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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR FOOD SAFETY AND APPLIED NMUTRITION

FDA PROPOSED REGULATION

CURRENT GOOD MANUFACTURING PRACTICES (CGMPs)

DIETARY INGREDIENTS AND DIETARY SUPPLEMENTS

PUBLIC STAKEHOLDER MEETING

Tuesday, May 6, 2003

9:00 a.m.

Ronald Dellums Federal Building
Third Floor, North Tower
Oakland, California

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C O N T E N T S

P R O C E E D I N G S

MS. McDONALD: I think enough people are here now so we can begin. There are still some people waiting to go through security, but the line, I understand, is not very long.

I'm Janet McDonald, Public Affairs Specialist with the San Francisco District Office of the Food and Drug Administration. And I have the honor to introduce Mark Roh, who will be doing the welcoming remarks, and then I will have the dubious distinction of doing housekeeping chores after Mark gives his welcoming remarks.

Mark Roh is the Deputy Regional Director for the Pacific Region. He's had that position since June of 2001. Prior to that, he was a Special Assistant to the Regional Director for two years. Before that he was the Small Business Representative. And we do have a slight change in the schedule today, because Marcia Madrigal, who is the current Small Business Representative for the Pacific Region is sick, and Mark will be doing her presentation this afternoon, right after the lunch break.

And then prior to being Small Business Representative for the Pacific Region, Mark was a

consumer Safety Officer, which you may better know as an FDA Investigator, with the San Francisco District Office for about nine years.

So it's my pleasure to introduce Mark Roh.

[Applause.]

Welcome and Opening Remarks

MR. ROH: Thank you, Janet. I don't know which one of these is on. Both of them?

I'm glad to have you clap, because all your faces look so very long and serious. I know this is a very important meeting, and I know that many of you manufacturers and distributors are--how do we say--reticent?--to look at these regulations. There is a smile. That's very god.

[Laughter.]

But I want to welcome you to this meeting today. As you know, this is the second, maybe the third, public meeting we've had on these proposed regulations for the manufacturing and packing and holding of dietary supplements.

I think we all agree that it is important that consumers have confidence in all the products they buy, and that includes dietary supplements. When the DSHEA was passed a couple of years ago, it was passed with the great support of the dietary

supplement industry and, I believe, also with the support of the consumers at that time. But we've received a lot of complaints in the past eight years about labeling and other problems associated with dietary supplements, and hopefully these regulations will help both you, the manufacturers and the consumers alleviate those problems and those complaints that we received in the past couple years.

And I think by attending this meeting you've taken the first big step into going in that direction, because you have the commitment to the consumer, and to make sure that the dietary supplement products that you put out on the market are not contaminated and are labeled accurately--which is really what we all want for all products.

And, really, that's what the proposed regulation is designed to do. And, as you well know, for the first time in history it will put some minimum requirements on the production of dietary supplements, and assure that the identify, purity, quality, strength and composition of those products is, indeed, what we purport that it should be.

Now, if you've read the regulation--and I understand that the proposal is not all out at the table. Only part of the preamble is out there. But I'm sure you've all read it. And it may sound--and it may be fairly complicated to begin with, but it's just--today we want to provide an overview of the regulation. And remember, we're still in the comment stage. So you do have an opportunity to comment on these regulations.

We want to receive your cements, and we want to know what you feel about it so they can be included in the final rule, because you are part of the decision--making process.

We know that this is a unique opportunity, and we ask the FDA to pay attention to what you have to say, and we ask you to work with us to get these rules out and make them something tat we can all live with--both us as regulators, and you as manufacturers and, of course, you also as consumers and us as consumers. The comments that we provide today orally should also be submitted in writing so that they can be included in the final regulation when it actually does come out.

As you know, if you've read the rule, we set a 90--day comment period--90 days from the date

of publication. That 90 days is up on June 11th. So you have to have your written comments in to the docket by June 11th. And, please, I encourage you to submit good, constructive comments that affect the rule, that we can incorporate into the rule, both for our benefit as well as yours.

There's going to be another meeting--in fact, actually this Friday, a satellite downlink--we're hosting another meeting here--the satellite downlink, we're hosting it here. And I was going to point out, Marcia Madrigal, who's in the office--or who was supposed to be in the audience today but she's home sick with 102 fever, who is organizing the downlink, but we have some information here that I can provide to you on the table out there--is her business card and some other information about the downlink. So if you want to register for that downlink, you can check that out.

I will not provide you the CFSAN website for all this information. I'm sure it will be provided on the slides--because it takes up the whole length of the paper, so I won't read all the letters. But the CFSAN staff--Center for Food Safety and Applied Nutrition--that's gathered here

today, we look forward to trying to explain these regulations to you, and listening to your comments and listening to your feedback, so collectively we can work to get these regulations out in a meaningful time frame, as well as having meaningful regulations that we can all work with, we can all live with, that also serve the needs of you the manufacturers, as well as the public.

So, with that, I thank you for coming. Please be seated. Plenty of chairs up front. Just like a church--you know, front is always empty.

So we'll get started. I'm going to turn it back over to Janet so she can introduce everybody. I'm going to come out and join you in the audience so I can actually watch the slides, because I haven't actually seen these slides from back here.

And thank you very much for coming. Welcome my colleagues from the Center for Food Safety. And, Janet, please take over. And thank you again for coming.

[Applause.]

MS. McDONALD: Well, there are some of the standard announcements that you get at every meeting. And the first one, of course, is to

please turn off your cell phones and pages. This meeting is being recorded and a transcript of the entire proceedings will be posted on FDA's website within several weeks after the meeting. So we need to make sure that the transcriber that's sitting in the front of the room gets to capture all of the information.

The restrooms--if you exit this auditorium, there is a small ladies' room to your immediate left, and a small men's room to your immediate right, just beyond the two registration tables. But the larger restrooms are located in the main corridor that you all came through to get here to the auditorium. So if you go through the double doors, head straight to the end, turn left and you will find the men's room first, on the right, and then the ladies' room is a bit further down the hallway, beyond the bank of elevators, also on the right--hand side.

There is also a no food or drink policy. You probably have already been a victim of the food police that are outside the door. It's a very strict rule for the General Services Administration, so we really will try to impress upon you to please abide by it. And this means not

only in the auditorium, but also in the immediate area where the registration is.

There is a cafeteria on the fifth floor. We will have a break in the morning session, and there are two elevators inside this auditorium area that go to the fifth floor. The cafeteria is on the fifth floor, and it is in the South Tower. We are in the North Tower. So if you follow the corridor, head back towards the center of the building, take a left and keep going across the bridge that connects the two buildings, and you will eventually come to the cafeteria. That will be on your left--hand side.

I hope that you've all picked up all of the handouts that are on the table outside. The two colored ones are the agenda and the restaurant list, respectively. We will have an hour break for lunch. And you have a choice of either going up to the fifth floor to the cafeteria, or going outside the building on the Clay Street side, and if you cross the street you will find the City Center complex that has numerous types of restaurants; everything from pizza to Italian, French, McDonald's, Starbucks. You will certainly be able to find something there, I think, that will appeal

to you.

The last restaurant that's listed on the salmon--colored restaurant sheet is a few blocks away. And I think that it might be tight if you try to go there for lunch and get back here within the hour's time. But that's up to you.

Now, if you do choose to leave the building to go out for lunch, you will have to go back to the main bank of elevators that you came up on. You cannot use these elevators that are right outside the auditorium. You'll have to go back through the security entrance. And then when you return you will have to come back through security again. So I just wanted to make sure you know that ahead of time.

Let me just see what else we need to discuss here.

I want to say a few words about the structure of the meeting. You do have the agenda. We're going to be handing out cards. If you didn't pick on the handout table, we will have a couple of ushers in the audience that will be able to provide you with four--by--six index cards for writing your questions. And you might want to be doing that throughout the various presentations.

