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Dr. Norris Alderson:

I want to personally acknowledge three people who spent considerable time and planning and making sure this event took place today Rick Canady, Catherine Lorraine, and Megan Clark. In particularly Megan. If there is something wrong talk to me about it, but please give Megan all the acknowledgement for all the work she's done arranging for the facilities and all the documents you've seen on the web page. I also want to acknowledge the FDA nanotechnology task force for their continued work on this subject and also particularly the session chairs which I will introduce shortly.

We trust that most of you have read our task force report. For that document, and I've got the first page of it for those of your familiar with it on the screen. If you've read this document you recognize that this document is our starting point in the path that FDA is on to address nanoengineered materials in FDA-regulated products.

So today, this meeting is a part of FDA's continued effort to identify science issues associated with inclusion of nanoengineered materials in FDA-regulated products. Is also in the context of continued national and international collaboration. This meeting is the opportunity for you as our stakeholder and collaborators, to inform FDA both on the need for guidance and the state of the science in FDA's vision of ensuring the safety and effectiveness of the products we regulate.

Please know that FDA is seeking input regarding the need for guidance as was framed by the questions in the federal register notice, in the questions you received for the specific breakout session, and also in the task force report. Potential guidance is meant to address safety, efficacy, and product quality issues for the products we regulate. In this respect we ask that your comments address the questions we've provided. While we are interested in anything that you want to present to us in the context of nanoengineered materials, our focus is on the issues which we provided associated with the safety and effectiveness and product quality. As there is a limited time today, and with consideration for others if you have come to listen please, provide information relevant to the respective breakout sessions.

So some pointers for today. We provided in the federal register announcement the opportunity for speakers to register prior to today. We also know from experience that individuals will come to meetings and decide they want to present that day. So we've also provided the opportunity for you to register if you want to make a presentation and you didn't do so prior to the meeting. We will cut that registration off at the end of the plenary session. We will limit those presentations to five minutes. Each of the session chairs will be running their sessions and take care of the scheduling for these additional presentations. These should be restricted to brief statements with the intent to add to the presentations already in place. Remember, this meeting has been designed for FDA to

listen, not to engage in debate on any of the issues presented. It is not a Q&A meeting with FDA. However, we expect your session chairs to ask clarification questions during the course of their particular sessions. As we will be recording all presentations for transcription, we ask all use the microphones when speaking.

This slide I presented the location of the breakout session, and let me attempt to orient you where these rooms are. On my immediate right, let me get this correct here, is the prescription drug in this corner and the cosmetics will be behind it. On this side will be the combination of food and what was originally to be the dietary supplements. However, we only had one presentation registered prior to today for dietary supplements. As a result we are combining the food and dietary supplement sessions together. So both food and dietary supplements will be in this area over here. Drugs, cosmetics. And in the center where you'll early are will be medical devices. Everybody straight? At the end of the plenary session we will have a break, they will reconstruct this whole area for the breakout sessions and we will begin the breakout sessions.

Another important item that I want to point out that OTC, over-the-counter drugs, will be in the drugs session. It is important to understand in that respect that sun screens are regulated as drugs. So if you were thinking about making a presentation about sun screens at the cosmetics session, please get with Megan or the sessions chair which I'll introduce shortly, to change that presentation. Sun screen presentations should be in the drugs breakout session.

I want to back up to point out one other thing. Please note on this slide that the prescription drug and cosmetic sessions will be a joint session during the first hour. So this area over here will be a joint session the first area of the breakout. This change has been made to accommodate a request form the personal care products council to provide a presentation that was made at a previous meeting and is related to both drugs and cosmetics. Following the presentation these two session chairs will provide direction and continuation of their respective sessions

I want to remind everyone of the questions that were provided in the federal register notice. Here is a brief summary of those. First, what are the characteristics of these products that impact safety, effectiveness of the products? What are the things that FDA should be concerned about as we consider nanoengineered materials in the products we regulate? Are the tools to make these assessments appropriate? Are they adequate? Are they available? Have they gone through the appropriate validation to be sure they work? Are there unique aspects of manufacturing, both in nanoengineered material and the products, that is different from the way we currently look at the manufacturing controls of similar products? Does product formulation, processing, and storage have effects on quality, safety, and effectiveness that we haven't experienced before? Are there considerations that we need to put into the evaluation process to address those particular issues?

