Building Effective Partnerships
FDA and Stakeholders Public Meeting

Searle Center
Duke University Medical Center
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Reported by:

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A P P E A R A N C E S

Mark Barnett – Moderator
Dr. Jane Henney – Commissioner, FDA
Dr. Linda Suydam – Senior Associate Commissioner, FDA
Dr. John Marzilli – Deputy Associate Commissioner for Regulatory Affairs, FDA
Dr. Bernard Schwetz - Acting Deputy Commissioner, FDA
Dr. Janet Woodcock – Director, Center for Drug Evaluation and Research, FDA
Dr. David Feigal – Director, Center for Devices and Radiological Health, FDA
Dr. Jessie Goodman – Acting Deputy Director, Center for Biologics Evaluation and Research, FDA
Dr. Robert Buchanan – Senior Science Advisor, Center for Food Safety and Applied Nutrition, FDA
Dr. Bert Mitchell – Associate Director for Policy and Regulations, Center for Veterinary Medicine, FDA

Dr. Tobias Massa – Executive Director of Global Regulatory Affairs, Eli Lilly Company
Dr. Victoria Durant-Gonzalez – Director of Community Service, Spelman College
Dr. David Lineback – Director of the Joint Institute for Food Safety and Applied Nutrition, University of Maryland

P R O C E E D I N G S (1:00 P.M.)

MR. BARNETT I guess we're ready to start. I'm Mark Barnett with the FDA, and I'll be serving as your Moderator today for this meeting on leveraging, which is actually a meeting to talk about how the FDA can work with outside groups in accomplishing its mission.

I think maybe the first thing to do is to introduce you to the panelists. Most of you probably can't see the little name tags in front of them, so I'll ask each of the panelists to raise a hand as we go around so you'll know who's who. We'll start with Dr. Jane Henney, who is Commissioner of the Food and Drug Administration. Dr. Linda Suydam is FDA's Senior Associate Commissioner. John Marzilli is FDA's Deputy Associate Commissioner for Regulatory Affairs. Dr. Bernard Schwetz is FDA's Acting Deputy Commissioner. Dr. Janet Woodcock is Director of FDA's Center for Drug Evaluation and Research. Dr. David Feigal is Director of FDA's Center for Devices and Radiological Health. Dr. Jessie Goodman is Acting Deputy Director of FDA's Center for Biologics Evaluation and Research. Dr. Robert Buchanan is Senior Science Advisor in FDA's Center for Food Safety and Applied Nutrition. And Bert Mitchell is Associate Director for Policy and Regulations in FDA's Center for Veterinary Medicine.

We also have three people on the panel who are not members of the FDA, and I'll tell you why they're here in a few minutes. Dr. Tobias Massa is Executive Director of Global Regulatory Affairs with the Eli Lilly

Company. Dr. Victoria Durant-Gonzalez is Director of Community Service at Spelman College. And Dr. David Lineback is Director of the Joint Institute for Food Safety and Applied Nutrition at the University of Maryland.

Let me tell you how the meeting is going to lay out in terms of format. We're going to start out with a few introductory words from Drs. Suydam and Henney in which they're going to be talking about, in a sense, setting the stage for this meeting and telling you why leveraging is such an important concept to the FDA at this particular junction in time. And then we're going to ask the non-FDA members of the panel to talk to you. And they have something in common. All three of them have worked on leveraging projects with the FDA in the past. Contrary to some of the rumors going around, they are not the only three survivors. But they have had good experiences with the FDA. And we thought that, since many of you in the audience might be in fact leveraging partners with the Agency, that you might like to hear about their experiences.

At that point, we will dive into the main portion of the program, which is to hear from the folks who are sitting at this table here about their ideas on leveraging. We are not looking for formal proposals, we're looking for ideas we can explore. And, from time to time during those presentations, I will ask the panelists up here to respond with questions or comments.

I should tell you a little bit about how this got started. Dr. Henney and her staff identified five (5) areas for potential leveraging that seemed to be very important to the Agency at this time and seemed to have a high likelihood of succeeding. Those five areas were published in The Federal Register along with an Announcement of this meeting. And in that Announcement we asked people if they would come to the meeting and explore with us their ideas. And we got a

very good response, as you can see, and we're delighted, and we're going to be hearing those folks.

The one thing that concerns me, I think, as the Moderator is the question of time. We have a lot of speakers, and we have a limited amount of time. We're eager to hear it all. And so we're going to do two things. First of all, we may run a little bit over. The meeting is scheduled for 3:00. We may run a few minutes beyond 3:00, and we hope that doesn't cause a problem for anyone. Although we can't go too much beyond 3:00 because there's another meeting scheduled.

The other thing I'm going to do is I'm going to promulgate an FDA guidance on the length of the presentations. Those of you who have worked with the FDA before know that a guidance is not enforceable under the law necessarily; but, on the other hand, it's not just a suggestion either. So. So we're going to go – my guidance for the speakers is going to be three (3) minutes. And that sounds like a short time, but actually we're not looking for a formal proposal, we're not looking for details. We're looking for ideas we can explore. So I think three minutes may be enough. And we are going to be in contact with you after this to explore those ideas further.

One more piece of housekeeping before we begin. There is an evaluation form in your packet. Please take the time to fill it out and let us know what you think about the meeting. Leave it on your chair, and we'll pick it up later. We may be doing more of these in the future, and so that kind of feedback is going to be very important to us in terms of future meetings.

Let me begin by talking to Drs. Henney and Suydam a little bit about leveraging.

Dr. Henney, the FDA has worked with outside groups before. This leveraging is not a brand new concept. And, yet, in your agenda for the Agency you've

elevated it to a conspicuous position, to a high-priority position. Why is that? Why is it so important now?

DR. HENNEY: Well, Mark, I think for you and all of you in the audience, you're all familiar that the FDA regulates a wide range of products that are important to American consumers. To be able to do that, we need to have the capacity to do that. Many of these products are becoming increasingly complex. The kind of issues that we deal with are often times controversial. And it seems to me that as we build our capacity, we need to think about our own internal strength, but how we use the strength of other individuals and institutions across this country to really meet our mutual goal of improved public health. So we are trying to really leverage the intellectual capital, the energies, the enthusiasms, and the desire to improve the public health on behalf of all of us. And it is why I am interested in seeing what opportunities we have out there to do this.

We started some of these other projects that you'll hear about a few years ago. I think some of them have really brought us many strengths already. Some are just still fairly nascent but have great promise for bringing us the kind of joint efforts that we needed, so that's why I've elevated it to this kind of level.

MR. BARNETT: Dr. Suydam, does that mean what was an ad hoc process—take it when you can get it sort of thing—now becomes a more formalized procedure in the Agency?

DR. SUYDAM: That's right, Mark. We've actually established mechanisms at all levels of the organization to make sure that leveraging is institutionalized into the FDA culture. And we think we have the systems in place to make leveraging an ongoing process, something that will last for many, many years.

MR. BARNETT: Dr. Henney, the FDA is entrusted by the Congress and the American people with

seeing to it that consumers are protected against devices that are ineffective or unsafe or misbranded or adulterated. Having outside groups help to do some of the job raises the potential for that trust somehow to be compromised. Is that a problem? Is it a concern?

DR. HENNEY: Well, it's an issue. And I think that, as a regulatory organization, we always have to be mindful of the relationship that we have, particularly with the regulated industry, so that we maintain the public trust and confidence in our independence in what we do.

And, before we have started nearly every one of these endeavors, we've probably had a room filled with as many lawyers as there are people in this room to make sure that these kind of relationships and organizational frameworks, if you will, are as they should be, and that is without conflict. And so that confidence in terms of what this body does, the FDA, can be maintained because it is critical not only to us but to what the industry is able to do as well.

MR. BARNETT: Dr. Suydam, what do you hope to get out of this meeting? I guess what I mean by that is, if you could visualize the best possible outcome for today, what would it be?

DR. SUYDAM: Mark, I think I have both a long-term and a short-term vision for this meeting. The short-term vision is that today we will hear some imaginative and innovative ideas about how FDA can partner with the people in this room to help meet our goal of promoting and protecting the American public.

But, from a long-term perspective, I think I have a vision of seeing some very concrete projects, ideas that come to fruition where FDA has long-term partners and we know that we have the capacity to serve the public in a way that meets the needs for the next ten to twenty years.

MR. BARNETT: Thanks.

Let me talk now to the three non-FDA panelists and ask them to describe some of their experiences. The first of those is Dr. Tobias Massa of the Eli Lilly Company. He worked with the FDA in developing a project called The Product Quality Research Institute, or PQRI. Dr. Massa?

DR. MASSA: Thank you. PQRI is a rather unique opportunity for industry, the Agency, and academia to work together on issues surrounding product quality. It's a unique opportunity because I think this is the first time that we have this in the area of product quality.

I'd like to talk a little bit about the PQRI process. The brochure tells you a little bit about what organizations are involved in PQRI. I would add that, since that brochure or that handout was written, three additional groups have joined PQRI. The International Society of Pharmaceutical Engineers, the International Council on Pharmaceutical (Excipients) and, most notably, the USP. So this is an idea that is catching on. And it's starting to take an international flavor in that EFPIA, which is the European version of Pharma, which is the innovator companies in Europe, are also interested in getting involved. So this truly does have a lot of interest.

The process is unique because all the players sit at the table, the regulators and the regulated. We jointly pool our resources, pool our strengths, together to identify what are the critical issues that need to be addressed and how can they result in good science that will lead to good regulation. Hopefully, that will result in a reduction of regulatory burden not only for the regulated industry, but also for the regulators as well. What we want to do is establish a science base, which will allow us to demonstrate that regulation can be modified so that we're regulating at the right level.

The way the process works is that there is a steering committee in which each member organization has a representative. And that includes FDA. The steering committee will decide what are the key areas that we will concentrate our efforts. Once those key areas are identified, a technical committee will be put together, which will help frame specific issues in each of those key areas, and a working group will be assigned to each of those key issues. The working group, again, will consist of an industry person or persons, because we have the generic industry as well as the innovator industry involved here. We will have people from appropriate trade groups involved as well as academia, which the primary input will come from the American Association of Pharmaceutical Sciences, and FDA. So everybody is involved in each phase of the process. The working group will define and crystallize what is the specific issue we are going to deal with, what is the specific area of regulation or guidance that this piece of work will address.

The protocol will talk about what specific work will be done and will also propose an outcome. If the data tells us "A" the guidance will be recommended to be modified along these lines. If the data points to "B," it will lead to a different way of modifying guidance. Ultimately, a report will be issued and will be approved through a couple of levels of review within the Institute and then sent on to FDA.

Now, Dr. Henney made a comment about concern of compromising confidence and conflict of interest. Well, this is where FDA gets to independently assess what PQRI has done. Because, although FDA has been involved in the process from the very beginning, it is not binding on FDA to accept PQRI recommendations. However, the Agency has agreed that they will either accept the recommendation and modify guidance or they will tell us in writing where the

recommendation is deficient and what we need to do in order to get a guidance changed the way we think it needs to be changed.

