviously during the formative stages of an outbreak, getting in there quickly, and fast, is key.

Similarly, once you have moved beyond that, and you know which food it is, what went wrong? Where did it go wrong? So, testing food, testing environmental samples is another key element of the need for sped, and it will all lead to identification of the problems faster.

The other thing that rapid detection can do, is it can actually eliminate negatives more quickly. Now, this is important in a variety of contexts -- particularly when you're dealing with, for example, a lot of food that may be held at a port, because you're unsure about whether it's contaminated. And under the current systems, it can take several days before a lot is tested, shown to be negative, and move on. So, there's clearly both public health and other impacts in terms of being able to identify negatives.

The public health gains, obviously, better protection, you're shutting down outbreaks more

quickly, and greater availability of products that are not implicated which -- as we've seen over and over and over again -- in these prolonged outbreak situations, where there is difficulty in narrowing it and knowing exactly where the problem lies, the public's reaction is, essentially, to move away from that food product completely, until all of the dust settles.

So, what are some of the challenges that we've got around rapid detection tools? Obviously, I've talked a little bit about outbreak situations, but you need tools that will operate in various types of matrices, and under various situations.

Obviously rapid detection of the human level. When you're talking about an outbreak, initial phases of an outbreak there's -- as you're dealing with human clinical samples -- how can you get those answers more quickly?

Then as you move forward, and you've identified the implicated food, you want to be able to test that food rapidly. And then as you continue forward, and you're saying "Okay, so we know it was,

for example, jalapeno peppers, in, with salmonella, St. Paul." What went wrong in the environment? So, you need the ability for rapid environmental detection, and that may be soil, that may be soil, it may be water, it may be other matrices that you've got to work on. And finally, with animals, again, you're looking at the ability to be able to test rapidly in animals.

So, rapid detection is not just about food, it covers the whole gamut in terms of dealing with public health impacts of food-related outbreaks.

Not only do you need it in outbreaks, but you need rapid detection during routine situations -- routine inspections. I've already mentioned the example of a food at a port -- we need to know quickly whether that food is contaminated with certain pathogens that we have concern about.

Similarly, when we're doing routine inspections. There is a shift at FDA to do more environmental testing during routine inspections, and clearly, getting fast answers to environmental

testing samples is going to be very important in terms of protecting public health.

Detection challenge is speed. You have got to nuance between speed and accuracy. Clearly there are tools out there that can be very quick, but have limited sensitivity, and limited specificity. That doesn't necessarily help you. So, it's the titration between sensitivity, specificity and speed which is going to get you to the point where you have a high degree of confidence that the test result that you got is meaningful, and you can take action on it.

It's got to be easy to use. Now, not all rapid detection has to be easy to use, but if it's going to be used in the field, it's obviously got to be easy to use using -- albeit sophisticated equipment -- but easy-to-handle, mobile-type, sophisticated equipment. So, there has to be that component in terms of thinking forward on this.

And finally, from FDA's perspective, whatever we come up with has to meet the regulatory requirements. This is a key element that you can do

all of this testing, but if at the end of that, you don't have enough confidence in the result to be able to take a regulatory action, it doesn't necessarily help you.

Now, that's different in other situations. In clinical situations, obviously there isn't a regulatory requirement, but purely from FDA's side, we have to keep in mind that where this project goes, a tool that does not meet regulatory requirements isn't going to help the agency.

So, that's really by means of background, and that was really a recap of the summary and the introduction that we gave in October, when w launched this progress

So, what process are we using to move forward on this? Well, we have identified a series of participants: FDA, CDC, USDA, DHS and DARPA. As colleagues in the Federal government who have either an interest in rapid detection, or have some expertise, knowledge of rapid detection technology. And you can see, it's pretty varied between the regulatory part of it, and the -- on the DARPA side,

more sort of innovative science.

An introductory meeting was held on January 30th, 2009 to basically frame this. That introductory meeting had high-level representation, it was chaired by Dr. Torti, from FDA. All of those various Federal agencies came together to hear, okay, what's the challenge? What are we trying to solve, here? And what's the approach that we're going to take?