Many of you in the room are working on products to bring to FDA. We'd like to hear your experience with these. We'd like to know the issues you've faced in the

development of the products, the development of the nanoengineered material. Is that something you can share with all of us that will help us facilitate bringing these products to the marketplace? What has been your experience with characterization? What are the important points from your perspective of the particular characterization issues? Do you think those similar issues apply to all nanoscale materials regardless of size, or does size make a difference? There is something in characterization and manufacturing that we've totally overlooked, that we haven't addressed, we would like to know about that. Your experience is very critical to us.

To help you identify who you are going to be working with during the breakout sessions I'd like to introduce the session chairs and I would like to ask them to stand so you know who they are. First in prescription drugs, Dr. Nakissa Sadrieh from CDER here to my left. From medical devices, Dr. Subhas Malghan from our Center for Devices. In the food, color additives, and dietary supplements Dr. Arthur Lipman, here. And for cosmetics Dr. Linda Katz. Linda is over here in the middle. Please work with these individuals today as you work for your presentations in the breakout sessions. If you remember the Federal Register we have established a docket for this issue. We encourage to submit you comments to that docket. It closes October 24th. This is another way you can impact our thinking about need for guidances for these particular products.

Let me stop right there and ask if there are clarifying questions relative to today's agenda?

Good that means I've done well.

Today the staff gave me two things to do. One, was to present today's agenda and guidances for how to make this successful. Since you had no comments about the first part, I feel better now. Second part was to introduce our two speakers for the rest of the plenary session. I'm going to introduce the first one first who is Dr. Rick Canady, who will be bringing us up to date on FDA activities since the task force report issued in July 2007. The real good thing about me having this opportunity is to introduce the next speaker. For those of that do not know Dr. Frank Torti, he's only been with us a few months. It has been a pressured packed few months for him, he's been on a steep learning curve, but it is beginning to level off…he thinks. But, Dr. Torti is going to talk this morning from his perspective of science and policy as it relates to nanoengineered materials and the science associated with that. I have chosen not to give you his extenseive resuem, because it is extensive, but I have also found from previous experiences that senior officials at FDA they do not need introductions through resumes because most of you in this room probably know his resume because you probably keep up with everything that is going on with FDA everyday. So in that respect I will only introduce Dr. Torti as our Principle Deputy Commisioner and Chief Scientist, Dr. Torti.

Dr. Frank Torti:

So thanks Norris. I am always hesitant to give these opening remarks because usually in my experience they are kind of vapid and just don't reach people and people want to get on to what they need to discuss, so I'm going to be brief. There is one thing about myself that I think is particularly valuable for this experience as some of you know before I came here I headed the Cancer Center at Wake Forest and was intimately involved in the nano center at Wake Forest which is in the department of physics since its inception so that I've have had a --- grounding from physicists and mechanical engineers in nanomaterials and nanoscience so I'm delighted to be here with you today and to learn from you some more and to increase my --- knowledge about these issues. You know the role of a chief scientist as I see it is in large part to be sure that we apply a full range of scientific expertise and judgment to the regulatory decisions that we make at the FDA. And that has been an exciting part of what I do here as we begin to strategize exactly how to approach those issues. I'm going to step back now and move from the issues of nanotechnology to just give you a little feeling about what that means and how I see how we ought to be doing it and how I want to engage you in helping me do it. When I first came here, just two weeks after I came here, I presented to the science board which is the external advisory board for science at the FDA made up of distinguished academics and people from industry and other areas sort of a vision for what science was at the FDA and where we ought to take science. I sort of developed three principles and I think I'll go over those briefly with you because I think they still hit the mark. The first one I think is particularly relevant to this audience, and that is the FDA cannot do it alone. That everything that we need to do in terms of our regulatory decisions is impacted by the stakeholders with whom we interact so that we have to be as smart as possible about listening to you and of course today is a critical part of that venture. We need to engage that dialogue on multiple levels and through multiple forums throughout our decision making process. So, we can't do it alone.

The second principle is that we need to build within the FDA expertise that is complementary and can assist in these regulatory decisions. Nanotechnology is one of those areas that the science board highlighted as an area growth at the FDA and we're very interested in your input as how we ought to build that infrastructure to better serve the regulatory decisions that we make. So that is principle number two.