Now, having said all that, we haven't run anything through the process yet. Our first effort is going to be on blend uniformity analysis. It's significant that FDA has put draft guidance out and has gotten a lot of comments on that guidance. Most recently, they have communicated to us their desire to formalize and finalize that guidance. Based on our input, they decided to wait until PQRI gives its recommendation at the end of this year before finalizing that guidance. So, although we don't have proof of principle that this process is going to work, at least there's a willingness on FDA's part to give it the opportunity to work.

Clearly, the Institute won't survive if the process doesn't work. So we've tried to pick research projects that do not require prospective research. We're going to look at existing data and try and analyze existing data. That's a lot more cost-effective for us. But, hopefully, we will get to the point where we can do prospective research.

That's going to cost dollars, and we are undertaking an effort right now to go through fund-raising for the Institute. That's one area in which we have divorced FDA from the Institute activities. They are not involved in fund-raising. This is being handled by a board of directors that's separate from the scientific steering committee.

I'll stop there.

MR. BARNETT: Okay. Thank you.

Our second case study in leveraging comes from Dr. Victor Durant-Gonzalez at Spelman. She worked with the FDA in a consumer-education program on medicines that was called Take Time To Care.

DR. DURANT-GONZALEZ: Okay. I would like to talk about the process that we established at Spelman. I'll talk about the process used in establishing the collaborative efforts used to leverage resources for the Take Time to Care, Using Medicines Wisely campaign that was conducted in Metropolitan Atlanta in April of 1998. And I would like to point out three features of the leveraging model, which we called a community participatory model for educating the public about using medicines wisely.

One feature of the process was tapping into existing relationships. Another feature was creating a strategy for developing buy-in and ownership of the campaign. And, thirdly, integrating the Take Time To Care campaign activities into the existing programming of the organizations.

Now, luckily for Atlanta and the campaign, the FDA had already started a partnership at Spelman College as early as 1996. And this partnership came as a result of the efforts of the public affairs specialist, a woman by the name of Joanne Pittman. She, with the support of her colleagues, came to Spelman and wanted to start a dialogue of how Spelman College and the FDA in Atlanta could come into a partnership and a partnership that would be mutually beneficial to both the FDA and to Spelman College. Out of that initial outreach came a dialogue between FDA staff members and Spelman College staff.

On Spelman's side, we had the VP of Student Affairs, we had the Director of our Health Careers Program, the Director of our Health Services Program, and the Director of Community Service. And we began to talk about what are some of the things that we can do that we could strengthen what Spelman does, educating its students, and FDA's interest in being more effective in its

outreach to consumer groups. So, out of that, came this partnership.

And what we decided to do in the first instance is that FDA scientists would come and serve as guest lecturers in Spelman's curriculum and that its Public Affairs specialists would be involved with us in our outreach programs to the community. That means that they would participate in some of our health fairs out in the community, some of our wellness walks, and some of the community health forums that we had.

Well, out of that some interesting things happened. At the community level, FDA's image began to change from that organization, which we see sporadically on TV that's either approving some drug or withdrawing a drug from the market. It got a face, and it got a face as an agency that sits down or walks or serves side by side with regular community people. Well, with that partnership intact when the campaign came to Atlanta, the Take Time To Care Campaign, we sat down to the table and said, "Well, why don't we simply broaden this partnership to include others?" So we broadened the partnership to include 30 other agencies, groups and organizations. And, out of that, we began to say, "How can we then take these 30 groups, have them buy into the Take Time To Care, make it their own, and make it work?"

So what we began to do was to develop some strategies. A planning committee was developed, and this planning committee had representations from major organizations around the city, and I chaired that planning committee. And then we decided on the planning committee, "Let's have a series of meetings." And what we did was look at who was part of the collaborative, and we had representations from women's groups, senior citizens groups, government agencies, colleges and other organizations. And we decided that

we would have four (4) major meetings, and these meetings would be held at different locations.

Now, what we thought, if we held them at different locations, then we would have to get someone from the collaborative to host the meetings and others would have to go into parts of the city in which they may or may not go. And each organization, when they would hold the meeting, they could call on anyone from the 30 collaborators to come and help them officiate that meeting. People began to take on that this is our campaign, this is what we want to do, and let's come up with a most effective way to reach people.

But, once we had the collaborative working and planning, the next thing we needed to do is that what was the most effective way that each organization could go out and take this education campaign about the effective use of medicine to the consumer and to the under-served consumer, to the consumer that's located in hard-to-reach areas of the city. Well, we decided that probably the best way to do this was to take the campaign and shape it and mold it into existing programming of each organization. This had the result of, one, organizations did not have to go out and create another program; organizations did not have to go out and create another venue. But then this could be smoothly integrated into what the organization does on an ongoing basis.

And I'll use how Spelman did its campaign in terms of integrating it into what we usually do. As Director of the Office of Community Service, Spelman women serve in approximately 95 to 100 service organizations around Atlanta. So our women are throughout metropolitan Atlanta doing service on an ongoing basis. We also concentrate a great deal of our service in the Atlanta university center neighborhoods. So we selected five (5) organizations in which Spelman women were

situated and decided that those would be the organizations whereby we would concentrate this campaign. We selected high-rises, the Atlanta Housing Authority high-rises, which house senior citizens. We selected a homeless organization called Cascade House. We selected Quality Living Services. We selected a CDC called Tyler Place.

Now, the homeless organization that we selected, the women did not meet the criteria, the age criteria, of the campaign of 45 and over. But we felt so strongly that this group usually is never touched, and since we worked so closely with the organization, we took the forum there. And when we would make a presentation, the presentation team would be made up of a pharmacist, it would be made up of students and myself. And the pharmacists, throughout the campaign we selected pharmacists from pharmacies that were located right in the community. So the pharmacists – is it time?

MR. BARNETT: I'm going to be perfectly fair and apply the FDA guidance even to the panelists. So it's almost time.

DR. DURANT-GONZALEZ: Okay. I will wind up.

So what happened? Using these three features of, one, tapping into existing relationships, creating a strategy for developing buy-in and ownership, and integrating the campaign activities into the existing programs of the organization meant that we were able to have a very, very successful campaign in which some of the educational programs that we started got continued.

Three minutes go by very fast.

MR. BARNETT: Thank you very much.

Our third example of leveraging comes from Dr. David Lineback of the Joint Institute for Food Safety and Applied Nutrition. His organization worked with the

FDA on carrying out the objectives of the President's Food Safety Initiative. Dr. Lineback?

DR. LINEBACK: Thank you. The Joint Institute for Food Safety and Applied Nutrition, or JIFSAN as it is better known, had its basic origin in the realization that the new FDA facilities were going to be constructed adjacent to the College Park campus of the University of Maryland, and in their facilities of White Oak are only about two (2) miles away. At that time, it appeared to some of the people there that a cooperative working relationship, or an improved cooperative working relationship, between FDA and the university would be in the best interest of both to leverage resources. It started with the Dean of the College of Life Sciences and Fred (Shankin), Director of Food Safety and Applied Nutrition initiating the discussions, which shortly thereafter spread through the Commissioner's office and the President's office at the University of Maryland.

In 1996, a Memorandum of Agreement was signed to initiate planning for cooperative programs between the two organizations. This was followed by a Cooperative Agreement, which was first funded in 1997. And we also have what's called an umbrella CRADA, a Cooperative Research and Development Agreement. We have that primarily because of the sharing of facilities and resources, so it covers that.

JIFSAN programs in education, research and outreach, all leveraged, are all built upon concepts of building partnerships. We have no program that does not. We are a virtual organization. We have a shadow staff and we put together partnerships. The partnerships primarily involve FDA and the University of Maryland at College Park, but reach out beyond this to the rest of the University of Maryland system, to other Federal agencies, to industry, and to other universities domestically and

internationally. So we have quite a few things that this has started now.

Just briefly, the area of leveraging of resources in terms of instrumentation. As the new building is being built, quite a bit of the sensitive instrumentation is being placed on the university campus in university facilities. These will be staffed by both university faculty and FDA scientists. This will enable cooperative programs to be performed and will actually enable us to leverage much better instrumentation than either one of us could have alone and to use it both in terms of the regulatory issues, in terms of research, and for teaching. This includes nuclear magnetic resonance spectroscopy, electron microscopy and other types of instrumentation.

In the education or outreach area, we have been working predominantly again with FDA, but we are initiating the development of training material and programs currently in Central and South America on the safe production of produce. However, this involves not only FDA and the University of Maryland, it currently involves the University of Arkansas, the University of Costa Rica, and FAO, all either under subcontract or leveraging with their own.

In the area of research, we are just beginning to get this started, because it takes longer to put together the research teams, the language, and the resources for this. However, we are working with the University of Rochester in a follow-up in the Seychelles Islands to a group of children who are now 12 years old and were exposed to methylmercury in their diets early on. We are looking at the neuro-physiological development and its impact. JIFSAN has been instrumental in getting the funding, which is involving some from the University of Maryland and the University of Rochester faculty.

We have an example of work that we are doing in the area of rapid diagnostic tests for food-borne pathogens, particularly of the *e. coli* type involving an industry, an individual in a start-up industry, one of our scientists and FDA scientists. And this is progressing very, very well.

These are the types of programs that we are putting together, and internationally we now have Memoranda of Understanding with the Central Science Laboratory in the Ministry of Agriculture, Foods and Forestry of the U.K. for reciprocal symposia every year and to initiate research programs. We have also just signed one with Agricultural Victoria in Australia in the education and research area.

MR. BARNETT: Thank you.

Before we go on, I'm wondering if anybody in the FDA staff up on the panel might want to respond to anything they've heard? Anything? Yes?

DR. GOODMAN: If I could just make one brief comment, which I didn't even know that this was a JIFSAN project, this study of methylmercury in the Seychelles, but this is something that recently was very useful to people in vaccines in considering (thermerasol) and mercury as issues in childhood vaccines. So I think it's an example that, if you do a good public health research or policy, it trickles across the Agency.

MR. BARNETT: Anyone else?

(No response.)

MR. BARNETT: If not, let's go on to talk to the folks that have volunteered to come here and share with us their ideas on leveraging.

Before I do that, let me just mention that those five things that were in The Federal Register which will be addressed by the folks today are not magic. As you sit here and listen to these things today, if ideas occur to you about leveraging, please let us know. We have a

mechanism for you to do that, and I'll tell you about that right afterwards. So, by all means, we want to hear from you beyond these five items.

That having been said, let's go to those five. And the first of those was a Safety Review for New Products, particularly Safety Assurance in Clinical Trials. We have three speakers in that area. We'll hear all three of them, and then perhaps ask the FDA folks to respond.

The first is Dr. Robert Califf of Duke University.

SAFETY REVIEW FOR NEW PRODUCTS
SAFETY ASSURANCE IN CLINICAL TRIALS

DR. CALIFF: I want to thank you all for taking the time to come down today. It's already been productive, and I'm sure it will be more so.

I do want to take a little bit of license, as I usually do, with the topic. The issue I want to address is bringing academia back to the table, because I would say the academic medical centers, by in large, have been asleep at the wheel for the last 15 to 20 years in terms of human therapeutics.