Each of the speakers will be giving their presentation, and then we'll have questions and answers at the end, just before the lunch break. So just so you remember what you wanted to ask, you might want to be writing those questions throughout the presentations. And then we will have people collecting--if you would pass your questions to the end of the aisle, we will have some FDA staffers collecting those questions and delivering them to the speakers at the podium.

After lunch, you'll get some more instructions, but there will be a breakout session this afternoon for about an hour and 15 minutes, after some introductory remarks about commenting on this proposed rule. And I would kind of like to get a sense of how many people in the audience plan to participate in the breakout sessions. If you could just raise your hands, and give us--okay. So we have a good number of you. Okay. Well, that's going to help.

And then, just another reminder that when we come to a point where any member of the audience might have to use the microphone, whether it's to clarify a question, or to speak this afternoon, we are going to have to use the microphones that the

court reporter has brought. So, again, it's important not to just get up there and pose your question from the audience. We do have to wait until we get a microphone in front of you to do that.

So, with that, I am going to introduce our first speaker. That will be Karen Strauss.

Karen is a Consumer Safety Officer in the Division of Dietary Supplement Programs, Office of Nutritional Products, Labeling and Dietary Supplements, in the Center for Food Safety and Applied Nutrition. That's back on the East Coast, currently situated in College Park, Maryland.

Her work assignments include drafting current good manufacturing practices proposed regulations, she's a major architect of these regulations that we're discussing today; and working with the Food Advisory Committee working groups on dietary supplements and regulatory issues having to do with dietary supplements.

So, with that, I would like to welcome Karen Strauss.

[Applause.]

Background and Proposal Highlights

MS. STRAUSS: Thank you, Janet.

What I want to do first is to introduce the other panel members that are here with me: Sara Dent Acosta is the Consumer Safety Officer for the Los Angeles District, San Diego Resident Post. She's worked with FDA since 1998, and has focused her work on food inspections, including dietary supplements manufacturers. During the summer of 1999, several of us who are working on the proposal visited several dietary supplements manufacturing firms, and some of them were in California. And when we came to California, we met Sara. She went with us. And then after that, she reviewed our proposal and also has participated with us in our presentation of the proposal on our outreach visits. We really appreciated her efforts in the past, and with being with us now.

Then Steve Musser is the lead scientist for chemistry, Center for Food Safety and Applied Nutrition, FDA, in College Park. He's also a chief instrumentation and biophysics branch officer of the Scientific Analysis and Support at CFSAN. He's really responsible for developing analytical methods for a number of CFSAN program areas, including dietary supplements.

And then Peter Vardon is our Economist in

the Office of Scientific Analysis and Support in CFSAN, FDA, and he's the primary economist on our analysis of economic impacts of the rule. And he will be giving some information on that part of the proposal.

I want to start by first expanding on what Mark said about the comment period, some of you may know that there is, in FDA at the present time, at least one request to extend the comment period, and the agency is considering that. But we are operating under the assumption that the comment period will not be extended, until it actually is--if, in fact, it is extended. And if there is an extension, it would be published in the Federal Register.

I want to first acknowledge, not by name, but that were many, many individuals that participated in the drafting of the proposal. Chemists, microbiologists, people who know manufacturing processes in the field--many, many people in FDA, as well as those in industry; from time to time I would call individuals and get some insight into things, as well as on our site visits, we gained a lot of insight into the kinds of manufacturing practices that were currently being

used.

So what my presentation will cover this morning are really an introduction to the rule. I'll summarize--give you some background, that is what is a CGMP designed to do and why it's needed. We used stakeholder input--and I'll describe the ways that we received input. I will summarize the legal authority that we relied on for proposing the rule, and then I'll highlight some of the requirements. Sara Dent will give over view of the production and process controls, and Steve Musser will give an overview of the laboratory operations.

I want to start by hoping that you all have read the proposed rule. It's a lengthy document, I admit, and we would actually rather that it not be so long but we, at the same time, wanted it to be an explanation of why we proposed certain requirements. And what I want you to know is that this presentation in no way will give you enough information about the proposed rule. You really need to look at it and see how it will impact on your business. And as you read it through, if there is a particular requirement that you really want more information about, to go back into the preamble and look up that particular

requirement to see how we explained it. Because we've attempted to interpret the why's of the various requirements that we've proposed.

And so our role here this morning is to clarify the meaning of particular requirements as much as we can. However, there are some requirements that we propose that give a manufacturers some discretion in how they would actually perform that requirement. And so for those requirements where there is manufacturer's discretion, those kinds of things would actually be followed up with guidance documents, following any final rule.

And we have encountered some questions in our previous presentations where individuals have asked for clarification on when we've given some discretion, if a particular action that they're--a manufacturer is currently doing would meet what is proposed. And those are really hard to answer because we are giving discretion, and those kinds of things would be clarified in later guidance documents.

Also, after Steve give his presentation, I will come back and give--specify some particular items that we've asked for comment about, and then

describe the next steps to get us to a final rule.

So what are CGMPs designed to do? Well, consistent with the FDA's public health mission, the CGMPs are intended to help protect consumers from adulterated product; that is, product that is contaminated. They're also intended to help protect consumers from products that do not contain what is claimed on the label. If it becomes final as proposed, it would establish industry--wide minimum standards that would ensure that dietary ingredients and dietary supplements are manufactured consistently, batch to batch, as to their identity, purity, quality, strength and composition.

Because dietary ingredients are included in the DSHEA--the Dietary Supplement Health and Education Act--within the definition of dietary supplements, we have included dietary ingredients in the CGMP proposal. It's important to note, however, that the CGMPs will not ensure the safety of a particular dietary ingredient, independent of whether it's manufactured under current good manufacturing practices, and it will not ensure that the dietary supplement produces any claimed effect. So the CGMP doesn't affect the safety of a

dietary ingredient, and it doesn't affect efficacy.

However under DSHEA--which amended the Food, Drug and Cosmetic Act--manufacturers have an essential and critical responsibility to substantiate the safety and efficacy of the dietary ingredients they use in manufacturing a product. Also, the proposed requirements will not affect other standards, such as organic standards.

So Congress saw a need for specific CGMPs for dietary supplements by including them the authorization for CGMPs for dietary supplements in the DSHEA. They gave the Secretary of Health and Human Services, and FDA, by delegation, the explicitly and express authority to issue dietary supplements CGMPs. And FDA has found manufacturing problems that have been associated with product recalls. And so it appears that there are manufacturing problems that can be improved by CGMPs.

We also learned of public support for CGMPs by comments--public comments--at several public meetings that we held. For example, the strategic planning meeting to develop a ten--year plan for dietary supplements urged the agency to give high priority to developing a CGMP rule.

Then, also, industry demonstrated their support by sending to us an outline of CGMPs--a coalition of trade organizations and manufacturers--and that was published as an advance notice of proposed rulemaking in the late '90s.

In the preamble, we have given some examples--it's not a comprehensive list--of product recalls, and also there have been some independent laboratory testing that's demonstrated the need from CGMP. The kinds of things that we found in inspection would be some poor sanitation that resulted in bacterial contamination. There have been examples of misidentification of dietary ingredients--one, in particular, is especially of concern: digitalis bonata was mistaken for plantain and digitalis can produce some very harmful heart effects.

We found super--potent selenium at 2 to 20 times what was claimed on the label. And at those high levels, it can have adverse health effects. And we found sub--potent folic acid; actually, the dietary supplement contained 35 percent of what was claimed on the label. And folic acid, it has a well--known effect of preventing--or helping to reduce neural tube defects; birth defects. And we

found dietary supplements were contaminated with prescription drugs.

Consumers want assurance of product quality. There are some consumer surveys that show some things that consumers have told the surveyers; for example, surveys show that only 37 percent of consumers thought that some supplements were adequately tested before marketing. A majority said that there is not as much regulation as is needed to make sure that supplements are pure and dosages are consistent. And only about a third of consumers were confident that products were accurately labeled. And surveys of people over 50 years of age said that the Federal government should review safety data and approved a product before it's sold. So there are some concerns out there by consumers.