And principle number three, I think again is particularly appropriate to this audience in that FDA needs [pause] to be proactive in terms of its interactions with its stakeholders and identifying issues that will come before the FDA. Again your presentations today will help us link to the future of how we need to regulate these devices. So, what about nanotechnology? I think there is a school of thought I don't entirely agree with but has been made, that the end points of efficacy and toxicity that apply to all other products can simply be applied to nanoproducts and we will be where we need to be. What are those? Does it work? Efficacy. Does it make people sick? Toxicity. But I think there are issues that you know better than I related to nanomaterials to make that statement, although in part certainly true, a little simplistic. The surface properties and structures of nanomaterials as entities as extremely complex, that there are issues related to nanoproducts that go well beyond their chemical structure that need to be conceptualized, understood, experimented with in order to reach firm and reasonable regulatory

decisions. And by understanding those the point is that I hope we can move more quickly because we can anticipate the landscape. That's the point, we want to bring products to the marketplace as quickly as you develop them, but do that fully accounting for the safety issues that we need to address so that again by trying to anticipate what is coming down the pipe scientifically that is unique to nanostructures this gives us an enormous opportunity to not only understand the regulatory issues better but to be able to work with you to be able to guide those issues to fruition quicker.

So, in conclusion, this is one day and this is one way that the FDA listens to its stakeholders. But I want to assure you this is not the end of the dialogue. This is a part of the dialogue that we are interested in interacting with you and to listening to your concerns about toxicity, your concerns about development, on an ongoing basis and there will be many opportunities to engage with FDA in meetings like this and in other forum throughout the development of the nano-approaches that are being discussed today. So I am glad to be here, I'm glad to listen, and now Rick, who knows the most about these issues, Rick Canady is going to bring you up to date on some additional issues.

Dr. Rick Canady:

Morning. A couple of housekeeping things I wanted to talk about first before we go into this. One, I want to make sure folks are aware we have a change of agenda, and instead of coming to plenary after the breakouts what we intend to do as let the breakouts end as they see fit at different time points, so there will not be a return to plenary and a closing statement. Second thing I want to make sure people are aware, for those of you who came here to find out about biologics issues or overlap with biologics issues, folks from the Center for Biologics Evaluation and Research (CBER) will be in both the devices and drugs sessions so there will be an opportunity to interact with them as well. There isn't an individual breakout session for them, so I just wanted to make sure that you were aware that they will be here.

So, it's my job today to give you a framework within which we can have the breakouts proceed considering the nanotechnology task force report that we issued a year ago July. And I want to make through this presentation the point very clear we have not changed any of the positions within the task force report. That the findings we came to within that report still hold. That we look forward to using those findings and referring to them as we continue in our development of guidance and other actions the agency is taking.

First of all -- can people hear me all right?

The scope of this talk it to provide a framework and information for the discussion in the breakout in terms of the FDA task force report. So I want to give you a sense of what the recommendations were within that task force report and then give you a sense of the actions that we've taken, or in some cases the direction we are moving with regard to those findings. Again this is to give you a framework of, a point of reference with which you can continue discussions with us or rather provide information to us in the breakouts that follow.

In that task force report, for those of you who haven't memorized it word for word as some of us have, it starts out with a section on definitions and gives recommendations about definitions for use in a regulatory context across all of FDA. It then provides a synopsis of the state of the science with respect to biological interactions of nanoparticles in products, nanomaterials in products that FDA may come across pursuant to its mission. We then go into two sections, one first talks about the science policy or science needs for nanotechnology as it applies to products that may come across FDA's doors, and then to analysis of the regulatory policy on implications as they apply to nanotechnology.

We have a number of bottom lines within the report, and I'm just going to go through those briefly, and again I'll go through the basic conclusions or findings and go through them one by one and try to give you an understanding of what we've done and our directions for them.