I'm just going to briefly mention two programs that are already funded and underway. Hugh Tilson is going to talk more about the Centers for Education and Research on Therapeutics, or the CERTs Program, that both Duke and UNC are very involved in. But I think this is an example of leveraging, bringing together academia, FDA, NIH and the medical products industry to work on issues that are in the public interest related to knowledge about human therapeutics and how products are used and assessing safety and efficacy. And Hugh will say more about that later.

The second one that we're going to have a bit of discussion about tomorrow, actually, is something

I'm very excited about. It's the concept of working with devices, which tend to get left out, by the way, in these kind of discussions. And, as I've learned in the research project, the device industry is 60 billion a year globally, the drug industry is 82 billion. They're not that different in terms of the overall scope of activity.

I've been concerned that the profession, the medical profession, has not been very involved in taking responsibility for evaluation of the usefulness of devices and their safety. And we've recently embarked on a program together with the FDA and the Society of Thoracic Surgeons. Professionals, particularly those who put in high-risk devices, now have to keep data to protect themselves professionally and hopefully increasingly in the future to develop quality improvement approaches to putting in devices better and having better technical proficiency. So data are being collected about devices in the process of doing particularly what surgeons do.

And so we now have a project to look at trans-myocardial laser revascularization. And this could be, obviously, applied pre-marketing as well as post-marketing. In this particular case, it will be post-marketing to use the STS Registry, which has the implantation devices and could easily have follow up built in as a natural part of the professional activity of the surgeons who put the devices in. This gives us a wonderful way to reduce the tremendous cost of both pre-marketing registries that are frequent in the device world and post-marketing surveillance. And as more physician groups become activated to collect data, like the American College of Cardiology, the Society of Otolaryngologists that we are now working with, I think it's a great opportunity to leverage.

And, finally, the area that I'm most passionate about is how do we teach medical professionals of all types, including those who are

reviewing for the FDA to understand quantitative things. And here I think we have just not done a good job as medical schools.

It's important to recognize that everybody practices medicine or other health care providers, almost 100 percent, go through one of 125 academic medical centers at some point in their career. You know, if you look at our curricula in terms of human therapeutics, it's pitiful. It's really almost not existent. Janet Woodcock and I have worked together for years and we have commiserated about this on multiple occasions.

So what I would like to see is an effort by the FDA and academia to work together on several fronts. One would be to develop a good exchange program between the FDA and academia. Because there is no better place to learn about clinical trials than listening to all the supplicants coming to the FDA with their ideas and schemes, and good trials and bad trials. You really learn it there.

And then, finally, I would really like to see a joint curriculum developed in human therapeutics that would focus on the quantitative aspects that practitioners need to know, but that those who review the literature need to know. I believe there is a body of knowledge within the FDA which is right now unexploited. There's a tremendous body of knowledge in academia, which is mostly suppressed by our previous habits of not being interested in therapeutics. That if there was a national emphasis on this, I think we could develop a tremendous curriculum that would transform the way clinicians think about their practices. As we have gone through (torglozone) and (cissipride) and other recent experiences, the absence of ability to even respond to package inserts and letters from the FDA to change practice patterns, I think is evidence that we're not doing a good job of just bread-and-butter training of those who

practice medicine about how to use medical products and how to think about their use.

MR. BARNETT: Thank you. I think I'll ask the lady who is recording this to strike the word "supplicants" and insert "applicants." I like it.

DR. HENNEY: Changing the record?

DR. CALIFF: I've been on both sides of this.

MR. BARNETT: Well, massaging it.

Anyway, our next speaker is Mr. Lee Evans of the SAS Institute. Mr. Evans, are you here?

MR. EVANS: Thank you. My name is Lee Evans. And, on behalf of SAS Institute, which is a global software company headquartered right down the road here in North Carolina, I would like to thank Dr. Henney and her colleagues from the Agency for this opportunity to discuss collaboration to benefit the public health.

As you know, FDA has eliminated literally tons of paper now that it receives electronic submissions. For the first time, data is part of a submission. And SAS Institute has worked closely with the Agency to adopt a submissions standard for data transfer formats. These are important steps in moving toward more efficient data-driven decision-making at the Agency. But we feel that there is room for additional improvement in regulatory information management. Existing technologies offer opportunities to improve the quality and usefulness of electronic data at the Agency.

And, as each of you well know, quality regulatory review depends on quality data. The systems to properly deploy that data to audit, review and analyze submissions are vital to proper regulatory decisions.

SAS Institute recommends a partnership with FDA to build a conceptual model for the optimal use of regulatory submissions data. We further propose a regulatory data sciences laboratory at SAS Institute, with

a replicate pilot laboratory at Food and Drug Administration, to demonstrate and validate that conceptual model with the Agency.

First, let me talk about what our two organizations could do together in this collaboration. Together, we can develop a conceptual model, which is based on good medical, statistical and computer science. The focus of the laboratory would be a framework to reliably serve standardized, analysis-ready data to support regulatory reviewers and their electronic tool set. It will utilize available metadata standards for research data warehousing through electronic portals to support data transfer, review, integration, control and familiarity at the FDA. The conceptual model is tested in the FDA/SAS collaborative laboratory to evaluate the human factors as well as the technical design of the system.

Now, how can FDA and SAS, together with stakeholders, make this partnership happen? We propose to unify data technology experts from SAS with regulatory experts from FDA to develop the conceptual model. These experts can collaborate using SAS Institute's physical facilities, hardware and software, and using our technical expertise to staff the data sciences laboratory.

We feel that this collaboration would have a number of benefits for stakeholders. The quality of data-driven review and decisions would be assured. Reviewers would have transparent access to analysis-ready data within and across submissions to make decisions to improve the public health. The mission of the Agency, therefore, is enhanced.

Secondly, the industry would get a clear understanding of a common data framework, an open framework, that will be used at FDA to deploy their submissions data to the review divisions.

My company, SAS Institute, and others like us would have an opportunity to better serve our important customer, the United States Food and Drug Administration, and leverage opportunities for joint education and cooperation between technology employees and FDA people to build better technology solutions.

In summary then, FDA and SAS Institute should collaborate on a conceptual model for submission data and demonstrate and refine that model in a controlled laboratory environment. FDA and SAS Institute people can make this happen by using our respective skill sets. The partnership will truly benefit the public health through better processes for electronic data review.

We propose to meet with the appropriate people at the Agency to plan our collaboration on the data submission model and the data sciences laboratory as soon as possible. SAS Institute, as a leading supplier of analytical software systems for the FDA, stands ready to take action on this matter, and we would appreciate your attention to this matter.

MR. BARNETT: Thank you.

Is Mr. Arthur Holden here? Yes? Mr. Holden, you're next. You might say where you're from as well.

MR. HOLDEN: Thank you very much for the opportunity to provide commentary. My name is Arthur Holden, and I am Chairman and CEO of something called the SNP Consortium. The SNP Consortium, which stands for singular nucleotide polymorphism, which is a genetic term I will come back to, is a non-profit consortium of 14 major pharmaceutical and information technology companies, along with the Wellcome Trust, which is the largest private foundation funding genomic and genetic research in a unique, two-year collaboration to complete a genome wide map of SNPs.

Our mission is to advance the field of human medicine and the development of genetic-based diagnostics and therapeutics through the creation of a high-density SNP map of the human genome. Our goal is very simple: By early 2001, we will have developed a standardized SNP map of between two hundred and three hundred thousand SNPs that will be placed in the public domain. All parties will have access to these data free of charge.

The Consortium believes this map will play a major role in supporting the development of pharmacogenomics and pharmacogenetics. In short, brief background, pharmacogenomics focuses on defining the relationship between genes and genetic markers and diseases in clinical conditions. Pharmacogenetics focuses on understanding an individual's genetics and their specific response to a specific drug.

The TSC is a working model of the type of collaboration you wish to define in this forum. We are a blend of diverse complementary parties focused on a clear and elevating objective. Our funding comes solely from our membership. And this support is an expression of the desire of all our members to see basic genetic information in the public domain, freely available to all researchers, unencumbered by patents.

I would like to make comments on three specific collaborative opportunities that could exist between the FDA and the SNP Consortium:

First. Joint education forums on pharmacogenetics and pharmacogenomicss for the FDA and the life sciences pharmaceutical industry. As everyone knows, the genomics and genetics fields are progressing very rapidly. It is clear form our members' interactions to date with the FDA that there are significant opportunities for key stakeholders to be educated on the current state of the genomics and genetics and, together,

to understand their prospects and the promise of applying genetics to the development of prescription drugs. Common definitions, a mutual understanding of the science is required if government and the private sectors are to effectively collaborate. A regular series of jointly organized and sponsored educational forums could meet this need.

Secondly. The use of pharmacogenetics to improve safety assurance in clinical trials: Pharmacogenetics should enable the doctor to use an individual patient's specific response profile to predict a patient's likely response to a particular drug that may be prescribed. Pharmacogenetics also holds significant promise also to streamline the drug development process and facilitate the development and targeting of medications to those patients who would most likely benefit and unlikely to experience adverse events, and to enable more effective post-approval surveillance of drugs. The FDA could collaborate with the life science and pharmaceutical industry through the SNP Consortium in two areas of pharmacogenetics.

First, the definition and development of effective protocols for clinical studies utilizing genetic markers or alleles for the development of new, safe medications.

Secondly, the definition and development of effective protocols for extensive regulated post-approval surveillance systems using genetic markers to better profile patient response and adverse events after a drug is launched.

Collaboration would focus on jointly and proactively defining with the FDA protocols that will serve both of these important activities.

And then, lastly, which I think addresses the fifth area that you wanted to focus on is what's called genotyping of genetic markers for pharmacogenetics.

Robust, cost-effective genotyping capability that will effectively characterize an array of genetic markers is absolutely essential to the development of pharmacogenetics and pharmacogenomics. Over the next six months, the SNP Consortium, in conjunction with the NIH, will be working collaboratively to define the user requirements, both for industry and large-scale academic researchers, for these types of systems. The FDA could participate in this critical study.

Thank you.

MR. BARNETT: Thank you. Before we go on, I might mention to the folks who are sitting in the back that there are three television monitors back there that you might find convenient. You can actually see the front of the guest speakers' heads instead of just the back if you just look at those monitors.

Before we go to the next one, let me ask the folks on the panel, the FDA people and the non-FDA people on the panel here, if they would like to respond to what they've heard so far with questions or comments? Anyone up here want to jump in? Okay?

DR. WOODCOCK: I don't really have a question. I would just like to say that all three of these areas really do bear great promise, I think, for collaboration, and they're all related, actually. In fact, and, as far as pharmacogenomics and genetics go, it is my opinion that, unless we obtain some of the clinical community like Bob Califf is talking about, we will not be able to translate the fruits of that research into effective patient care. Because we must have an informed clinical community ready to utilize that knowledge. And we probably aren't there yet.

As far as the data, of course we have been extremely interested, and we are moving along in accepting electronic data. And standardization is clearly the next step, I think. And Dr. Califf made some comment

on this. It may help not only the FDA and the submitters of the data, but the whole clinical community, in fact, to have these data is available in analyzable form.

MR. BARNETT: Anyone else? Dr. Henney?

DR. HENNEY: I guess the only question, and maybe it's a comment, for Dr. Califf, and perhaps you would want to follow up in writing, but your first suggestion in terms of a joint effort between medical schools and the Agency. I think, if anybody knows the trick to how to crack the curriculum committee, I would appreciate that suggestion being sent in, having worked at a couple of academic medical centers in my lifetime.