This slide summarizes that approach, and essentially what it is, is a series of steps that is linked together by iteration, as you go down a step, if something doesn't look right, you can readjust.

So, the first step is the interagency technique evaluation. So, with these different Federal agencies with their different experiences, their different methodologies, what techniques have we got? What's sitting on the shelf? What could be moved forward to meet some of these requirements? What techniques are there out there, and how can we evaluate them? And, in a moment I'll get to the more specifics of how we're going to do this. So,

interagency technique evaluation is step number one.

That is, then, going to be taken -- in a more public forum -- to academia and industry. What do they have that they can put on the table, what can they bring forward that will further, essentially, develop some of these techniques into reality?

And then the third step, once you have reached an idea or ideas of a detection tool, is to test it. Now, testing it sounds easy, but, in fact, what it's got to be -- it's got to go through a series of validation steps within the Agency, and that is complicated, because remember -- for FDA's perspective, it has got to meet those regulatory requirements. So, it's got to be thoroughly validated, and it's got to be tested. And ultimately the goal would be to implement it in the field.

And the -- obviously the white arrow going around the side is to illustrate that there is constant iteration going on in this process, so if something starts to fall apart, there is an

opportunity to readjust, reevaluate the technique, continue the interaction of dialogue with the public sector through academia and industry and then test a second version.

Finally, what are our next steps, here? As I said, there is high-level agreement on this approach across these Federal agencies, that has moved forward, we're moving forward on this plan, there was agreement on the general areas of what the needs were in terms of the scope that I've presented to you.

There is going to be a meeting of subject-matter experts that's slated for March, so just next month. This is a meeting that we're adding on to an already -- a meeting that's already on the books. This will be subject-matter experts from those Federal agencies, who will get together to begin this process of evaluating techniques -- what techniques are out there, how do we set up the evaluation process?

The second step, which is slated to happen spring/summer this year, is to get to that second

part, to hold a workshop, to solicit that outside input; from academia, industry, States and locals, and others who can look at some of these techniques, bring some of their own ideas to the table, and move it forward. And then, hopefully that will, then, lead to some very specific detection tools, that we begin the field testing, the evaluation process, actually both -- within the Centers within FDA at first, and then out into the field, beginning in the summer of 2009.

So, it's a pretty aggressive timeline. We want to move forward on this, but as I said when we met in October, there is a real need to do this. We were certainly slowed down with the salmonella, St. Paul, on peppers and tomatoes, because we don't have these rapid tools.

I think we've not been so slowed down with peanut butter, because it was a very different situation, but there is no doubt that if we'd had these tools, we could have probably shaved off hours, if not days, in terms of protecting public health.

So, there is a constant need, an urgency to make this happen. And under Dr. Torti's leadership, we're pushing forward with an aggressive track, here. And I think we recognize it is aggressive.

That, essentially, is a summary of what we're doing, why we're doing it, and where we're going. And I'd be happy to take some questions.

Dr. McNeil: Questions? Yes?

Dr. Broach: I notice that you didn't include Homeland Security. This is obviously something that they have been worrying about for -- at least ever since the anthrax outbreak, and I've worked with several groups that have approached a number of different techniques for developing hand-held devices for rapid detection. So, I wonder how much you can leverage off what has already been accomplished along those lines?

Dr. Acheson: Absolutely. Well, DHS is part of the group, so Department of Homeland Security is one of the groups that we're meeting with. I was -- were you wondering whether they were

involved? Because they are.

And you're absolutely right -- they've got a lot of experience in this area, so we're looking forward to their input.

Dr. Woteki: Thank you. Two weeks ago the National Academy of Science's Government, University, Industry Research Roundtable had a day-long session about food safety, and there were representatives there from the DOE labs, who were -- Oak Ridge National Lab, and Pacific Northwest National Lab -- that were speaking to the kinds of technologies that they have developed that they believe have applications in this early detection phase, as well. Have you reached out to the DOE lab system for inclusion on this project, as well?

Dr. Acheson: We've worked with DOE labs in other areas. We haven't specifically reached out to this one. I think we've made this as a starting point. And I think to your question -- obviously reaching out, as you provide us input and others provide us input, DOE or other groups -- it makes all kinds of sense for us to do that.