The first conclusion, which is not a surprise to most of you in the audience, is that we anticipate that nanotechnology will be used in most products that come across FDA's door. Nanotechnology is an enabling technology, in some ways it's like chemistry. It is something that is used and will be used in most products eventually over time. Nanoscale materials present challenges similar to those we come across with other technologies over the past decades, and so we've learned from the technologies we have come across in the past and we feel that nanotechnology presents challenges that are similar. There is one thing; the fact that size influences efficacy and safety can complicate the challenge of the new technology towards is application and regulatory approaches that FDA has within its arsenal. Another bottom line is that it's not apparent that nanoscale materials as a group, considering all nanoscale materials, comparing them perhaps to chemical materials, bulk-scale materials, and so on, it is not apparent that they have would have more inherent hazards that other materials as a group. And our final bottom line is that we recognize that steps should be take to better inform FDA reviewers, and also those manufacturers, producers that are bringing products to us, what is known and what is expected for the analysis of those products as we go about our regulatory mission.

So now I want to go into the individual recommendations of the task force report and provide a table that provides some indication of what we've done and what we're intending to do. The first science recommendation that we have is that there is a need to pay attention to testing approaches. To evaluate the adequacy of the approaches with regard to assessing safety, efficacy, and the quality of nanoscale materials within the products. We also recognize that we need to promote and participate in the development of data characterization methods, standards for nanoscale materials and develop better understanding or modeling of how materials can relate to one another so we can extend knowledge from one material to another using various modeling approaches and invitro, and invivo analysis results. A second finding with regard to the science recommendation was that we do need to develop information regarding the biological interactions of these materials to improve our understanding of those. Within this there is the need to promote, both externally and also participate and direct ourselves, research regarding biological interactions. We also need to build in-house expertise, build upon our in-

house expertise that we already have, and build upon the infrastructure in order to ensure that we, as Dr. Torti alluded to, keep up with the developing science and anticipate the issues as the come to us. We also need to ensure that there is agency-wide coordination. We would like to be fairly consistent in our approach to providing policy indications, directions to the outside, so that's clear when you come to us, when you come to us, that you will get an consistent answer not depending on who you come to. I hope that made sense.

[Side conversation]

I have a table here that goes through the recommendations and in the left hand part of the table I've gone through what I distilled to the previous two slides and I'm going to talk about some of the actions that we've taken and the direction we're going. So with regards to developing knowledge, building infrastructure, evaluating testing approaches, developing methods standards, and models we've done a range of things. These all fall within either the data development, the collaboration, the promoting participating framework of both developing data and developing models and approaches to use that data and improve understanding. FDA is doing its own research. It's evaluating some toxicity assays with regards to nanoparticle actions. We're participating heavily in the National Toxicology Program collaborating with the Nanotechnology Characterization laboratory and the National Institute of Standards and Technology. I'm going to go through this in a little more detail in subsequent slides. The Organization of Economic Cooperation and Development has a testing program on nanomaterials that we're involved in. We're also working with academic and public/private partnerships in a way to establish data development avenues for FDA to get ahead of the problem, or anticipate issues before they arrive to us. With regards to coordinating regulatory science we have the FDA task force, interactions with various working groups at the White House, the Executive branch, coordination. We have bilaterals, or informal or in some cases more formal interactions with our major trading partners with regard to policy and science issues. With regard to research the FDA is doing, and I'm just giving some examples of this, we have research for example on silver nanoparticles we're doing, actual toxicity assays we're doing in the Centers. We've been looking at dermal penetration of metal oxides in particular and ----, we've had some papers published on this recently. We're working quite heavily with the National Toxicology Program, which as many of you I'm sure are quite aware, have taken on a number of nanomaterials as part of their research agenda, or rather nominated and accepted as research topics. FDA is for example, the lead on metal oxides including titanium dioxides, zinc oxide, silver nanoparticles, gold nanoparticles and we're collaborating in the development of study designs and so on with NTP with regard to fullerenes, carbon nanotubes and quantum dots.

We're working with the National Cancer Institutes, Cancer Nanotechnology Alliance, and again I mentioned earlier the Nanotechnology Characterization Laboratory, which is just a work horse of an organization that is developing assays and forging ahead with some of the development of new technologies to understanding biological interactions through its evaluation of cancer therapies. We sit on the oversight board for that and we're actually collaborating with them and they're working with us to develop some

dermal penetration information on metal oxides. We co-chair the interagency Oncology Task Force's subcommittee on nanotechnology.

We're also working with the National Institute on Standards and Technology as we move into evaluating nanomaterials it is essential to have standards, standard reference materials, standard approaches, and NIST is just a power horse in terms of developing that information as you all know, I'm sure.