We also are aware that industry has some challenges with the kind of recalls and media publicity, there has been some eroding of strength of consumer confidence in the dietary supplements they purchase. They have some safety concerns and quality issues about some products. And there are also some concerns about inaccurate or unsubstantiated label claims. And if a final

regulation--if there is a final regulation as proposed--as we propose it--we believe that there will be enhanced consumer confidence in the dietary supplements that they purchase.

Now I will go over some of the legal authority that's cited authority for the proposal as a whole, as well as some specific requirements that we propose. It starts with Section 502(g)of the Food, Drug and Cosmetic Act--and this was an amendment that came through DSHEA. And the Act, as I mentioned, gives explicitly authority to FDA to propose the CGMP. And it further states that once there's a final rule, if a product is manufactured not in compliance with CGMPs it would be an adulterated product, because it has not followed the CGMPs.

Also, Section 401(g), Congress stated that regulations were to be modeled after current good manufacturing practice regulations for food. And when Congress used the term "modeled after," we wanted to get a sense for what that meant, as far as giving us direction, so what we did is we went to the dictionary and found that "model" means a preliminary pattern. And so we've used the food GMPs as a preliminary pattern in developing the

CGMP for dietary supplements. If Congress had intended that as a food CGMP was the only CGMP that dietary supplements were to be subject to, they could have explicitly stated that; that they were subject to food CGMPs.

So we've modeled it after food. And the proposal is modeled after food in that it covers some of the same practices relating to receiving, inspecting, segregating, storing and distribution; used many of the same sanitary practices that other conventional food production, in order to produce a product that's not adulterated.

However supplements have their own unique set of requirements, as the result of their own characteristics and hazards, because there are different preparation methods, there are different dosage forms, ingestion forms--different from conventional foods. There are different product processes to insure that they're not adulterated, and that they're produced in the same way from batch to batch.

The scope of legal authority also relies on the same kinds of authority for determining when food is adulterated in that section 402, and it says that when a whole or a part of any product is

filthy or decomposed, or if it's otherwise unfit for food, then it's adulterated. And section 403 describes when a product would be "misbranded." This is also the section that gives authority for nutrition label information and the supplement facts panel.

And, in order to have an accurate label, a product would need to have the identity of the dietary ingredient, as well as the quantity. And this indicates that some testing was necessary.

Then we also used section 701 and 704, and these two sections give authority for requirements for efficient enforcement. 701 gives the authority for record--keeping, and we note that there are record--keeping requirements for other commodity--driven food CGMPs or manufacturing regulations.

704 gives the agency authority to inspect factories, warehouses and other establishments. Then we've used section 361 of the Public Health Service Act, and this section gives authority to the agency to propose regulations and have final regulations to prevent introduction, transmission or spread of communicable diseases from one state to another; and we're especially thinking of plant

and animal dietary ingredients that come from natural sources that could have contamination with soil, or animals or other--become contaminated during handling and transportation.

So how was the proposal developed? What did we consider? Well, as I mentioned before, we considered the unique characteristics: how they're manufactured. There are tablets, capsules, powders liquids, versus canned, frozen. So there are different processes there. And we looked at the unique properties of dietary ingredients and dietary supplements. For example, if you're going to identify the difference between two conventional foods, most often you can tell by just visually looking at two green products--a green pea, a green bean--you can really tell the difference by looking. But if you have two white powders, you can't tell the difference by looking. So, some different kinds of identity tests would be needed.

Then we considered the desire for a clear, enforceable regulation. On the one hand, we used plain language techniques, which would--say, if we took a paragraph from 110, the food GMP in it had many, many requirements in a paragraph. What we did, we would have a heading and bullet kind of

enumerations of those various requirements, being much more plain, rather than bunching them in a paragraph. And there's a trend in government to have plain language in regulations, and that's one of the techniques. So sometimes it looks like we have a page and a half versus a paragraph, and it really is not more there, it's just formatted different.

And we wanted a clear, enforceable regulation. You'll hear from Peter--and you know, maybe, yourself--that many of those in industry are small manufacturers, and some of them are actually doing no CGMPs at all. So we wanted to strike the right balance between enough detail so that the firm that's not using any GMP can understand what we're saying, but at the same time have performance objectives that leave some flexibility and discretion.

Then, lastly, we considered the estimated cost and benefits, not only for the rule as a whole but to look at what were more expensive requirements, and trying to really consider the cost and benefits.

We also looked at several different documents. And with DSHEA came the establishment

of a White House Commission on Dietary Supplement Labels. And they prepared a report in 1997, and this commission supported CGMPs in two ways: one, they encouraged industry and FDA to work together to develop the regulations; and, secondly, they endorse CGMP record--keeping as important in substantiating dietary supplement labels.

There was a Food Advisory Working Group, 1998 and 1999, and I worked on that working group, and the two topics there were identity--testing of dietary ingredients and record--keeping. And that report gave us some insights into those two topics. Actually, the report contained much more detail than would be appropriate for a rule, but they will be no doubt used later as guidance documents, or as the fodder for guidance documents.

Dietary supplement manufacturers were visited by FDA in 1999. We visited eight different firms, and really wanted to see what operations were currently being used, as far as GMPs, and they were very helpful to us. We also conducted small business meetings, and these were looking at the industry outline, and we wanted to get their input as to what their concerns were about costs, based on the requirements included in the industry

outline. And those also were in 1999.

Then, when we actually sat down to draft, we started, as I mentioned, with the food CGMPs. And we looked at other food commodities manufacturing regulations. And those that we looked at were low--acid canned food, the juice, fish and fishery products and infant formula--both existing and proposed. What we wanted to do was to do some updating. The food GMP--the umbrella GMP--is really pretty old, so we wanted to be sure that it was scientifically accurate.

Then we also looked at the drug and device GMP for organizational principles. And then, lastly, once we looked at the food GMP, decided our organization, we looked at the industry outline that was submitted and published as the ANPRM--or Advance Notice of Proposed Rule Making. USP has an outline, and MNFA has an outline, and we looked at these as well.

Well--this is a kind of schematic that shows kind of how we approached this, and also shows where there are some of the requirements that we have. When we looked at the developing the proposal we decided to come--start at the door--warehouse door, and end at the warehouse

door: when the materials come in is where we start, and where they're going out for distribution is where we stopped. So we haven't included raw agricultural commodities, and we have not included retail.

Components--Sara will talk a little bit more about these--but they include packaging, labels--outside of the components. And then the components are ingredients that are in the final product--dietary ingredients and things that aren't in the products but are there during the time they're manufactured, like a solvent.

And ingredients must either be an approved food additive or a graft food additive, or self--graft. A dietary ingredient is not treated that way. So--let's say that again. Anything that's not a dietary ingredient, but stays in the final product must either be an approved food additive, a graft food additive, or a self--graft by the manufacturer. We've received several questions on that, so I want to just mention that aright up front.

Then looking at--once things come into a warehouse, they would need to be segregated so that it wouldn't get mixed up from other things. The

manufacturers would have a formula or recipe for producing that dietary supplement, and we call that a "master manufacturing record"--kind of like a recipe. And they would produce some bulk product. Then you'll see above that there's "flexible testing." And there are two prongs going from flexible testing--and Steve will talk more about this, as will Sara.

But to get a handle on cost and diminish costs, we've proposed a flexible testing requirement, where a manufacturer could choose to test, based on some parameters that will be discussed later, either finished product testing, final product testing, or, if that's not possible, then they could test incoming materials and in--process materials. And the objective here is to be sure that what is in that product and what's on the label are consistent. So you need to know what you're starting with and at the end that material is still there in the quantity and that it's not contaminated.

Then the product would be packaged and distributed or shipped. And then we also have some requirements proposed for consumer complaints, and a consumer complaint would come back to the firm,

and then they would--it could impact anywhere along the manufacturing process.

And then the records kind of underscore the whole process. There are only certain records that we've proposed in our rule, and I'll talk about these in a minute.