It's a matter of, okay, if you make the group too large, we won't move forward, but we want to focus in on the areas where there's some good detection tools that we can build off of. So, thanks for that suggestion. We will reach out to DOE.

Dr. Parkinson: I think it's a really important initiative, of course. And as part of the comments I'll make later about peer review of the scientific priority -- prioritized projects -- it was clear to me that at least three of the Centers have rapid detection initiatives.

Dr. Acheson: Yes.

Dr. Parkinson: And, just -- I've had the opportunity to look at the proposals, and it seems like there might be very good opportunities for cross-Center interactions. Do you know if those are occurring yet, and could they be integrated into some of the activities that you just discussed?

Dr. Acheson: Excellent point -- they are occurring. Part of my role in the Office of the Commissioner, is to facilitate those inter-Center

interactions. And we actually have a separate group that is focused on exactly that -- that is running in parallel to this -- internal within FDA to make sure that there is dialogue going on between SIF CEN, and NCTR, and Center for Veterinary Medicine, and also talking to ORA, who ultimately are going to have to use those tools to move this forward.

So, yeah, there is the internal process, but obviously this is looking at a bigger universe of potential tools.

Dr. Hewlett: David, there's been a lot of focus, obviously, on your office in the context of resolving these issues, but the list of participants that you have here for developing new technologies are also the groups that are going to be important in the early detection of the cases.

And I'm interested in the nature of the relation -- the operational relationship, independent of new technology -- that you're having to work with. Because it seems to all end up with you, by virtue of an enforcement part --

Dr. Acheson: Yeah.

Dr. Hewlett: -- but you must be getting data from all manner of sources?

Dr. Acheson: Absolutely, Erik. You know, and I think -- I mean, this, obviously, is a narrow focus on one piece of the puzzle -- is figuring out where is the salmonella and can you detect it in the human sample or the environment? I think what you're alluding to is the bigger picture of how do you get in there more rapidly?

Lonnie King, from CDC, who's part of your Board -- when he puts his other hat on -- he and I were working very closely together on trying to address some of those issues, specifically. And to give you examples of where we're headed -- developing closer ties, and greater integration with the States and locals is a key part of that.

And just to go off on a slight tangent, to answer your question, last August we had a 50-State meeting where we brought representatives together of over 200 individuals -- States, locals, tribes and territories -- to discuss how can we better build an integrated food safety system in the United States?

That led to a series of ideas around improved information sharing, training, risk-based initiatives and response, and now we've established four work groups to focus on those areas, and we're doing it collaboratively with CDC.

So, that part's not being forgotten, and you can't simply build a better detection tool and not have that other public health infrastructure piece as part of the mission, as well.

Dr. Pagano: I think the plan -- as I'm first hearing about it -- is impressive, and what I'm wondering, though, I can get a better feel for it if you can give me an example, or do you see any promising techniques, tools, or some specifics? Even if it isn't completely, fully developed, so I can see exactly where you see opportunities ahead?

Dr. Acheson: The short answer to that is, is I don't have any specific examples, yet, of what's going to work. I think, to give you examples of the areas that we need to focus on is, number one, is how do you deal with the matrix? Which is the type of food that you're dealing with; how do

you take -- because there are many fast detection tools. If you've got DNA in your hand, you can get an answer real fast.

The challenge with yogurt, cheese, tomatoes, is getting that sample to the point where you can run it through a piece of equipment, is a challenge. So, part of it is matrix challenges.

Part of it is also the identification of the organism itself -- is there salmonella in there? And that alone, from a regulatory perspective, will say, "Yeah, there's salmonella in this product, it shouldn't be there, it's adulterated, we can take regulatory action." That doesn't necessarily mean it's linking you with the outbreak strain. So, looking at the technologies for, say, rapid serotyping is important.

And then the next layer is, what are the genetic tools that we need to be thinking about in terms of the next generation of PFGE? PFGE is great, but obviously it's old technology, there's different ways to go on that, and you have the challenges there of trying to establish a system of

genetic tools that's actually applicable across the whole of the United States. The great thing about PFGE is every State's doing it, and CDC have worked very hard to get folk to that point.