But I think that you are absolutely right on target in terms of the proper use of therapeutics. We have to really look at not only our programs of outreach to help patients and consumers how to use medicines more wisely, but to inform health professionals in training and in the disciplines of the practice of medicine, particularly as our medications are becoming much more complex and much trickier to use.

So I would encourage any insight you have into that curriculum-committee cracking that we could do.

DR. CALIFF: Well, now you've been a Dean and I haven't, so ---

DR. HENNEY: That's why I'm speaking from experience.

DR. CALIFF: And after years of struggling with this in what I consider to be a relatively enlightened academic medical center, I think this is so much bigger than any individual AMC to overcome this sort petty resistance to really dealing with human therapeutics that exists in medical schools. I think it's going to take, frankly, in the true sense of the word leveraging, it's going to take federal agencies saying, "This really needs to happen."

Hugh is going to talk about CERTS about drug-drug interactions and the fact that most of us can't even interpret drug-drug interactions now, even those of us who deal with it every day and are in practice. So tremendous things need to be done. And it's going to take a group of AMCs and, I think, something like the FDA saying, "This really has to be done" and the public saying, "We want doctors who know how to write a prescription so it makes sense."

I would also comment on Dr. Woodcock's comment and Lee Evans' here. Nomenclature is absolutely critical to this. Not just standards of data transmission. But, if we have 130 different definitions for unstable angina, as we currently have, it doesn't matter how well you transfer the data, we still don't know what we have at the other end. And I would argue that the NIH, the FDA, outcomes researchers and managed care organizations all have in common that we call the same phenomenon the same thing, we would be able to improve practice and get better drugs on the market.

MR. BARNETT: Thank you.

Dr. Feigal?

DR. FEIGAL: Just one comment that I would like to make about particularly some of the efforts that focus on being able to automate data and standardize data. It is that it's often easiest to begin with the process that served us well last year or five years ago. And the challenge of thinking about where we're going with pharmacogenomics and SNPs where having a diagnostic tool, that instead of telling us a single piece of information, may give us an array of information, some of which may be well established and easy to interpret. And the other may be totally exploratory.

How we can think about that as clinicians, let alone as regulators, let alone think about what our data needs would be to serve that and whether or not it's a

fixed and static process. So I think I applaud where we're beginning and we need to look ahead to where we want to go at the same time.

MR. BARNETT: Any other responses?

(No response.)

ASSURING INDUSTRY COMPLANCE WITH SAFETY REGULATIONS – GENE THERAPY, HUMAN CELLULAR and TISSUES-BASED PRODUCTS

MR. BARNETT: If not, let's go on to the second of the five items, which is Assuring Industry Compliance with Safety Regulations, particularly with Gene Therapy and products that are based on Human Cellular and Tissues, cells and tissues.

Our first speaker there is Ms. Mary Rose Tully. She's with the Human Milk Banking Association of North America.

MS. TULLY: I thank you very much for letting me be part of this program today. And I'm going to start to take off to a very direct clinical application in ways that the other speakers have not.

There appears to be an increasing need for federal oversight of donor human milk-banking, as witnessed by current concern expressed at USDA over use of donor human milk banks for providing to WIC recipients. And there have also been a few random attempts by breast-feeding mothers to give away or sell their milk on the Internet and in different communities. With this need in mind and given the fact that the Human Milk Banking Association has developed guidelines under which member banks have operated since 1991, a collaborative effort between the FDA and HMBANA to set federal guidelines is an ideal leveraging opportunity for consumer safety.

The FDA staff have regularly given input into the development and updating of the *Guidelines* since 1987. From 1987 until 1990 when the initial guidelines were finally completed, two FDA staff members—John Wallingford of the Clinical Nutrition Branch Center for Food Safety; and James Weixel of the Consumer Safety Office—reviewed each draft of the guidelines. Dr. Wallingford even found funding for testing of the milk-processing procedure to ascertain that it would both destroy HIV and minimize damage to the unique immunologic and nutritional complements of human milk. Both of the men continued to advise HMBANA until they left the FDA. Since that time we haven't had very good collaboration.

Dr. Edgar Marcuse also reviewed the initial *Guidelines* as a representative of the American Academy of Pediatrics Committee on Infectious Disease Disease.

Since 1990, the *Guidelines* have been updated annually, and you have before you the 1999 edition. The six U.S. milk banks and one Canadian milk bank will be meeting again the first of May to review the *Guidelines* in light of new blood-banking and other medical information that's come out in the last year.

In 1991, HMBANA sent a representative to the Tissue and Organ Transplantation Regulation hearing, and she was one of the authors of the final document *U.S. Public Health Guidelines for Prevention of Transmission of HIV through Transplantation of Human Tissue and Organs.* These guidelines have been incorporated into HMBANA's guidelines were applicable.

HMBANA's guidelines include verbal and written questionnaires, which are closely patterned after blood banking screening forms, with a few additional questions. For example, our potential donors are asked about smoking and alcohol consumption. And we also require a written statement from both the donor and the

donor's child's physician that this person is an appropriate donor.

A little background on donor milk banking in the U.S. might give you some perspective on the issues involved. There are currently six (6) milk banks operating in the country. Four (4) of us are in tertiary medical centers and two (2) are freestanding, non-profits associated with tertiary medical centers. The oldest milk bank is located at Christiana Hospital in Delaware. It has been operating since 1943 continuously and with great success. And the newest bank opened in Austin, Texas, last year as a collaborative effort among three tertiary medical centers.

All the milk is donated. There is no payment to donors. We operate very similarly to Red Cross blood banks. Milk is only dispensed to a hospital or on physician order to an individual recipient. Recipients are charged a processing fee to help defray the cost, but they are not paying for the milk. And, as with other health care, no recipient is denied because of lack of ability to pay.

Obviously, with so few clinical facilities, the need for donor milk across the country is met through a collaborative effort. This alone has motivated member banks to agree on both donor procedures and milk processing procedures. An additional reason for FDA recognition of the guidelines is the necessity to ship milk across state lines. We in North Carolina supply milk to babies all over the country.

The States of California and New York have licensing requirements by statute for milk banks. California is the only state that actually has a milk bank that they have licensed under their statutes. New York does have one milk bank as an in-house research facility, but it doesn't operate as a distributing milk bank.

With the increased recognition in the literature of the superiority of human milk for human infants, especially for pre-term and sick infants, other tertiary level hospitals around the country are considering opening donor milk banks. Some are also negotiating to become satellite banks, which will serve as collection depots and also dispensaries for pre-existing milk banks.

In 1999, among the six milk banks, approximately 200,000 ounces of milk were processed and distributed. To give you some comparison, in the Country of Germany, about 196,000 ounces—they gave me the number in liters, I had to figure it out.

MR. BARNETT: I want to remind you about the guidance.

MS. TULLY: Okay. The last thing that I would like to say is that where I think HMBANA has done a very good job of setting up standards and the FDA has given us a lot of guidance up until now, all of our milk banks are operating in a very good safe manner, I think that this collaboration would establish standards across the country that would make more clinicians feel comfortable with the milk and assure a safe product.

MR. BARNETT: Thank you.

Any response by the panel?

DR. HENNEY: I did just want to let you know that we have been in contact with the Undersecretary of the USDA who runs the WIC Program who, I believe has had some fairly recent conversations on this topic with Janice (Albert), who is our Deputy in the Center for Foods, who I think is well aware of these issues. And I'm sure that your organization will be party to those discussions as well.

PATIENT/CONSUMER EDUCATION on the SAFE USE of PRODUCTS – RISK MANAGEMENT

MR. BARNETT: Thank you.

Okay. Let's go on to the next issue. And that is educating patients and consumers on the safe use of products. And we have several speakers there. The first is Dr. Peter Kussin of the Duke University Medical Center. Is Dr. Kussin here?

DR. CALIFF: I know him well, and I don't see him on this panel.

MR. BARNETT: All right. Dr. Elizabeth Brooks?

(No response.)

MR. BARNETT: Dr. William McCready?

DR. McCREADY: Yes, sir. He's here.

DR. HENNEY: You don't get to take their time.

DR. McCREADY: No, no. And, although I'm from Chicago, you'll notice I didn't even ask. I'm trying to behave myself today.

I'm Bill McCready, and I'm currently on leave from my university working in Stanford with a start-up company called InterSurvey out in Menlo Park. As far as I know, I am the oldest Midwesterner actually working for a start-up company in California. I have been told that they needed an adult, therefore --- I was on leave. But I am not going to write a book about my experience, however.

InterSurvey is trying to create and has indeed created, I think, a facility that I wanted to bring to the attention of the panel, and that is why I got involved in this conversation.

Doing surveys over the Internet has become something more popular lately, but all of the companies doing it are doing it without any sampling. They are not samples at all, they are what I refer to as BOP's, bunches

of people. It's the same thing as if you stood on the street corner and said, "Please do my survey."

What we did was create the sample first. We did a traditional random-digit dialing telephone sample and, in those households, we then placed an Internet device, and we provide free ISP service. So the respondent gets to use the WEB and mail, et, cetera, and, in return, they do about one, ten-minute survey a week. And the sample runs through the household. Everybody over 14 gets their own e-mail, et cetera.

In effect, what we've done is create a random sample of American households that are available through the Internet. We can download questionnaires to them, videos, sound, et cetera. We are up to about 25 or 30,000 households at the moment, and we're heading for 100,000 households by the end of the year and 250 by the end of next year. So this is a very large panel, in effect. Remember that word.

The work that I would bring to the panel's attention are evaluation studies that we are doing right now for the U.S. Census. The Census mobilization effort is being tried in lots of different places. We're doing a project that allows us to test and evaluate the efficacy of education messages. That's not very far away from what the FDA wants to do on many cases. Test education messages with sub populations. There's no screening cost on the sample because we've got them pre-screened. We now have 2,000 minority households in this sample, because that's the number in the case, and we can screen them on any issues that we need to.

The rapidity of the response, in effect, what the company has really done is broken the link between case size and field time. We can field five cases or 50,000 cases at exactly the same time. We just did a small study for NSF on the Elian Gonzalez issue. It was a time, one-time-time-two, study originated by a professor.

They got the funding last Monday or so. The program officer called on Friday and said, “It’s already breaking. We’re sorry. The father is coming. The time line has changed. I guess we better pull the funding.” And the professor said, “I’m sorry, we’ve already collected the data.” And he said, “Well, what do you mean? We just gave you the money on Tuesday.” And she said, “I know. We fielded it on Thursday and had all the data the next day.” We had 600 cases the next morning. Partly because people were interested. But that’s a 78 percent response rate, which is not bad.

So this is very different than what we think of or what people think of in terms of Internet surveys. This is really a traditional sample survey being done over the Internet.

Our research partners involve currently people at RTI, down the road, and we come from an academic setting. The company was founded by Stanford as a partner of ours.

What we are interested in doing in terms of leveraging is taking this facility and making it available for primarily not-for-profit government work, foundation work, et cetera. As I said, the Census project is right now one of our largest projects. We’re doing a big project for the University of Pennsylvania. We’ve done several NSF projects as well.