Now, just some highlights. General provisions would apply to domestic firms, as well as foreign firms. And, clearly, FA does monitor dietary supplement imports when a problem is suspected and then tests them as needed. And also, generally, when FDA establishes a final rule for a product and a foreign manufacturers wants to bring it into the country they're usually pretty good about complying with whatever is necessary as far as U.S. regulations are concerned. A dietary supplement firm would also be required t comply with other applicable statutory provisions that would be required under the act related to manufacturing, packaging or holding. For example, a manufacturer produces a dietary supplement that includes fish or fishery products, such as fish oil, would have to comply with HACCP regulations as required by Part 123, as well as these CGMP provisions.

Other statutory provisions or regulations may apply because of particular ingredients. There are also some bioterrorism regulations that would require registration, and these are proposed. And if these become final, they would also be something that a manufacturer would need to comply with.

So CGMPs would apply to activities associated with manufacturing, packaging, holding and distributing. A manufacturer would need to comply with requirements applicable to the operation that they're performing. A contractor would need to comply with the applicable requirements and a contracting firm responsible for a contractor's performance is also--has a responsibility. For example, if a manufacturer contracts with a packager--labeler, that package labeler would need to comply with the CGMPs, and it would be the contractor's responsibility to see that they comply. Neither one is off the hook, so to speak.

Same with a distributor. The distributor gets the products, you know, puts a label on it and then distributes it, it would need to--the distributor would need to ensure that what's on the label is what's in the package, as well. How they

do that, we have not proposed a rule on, although we may in a final rule provide more detail on that to be sure that it's understood. But there is a responsibility there.

We've proposed requirements for personnel. And these model Part 110--the food umbrella CGMP. Basically, they help prevent contamination. The personnel would need to be qualified by training and experience to perform their assigned duties. The firm would need to institute disease control and hygienic practices to ensure that an employee doesn't contaminate a product. They would also be required to assign qualified supervisors to oversee implementation of the CGMPs.

The physical plant and environment--these also really model Part 110--the food CGMP. And they too are intended to help prevent contamination. It deals with the design and construction of the physical plant: ceilings, floors, walls would need to be easily cleaned and maintained. There needs to be separate areas to prevent mix--up, and screening to keep out pests.

A manufacturer would need to keep the firm in good maintenance and clean and sanitized as necessary. Water that is used in the physical

plant, where it's used as an ingredient, or component, or where--would, at minimum need to meet the EPA drinking water requirements. That doesn't mean that a firm couldn't use a more purified water if they wanted, but this would be the quality that would be required. And the aim here is really to get at private wells. Those private wells would also need to meet the EPA drinking water requirements.

We propose plumbing, bathroom, lighting, and ventilation and trash requirements to prevent contamination. And these really follow the umbrella food CGMPs.

We have proposed requirements for equipment and utensils. Again, these really follow Part 110 of the food CGMP quite closely. We would require that manufacturers use equipment of appropriate design, construction and workmanship for their intended use, and provide for adequate cleaning and maintenance.

Under the proposal, the manufacturer would be required to maintain, clean and sanitize as necessary all equipment, utensils and contact surfaces that are used to manufacture, package or hold dietary ingredients or dietary supplements.

In the proposal, we've required that if a machine is used--or equipment is used in producing a batch, that the maintenance, cleaning and sanitizing records be kept in that batch record.

In the answer rounds there was a comment that, I think--included a log, and so that we don't have a log, you put it in the batch. And because we're minimizing the number of records we're requiring, we decided to propose that it be kept in the batch. In question and comment meetings, they said it would really work better if you had a log. So maybe there's some--that's an area for comment. Should it be one place or other, or should there be an option. And if you propose one or the other, give us some why. Tell us, you know, why we should do it that way.

We have not proposed equipment validation or process validation. The only validation we've proposed has to do with analytical method. So, there has been some questions that--we proposed equipment validation or process validation and we had not. But we do ask whether that should be included in a final rule. What we've said is that a manufacturer needs to ensure that equipment functions as intended. And we've not given--so we

have given discretion in that area.

At this point, that's where I stop and Sara takes over, and she will give some highlights of the production and process controls.

Ah--no, she's not. She'll be down.

Proposed Production and Process Controls.

MS. STRAUSS: I will give just a little bit of overview of the production and process controls, and just kind of the basic elements that we've included in this proposal. And Sara will give more details.

There's a quality control unit that we would require; a master manufacturing record and batch production record; specifications for incoming, in--process and final product; and then flexible testing requirements that I've mentioned before. And you'll hear more about it as we go on. And I'm sure you'll have question about them--everyplace else has, as well.

Testing of final product, when that's possible, or incoming and in--process testing.

Consumer product quality complaints. We have proposed a requirement for handling consumer complaints. And this is an area that

[Technical difficulty.]

First of all, we would require that the manufacturer keep a written record of each consumer complaint they receive that is related to CGMPs. Some examples would be super--potent or sub--potent--you know, having more or less than claimed on the label. Having a wrong ingredient, and having a contaminant--like a drug contaminant or other contaminants like a bacteria, pesticide, toxin or foreign material. So complaints about prices, package sizes, shape or other matters that couldn't possibly reveal the existence of a hazard to health, or do not concern the purest case order of quality of the dietary ingredients are not considered consumer complaints under this regulation, although CGMP relating to consumer complaints about quality could be related to a health hazard or an adverse event.

The quality control unit would be required to review the CGMP--related product quality complaints to determine whether there was a possible risk of illness or injury that is an adverse event. They also need to look at them to see if there's a possible CGMP failure, or maybe the specification wasn't met. And if there was an adverse event, and it was related to the CGMPs,

then the quality control unit would need to do an investigation into what was--what had happened, maybe with that batch or other batches.

But here's where it's difficult to kind of understand. What is not included in a CGMP--related consumer complaint is a complaint that's related to the pharmacologically active substance of the dietary ingredient. These we don't consider to be CGMP--related practices, and aren't related to practices. So they're not a consumer complaint under this proposed rule. So it's only those complaints that are related to manufacturing practices that we have proposed to be handled under this rule.

We have holding and distribution requirements, and these really are to ensure that products are not contaminated or that they don't get mixed up, or that there's deterioration. So it really relates to temperature, humidity, light and kind of how they're handled.

We proposed records and record--keeping requirements. The record--keeping requirements we propose would be for calibration of instruments and controls, for the master manufacturing records, for the batch production records and for consumer

complaints. And what we've proposed is that records would be kept for three years beyond the date of manufacture that would be associated with those particular records, and that FDA would have access to records when requested.

We've chosen the three year date because we do not propose expiration dating. We don't propose a requirement for expiration dating because we feel that in order to have a meaningful expiration date you would need to know the active ingredients in a dietary supplement. So if, for example, botanicals, the active ingredient is not know, an expiration date really wouldn't be related to an active--you wouldn't know what it is. So what we've done is tied that back to the manufacture. We don't prohibit expiration dates. If a firm chooses to use one, they must have the data to support that expiration date.

And that's where I'll stop. Sara?

I should add that if you have questions, write them down on a card and raise your hand, and then what we'll do when we answer the questions is we'll give you an opportunity to ask a follow--up question if you felt we've not answered the question.

And we'll do those questions after all of our presentations.

MS. ACOSTA: Hi. We have no reached the part on production and process controls. The proposed regulations would require that the manufacturer have a system of production and process controls.

That system would be required to cover all stages of manufacturing, packaging, labeling and holding dietary ingredients and dietary supplements. The purpose of the control system would be to ensure that the dietary ingredients or dietary supplements are manufactured, packaged and held in a manner that would prevent adulteration. And that's the important part--preventing adulteration.

The production and process control system would be required to be reviewed and approved by the quality control unit. The production and process control system would also be required to include the quality control unit, and also all manufacturing operations, including laboratory operations, the holding and distributing and, finally, record--keeping.

Louder? Okay. Sorry.