So, I think -- I don't have specific examples, yet. But those are the sorts of areas that I think we can make progress on.

Dr. Pagano: That's fine. Thank you, that gives me a much better idea.

Dr. Applebaum: Yes, thank you.

And, David, an excellent presentation. And I'm probably going tangential to what you're doing; and what you're doing, and what FDA's doing is absolutely, you know, right on key in terms of what -- speaking for the food industry, what the food industry needs.

But I'm going to ask maybe, we could discuss this over coffee break. Going after the pathogens, absolutely. Absolutely. But, I'm just wondering what FDA's research program is on, number one, looking at surrogates, so that industry can work with those and not bring anything hazardous

into a plant, but also, you know, from that same area, what are you doing in terms of preparing for the next one? I.e., when that bug jumps the hurdle, and can now be somewhere else that we're not currently looking at? Or, perhaps that's too long, and we could do that over coffee break?

Dr. Acheson: Well, you know, Rhona, those are key questions. There's probably a two-hour answer to that short question.

You know, the quick answer is that we need to be focused on preventive controls. I mean, that's where the emphasis needs to go. This solution that I'm putting out here is largely a reactive one, which we need when things -- when we've got us a situation.

But rapid detection can also help us with prevention, and I think your thought about surrogates is an interesting one. It's not something that we have focused on a great deal. I know that our colleagues at USDA have focused on surrogates, and they're a mixed success, in terms of whether generic e-coli tracks with e-coli 0157.

And, you know, some say it does, some say it doesn't, but there's nothing like looking for the pathogen itself.

You know, listeria species versus LM, in terms of environmental contamination in a facility. Again, interesting questions. And it's not an area that we have focused on specifically, but it's a good thought.

But, I think, ultimately where you've got to go is to figure out what are the preventative controls, that are going to stop these problems in the first place, and that is another huge research endeavor that we need to pay attention to.

Dr. McNeil: So, I have two people who want to talk, and maybe that should be it before the break.

So, Lonnie, and then Alan? Short question?

Dr. King: This is short, because Rhona actually kind of hit my point on this.

And, first of all, thanks very much, David, and Dr. Torti, thank you for your leadership

to put this group together, CDC is very excited to participate.

But, not only is there a benefit for diagnostics in regulatory work, but as Rhona pointed out, I think one of the real values that's added to this is in infectious disease ecology, which now we see as a new niche and an expanding niche in public health.

And the identification of moving upstream to find out more about the natural history of these microbes and pathogens will actually change intervention strategies. So, that's another reason that we're really anxious to be involved with that, because we see a broader use of the techniques and technology.

Dr. Acheson: I think it's a good point. Microbial ecology is something I didn't specifically mention, but absolutely.

Dr. Russell: Thank you.

Thank you, Barbara.

So, I was undoubtedly not asked to join this Board because I know anything about food

safety, but a back-of-the-envelope calculation would tell me that we must serve around a trillion meals a year in the U.S. And undoubtedly it's one of the safest things that we do as humans, and I'm sure a large part of that is due to the work of the FDA. So, problems like the ones that you talked about are incredibly rare events, and it goes back to the need for good communication about how effectively you're already doing the job.

But, given that, what's a win? So, in your designing a scientific program, here, it really only makes a lot of sense in the context of defining specifically what you're trying to achieve. You've already got an incredible event, so how much better do you want to do, and how much is it worth spending, doing that?

Dr. Acheson: Well, that's an interesting philosophical question.

My personal view is we want to do it better, and we want to do it faster. I think we -- in the last two or three years, we have seen several large, multi-State outbreaks in which hundreds of

people have got sick. And obviously, in this most recent one, 9 have died, linked to this. That's clearly unacceptable.

To your point, you know, you are consuming -- I'll take your word for it -- trillions of servings. Certainly, I think of it as, you know, you're feeding 300 million people, 3 times a day, 365 days a year -- it's a huge number.

We can do a better job at preventing these problems occurring in the first place. I have no doubt about that. So, you're taking something that is good, and making it better.

We can do a better job of when these outbreaks occur of identifying them more quickly, and shutting them down faster. We'll never reach the point of zero. And you're right -- there are economic diminishing returns in terms of the investment of public health infrastructure, versus reducing food borne illness.