The possibilities also are to create sufferer panels. We can do prospective sufferer panels. We can also—we’ve thought about this on occasion—do conditional sufferer panels where as our panelists, imagine we have 100,000 households out there and we say, “If somebody in the household gets a diagnostic screening of diabetes or something else,” pop up, and we can tell very quickly what’s going on so we can monitor the panel.

This is a new facility. I think it's going to change the face of survey search. I've been in the survey search business since I don't know when, 30 years or more. And I did my training and a good deal of my work in 20 years at the National Opinion Research Center at the University of Chicago. And this is perhaps the most revolutionary thing I've seen come down the road.

And what I'm suggesting is that, one, there's immense leveraging possibilities. But the nice thing is, unlike most so-called Internet companies, we actually are already doing it. The Census didn't hire us because they thought we could do it. We're actually running those cases. And we're actually doing the NSF work. We're actually doing the University of Pennsylvania work. So I think it's an exciting opportunity, and I wanted to bring it to your attention.

Thank you.

MR. BARNETT: Thank you. We'll come back and get some responses after we do the rest of the group.

Mr. Anderson?

MR. ANDERSON: Yes. Thank you for the opportunity of testifying today.

I'm Holt Anderson, and I represent the North Carolina Health Care Information and Communication Alliance. We are a unique 501(c)(3) made up of a very broad membership of over 150 organizations, including providers, academic medical centers, among those, health plans, professional societies and associations, pharmaceutical research, academic medical research, contract research, technology and communications vendors and State and Federal agencies.

Our primary focus is on the implementation of standardized secure information and communications technology to improve the delivery and the efficiency of health care. Currently, there are projects underway to

deal with the secure use of the Internet to gather, transmit and provide access to sensitive health information in standard formats.

NCHICA has been dealing with the development and use of registries for a number of years, including secure Internet access to immunization records and the electronic collection of standardized emergency department information for community assessment and best-practice development. And that's done with the CDC.

NCHICA is part of a five-state consortium developing secure Internet, or PKI technology, procedures and best practices for application in health care. These efforts are funded by a multi-year grant from the Robert Wood Johnson Foundation.

NCHICA has been a leader in the area of public policy development for privacy, confidentiality and security of health information for over five years and are deeply involved in figuring out how to implement (HIPPA) and the transactions, administrative simplification part of (HIPPA).

The professional societies that are members of NCHICA, including medical societies, Hospital Association, Nurses' Association, Association of Pharmacists, local health directors, have adopted a common vision, and each of them have adopted it as policy of paperless, person-centered health records by the Year 2010. And a fundamental principle included within that resolution is that **"…prompt access to complete and accurate information will improve the quality of care through the communication of patient wishes and the prevention of mishaps related to drug interactions, allergies, transmissible diseases, et cetera.**

What we propose is that there's an opportunity here to undertake discussions with the FDA

to lead to a strong collaboration to develop an understanding of the policies, practices and the technology, which is a small part of this, and the implementation issues that will enable the secure monitoring and reporting of adverse events and the improvement of care consistent with the vision and mission of our organization.

Thank you.

MR. BARNETT: Thank you.

And, Dr. Veronica Scott?

DR. SCOTT: I would like to say good afternoon and thank you for allowing me to speak today. I am a geritrician, a physician educator from Nashville, Tennessee.

I feel that there is a need to educate older adults, patients and consumers on the safe use of products. Areas of education would be primary, secondary, and tertiary prevention of public health conditions that are responsible for most of the morbidity and mortality in this country, particularly among older adults. I think that this education needs to address gender-specific issues as well as overlapping gender issues. For example, pharmacokinetic handling of medications differ across genders, and I think that patients and consumers need to be made better aware of those medications and where those differences exist.

Some of the issues for education are gender neutral. For example, educating older adults in certain preventions, as in diabetes management, cardiovascular risk profiling and similar. I think that the education needs to take into consideration the geographic diversity in this country, particularly rural versus urban settings. The differences have distinct issues relative to access, and I think that patients and consumers need educating in these areas. For example, supply and distribution of certain services affect travel time, availability,

appropriateness and cost of certain services. And I think patients and consumers need to be made better aware of these.

In addition, pyscho-cultural barriers that can be directed by both the buyers and consumers, because of their values and belief systems, need to be addressed. I think that if consumers are better educated in these areas, that they better combat or address the problems. They can become more participatory in bringing about change in their communities.

I think that the education needs to address the ethnic diversity in the population. Again, with medication use, we know that there are different mechanisms of drug handling across ethnic groups, and I think that the public needs to be made better aware of this.

So, to collaborate, I think then that we can do one of three things, or all three things:

We can use existing networks of national programs, especially those that are federally funded, to provide the consumer education. An example of some of those programs are the VA's Geriatric Research Education Clinical Centers, there are 20 of those in the country and more then 40 Geriatric Education Centers, and the more than 20 Bureau of Health Professions Rural Inter-disciplinary Training Programs. These are all based in academic institutions. These are educators who were funded to provide education, and these can become, I think, legitimate vehicles of information dissemination.

In addition, particularly for special populations, I think we need to use more historically black colleges and universities, Hispanic colleges and universities, American Indian colleges and universities, Asian colleges and universities--these have been identified in the country--as well as organizations that particularly target these groups so that the special

avenues to reach these special populations can be used as well as perhaps better identifying how best to deliver the consumer education.

I think that FDA, actually, can make available its databases to these educators and/or provide staff as consultants so that the best and most up-to-date evidence-based information can be provided to the consumer.

And then we can use the WEB in more effective ways. For example, there is a new WEB site about to be launched on May 1st that's called "Minorityinterests.com" where educators or those who want to write for consumers are invited to write evidence-based material for consumers. And I think that these are three strategies that we can consider for better collaboration.

Thank you.

MR. BARNETT: Thank you. And now let me turn to the Panel and ask if there are any responses, questions, comments to the things we've learned in this section on education of the patient and the consumer. Yes?

DR. BUCHANAN: This is a comment directed toward Dr. McCready. One of the critical needs we have in executing risk assessments is the ability, at least in the foods area, to get an understanding of how the consumers differ in their practices in the home. I can see great potential for the approach you're doing to greatly accelerate and to increase the accuracy of that kind of activity. I know we've attempted to do this in conjunction with our partner JIFSAN in the development of a risk assessment clearinghouse. And the approach you're taking sounds like it could be extremely beneficial if it could be modified to find out more about what consumers do.

DR. McCREADY: One of the things that we think has some utility is this will be a magnification or an amplification or an improvement on the old traditional diary systems which are fairly intrusive. One of the reasons our panelists stay with us and like this experience is nobody calls them during their dinner hour, and they don't have to fill out anything. They actually respond to surveys, at the moment, on their television. I mean, that's where it appears.

And the thing that I was fascinated by is every one that we've done so far, we're getting a slightly larger proportion of male respondents than female respondents, which is absolutely unheard of in telephone surveys. And we finally figured out the reason, it's a human factor, guys like the remote. So they're more likely to use it. So we get a much better balanced gender finding.

MR. BARNETT: Do they flip around a lot? Yes?

DR. SCHWETZ: Also a question for Dr. McCready. I assume the responses can be stratified by age and by sex and by other preference kinds of categories?

DR. McCREADY: Yes. One of the nice things about it is, remember, it's a panel set. So everybody downstream gets the panel data from upstream. So the nice thing is you're not burdening the respondent by asking the same response a bunch of times. You get the demographics up front, which we do, and then we can sort by all demographics and they never have to do it again, unless of course it changes, their age changes, et cetera.

MR. BARNETT: Yes?

DR. WOODCOCK: This is for Mr. Anderson. You just sort of glanced on adverse reactions

and how you might be able to provide data. Could you elaborate a little bit on that?

MR. ANDERSON: Yes. As we've worked through a lot of the privacy and confidentiality issues in working with sensitive information, in working with clinicians and other providers, they recognize the need to have adverse event reporting. But the concern about liability is a great driver. We need to find ways to not drive people underground, but to have that reported in an anonymous enough way that it doesn't necessarily go back and affect them directly, so we can develop best practices. So how do we use technology to gather that information in a useful format and really get people to come forward with it. I think that's one of the areas that we would like to explore.

DR. WOODCOCK: Okay. Thank you.

INSPECTIONS – INTERNET

MR. BARNETT: Let's go to the next group, which is Inspections, particularly having to do with the Internet. And Mr. John Mack of Internet Healthcare Coalition is here.

MR. MACK: Thank you for inviting me today. Aside from being the President of the Internet Healthcare Coalition, my real job is Director of Drug Information with Mediconsult and site manager for PharmInfonet, major consumer and healthcare professional WEB sites on the Internet.

The Internet Healthcare Coalition is an international, non-profit and non-partisan organization dedicated to identifying and promoting credible health information and resources on the Internet. We are actually not an organization that is a front for the industry or from any one particularl interest group. We are actually a membership type of coalition that consists of over 500

individuals, not organizations. And we actually were formed as a result of one of the public hearings the FDA held in 1996 where you were trying to determine how to regulate the pharmaceutical industry on the Internet. And I thought some of the principles that were talked about there were applicable to all WEB sites on the Internet.

Our membership represents every sector of the Internet healthcare space worldwide, including consumers, providers of healthcare information, government representatives. We do have an official liaison with the FDA. We also represent academic institutions and so on.

The Coalition is focused on educating healthcare consumers and professionals about the evolving issues relating to the quality of Internet health information. As a part of our ongoing educational campaign, we've developed, for example, tips for health consumers finding quality health information on the Internet. And we've also launched an e-health ethics initiative and developed a draft set of ethical principals which can been seen on our WEB site. Our tips have appeared in major national newspapers, like The Wall Street Journal and in books like The Complete Idiots Guide to Online Medical Resources. So it's really written at a very basic level that most people can understand.

And, actually, the tips have been featured in an Eckerd Every Day public service announcement. And that's part of what I want to propose to leverage what we can do with the FDA's campaign regarding the sale of pharmaceutical products through the Internet. For example, I'd like to develop, the Coalition would like to develop, tips for helping consumers on purchasing drugs and medical supplies on the Internet.

My site, actually I just discovered yesterday, is linked to by a Mexican drug site that uses my information on my WEB site to claim to be their

information. And they are actually selling drugs. We don't sell drugs. And I want to stop things like that.

So one way would be to put these tips right on that page that they're linking to us and put the FDA on that page as well so people that link over. That page gets hit about 100,000 times a day by people looking for drug information. So we can help. That would involve my company, which is Mediconsult, but the Coalition does work with companies, like Eckerd, who want to provide this kind of information in a credible way. They don't want to develop the tips themselves because that would not be credible. So we've given them permission to use our tips under certain circumstances.

We also would like to work with the FDA in our other educational activities. Every year we do a conference called The Quality Health Information on the Net Conference in the fall. And I think we've had some FDA participation in that conference in the past. You get over 600 attendees to this conference. This year we're going to be in Las Vegas and we're going to be focusing a lot on ethics. Our goal is actually to get more West Coast participation, and it's a long story of how we got to Vegas, but we'll se what happens.