We would require that the system of production and process controls include specifications and testing to ensure those specifications are met, and that's covered in the later part of this talk; monitoring, material review--sorry--and disposition decision, and the manufacturer would also be required to use the master manufacturing records and batch production records.

Specifications would be required anyplace that control is necessary to prevent adulteration. For example, a control specification might include hearing temperatures, drying times, or cooling specs. If used, the manufacturer identifies that a particular specification is necessary to prevent adulteration, then that specification is part of these required regulatory specifications. However in addition to that, we have identified certain steps when specifications would be required.

Specifications would be required for the identity, purity, quality, strength and composition of incoming components, and within incoming components we include the dietary ingredients, ingredients and any other component. And let me define that a little bit further.

The term "component" is define as "any substance intended for use in the manufacture of a dietary ingredient or a dietary supplement, including those that may not appear in the finished dietary ingredient or dietary supplement. A solvent is an example of a component that may not appear in the finished product. A component would also include ingredients and dietary ingredients as described in the definitions of Chapter II of the Food, Drug and Cosmetics Act, Section 201 (ff)."

"Ingredients" would be any substance that is used in the manufacture of a dietary ingredient or a dietary supplements that is intended to be present in the finished dietary ingredient or dietary supplement. And that includes, but not necessarily limited to: dietary ingredients as described in 201(ff).

Janet is asking me to speak a little bit louder. Can you hear me in the back now? Sorry about that.

We would require that any substance other than a dietary ingredient within the meaning of Section 201(ff) of the Act which, when used, is reasonably expected to become a components, or other affect the characteristics of the dietary

ingredient or dietary supplement, be it either an approved food additive or generally recognized--

[Technical difficulty.]

And, as I was saying, let me go back a little bit--specifications for the incoming components--also we would require specifications in process, anytime the control is necessary to prevent adulteration, for the identity, purity, quality, strength and composition of the final product, and for packaging and labels.

Then I'm also going to define a little bit--and I'm sorry, this is a long slide--what we have interpreted "identity, purity, quality, strength and composition" to mean. That means that the product, on a batch--by--batch basis, is consistent with the master manufacturing record, and is also what it is represented to be on the label, the identity; it is without impurities, and it's the desired product, the purity. Quality would be that it has the identity, purity and strength for the intended purpose. "Strength" is--you know, this is common sense--the concentration or the amount intended to be in the product. And the composition is the intended mix of product and the product--related substances.

A little bit more on packaging and labels. Specifications would be required for the packaging and labels. They should be safe and suitable for the intended use. They should comply with all other applicable statutory and regulatory requirements, and they should not be reactive or absorptive to affect dietary ingredient or dietary supplement safety. The packaging should also be intended to protect the ingredients from contamination and from deterioration.

The manufacturer would also be required to monitor operations to ensure specifications are met and detect unanticipated occurrences. The manufacturer would be required to conduct a material review and disposition decision when specifications are not met, or an unanticipated occurrence may lead to adulteration; whenever a master manufacturing record step is not completed, if an instrument or a control calibration suggests a problem or a dietary ingredient or dietary supplement is returned to the manufacturer.

All those actions need to be documented, and that documentation would be required to identify the specific deviation or unanticipated occurrence, describe the investigation, evaluate

whether or not the deviation or unanticipated occurrence resulted in or could lead to adulteration; identify the actions taken and show that the quality control unit approved the material disposition decision.

A manufacturer must establish and use the quality control unit. We do not require that a quality control unit have a particular number of employees. WE do propose requirements for the authorities and responsibilities of the quality control unit. The requirements would include that the quality control unit must approve or reject procedures, specifications, controls, tests and deviations or modifications from any of these; approve or reject materials received and products manufactured, packaged and labeled by the firm, and review and approve master manufacturing and batch production records.

An appropriately trained person in the quality control unit would be required to review CGMP--related consumer complaints to determine if a quality problem exists, and to determine if it is associated with an adverse event. If a quality problem exists, and there is a possible relationship between the quality problem and the

adverse event, then the quality control unit must conduct an investigation of the consumer complaint. That investigation must extend to all batches associated with the consumer's complaint.

The manufacturer would be required to keep this CGMP--related consumer complaint record. And we, in addition, recommend--but we would not require--that a manufacturer report serious adverse events to the FDA.

The manufacturer would be required to prepare and follow a master manufacturing record. The master manufacturing record would be similar to a recipe, and we would require that the master manufacturing record include a list of components; and, as stated previously, components include dietary ingredients, ingredients that remain in the final product, and substances that do no remain in the final product.

And here I'm going to read--this is almost word by word the definition in the Food, Drug and Cosmetic Act, Section 210(ff), which defines a dietary ingredient as "The vitamins, minerals herb or other botanical and amino acid or any dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a

concentrate, metabolized constituent, extract or combination of any of the above."

The master manufacturing record will also include any other ingredient that appears in the final product, and any substance that does not appear in the finished product. As mentioned previously, this could be a solvent.

The master manufacturing record would be required to include specifications anyplace that control is necessary to prevent adulteration; the weight or measure for each component; instructions for adding, mixing, sampling and testing; the expected yield; and specifications for packaging and the labels to be used. And the manufacturer must also keep the master manufacturing record.

In addition to the master manufacturing record, the manufacturer would be required to prepare a batch production record every time the batch of dietary ingredients or dietary supplements is manufactured; and that includes reprocessed batches.

The proposal would require that the batch production record include complete information relating to the production and control of each batch. Generally, the batch production record is

the mirror image--it accurately follows the master manufacturing record. And we would require that the quality control unit review and approve the batch production record, including cross--referencing of the receiving and batch production records, any material review and disposition decision, reprocessing, as well, also release for distribution. The batch production records would be required to be kept for three years beyond the date of batch production.

What is going to be included in the batch production records? It's also going to include the batch, lot or control number for each batch; the identity of the equipment and processing lines that were used in manufacturing, the date and time of the maintenance, cleaning and sanitizing of the equipment and processing lines used; incoming shipment lots identifier and the identity and weight or measure of each component used.

It's also going to include the documentation of the time of performance, showing the date and initials of the person performing and verifying each step of the master manufacturing record. It's also going to include the date the batch was produced, the actual test results for any

testing that is performed during the batch production, material review and disposition decision; documentation that the dietary ingredient or dietary supplement meets the final specification, and the copies of all container labels used, and results of examinations conducted during labeling operations to ensure that the containers have the correct labels.

The signature of the quality control unit would be required to document the batch production record review and any approval for reprocessing or repackaging.

Manufacturing operations need to be designed or selected to ensure that the specifications are achieved. They need to be conducted in accordance with sanitation principles, and also to take precaution to prevent contamination. Precautions to prevent contamination would include protecting against growth of microorganisms and the potential for contamination; washing or cleaning components that contain soil or other contaminants; preventing the growth of microorganisms and decomposition by methods such as sterilizing, pasteurizing, freezing, refrigerating, controlling pH, humidity

or water activity; preventing against inclusion of foreign material by using filters, traps, magnets or electronic metal detectors, and identifying all processing lines and major equipment used during the manufacturing to indicate their content.

It's also going to include the batch and lot number, when necessary, and the phase of manufacturing.

And this is my last slide. And now I'll leave you with Steve Musser, who's going to discuss the laboratory operations.

Proposed Laboratory Operations

MR. MUSSER: Good morning. This is--I'm going to talk to you about laboratory operations. You know, this is a very small portion of the proposed rule. It really has led to the vast majority of the questions that we've gotten about the rule. And I'm going to attempt toe address some of those questions. And I realize that I won't be able to address all of them. And, of course, we encourage your questions and comments.

Laboratory operations consist of about three parts. One of them is to establish and follow the laboratory controls. That means as you decide what your specifications are, and then you

follow those specifications; that you use adequate facilities, either in your facility or from outside sources to perform the testing and examination. What that means is that you can use a third party or a supplier to do the testing. You can use a contract laboratory. You can use any outside testing organization that you choose.