I don't believe that we are at the point, yet, where we've said, "We've maxed out. The investment is matching the return." I think we

should, we need to do more.

The other point is, that we're not dealing with a static system. The food supply is getting more complex, particularly if you think of it in the context of the global food supply. We're importing more and more and more foods, and obviously there is a concern that, what do we know about the way food is being produced in certain countries that we are importing more and more foods from?

So, establishing those preventative controls domestically, internationally. Being able to target inspections based on risk. And to your point, you don't want to inspect everything, and test everything -- that's not a good ROI. And then having a fast, targeted, laser-like response system when something goes wrong. And that's -- that's the goal. We're not there, yet.

Dr. McNeil: So, thank you very much, David. We're going to take a 20-minute break, now. And Carlos reminded me that I erred in my remarks about saying let's carry on this discussion over coffee, because over coffee we talk to ourselves, or

we talk to each other about the weather, or the stock market, or housing prices, or whatever you want. But we don't talk about rapid testing.

[Laughter.]

Dr. McNeil: So, we can potentially have room, perhaps, later in the agenda for something like that, but let's take a break now, and come back in 20 minutes.

Thank you.

[Recess.]

Dr. McNeil: We're going to start, because we have an important presentation now by Randy Lutter, to expand upon the food contaminants, and economically motivated adulteration. Which, I must say, is something I'd never heard of until I came to the FDA Science Board. Goes to show my naïveté, but go to it.

ECONOMICALLY MOTIVATED ADULTERATION OF FDA REGULATED PRODUCTS: UPDATE BY RANDALL W. LUTTER, PH.D., DEPUTY COMMISSIONER FOR POLICY, OFFICE OF THE COMMISSIONER

Dr. Lutter: Thank you very much, it's a

pleasure to be here.

I'd like to give you a progress report, an update on our efforts to anticipate, and ultimately prevent, future economically motivated adulteration.

And for those of you who participated in the Science Board meeting last fall, you'll remember that this is a term that we've used previously, and the problem that we're addressing is one that is fairly evident to people who followed popular press accounts of problems associated with FDA-regulated products.

In the case of the first major episode, dates back to March 2007, melamine was reported in animal feed -- it's an industrial chemical that was added to gluten by manufacturers in China, apparently to enhance protein content. It was also added to flour. And the effect of adding melamine is essentially to defeat an assay used to infer protein content, which in fact measures nitrogen.

Subsequently, in January of 2008, there was an episode of heparin that CDER was very actively involved with. Over-sulfated chondroitin

sulfate was found in heparin active-ingredient pharmaceutical -- active pharmaceutical ingredient from China.

The over-sulfated chondroitin sulfate is known in the scientific literature as an effective anti-coagulant, suggesting that this had been deliberately contaminated.

Subsequently, in September of last year, melamine was reported in dairy products. It was apparently added to milk in order to enhance its perceived quality and value. This was an instance where, fortunately, there was no exposure to U.S. residents. There was, however, very significant exposure in infant formula to -- through infant formula to infants in China, and as many as 300,000 infants were reported to have needed medical attention there.

So, the broad concern that we have is there's a pattern that's evident, here, and all of these products appear to have been purposefully adulterated for economic gain. Which poses, if you will, the challenge for us, how can we anticipate

future economically motivated adulteration of FDA-regulated products?

As we mentioned last fall, this is, of course, not a new problem. It's one that has a history of at least 100 years in the United States, and that's a reassuring perspective. It suggests it's a problem that -- with effort, tenacity and thought and energy -- we can successfully control. But it's re-emerged, now, in a different form that requires our deliberate attention.