We would also like to develop a part of our WEB site to help consumers report not only health fraud, but companies like this Mexican company trying to sell products and working unethically. We have been working with the FTC in a similar proposal to develop a global health fraud reporting WEB site. So we would like to work with the FDA to try to leverage the reporting of unethical and illegal sale of products on the Internet.

And, finally, we would like to have some kind of way to keep our members informed about FDA actions relating to the quality of health information and services on the Internet. And we have an e-mail newsletter

reaching our constituents, and we can work with the FDA in that capacity as well.

Thank you.

MR. BARNETT: Thank you. You talked about that Mexican drug seller – you're sure it wasn't a Colombian drug seller?

Okay. Let's have some response, if there's any, from the panel for these two on the Internet.

DR. MARZILLI: Of course the Internet is an incredible resource in terms of information and also misinformation. We've worked closely with the Federal Trade Commission and also with the States Attorneys General. Are you working with them as well in terms of ---

MR. MACK: Right. That was the basis of our collaboration on what was called the (Munch) project or something like that?

DR. MARZILLI: Yes. I think.

MR. MACK: Yes. The FBI is also involved in this health fraud reporting system whereby, hopefully, we can feed into the law enforcement database so that they can follow up on complaints that they receive through the Internet.

DR. MARZILLI: Yes. That's excellent. And the (Munch) Project also involves the governments of Mexico and Canada as well, because, you know, the lines go internationally as well as it's a great use of resources. Thanks.

MR. BARNETT: Dr. Feigal?

DR. FEIGAL: One of the challenges for medical devices is that there's no reference like a PDR that has a collection of labeling. The devices are often designed to be cleaned and reused and repackaged and shipped out, but where do the instructions go? And one of the things we've wondered is whether or not the Internet can step into that breach, and how to do that, given that there are six or seven thousand device

manufacturers and tens of thousands of device types. But if there's a technology that's up for it, it's probably the Net.

And the leveraging that we've wondered about is sort of how to tie our own news about devices and approvals and safety and reporting mechanisms with company or neutral party sites where part of how we would allow the use of our good name, if you will, to be linked to it would be some agreement with the quality of the information would have to be in the other areas. And that would leverage a little bit in the way of getting some consumer confidence in that quality of information in multiple sites.

So I think there's areas that are very interesting to explore, particularly in the products that could turn over very rapidly and the hard-to-find information.

MR. BARNETT: Any other response to this one?

(No response.)

MR. BARNETT: Okay. We also have Dr. Jim Jarrett of the emerging Association of Bovine Practitioners to talk about a similar issue. Doctor?

DR. JARRETT: Thank you. First of all, for those watching on monitors, I can assure you that the view from the front is no better than the one from the rear. And, hopefully, for my sake, there are no remotes in the audience.

My name is Jim Jarrett, I'm a veterinarian. And my current day job is the Executive Vice President of the American Association of Bovine Practitioners. However, I have spent the majority of the last 35 years in a private dairy practice specializing in dairy production medicine.

The AABP is an organization of almost 6,000 veterinarians interested in cattle medicine. Most of our members are self-employed private practitioners. The

primary mission of the AABP is to provide continuing education and other pertinent information to our members. The information is provided and transferred in such ways as print media and electronic transmissions. Electronically, we communicate by e-mail, through members-only list-serve and with an Internet WEB page, AABP.org.

Like other professionals who depend on technology, we need current information in order to assist the cattle industry, both dairy and beef, to continue to supply safe and wholesome foods for the consumer and to prevent and relieve animal suffering. Examples of the information we need and use would be included in such things as product labels and other public information developed by the FDA Center for Veterinary Medicine in the area of veterinary therapeutics and information like that contained in the anti-microbial use data base currently being developed by personnel at the Iowa State and at least two additional veterinary colleges around the country. Funding for the database development has been provided by the American Association of Bovine Practitioners, the American Association of Swine Practitioners and the Veterinary Medical Association.

Public funds added to those provided by these organizations would insure that this project is completed as soon as possible and the information made available to practicing veterinarians and anyone else interested in maintaining the health of the nation's cattle herds and insuring the continued safety of the foods they produce. This data base information will help to insure the judicious use of anti-microbials and thereby reduce the possibility of anti-microbial resistance.

The Internet has become, as already alluded to, a useful and valuable tool in the transfer of information. Through its use information such as I've described could

easily be transmitted to practicing veterinarians and others.

With this in mind, I would urge the FDA Center of Veterinary Medicine continue to support the data base development at Iowa State and develop ways to use the Internet to provide important information to bovine practitioners and other interested parties. With this information and other efforts, we, the cattle industry of the U.S., can continue to supply safe and wholesome foods of animal origin to the consumer. The American Association of Bovine Practitioners is ready to partner with the FDACVM in these efforts.

And I think you for the opportunity to be here.

MR. BARNETT: Thank you, sir. Any comments here?

DR. MITCHELL: I would respond that we are aware of the database that's being developed at Iowa State and have a grant proposal actually under consideration at the moment.

SAFETY-RELATED RESEARCH – NCTR CHIP TECHNOLOGY

MR. BARNETT: Okay. Thank you. The next group has to do with safety-related research, particularly the NCTR chip technology. And we have two speakers there. The first is Dr. Hugh Tilson of the University of North Carolina School of Public Health. Dr. Tilson?

DR. TILSON: Thank you, sir. And thank you for pointing out that I'm from the University of North Carolina. Sometimes one doesn't say that quite so loudly around the halls of Duke. But I assure you the friendly rivalry enjoyed on the basketball court is not reflected in the kinds of partnerships and synergy we enjoy when it

comes to patients' health and the protection of the public health here. We work together as partners in an extraordinary way. In fact, it stuns me that I'm number ten on this panel and no one has said, "Welcome to Research Triangle Park" and told you a little bit about that as a metaphor for the synergy you're talking about as well. You know that the Triangle is three great cities, well, we won't name them, and several others think that they're great as well, and they're also in the Triangle. Three great universities. Those you know. And there are other ones too.

But also it's a metaphor for the intersect of academia, government and industry, which have collaborated to create this wonderful atmosphere that you're observing here. Truly synergy everywhere. Partnerships, particularly public-private partnerships and government-industry-academic partnerships. We have learned how to work together with mutual respect developing proper arms-length relationships where that's necessary, but helping one another and particularly helping one another with financing when one has and the other does not have the resources to do necessary work.

For example, in the funding of some major pharmaceutical activities, several of the large pharmaceutical companies in the Triangle have helped immensely the universities in the area to get our programs going. The University of North Carolina, for example, with the Glaxo-Wellcome funded program in health outcomes research, which then allows us to do the kinds of arm-length partnering that one needs to do.

I want to thank Rob Califf for giving my talk and, therefore, I'm going to give you my written comments, and I'd rather speak a bit more extemporaneously to be sure that the extraordinary opportunity that Dr. Califf mentioned in the first of his four

major points is clear to you, and perhaps we can have some dialogue about that.

I refer specifically to the Centers for Education and Research and Therapeutics or CERTs for short. There are four such centers funded by the Agency for Healthcare Research and Quality as part of a Federal mandate from The FDA Modernization Act of 1997, itself a tribute a leverage and partnership to get to where we are today. And FDA has worked with the Agency of Healthcare Research and Quality to be sure that CERTs are there for the whole public good and therapeutics and not just for outcomes research or the sorts of things that one or another agency might be interested in.

The Agency for Healthcare Research and Quality did an unusual thing when it funded these four centers. Many government agencies fund centers to build capacity, and this capacity was much needed for education, research and therapeutics. Like Rob, I have a fire burning in my gut for proper education of our current practitioners and getting word out in a way that will change their behavior so that they can act positively on behalf of their patients through smooth, swift product labeling.

But, in addition to creating four excellent centers through Federal money to support an infrastructure around which then leveraging itself could occur, the Agency for Healthcare Research and Quality added a coordinating center—Rob Califf chairs it—and a steering committee to help them to steer the overall affairs of the center to create a true national program and not just for silo centers doing excellent work. That steering committee I have the privilege of chairing and, therefore, I take the liberty of telling you a little bit about it today.

Now, the leverage opportunities here abound. Four (4) excellent centers. One at Duke, and you've heard a bit about that. One at Georgetown with a

particular expertise, very strong expertise, in clinical pharmacology and leadership in the National, the American, Association of Clinical Pharmacology and Therapeutics, pharmacogenomics activities abound there. And so the opportunity to leverage your interests in that area through that center quite clearly.

The University of North Carolina is an interesting CERT because it's co-directed by the Dean of the School of Pharmacy and the School of Public Health. And, therefore, it involves all of the public health issues you've talked about today and many of those happen to be relating to the expertise that pharmacists can bring to the table and here particularly getting education out into a community in an effective way which involves all of the partners in the therapeutic enterprise, particularly relating I think to some of the FDA's initiatives in patient care quality, error reduction and of course for the reduction of adverse reaction. So those are going to be part and parcel of all of the CERTs with particular emphasis at Chapel Hill.

And then, finally, Vanderbilt, which has superb programming in all of the four areas of emphasis of the CERTs: clinical pharmacology, clinical research, pharmacoepidemiology, and patient safety monitoring, and then translational research and translation of the message into effective educational activities. But their particular emphasis is one that I want to be sure you know about and we might talk a bit about. And that is the use of the large automated population-based databases for going beyond individual reporting, for example, adversity or errors where blame and fear and fear of litigation may deter people from doing the right thing, but using databases which record events so we don't have to wait for people to tell us to monitor things that may be going wrong. Or, because they are automated and they're monitoring all events that are occurring in those

populations, can tell us how people are changing their behaviors in accordance with our instructions, directions, warnings and, of course, new opportunities.

So, in summary, the CERTs provide four (4) centers now—there will be more—in these areas of expertise, particularly funded for the core to be sure that we have centers to turn to. And our job now is to build on them with the many efforts that you've initiated in the excellent Commissioner's Report on Risk Management, for example, Population-based Pregnancy, Drug Exposure Monitoring. For example, how would one get multiple pharmaceutical companies to finance a national approach to that, perhaps arms length or separate from the agency? Well, maybe a CERT.

How about building onto the excellent extramural programs on data bases already present in CDER where we contract with HMO data bases and other insurance data bases to monitor for adverse drug reaction? So those are methodologic questions here that need to be pursued. How best to do so. How to be more proactive.

Hospital-based adverse reactions monitoring. How to harness the power of drug information, pharmacy, for example, in hospitals. Well, those are the sorts of questions that this device is, therefore, just waiting for us to build a leverage agenda.

And I point out that FDA is already a part of this. There is a steering committee made up of the four principal investigators, coordinating center director, three Federal agency representatives, one from the National Institutes of Health. We certainly can't leverage much of they do and need in therapeutics, the agency built their Research and Quality. And Peter (Honnig), who provides excellent voice for FDA. And then three large representatives, one from a pharmaceutical company, one from the National Pharmaceutical Council, and one

president of the National Consumers League with myself as chair.

So I give you, colleagues, a wonderful leverage opportunity and look forward to having a chance to pick your brains about how we can work better together.

MR. BARNETT: Thank you. You mentioned my courage in mentioning the University of North Carolina out loud. We're going to bleep it out later. The audio-visual folks here will take care of that.