However, if you do choose to use an outside testing laboratory your quality control unit would need to inspect that facility on a routine basis to make sure that they are following the tests that you've specified, and that the records and documents that are required by the proposed rule would be kept in accordance with the rule, and for the appropriate length of time; and then, finally, regardless of where the testing is performed, that the laboratory test and examination records are kept for the specified period of time.

Within the establishment and following of laboratory controls, as well as most of the other items that are listed within this particular portion of the rule, there are two basic criteria. And the criteria are split into two sections. One is that the testing either be performed on the finished product, and if finished product testing

cannot be performed, that the components or dietary ingredient and dietary supplements as they are received are tested; that any in--process materials that are specified in the master manufacturing record be tested; and that if water is used as a contact or as a mixing agent, that it meet EPA national drinking water regulations.

Food GMPs require a fairly stringent use of water, however we thought that by adding EPA's guidelines or regulations, that that would be a much clearer specification as to what water could be used, and what the specifications would be appropriate for use of water in the manufacturing of dietary supplements.

This provision does allow the use of municipal water or well water--if you have well water on your facility you can use it, as long as it conforms to EPA's national drinking water regulations.

Within the establishment of these guidelines you would need to establish such things as what criteria are used for the tests; what will be tested; and what performance criteria must be met.

So each batch must be tested, to test the

finished batch for identity, purity, quality, strength and composition, according to those criteria that you have outlined in the previous establishment of the criteria you're going to use. And if analytical methods are not available--I'm sorry. I'm getting a little ahead of myself.

If analytical methods are not available for testing the finished batch, then you must test incoming components, dietary ingredients or dietary supplements, to determine whether the specifications are met, and you must test in--process, in accordance with the manufacturing record to ensure the identity, purity, quality, strength and composition of dietary ingredients or dietary supplements.

You would need to test for types of contamination that may adulterate your product. And those things may include filth, insects, other extraneous materials such as glass or metal, microorganisms. If you know, for example, that your particular raw product is contaminated--or routinely contaminated with microorganisms, then you would need to test and remove that contamination. And toxic substances--and those toxic substances can be organic or inorganic,

meaning things such as lead--inorganic--and organic substances could be things such as naturally occurring toxins.

Also, if there is historical confusion--this is particularly applicable to botanicals--if particular products are routinely confused with other botanicals, then the types of adulteration that might be wanted to be checked for would be whether that particular botanical that you've specified is indeed that botanical and is not mixed up with one that has historically been misidentified.

The proposed rule indicates that tests or examination must use at least one of the following, and they may be gross organileptic, microscopic, chemical or any other test that is appropriate and can be validated for that particular specification or criteria for which you've identified. We leave this open to your discretion. These are your products, and we feel that you can identify the testing requirements that are needed for those products.

Now, because the rule only says that you must perform at least one, it doesn't mean that you have to perform just one. If more than one

particular testing method is appropriate--for example, microbiological and chemical contamination are appropriate--then it would be then appropriate to use more than one testing method.

One of the most difficult to understand--not necessarily to understand, but for what we've had the most questions on in the proposed rule deals with this particular section, which is the establish and following laboratory controls; to select and use appropriate validated testing methods.

FDA interprets this to mean that the test is appropriate for--suitable for the test being made, or the measurement being made. So, for example, if you were using a balance to measure the UV spectrum of a particular chemical, that would be not appropriate for the test being used; and also that it be validated. And by "validated" we mean that the method is validated according to guidelines. And these may be from any of a number of organizations, such as FDA, or any other internally accepted guidelines, such as ISO 17025.

We've included in the rule some sources for validated methods--or just methods in general. They may be the AOAC, the USP, or any other

compendia that is commonly used for these types of methods. They may include peer--reviewed journals, or they may be in--house or proprietary methods for which you've developed and validated for your particular product.

Regardless of the source, however--regardless of whether you've got a fully collaboratively studied validated method that you're using, you must validate that method in your particular laboratory and show that it demonstrates the result and meets the criteria for which you've specified in your origination of those products.

We've had a number of questions already concerning commonly used test practices, and ones that would not apply in this particular rule--proposed rule. One of the biggest ones deals with suppliers or laboratory certificate of analysis for a shipment that's not supported by testing of all specifications. So simply accepting the certificate of analysis from a supplier without any kind of investigation by your quality assurance unit--or quality control unit--and no validation of that testing results would be inappropriate for this particular rule.

Skip lot testing--this is where you've

determined that a particular lot has met your testing criteria and you've done all the appropriate tests, and then you accept the next two or three batches without any testing at all, and then randomly test in between those batches--within the guidelines of this proposed rule, skip lot testing as that definition applies would not be acceptable.

And single test certification of a supplier or an ingredient manufacturer, in this case you would have performed the appropriate testing on one particular lot, certified that manufacturer, and then not tested any other batches. The rule is very specific, in that it specifies that all batches must be tested.

And, finally, then, for all tests that are performed, you must keep laboratory tests and examination records of finished dietary ingredient and dietary supplements tests, or components, dietary ingredient or dietary supplements received, and any in--process materials, where specified in the master manufacturing record, and water, once again, the test results from that, to assure that it conforms to the EPA national primary drinking water requirements.

And the specifications do--the proposal does say that they must include documentation of all examination and testing records performed.

Thank you. And that concludes my portion of the talk.

Public Comment Period and Next Steps

MS. STRAUSS: Throughout the proposal we've asked for comment on many, many, many issues. And there are some in particular that we've asked for comment on--and I'll identify some of these, and then I'll describe the kind of information that will be useful to us, in addition to, or as part of a comment.

We've asked--if you'll look at the handouts that you received that was a portion of the proposal. What is included there is the "highlights" section, and that really parallels some of the information that we've given in this presentation. It also gives some additional information on the comments that we've requested, in particular, and then what kind of information would be necessary for us to change something that we've proposed.

We've asked for comments on whether there should be certain additional personnel records: for

example, training records, consultant records. We have not included any written procedures. The only written procedure that might be required under the proposed rule would be for calibration. If you look at the calibration section, option, there as far as whether a written procedure is developed and then used as the documentation, or whether just the calibration procedure itself is documented. But we have asked for comment on whether there should be SOP written procedures.

Expiration dating and relating testing--we've, as I mentioned earlier, not included it as a requirement, but perhaps we should. Perhaps there should be expiration dating for certain dietary ingredients and not for others; for example, for vitamins, but not for botanicals.

Then we asked for comments on whether there should be specific requirements for animal--derived dietary ingredients, especially those that might be related to the importation of material that might be animal--derived that might be associated with BFC, or mad--cow.

So look at that highlights section in particular for those places that we've asked for comments.

We also have excluded persons who handle raw agricultural commodities. That's just the harvesting and transporting. If there's any drying or chopping, those kinds of operations would be considered manufacturing operations. Unless those are something that occur before it actually comes to a manufacturer's warehouse--and perhaps there's an area there where we need to make some more clarifying detail.

Now, what kinds of information would be needed if you submit a comment to us? If you submit a comment, for example, that says the final rule should not include a particular requirement, you need to tell us why or how, in the absence of that requirement, we could achieve the goals that we're wanting to achieve with the CGMP. How could we prevent adulteration? How could we ensure the identity, purity, quality, strength and composition of the dietary ingredient and dietary supplement without that particular requirement? Or how could we ensure an enforceable regulation? FDA's not on--site 100 percent of the time, so we rely on records for efficient enforcement of the Act, so that the inspector can tell whether or not the CGMPs are implemented over a long time period, not

just what's happening that particular day.

If you thought we included a requirement that should have been there but we didn't include all the reasons, it would be helpful to know if there are reasons we didn't include in our preamble discussion.

And, then again, as I mentioned earlier, if you wonder why we proposed something, go back to the preamble. If you look at a particular requirement, it has a number associated with it, we've talked about that particular requirement. So go back and look at it, and see if it helps you understand.

The next steps are to analyze the public comments. By Federal law we're required to look at all of the public comments and consider them in making changes to the final rule. But then they need to tell us the why's as well; convince us that the requirement should be added or revised or--let us know if something's not clear.