The Organization of Economic Cooperation and Development is an international organization within which has been established a testing program that is looking at up to 14 different nanomaterials representative of those materials in commerce, and is intending to test, and actually already initiated testing, on 59 different endpoints of those materials including characterization, mammalian toxicity, ecological toxicity, --- transport, and so on. And FDA has played a role in both developing that program and is part of the sponsorship team on several of the materials for those programs. We're actively involved in developing data in cooperation with these other countries. We're working with the development of guidance for how to do the actual test program within that, reviewing test guidelines, adapting what OECD already has in terms of test guidelines for chemicals to their application to nanomaterials, participating in the review of risk assessment methodologies with respect to nanomaterials. I'm going through this as a way of giving you a sense of active participation in the development of information that would lead to anticipating issues that are coming down the pipe and also in being able to better answer and address issues as they arise through product reviews.

We're also working with academia and in the interest of developing public/private partnerships [side conversation] so that we can again develop information, develop collaborations to facilitate our infrastructure and data and knowledge. We're working with the Foundation for the National Institutes of Health for example to develop data about biological interactions, modeling and so on. Both they and the Alliance for NanoHealth down in Houston have had prioritization workshops where we have looked at what are the information needs that are most pressing to help us get ahead of the information needs in order to better address nanotechnology assessments.

I want to move now into the coordination of regulatory approaches across the agency. FDA has cross-Center and cross-product area coordination through the nanotechnology task force which is responsible for the report that I am talking about. The nanotechnology task force coordinates science and regulatory policy issues both and also links us down to the Center-specific groups that exist within some of the Centers.

At a national level FDA is a heavy, active participant within several of the working groups and committees that exist within OSTP and more generally within the White House. There is a Nanotechnology Environmental Health Implications Working Group which Dr. Alderson co-chairs with Dr. George Gray of the Environmental Protection Agency. We have been a chair, co-chair of that group since its inception. So we've been quite involved with that. There's also group within the general interest or a specific interest in terms of international collaborations and interests for nanotechnology called

the GIN group. Nanotechnology Policy Coordination Group is a group that is more specifically involved with looking at policy issues across the government so that learning in one agency can extend to another agency and so that again we can more consistently provide a message that takes advantage of all the knowledge across the agencies.

International regulatory science we have informal but actually quite direct and clear interactions with our major trading partners on nanotechnology. It's a quite good communication at this point and I think you can note that in terms of the various policy documents that have come out across the different major economies in terms of how they deal with regulatory adequacy and data development issues. OECD I've already mentioned, and I don't think I need to go into that more. We're also paying attention to converging discussions that are coming out in ICCR, CODEX, U.N. Agencies and so on as those discussions start to develop so we're keeping an eye on things and making sure the coordination happens as appropriate.

And now I want to get into the regulatory issues that were addressed in the task force report. We focused on four issues in the report itself based on our analysis. The first was the ability to identify products that contain nanoscale materials; the second was authorities with regard to evaluation of the safety and effectiveness of products that may contain nanoscale materials. Then we addressed the issue of labeling and finally we looked at the national environmental policy act. With regard to the identification of products containing nanomaterials, we came to the conclusion, and the finding within the report, that FDA's authority to obtain information about particle size does vary across regulatory authorities. It's comprehensive for products subject to premarket authorization; it's somewhat more limited for products not subject to premarket authorization. And then for some product categories for example over-the-counter drugs and food and color additives information requirements can vary and we have further discussion on that within the report. Our recommendation with regard to the identification of products is that we should issue guidance regarding when and how to identify size and when warranted request data under other situations for example with over-the-counter drugs or food and color additives.