DR. TILSON: Thank you. I assure you we are grateful to have you here today at the University of North Carolina.

MR. BARNETT: Thank you. Our next speaker is Dr. Samuel Wilson of the National Institute for Environmental Health Scientists. Doctor?

DR. WILSON: Thank you. It's a real pleasure for me to participate in this event. And I, too, would like to welcome our Federal Government colleagues to the Research Triangle Park area, especially colleagues from the Department of Health and Human Services.

Let me just start off by noting that our organizations have extensive scientific overlap. For example, in the area of safety assessment, in the area of drug response, and in the general area of assessment of efficiency of tests in various trials. And, indeed, our organizations have recognized this overlap for many years now, and we have a number of very significant partnerships in place at the present time.

The NIH and, in particular our Institute, NIEHS, we're all working as a team to stimulate capacity-building. That is, growth toward the use of new molecular tools in toxicology, in the area of safety assessment. And I think it's important that we all realize that we have entered a new era of opportunity in the study of proteins

and in the study of nucleic acids. For example, the gene-shift technologies that we've heard so much about and also in the study of messenger RNA expression technology.

These areas represent revolutionary new scientific opportunities for our field and for both of our agencies. There will be major and costly needs in both of these areas. For example, in the area of databases, in the area of risk modeling and risk profiling, and of course in the focused area of dose-response relationships. Partnerships addressing these needs are most appropriate.

As I said, we are just now embarking on new science. And this science truly will change the way we practice medicine in the relatively near term. And it will also change the way we define disease so that disease will be defined by protein marker changes, messenger RNA profile expression changes, and be interpreted in the context of gene-shift results. So, indeed, we are facing a new generation in the practice of medicine and truly a new science.

Preparations, in addition to these areas that I've mentioned that are most appropriate, are in the area of problem definition as we approach this new science and identification of issues, especially ethical issues, issues of communication and education.

Finally, in closing, I think it is very important that we stimulate our partnerships between our respective organizations and continue to collaborate to more effectively translate the new science to impact public health.

Thank you.

MR. BARNETT: Thank you. And let's see if we have some response from the panel on these two?

DR. WOODCOCK: Dr. Tilson, I think the CERTs do offer a tremendous opportunity. Could you

elaborate on your idea for getting better link access for the Agency, perhaps where the Consortium, or what-have-you, to link to databases?

DR. TILSON: Thanks. I should point out that happening right up the street today is the board meeting of the International Society for Pharmacoepidemiology co-sponsored by the UNC CERT, bringing all of the leading international pharmacoepidemiologists to town for a symposium on Friday on better harnessing the power of the large automated linked databases. And one of the things we can do is to talk with each other and reason and work on methods of access. Obviously, it cost money to manage data, and we have a real scarcity of well-trained people who can work in these large databases. It's easy to be fooled and to find associations that are there but for reasons that are other than causality, as you know.

So, one is certainly for us to learn together about best practices. That, the CERT is already doing.

A second is that each of the CERTs will be working with one or more large databases or with one or more other centers. I mean, this needs to be seen as a national program, not four places or not four research activities in four places. So particularly the large database world now allows us to import data from the Province of Saskatchewan into Research Triangle Park, as we do, and analyze drug-disease linkages there and come up with best practices.

So I think that the Agency will be able, solely by participation with the CERTs, to have better access to those databases. But you know all about this. I mean, the Agency was the one that started this thing 20 years ago under the Experimental Technology Improvement Program and still funds five (5) extramural grants in a cooperative agreement to work on them. So I think the Agency can bring its databases to the CERTs table as

well and we can work together on best practices. And I see this as the embodiment of this bi-directional linkage that you're talking about.

MR. BARNETT: Would anyone else like to speak on this section?

(No response.)

OTHER

MR. BARNETT: Okay. Our final three speakers are going to be discussing a potpourri of topics that didn't quite fit into the five that we had anticipated. The first is Doug Saunders of the Association of Food and Drug Officials. Mr. Saunders?

MR. SAUNDERS: Thank you very much. The Board of Directors of the Association of Food and Drug Officials, or AFDO, is pleased to provide the following comments to the U.S. Food and Drug Administration regarding leveraging:

During the past two (2) years, AFDO has advocated an integrated food safety system for the U.S. to eliminate duplication and gaps in our current system of regulating foods. This vision provides FDA one of the largest, most far-reaching and effective leveraging opportunities in the implementation of AFDO's vision for a truly integrated food safety system.

Fundamental to integration is the leveraging of all state, local, and federal resources to meet statutory requirements in consumer protection in foods, drugs, cosmetics, and medical devices. This Federal Register announcement failed to identify integration as a means of leveraging. The success of integration is critical to fulfilling the Agency's mandate and outreach. Through this effort, other agencies can assist the FDA in meeting its annual work plan goals.

That said, AFDO would like to address specific areas for leveraging in response to the requested information in this Federal Register announcement. Leveraging requires a relationship of equality and trust between parties to that results are equivalent and useful to the FDA and the parties involved. Any leveraging will require a Federal oversight component. Most state and local governments have a history of working cooperatively with the FDA through partnerships and contract programs. These programs have, particularly over the past five (5) years, resulted in less duplication and increased coverage of areas of mutual responsibility and priority. However, these contracts and partnerships fall short of establishing a formal mechanism for FDA recognition of state inspection.

Basically, AFDO recommends that the FDA establish a mechanism for formalizing a recognition of state inspections and laboratory results that includes recognition criteria, a quality assurance program, periodic management evaluation, mutual training to maintain quality and uniformity, routine joint work planning, and common or mutually accessible databases for inspection, analytical and compliance information.

It must be understood by all concerned with using partnerships and contracts for leveraging that states operate on budgets similar to the Federal agency, and planning is a critical element. These programs need to move beyond a year-to-year funding that limits states' ability to plan for an appropriately trained workforce to carry out the functions.

FDA already partners and contracts with states in many areas of food inspection, food testing, mammography inspection, medical device inspections, and education. The following listing provides some focus areas for continued and improved resource leveraging with state and local government partners:

Those things would include topic areas such as dietary supplements, fresh fruits and vegetables, imported products, assessment of the bacteriological quality of fresh juice in the marketplace, enforcement of various new FDA regulations and policies, incentives for the adoption of the FDA Food Code, drugs and medical device inspections, and monitoring of the Internet for inappropriate advertising of prescription drugs and dietary supplements as well as the unmentioned area of veterinary drugs and animal feed.

The current level of funding for contracts FDA has with the states to conduct inspections of regulated industry is minimal and has been in a state of serious decline. FDA should, therefore, identify where high and medium risk establishments exist, then increase funding for contracts with those states for foods, drugs, and medical devices.

AFDO is in a position to assist FDA with training in many different areas, including dietary supplements, drugs, medical devices, food, good manufacturing practices, dietary supplement good manufacturing practices, retail processing and other areas of mutual concern. AFDO is also in a position to conduct surveys of the states with respect to any number of issues, including capacity, resources, and other leveraging parameters. FDA should consider partnering with AFDO in these areas.

AFDO appreciates this opportunity to comment on leveraging opportunities through the AFDO organization as well as the states and locals that it represents.

Thank you very much.

MR. BARNETT: Thank you. Dr. Alan Hanks is with the Association of American Feed Control Officials. Dr. Hanks?

DR. HANKS: Yes. Thank you. I, too, wish to thank you for the opportunity to contribute to thoughts and comments on how FDA can leverage its resources.

The Association of American Feed Control Officials, or AAFCO, has been conducting inspections of medicated feed mills with FDA for many years. And in the last two years we have been involved with doing inspections of mills for basically use of prohibitive proteins in ruminant feeds, basically an inspection program designed for BSE.

During these past two years, the support for continuing the number of inspections in medicated feed mills is off, and those are required every two years. These are GMP inspections.

And I would just like to comment I think we can leverage the efforts of the states to continue BSE, all mills that might be using prohibited protein every year, at least at this stage of trying to prevent the emergency of BSE in the United States while also the little extra funding would probably continue the biannual inspections of the medicated feed mills.

Along this line, I'll point out, there are only about 20 states that are involved in contracting for the medicated feed mills inspections. That leaves the remaining mills in the other states for FDA to inspect. AAFCO has suggested a way of relieving some of this inspection pressure on the FDA through a program we believe which would be very useful in giving us all opportunities to emphasize other things and work on other priorities.

A program that was basically initiated by FDA is an industry program for voluntary self-inspection or what we would call a VSIP program. It integrates very well into a model national medicated feed mill program that has been developed by AAFCO. Those two programs, together, would allow us to leverage the

inspections conducted by industry to give us the opportunity to do other things.

Along this line, AAFCO has also proposed, along with industry, a change in the GMP inspections and basically, through a citizens' petition, requested that these be adopted. If adopted, integrated with the AAFCO BSE program and VSIP, we believe that it would enhance both of those programs and our opportunity to get those inspections done and do more with our resources.

Along these lines, we have submitted a proposed pilot program, and we believe this is an opportunity for FDA to be involved and to be part of the pilot, and also we will need a little support in conducting that pilot program.

Finally, I would like to mention that AAFCO has been emphasizing feed safety for the last several years. We have a strategic plan that's the primary emphasis in the plan. In our philosophy of feed regulatory programs, feed safety has great emphasis. In 1997, we created a task force on feed safety to develop a model program for the states. This program of development continues, and we are now working on basically a generic quality control program for feed manufacturing. Basically an approach to process of control.

And, as we work on that together—and we do indeed work with the FDA on many of these things—we believe greater opportunities will be ahead for us to leverage and collaborate through that type of program.

I would like to also mention, hearing everything mentioned on the Internet, we too are taking a look at the Internet and working both with FDA and the Federal Trade Commission. And we, hopefully, will be able to this fall launch at least a (surf day) on what we call, for lack of a really better name, novel ingredients.

Thank you.

MR. BARNETT: Thank you.

Before we go to our last speaker—I've been watching the time, and I think that we may, at the end, have some time for the audience to ask questions of the FDA about the leveraging process in general. So, if you want to be thinking about a few questions, by all means, do so, and we will go to those when we have time. There are a couple of microphones here that you can go to. So let's watch the watches to see what we can do.

Our final speaker is Mr. Michael Ferrante of the American Society for Quality. Mr. Ferrante?

MR. FERRANTE: Thank you. And I begin, like everyone else on the dais, I want to thank you for the opportunity to speak.

Specifically, the American Society for Quality Control, I am actually representing the Food-Drug-Cosmetic Division, which basically has a long history of cooperation with the Agency. I just want to be sure that everyone was aware that we have in the past cooperated on an annual basis, we hold conferences jointly with the FDA, we ---

MR. BARNETT: Excuse me. We'll need a microphone a little closer to you, I think.

MR. FERRANTE: Okay. Hopefully, that's better.

MR. BARNETT: Yeah.

MR. FERRANTE: Again, we have held conferences in the Northeast, the Southeast, the Midwest and the West Coast with the FDA for both our memberships and also anyone else in the industry who wishes to attend. Agendas are agreed to jointly by the Agency and by the Society with the idea being that it's a forum for both the Agency and industry people present. It's a training issue for our people. And, again because it's on a regional basis, most of the attendees are from that region. It's something that a lot of them look forward

to annually. We have basically been trying to present these cost-effective programs for the membership.