Then we will prepare a final rule. We expect that it will be a final rule and about a year after the public comments close, it will be published in the Federal Register, just as a proposal. What we're proposing is one year after

it's published for the implementation of large businesses, and we proposed a three--year phase--in for small businesses. And these are proposed. And depending on what comments are received, whether or not it will be this or something else.

There is one more event that we are having: the May 9th satellite downlink. There is information on the table. Also, if you want a copy of the proposal electronically, there's the website, under "What's New," just in the same places that you get all the documents, the backgrounders. You can pick up a copy of the electronic version of the proposal.

I'll leave this up while we answer questions, and this indicates that there's a 90--day comment period ending June 11th. But, as I mentioned, there's an extension request with FDA that is being considered. Comments can be sent either electronically or by mail. And the address, both electronically and the mail address is on this slide.

And, at this point, we will have a break, and Janet will give us some information. And then following the break, we'll have the presentations by Peter Vardon. And then after that we will

answer the questions or address comments.

MS. McDONALD: I just want to let you know that we are, during the break, try to get rid of this static in the microphone. So we will try to do it. I won't make any promises, but we are going to work on that.

Also, for those of you who came in late, there is a cafeteria on the fifth floor in the South Tower. We are in the North Tower. There's a bridge that connects the two towers. You can take either the elevators right outside the auditorium up to the fifth floor and head to the center corridor, turn left, and cross the bridge, and you'll find the cafeteria on the left--or you can go to the main bank of elevators that you came up on, and take that to the fifth floor, and proceed to the cafeteria.

And we're going to try and be back here by 11 o'clock to resume this morning's presentation. Thank you.

And, remember, no food or drink in the auditorium.

[Off the record.]

Economic Impact Analysis

MR. VARDON: Okay. Well, why don't we get

started. Thank you all for coming today.

As you might have guessed, the underlying theme of this public meeting is that this is a draft document that merely reflects our best understanding at the time the document was published.

But the purpose of the comment period is so that you can provide reason and evidence to fight city hall, as it were; that we can be persuaded, where to amend the document, to revise the document, to reflect your concerns. And that is particularly important with the economic analysis. One of the beset ways to provide reason and evidence to make a better document is through the economic analysis. If you can show that benefits can be achieved without the same compliance cost, then clearly that would benefit everybody.

So as I go through the economic analysis, think of ways that you think either you can provide evidence or data that would strengthen the economic analysis.

A large staff of the FDA economists and epidemiologists conducted the analysis, and the analysis was conducted with Executive Order 12866,

which requires, essentially, a cost--benefit study. And based on the cost--benefit study, we're required to select the approach that maximizes net benefit.

And we determined that rule, if adopted, would be significant--that it would have a significant impact on the economy, which means an impact greater than $100 million on the economy. And we felt that it would be significantly large than $100 million.

And we also felt, based on our analysis, that it would have a significant impact on small businesses. And because it's going to have a significant impact on small businesses, we looked at regulatory options for those small businesses.

The economic rationale for the proposed regulation is that there is a market failure; and by that we mean, consumers cannot take control of their own choices; that there are hidden product defects that aren't detectible through observation, and consumers can't know what they're buying. They can't know whether the product's adulterated or not merely from observation. And there are private incentives now to adopt sufficient controls to prevent adulteration. And controls are costly, and

so those firms that do adopt preventative controls would be at a competitive disadvantage if they're done voluntarily.

We looked at several regulatory options--we looked at six regulatory options, in fact, to see if there is an alternative to the rule that we propose. And the first regulatory option that we looked at was no new regulatory option, and that would mean the voluntary adoption of stricter standards as an alternative. And from survey evidence, though, we determined that 48 percent of very small firms, and even 11 percent of large firms now don't follow any GMP model. So we didn't feel this regulatory option would be a real option--or a better alternative.

We also looked at the option for fewer requirements for vitamin and mineral manufacturers than for the other dietary supplements manufacturers, such as plant-- and animal--derived dietary supplements. And we thought that might be an important option, because there may be greater variation in product quality with plant-- and animal--derived products than with synthetically--derived products. And the advantage of an option like this is that would be fewer

products and firms that would be affected so the total compliance cost would be less. But the disadvantage is that we don't have any evidence at all that there's a difference in health risk between synthetic and naturally manufactured dietary supplements.

So we looked at a third option of more restrictive regulations, and we looked at the possibility of product quality testing for each shipment lot, in addition to the finished product testing. And we looked at mandatory written procedures for each provision. But we felt the disadvantage of this would be that it would be costly and difficult to link to health benefits.

As a fourth regulatory option, we looked at HACCP, and we defined this as the hazard analysis and critical control point option, where manufacturers would determine how best to eliminate or control hazards. But we felt the disadvantage of this option is that it wouldn't create uniform minimum product quality across the industry. And we, as you'll see soon, that we found that there's a major benefit in having minimum product quality standards.

We looked at a fifth regulatory

option--final product testing only--without all the other provisions; just finished product testing. But we felt the disadvantage is that not every finished product has a test that confirms the identity, purity, quality, strength and composition. So finished product testing can't ensure the discovery of all contaminants when there are hot spots or false negatives. So we felt the other provisions were important.

And, as a sixth regulatory option, we looked at just regulating high--risk products, or high--risk hazards. But the disadvantage is that we just don't what those high--risk products or hazards are. There's significant under--reporting; FDA just doesn't have a bird's--eye view of real the real harms are, where the real hazards are. And what may have been reported may not actually be the highest risk. So we felt that this regulatory option wasn't feasible.

To conduct our economic analysis we did a survey of the industry, and the survey was conducted in 1999. And it's entirely possible some of you participated in the survey. And the survey was based on a database of firms that were developed from several sources. We used FDA's

official establishment inventory, and we were given the names of the firms from various trade organizations, and then we also had electronically databases-- privately published electronic databases, especially InfoUSA, which is a database like Standard & Poor's, which collects business information.

And we found, based on these various sources, that about 1,566 firms would be covered by this rule--are some way related to the manufacture of dietary supplements. And those covered firms are those firms that manufacture, package, or are dietary ingredient suppliers or repackers or holders. But the large majority, as you can see from the slide, are manufacturers. And we found also that most firms are small, as classified by the Small Business Administration, which means firms with 500 or fewer employees.

And we sent our survey to about 966 firms, and we received about 240 responses. So, from those responses, we were able to derive statistically significant results,

We also looked just at what's happening to the consumer market. And we found, largely from industry sources, that there's significant growth

in the market, which means that there are also very large competitive pressures. But we found that the growth rate is about 10 percent per year for the last decade. So this is a growing industry, and per capita consumption is growing; the number of units per U.S. resident--as measured by the number of units per U.S. resident shows about a 3 percent growth in consumption for the last decade also. And the industry size from about two years ago, it's about $15 billion per year.

We use the survey to look at producers' manufacturing practices today, and we stratified the survey by product type and by size. The product types we looked at are those manufacturers that make vitamins and minerals, is one strata. And we looked at those that manufacture and herbal products as a second strata. And we looked at those that manufacture amino acid, proteins and animal extracts as their primary product, as a third strata. And we looked at all others as a fourth strata.

And then we also stratified our results by firm size. WE looked at those that have more than 500 employees, and we defined those as being large firms. We looked at those that are small, and we

defined those as between 20 and 500 firms, and we looked at those that are very small, which we defined as those that have 20 or fewer employees. And looking at those that have 20 or fewer employees is important, because this industry is characterized by many very small firms. We found the median firm actually only has about eight employees, which is astonishing. And as we've gone to other meetings--somebody didn't really believe that. But that has been the results of our analysis.

And we also found that there's a very large turnover in this industry; that about 20 percent of industry enter every year and about 20 percent leave every year. So there's a great deal of change in the industry, too, as people come and go. And so there's a quite a bit of uncertainty because of that change.

And, maybe the most startling thing about our survey results was that as many as 35 percent in the industry have told us they don't follow any GMP model--including food GMP.