For product safety and effectiveness FDA's oversight authority for product safety and effectiveness varies. We have again most comprehensive authorities for products subject to premarket authorization but less comprehensive authority for those not subject to premarket authorization. But in the second case manufacturers are clearly responsible for the safety of the products as they are for all other products. The presence of nanoscale materials may in fact change regulatory status, and our recommendations within the task force report are that we should issue calls for safety and effectiveness data, in fact the federal register notice that was issued with respect to this meeting has such a call for data on safety and effectiveness. There was also one within the over-the-counter drug proposed rule for sunscreens. We also recommended for consideration that guidance be issued with respect to manufacturing devices, generally recognizes safe food ingredients, food and color additives, cosmetics, and dietary supplements. And I'm going to show you a table again and go through some of the things we've gone through, or rather some of the actions we've taken and direction we're going in the regard to these issues. First

with regard to particle size identification, we actually issued guidance last December for food contact notification indicating that size is a relevant data need within those submissions. And we're examining similar sorts of situations where we can issue guidance identifying where size is relevant and it should be submitted to us. We've requested comment on the over-the-counter sunscreen rule, and of course today's meeting is another opportunity for seeking information on what should be included in guidance on particle size identification. Calls for safety and effectiveness data there was the proposed rule on sunscreens and the data call within this meeting notice, and we also are generating data ourselves through National Toxicology Program as I indicated, through FDA research and through the --- test program. In regard to labeling, finding of the task force report as I said was that case by case evaluation based on the materials in the product wasn't binding and with regard the national environmental policy act area it was indicate that a case by case evaluation was indicated and that we should, and in fact do, have an agency wide of coordination mechanism for that area of authority. Safety and effectiveness guidance with regard for manufacturing, we did have a request for comment within the sunscreen proposed rule that would apply to this. We had case studies that we provided expertise for with regard to food contact notification that gave us information that was quite useful with regard to this. And again, today's meeting we're looking for your input with regard to these issues so that we can move forward with developing guidance expeditiously. --- recognize safe food ingredients, again the case studies provided information that is helpful to us for developing guidance and we're considering further case studies with regard to that. Particular issue, we've had extensive bilateral discussions around this issue and other issues regarding foods and nanomaterials within them. We've had additional discussions with UN Agencies, World Health Organization, World Agriculture Organization, with regard to expert meetings surrounding the application of nanoparticles in foods.

For devices we participate in the Global Harmonization Task Force and have monitored for discussions within that group. We're also engaged in bilateral discussion with various trading partners in regard to their policy, directions on that. And seeking to, as with other issue, maintain convergent approaches to those technologies. How those technologies interact with regulatory structures.

Cosmetics, again I mentioned ICCR earlier. That is one way we are keeping track of this, and again we're looking for your input in today's meeting. And dietary supplements we're looking for your interactions in today's meeting to help us move forward with guidance. And I wanted to say with regard to next steps, we're looking for your input as a way of helping us move expeditiously through the development of guidance. We've been collecting information and we're to a point that we would like to move forward and develop the guidance as we indicated within our task force report.

I do want to say a few things in closing, and first is that the very fact that nanotechnology and its application within products is an emerging technology, that understanding its development highlights the need for us, for FDA, working with stakeholders, working with you, to develop a clear, transparent regulatory pathway. So we anticipate the needs, so we get ahead of the needs, so you know how we're going to address things when you

come to us and so on. So we're really looking forward to your input to help us figure out how to get to that. We want to have your thoughts on that; we're here to listen to you in this session. And it's important within FDA's process, and this is standard practice for FDA, to have early consultations and for an emerging technology like this it is especially important. That if you're thinking of developing a product, you're in the early development stages for a product, or you have questions about a product, come in and talk to us. Come in and talk to us early. We need to hear from you, we like to hear from you. With regard to nanotechnology which is one of these technologies where you can converge various modalities it may be in fact important to come in perhaps even little earlier and interact for example with our Office of Combination Products to consider pathways within FDA that may work best for you. Actually, pathways within FDA that might work best for the evaluation of the product.

So consultation with us early and often, provide data to participate in the research and the planning for FDA's evaluation of those products, and engage in international harmonization work with us. It is important that one regulatory approach doesn't get ahead of another. It is important that we keep ourselves working well with each other and maintain the safety and effectiveness of these products as they come to market.

With that, thank you very much. At this point what we will do is break the room, go to break rather, and then divide the room into the various breakout sessions. Again, after the breakout sessions you are on your own. Lunch is at 12:00 o'clock, it is up to the sessions when you go to lunch that's correct. The very first session, again, is the drugs session combined with the cosmetics session over in this area, which will then break up into two separate sessions. Devices is here and the foods area is over there. Thanks you very much.

FDA, the leader is now disconnecting. This call will now end.