In terms of what we're looking to do in the future, again, one of the things we want to do is continue this initiative that we have had for almost, I'd say, as long as I've been a member of the Division, over 15, 20 years with the Agency, and to tell you where we're going with some of the other industry that's going on. Right now, the Division has been working on certification exams. They've been doing that for over two decades.

But right now, for the first time, we've gone to one where we've had a membership request and we've responded to it, to have examinations and training specifically in HACCP requirements, because there have been – I think as we go forward, and I've heard a lot of advances that we've talked about today, a lot of times we find out that we sometimes overlook the basics.

And there are a lot of people constantly coming into the industry that need basic training. And the basic core science is the one thing we emphasize, the quality sciences. Because I know we can talk about the compliance regulations and the regulations dealing with CDER or CBER. But basically we have to remember there are core—there's a core knowledge curricula that has to be continually emphasized. And I think that if we look upon many of the things that are coming out of the Agency as far as the Internet warning letters that we all look at on a constant basis, we can see that a lot of things that are occurring are things that occurred 15 years ago, 20 years ago.

And so what we, again, have been doing and what we propose to do in the future is, again, building on the joint training from the Agency and the Division. Because we can offer a number of courses and a number of criteria. But it's the influence and the involvement of the Agency in these key education issues that make it

very, very valuable to the membership. They want to know both from a quality and a regulatory and a compliance initiative where everyone is going. We want to make sure we wind up on the same road.

So, again, to summarize, basically what we're talking about leveraging is continuing and bringing forward and advancing the joint training issues.

Thank you.

MR. BARNETT: Thank you. Do we have any response by the panel on these last three? Yes?

DR. BUCHANAN: Thank you, Mark.

In 1997, the President called upon the Food and Drug Administration and other Federal agencies to develop a food-safety initiative to reduce, to the lowest level possible, food-borne disease. This was based, Doug, as you correctly pointed out, on the concepts of partnerships, partnerships within Federal agencies, between state and local government, between industry and all of these partners. I think this is probably one of the most significant success stories in public health and those partnerships. We've seen, based on the latest CDC data, a decline by 19 percent in the overall rate of food-borne disease in this country, certainly emphasizing the importance of partnerships and focused activity can have on public health.

MR. BARNETT: Anyone else want to respond here? Yes?

DR. HENNEY: Well, I guess I just want to issue a word of warning, Mark, in terms of opening up for questions. Last night, Janet gave a talk, I think in this very room. The questions went on for so long, they got kicked out of the room. They moved into the hallway. Then they got kicked out of the building. Then they moved out to the parking lot and the police kicked them out of the parking lot. We don't need to repeat ---

MR. BARNETT: All right. I'll exert better control. Yes, sir?

DR. MITCHELL: I wanted to follow up on Dr. Hanks' comments there from the perspective by AAFCO and invite you to comment further for the record on your view of how the relationship between the Agency and your own state, Indiana, and whether you regard that feed inspection model that we've used there as one that could be applied more widely with other states. With your association of other representative states, it would be helpful if you could comment, I think, from that standpoint.

MR. BARNETT: If you could do it pretty quickly.

DR. HANKS: Well, currently of course our GMP inspections follow 21 CFR 225, which are basically the standard GMPs which were revised, not too many years ago, to emphasize mills using drugs that would require withdrawal.

We also inspect all the non-licensed mills that use drugs, as do many other state feed control programs. And certainly there's an opportunity for leverage there. The only difference in what they're doing is the concentration of the drug. And so we feel that's a very important inspection program.

Part of the suggestion for revision of the GMPs would put both of the mills—that is, the licensed mills today and non-licensed mills—somewhat on the same plane, not quite, but close, with perhaps a little better assurance that we will not have drug residues.

MR. BARNETT: Any other response from the panel?

(No response.)

MR. BARNETT: If not, I would like to thank all of our speakers for sharing their thoughts with us. Our official transcriber has asked that, if you have things in

writing, to supply them to her and that will be of help in preparing the transcript of the meeting.

Dr. Suydam, do you want to make a few closing comments?

DR. SUYDAM: Well, the first thing I'd like to say is that my short-term vision for this meeting has been realized. I think the breadth of the ideas that were presented today certainly provided us with adequate opportunity to apply them directly to the breadth responsibilities that FDA faces every day. And I want to again reiterate how important our leveraging projects are and to say that we will be following up with each of the presenters and to ask those of you who are in the audience, if you have ideas for how FDA can leverage our resources with yours to promote and protect public health, we are anxious to hear from you. So each of the ideas that we have heard today will be followed up on, and hopefully we will be able to move toward that longer-term vision that I had earlier today.

I do want to thank all of our panelists for being here with us today and all of the speakers, again, for the thought that they put into the proposals that they've highlighted. And I'm sure that's just a highlight of what you've thought about in terms of what you've done for us today. So thank you.

And, Mark, I guess we do have time for audience questions.

MR. BARNETT: Yes, I think we do have time for a few questions from the audience. This is not going to be a general Q-and-A session, talk to the FDA. That's certainly fine, but not in this venue. What we want to have are questions about leveraging in particular, and we would be delighted to answer those. Yes, sir?

MR. BUSH: In deference to Commissioner Henney, I have a comment as opposed to a question. So this won't take any time at all.

MR. BARNETT: Say who you are.

MR. BUSH: I will get there in just a minute. I just want to say that you left out a model today that I would like to commend FDA for, and that is the evolving use of third-party review in medical devices.

My name is Milton Bush. I'm a lawyer. And I would have to say I'm a little nervous being in a room full of doctors, because usually we out-number everybody else.

But the commitment of Dr. Feigal's office to the increased use of third-party's review for medical devices is very encouraging to my clients. And all the stakeholders are involved in this process, both the manufacturers, the users, and the third parties. And the system that is envisioned is one that will allow the current inequities that exist in the U.S. – E.U. Mutual Recognition Agreement and will allow U.S. manufacturers to participate in envisioned third-party quality system review audits on an equal basis with their European counterparts.

The grassroots support is there, we've demonstrated that to FDA, and we would like FDA to initiate that program before year's end. Thank you.

MR. BARNETT: Thank you.

Other comments? Okay. Yes, sir?

DR. KRUCOFF: Just a question on the scope of the vision of the leveraging initiative. Obviously, as we all know, the central mandate of the FDA is to protect the American people and the majority of resources, therefore, are national in scope. And yet many of us also know that the healthcare community is just one version of how globally we are continuing to interact and even be able to be proactive.

Does the leveraging vision involve a global dimension or a national dimension or some of both? What comes to my mind is, is leveraging with a comfortable array of partners potentially directed towards

Ministries of Health outside of the United States as well as our global industry and global independent communities.

MR. BARNETT: Thank you.

DR. WOODCOCK: I think the best example of that, and it is already going on, is the model within the International Conference (on) Harmonization, technical requirements for pharmaceuticals, also affectionately known as ICH. And, because of the globalization and use of therapeutics, we have worked with the regions of Europe and Japan. Both regulators and regulated industry have come together and have harmonized a wide variety of requirements that mean basically that patients don't have to – tests don't have to be repeated on patients, or animals for that matter, multiple times in different regions around the world, and it's created streamlining and harmonization clarity in the requirements.

We also have harmonized the terminology for adverse events so that it can be used worldwide. And that is up and running and the FDA is using it now. So I think that's a good model for where coming together in international and global issues to really provide a win-win situation for a lot of people.

MR. BARNETT: Thank you. Dr. Henney?

DR. HENNEY: The other extension of that, and I think it is a bit using what's happened in ICH in the drug world as an example, but also spring-boarding off a lot of difficult problems that Europe and other countries have had in the food safety. Other countries are looking toward us for what has been a food-safety paradigm and regulations of food products in our country. And so we are engaged in a number of activities that are trying to support other countries in terms of developing their approach to regulation and hopefully on safe foods. And we would hope to bring forward, then, perhaps more worldwide and more uniform approach to food safety

because we all know that foods are clearly one product that is happening at a global pace.

MR. BARNETT: Dr. Feigal?

DR. FIEGAL: Just a final area to comment on that's very international is the international standard-setting process and the increasing role of conformance to standards in substituting for part of the traditional approval processes. And, right now, there is a certain amount of redundancy in some of the efforts, and we are looking very hard at how to streamline these processes and focus them together.

MR. BARNETT: Thank you.

Any other questions from the audience? Yes, sir?

UNIDENTIFIED SPEAKER: Mark, you mentioned that you would outline the procedures for purchasing the FDA formally.

MR. BARNETT: I will do that. Yes. I will do that in a moment. Thank you. Yes, I will.

Anything else? Yes, sir? Just come to the mike, and we will take one more.

MR. GARRETT: My name is Dan Garrett, and I am the Executive Director of the North Carolina Center for Pharmaceutical Care.

About two years ago, we began an experiment in Asheville, North Carolina, with the City of Asheville and their employees to put together a community-based project on care of their employees for diabetes and asthma. We now have two years worth of outcomes data, humanistic, economic and clinical data that we think is pretty telling. And we also are working with actually a class to develop a tool kit on how we can replicate this community health project throughout the country.

The question is who do I call? When I looked in this pamphlet, there is not a list of people ---

MR. BARNETT: Okay. I'm going to cover that in just a moment.

MR. GARRETT: Okay. But I guess what I'm saying is that I don't know if that's within the scope of your project, but this program did get a Harvard Community Innovations in Government Award. So these are the kinds of things that, if you replicate them, and hopefully the FDA can help us do that.

MR. BARNETT: Thank you.

Dr. Henney, I don't think we're going to get to the parking lot, but we do have time for a few closing comments, if you like.

DR. HENNEY: Well, let me say on behalf of the Agency thank you, first of all, to Duke for being willing to host this meeting. I think that we have really enjoyed our day here and the logistical help that we've had from many on the staff that have made that all possible.

But the biggest "thank you" I think should really go to you on the panels, both on our panel from outside the FDA for being willing to come down and explain your experience in terms of these leveraging activities, you on the panel who have shared your ideas, and you in the audience who have listened patiently to this and hopefully have been thinking within your own sphere of influence or scope of activity that you have about other opportunities that we would have to really work on mechanisms and ways to improve the public health. That's really what this is all about, increasing that capacity and capability within the scope and span of our jurisdiction. It's been a very good afternoon. I have enjoyed the time here at Duke, but I also enjoyed yesterday afternoon at UNC. So thanks – and this morning at N.C. State. So we did it all. And for somebody from Kansas, that is hard to do. I'm just glad we weren't in anybody's fieldhouse. Thank you again so much.

MR. BARNETT: Thank you, Dr. Henney.

And now several people have asked, "How do you follow up?" We have a sign-up station out at the registration desk where you came in. If you sign up, you will be contacted to explore your ideas about leveraging. This is not an ordinary sign-up sheet where you get on a mailing list. This is for real. This is the beginning of an active process. We will contact you. Doesn't mean you have to commit yourself, but it means that you will be contacted, but we won't call during the dinner hour.

Anyway, thank you very much, everybody, for coming. Fine meeting.

(Applause.)

(Whereupon, the meeting was adjourned at 3:10 p.m.)

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