What is our strategic approach? What we've done, to date, is created an internal workgroup to develop an approach to anticipate future economically motivated adulteration so as to prevent or control the risks. And the paradigm in the workgroup is based on the presentation that I made in the fall, or consistent with it, which is that the motivation here is essentially an economic model. That there are private actors who are deciding what products to adulterate, based on an assessment that they make that the benefits of such adulteration, in purely financial terms to

1 themselves, outweigh the cost, to them, of doing so.
2 So, what that means from our perspective,
3 is that we should be thinking about products where
4 there's a relatively high value to the market, where
5 there are cheaper and risky substitutes in the
6 ingredients or in the components of the products,
7 and where assays to detect purity -- to verify the
8 purity of the products, or to detect potential
9 adulterants -- can be easily defeated. And that's
10 what I'd like to pursue, here.
11 What we've done, to date, is developed a
12 set of questions that I'll share with you to ask
13 Federal, State and international partners in
14 industry, pertaining to economically motivated
15 adulteration, and this structured approach, as I
16 mentioned, assumes that adulteration is driven by
17 economic motivation.
18 To date, we've met with a variety of
19 Federal partners, including at USDA, and with
20 Homeland Security, and we are planning a public
21 meeting on this topic for this spring at a date and
22 location to be announced later.

The purpose of that would be to pose these questions to the public to solicit their input on them. And let me say that there's a -- in developing this workgroup, and in pursuing next steps, there's a little bit of a balance, if you will, that we strive to maintain between a couple of approaches.

One is, how much information we should solicit publicly, versus through other forums? And we're pursuing, of course, both options. What we've announced through this -- what we expect to receive through this public meeting, is a set of public information.

But, simultaneously, we invite members of the public to provide other information to us more confidentially. On our website is a new link, which goes directly to the Office of Criminal Investigations. It is www.fda.gov/oci/contact.html and people with information about potential criminal activities pertaining to FDA-regulated products are invited to provide that information to our office of criminal investigations.

So, a schematic overview of our strategic approach suggests that it's iterative, an idea that I think David Acheson mentioned to you earlier today, and consultations, because we're doing something new that we don't think has been done recently by any regulatory agency in any similar arena.

So, we begin with consultations with partners, by which we mean, other regulatory agencies; a public meeting and a solicitation of comments, a consultation with outside stakeholders, which would include private industry -- either trade associations or companies themselves, be they manufacturers of the products or companies that are engaged in selling consulting services about security.

The purpose of all of these consultations and meetings is to identify -- if you will -- four major questions. What products are high-risk? Defined in the sense that I alluded to earlier, likely to be targeted by economically motivated entities who may be adding adulterants. What

substances are at risk of being used as adulterants? What assays are there that need improvement and greater sensitivity, and then are there potential signals of economically motivated adulteration that we should be worrying about, should be following, and that might provide us early warning, if you will, of economically motivated adulteration in the future?

All of these are, if ongoing -- one can think of -- as ongoing work products that we'll iteratively refine, and we're currently engaged in developing these, to date. And based on the state of that refinement, we'll then share these, again, with partners, or through public meetings, or through consultations with outside stakeholders.

Ultimately, this will lead to our use of information to help better inform and manage FDA's activities on a regulatory front, and we hope also to have results that we can share with stakeholders in the regulated community, but we're not at that stage, yet.

So, what I'd like to do now is share with

you some of the questions that we propose to ask at the public meeting, and the purpose is to get your feedback on these questions. And, so that when we formally announce them to the public for the -- in the context of that public meeting, they will benefit from your input.

And there's several sets of these, the first one deals with questions pertaining to attributes of the products, or components and ingredients that may be faked. And largely the questions are inspired, if you will, by our experience with the two melamine episodes, and with the heparin episode, as well. There are related episodes that are not quite as prominent, dealing with diethylene glycol.

What products -- so, the questions are -- what products or components or ingredients used in products have attributes that can be faked by using lower-cost substitutes? What are such attributes, and what are the lower-cost substitutes?

What products not reported in the press contain melamine or diethylene glycol? What other

known or potential adulterants have been used in the manufacturing of products, or added to products for economic gain? And the last one, what food products are paid a premium based on measured protein content or on measured fat content as inspired by the experience with melamine, where our understanding is that the motivation for it was that gluten was paid a premium in China based, in part, on measured protein levels. And also milk, similarly, was paid a premium based on measured protein levels. So, this speaks to the possibility of developing signals, if you will, of similar risk of economically motivated adulteration in other areas.

Questions pertaining to changes in the marketing environment, what dramatic changes have occurred recently in the marketing environment of products who are ingredients in the geographic origin of products? In the price's output or exports for products or ingredients and in the supply of ingredients or source materials for products?

Inspiring these questions is information

that there was a fairly large shift in the supply of gluten coming into the United States from other sources, to China, in the years immediately prior to the episode of contaminated gluten, and also there was a shift of Chinese exports of gluten by some accounts, away from other markets, toward the United States at the same period of time.

Other proposed questions are, what scientific research -- published or otherwise -- indicates that a specific material could be used as a substitute for another legitimate material? Inspiring this is the observation that the over-sulfated chondroitin sulfate was actually an anti-coagulant in the scientific literature. And, in that sense, somebody very clever and very shrewd, presumably thought of adding this to heparin, as a way of making money.

What analytical equipment or methods -- although used by industry and regulators -- are, in fact, unable to detect faked products or ingredients? A fairly broad question. Other proposed questions are, are you aware of products or

ingredients with a supply chain more complicated than it would appear to be necessary for distribution, or where the supply chain has recently become more restricted or complicated?

And finally, what recent examples of economically motivated adulteration should U.S. regulators study and learn from? We're aware that not all of these cases may be made public. And earlier conversations with some stakeholders we were informed companies themselves -- if they're able to control these problems at a relatively early stage -- may not bring it to the attention of the regulators. It's embarrassing for them, for a variety of reasons. It poses, also, other security concerns, and therefore there may be issues here.

From our perspective, there's a dilemma. How do we elicit this information? We're trying to elicit it as best we can, but we seek your advice on how to phrase this -- these questions -- and how to best get information about them here.

We have other questions -- what further information should U.S. regulators request to help

predict and address economically motivated adulteration? Does this broad approach make sense? This is a question, not only for you, but also from the broader public in the public meeting that we'll convene later this spring. How might we best address this problem more broadly?

What other organizations may have information that would help U.S. regulators predict and address economically motivated adulteration? This is a new endeavor for us, we've not previously done it. We believe the pattern that has been described earlier with respect to melamine and heparin is one that, unfortunately, may not have seen its final day.

And in that sense, to the extent that there's another episode of harmful economically motivated adulteration that will loom before us this year, next year, the year after that, we're remiss if we don't take whatever thoughtful, organized, comprehensive action we can now take to try and anticipate it and predict it. But because this is a new endeavor, we're exploring, if you will, how best

to do it, and soliciting your input on that.

So, this is where we stand, and I welcome comments.

Dr. Spielberg: I think it's worth pointing out that in, really, all of these episodes that children have borne the brunt of toxicity, which is ironic.

The ethylene glycol, diethylene glycol, situation, for Heaven's sakes, it was 1938 and the Pure Food and Drug Act that created this Agency, and it was a result of use of diethylene glycol to suspend sulfanilamide as a pediatric elixir.

And the current diethylene glycol adulteration of acetaminophen internationally, has again been a tragedy that has been borne on the back of children. The melamine situation -- baby formula -- and even the deaths associated with heparin, the majority of the deaths were really dialysis patients and children, again, because of the dosimetry associated with the contaminants.

So, one area to think about is the fragility of pediatric formulations for foods, as

well as pediatric medicines, because pediatric medicines often have to be given in liquid forms, which leads to folks looking for cheap substitutes for glycerin, and using diethylene glycol which, after all, tastes great, and is a very fine antifreeze, but is incredibly toxic to children.

And again, from a dosimetry point of view, if you think about the morbidity that you're going to see from contamination, it's again going to be in the pediatric population, and often hardest to see, particularly when we're dealing with the developing world's children, who have such high mortality to start off with -- 15 percent of children don't make it to age 5 in most countries outside of the United States and sub-Saharan Africa and such, and then Asia -- so that we're dealing with a major international issue, and focused on kids. Focus on liquid formulations -- any time a medicine has to be suspended. And I know that the USP is involved in this.

And the second point, relative to USP, is that the assays we're using to detect things are

ancient -- the old keldol reaction for nitrogen, as a way of determining protein content. So, we need much better specificity on our assays to determine those things that might be viewed as economically important -- how much protein is in your product?

And similarly, with heparin, I know USP is revising all of its standards for looking at what heparin really is, and the super-sulfated chondroitin issues.

So, going forward, I think, those of us in the pediatric community are very worried about this. The strange part is that the pediatric marketplace is always viewed, economically, as a tiny portion. And it's so hard to drive the development of pediatric medicines, because they really don't have high returns.

Which raises the question, again, of why diethylene glycol has been sneaking into the acetaminophen supply, where pediatric acetaminophen is really so cheap. I suppose the margin between glycerin and diethylene glycol is enough for people to consider doing these things, but I think we

really need to think about liquid formulations, and atypical formulations.

We know that in the sub-Saharan African situation with respect to AIDS, a lot of pediatric HIV drugs are not. The don't contain the active product, and they often contain adulterants. So, this is truly an international issue, and I suppose one plea is that on behalf of kids internationally, that the Agency engage heavily with WHO and other regulatory agencies -- EMEA -- but also the agencies responsible for care of children internationally, because they are going to take the major brunt of what's going on with unethical production of pharmaceutical products, and obviously now, as well, baby formula.

Dr. Kushner: Thank you, that's a wonderful presentation.

I just have a, sort of, a two-part question related to one issue. You stated, and I think it was a really good idea, to have a place where the public can call in on the website for the FDA -- it's a very complicated URL, is there a link

on the front screen of the FDA.org website that links to that URL? So that people don't have to try to search for that?

Dr. Lutter: I can verify it, actually, it went live only yesterday, but I think it's two click from the home page.

Dr. Kushner: But can you see it on the home page, actually?

Dr. Lutter: I have to check, I'm not sure.

Dr. Kushner: I would recommend that you have it on the home page for people who might have difficulty finding that.

And my second part of the question is, since a lot of this is international now, our food base and medicine base is becoming international, have you given any thought to developing human intelligence sources, or the ability of human intelligence sources in other countries to alert us to these problems? Some may be potentially through the websites or something else, or through networks of human intelligence that might -- in the

industries involved -- that might be able to alert you before a problem becomes evident?

Dr. Lutter: Yes.

Dr. Woteki: My observation and comment are exactly like Fred's.

The first observation is that I know within the major food companies they're -- each one is conducting the same kind of analysis. Your questions are spot-on. They're the kinds of things that companies are looking to their own supply chains to try to make them as secure as possible. I imagine the same thing is going on within the pharmaceutical industry.

But, to Fred's point, this question of human intelligence is one that is, I think, encompassed in your last question, here, but one also that is going to be extremely important for prevention of these types of situations in the future. So, how to do that marketing analysis, how to get coverage within trade shows, we know that some of these substances actually have been featured in trade shows in developing markets.

So, you know, how do you get that information and brought in, in such a way that it can be actionable? Is, I think, a big challenge.

Dr. McNeil: Is that a question, or is that -- ?

Dr. Lutter: I can talk a little bit about that, if I may.

One of the concerns here -- I guess I can go all the way up -- is signals. And we need signals that are valuable to us, where the signal, the noise ratio is ultimately actionable, and we have spent a fair amount of time developing detailed timelines, retrospectively for the heparin and melamine cases, and we are exploring what types of signals might have been helpful in those instances.

We're aware, simply from the press accounts, that there was a large-scale trade of melamine within China, apparently for the purpose of being used as a magic protein powder. And I don't know whether that was actually known in a trade show, or known in some way, but there are clearly examples based only on the press accounts that, had

we known about that at an early stage, it should have triggered a whole collection of actions and further inquiries on our part that weren't -- that we didn't take at that time, because we didn't know about it, and we hadn't thought about it.

So, that's the -- the broad recognition, we share with you that there is an opportunity for us to act proactively, early on, but there's also a very large challenge of managing the information. Because one could easily see that, for example, the -- there's a blue ear disease in pigs that may have been linked to the heparin, it had the effect of a substantial reduction in the pig supply in China.

At the same time that the heparin shipments, which are derived from pig intestines, the API was unaffected, coming to the United States. Had one known that at the time, presumably that would have also triggered a signal to us, and further action.

But then the question becomes, how many other pieces of information are there like this in the world that we would need to follow, to track, to