We felt the advantage of adopting this rule as it's currently written, is that consumers would enjoy better health. If you can reduce the

adulteration, consumers are less likely to consume contaminated products and they'll enjoy better health. And some of the risk from contamination, as Karen mentioned, are that--we found from our recall evidence, that there's a reduced risk of glass fragments, and salmonella, and selenium poisoning, and super--potent zinc and iron poisoning--among many of the things that we found, actually, in the products that have been recalled. And those risks were identified by FDA epidemiologists from our recall data.

We also felt the second benefit to consumers would be that consumers would spend less time searching for safely manufactured products. With standardization, or with uniform quality standards, consumers can spend less time shopping. They can spend less time worrying about whether this product's adulterated or whether that product's adulterated. And so they don't have to go to a website to see which manufacturers are better than other. They don't have to read literature. They don't have to spend----less time comparing labels. There's a greater assurance. And if you can just reduce that amount of time--a small amount of time across the adult consumer

population in the U.S.--I mean, to spend a few minutes every year across--if you can save consumers a few minutes every year across the entire adult population, you can save an enormous amount, actually, for the entire population. And we found that that is a significant source of the consumer benefits from this rule.

And we also felt that by adopting these rules we'd also just have fewer product recalls.

The major cost, through, from adopting this rule--if it were adopted in its current form--is that firms that currently were not maintaining records would now have to keep records, and that's potentially a significant cost. And they would also have to adopt final product testing if they weren't already doing that. Of course, we recognize that there are a whole range of other costs associated with this. There will be capital improvements to your building, or you may have to buy new laboratory equipment and other things. But we felt the major costs are from product testing--the final product testing and the record--keeping.

Now, I'll just mention a little about how we actually estimated the health benefits from the

rule. And we should acknowledge that it is very difficult to estimate the health benefits. There's just a great deal of uncertainty.

But we estimated the cost--or the health benefits, by reducing the cost of illness for a variety of types of illnesses that we found are associated with poorly manufactured dietary supplements. And we looked at the severity of those illnesses, and we used a technique know as "quality adjusted life day" to assess the cost, per day, for each type of illness that are associated with--the illnesses that we found are associated with poorly manufactured products.

And we looked at the loss of functionality. If somebody had lead poisoning, they wouldn't, perhaps, be able to walk up and down the stairs. So there would be a cost associated with that loss of functionality. But also they wouldn't be able to go to work, perhaps, for a few days as they recover. And so there's that loss in productivity. And then also there would be the direct medical cost associated with the loss from lead poisoning, let's say.

And then those losses would all be associated for a number of days. So, let's say

they're in the hospital for two weeks with whatever illness they have, then the loss would be over that two week period.

And we tried to estimate what all those losses would be, and we came up with an estimate. And so we'd very much like your opinion on whether you think those estimates are plausible or not.

We feel that there would be a considerable consumer benefit from reduced search costs, because consumers will spend less time searching for quality products. But, more precisely, they would spend less time shopping for purchase, which means they'd spend less time reading product labels and other literature, and comparing one product with other products, and less time searching on the internet or examining the product itself, or thinking about the product, or second--guessing their final decisions. And that's very difficult to actually measure. And so we had to rely on studies that were conducted in other closely--related industries, but still different industries.

And so we looked at the drugstore model, and the literature associated with shopping for pharmaceuticals. And we also looked at the

literature and models associated with consumers as they shop in the grocery store. And we looked at a series of use--of--time studies to derive our estimates.

And there was some convergence from these various sources, about how much time consumers would likely spend shopping for dietary supplements. But, in the end, there's still quite a bit of uncertainty, and so we relied on a technique known as Monte Carlo simulations to help us characterize that uncertainty. And we found that if consumers spend between saving 1 percent of their time shopping and 50 percent of their time shopping--I should say we felt the truth is somewhere between these boundaries--between--consumers would spend less than 1 percent of their time shopping, and between 50 percent less, with the most likely amount of about 33 percent less time shopping. And that's also based on the expert opinion of pharmacists. Apparently there was a study done, while we were doing our own analysis, that showed the consumers would be likely to spend about a third less time shopping if we adopted these rules as they're currently written.

But we'd very much like your comments on that.

So this slide summarizes our analysis. We felt if this rule were adopted as it's currently written, we'd have about $105 million in fewer illnesses; about $109 million in fewer--in the reduced consumer search; and about $3 million less in product recalls.

And I know these numbers are precise, but don't let that precision fool you. We recognize that there's a great deal of uncertainty about that, and that although these numbers are presented, what they really reflect is the mean estimator of the true value. And so I wouldn't let these few numbers provide a false precision. We recognize there's a great deal of uncertainty in our analysis.

But the total social benefits amount to about $217 million per year. And we feel the average industry compliance cost per year will be about $86 million per year. So we believe that the social benefits exceed the social costs; but that the impact to small firms, and to other firms, is potentially quite large. And we feel the average very small firm will incur an annual cost of about

$38,000 per firm, and the average small firm will incur a cost of about $61,000 per firm, and the average large firm will incur about $47,000 per firm.

And at previous meetings several have mentioned that these costs seem very low; that you can't even hire one person, and that this rule will probably require you to either hire several or fire several. But we have to recall that this is an average cost, and we have survey evidence that shows many, many firms are actually following many, or most--or all--of the proposed provisions, and that this compliance cost would really be--would fall on those who aren't following most of those provisions. So if you're following most of the provisions now--and we have survey evidence to show that most are, then these costs will be considerably less. This is just an average cost, per firm.

The key sources of uncertainty in our analysis is that those firms that currently aren't following the practices will now have to--must now comply. Which means that to comply with the physical plant requirements, if they don't currently have floors and walls that are smooth and

hard, then they'll have to adopt those smooth, hard surfaces. If they don't have equipment and instrumentation controls that are required, then they'll have to get them. And if they don't have a quality control unit--and we have survey evidence that shows about 85 percent of all firms have a quality control unit, and would therefore comply with the rule; 15 percent do not. And so, for those 15 percent that don't already have a quality control unit, they'll have to incur the cost of adopting a quality control unit.

But the key sources of uncertainty in our analysis are the number and cost of tests per batch for product quality testing. We have some survey evidence of how much is done now, but we'd be very interested in your opinion--or getting information about how many you would have to do. The number and cost of contamination testing per batch, the cost of creating and using new records, and the cost to investigate consumer complaints for adverse health events that are associated with the manufacturing practices.

As I've mentioned, we do believe the requirements are going to be significant to many of you. And to estimate the number of firms that are

at risk of going out of business, we looked at those that have revenues of $500,000 or less. And we felt if those firms incur an average--or higher cost of compliance, they would be at significant risk of not being profitable, and they would go out of business. And we determined that several hundred are actually at risks of that.

So, because it is going to have a significant impact on a very large number of small firms, we looked at the regulatory options. And it's based on that analysis, we determined that giving small firms a three--year compliance period would reduce the compliance cost to them.

But--I'm going to repeat a couple of slides--or I'm going to mention a couple of slides now that I'm going to repeat this afternoon where I go into a more lengthy explanation about the small--business impact, but I know not everybody's staying for this afternoon. So for those who will leave, I'm going to go through the next couple of slides.

We'd be very interested in hearing your comments about the need for the rules. We identified it as a market failure; that voluntary controls aren't sufficient, in that consumers can't

distinguish between adulterated and non--adulterated products. We'd be very interested in hearing your comments about that. Do you agree with that basic premise? And we'd be very interested in knowing what it will cost you to comply with the rule. If you could provide data to us--just the hard data--what does it cost you to test? What does it cost you to maintain records? That would be very helpful for our analysis.

And we'd also be very interested in hearing your opinion about whether you thing the rule will accomplish the goal--if we adopt the rule. Will there still be significant quantities of adulterated products? Will there not be? Does this rule work as it's intended, or are there other ways to accomplish the rule that are less costly and do more? And are there other regulatory options that we neglected? Let us know that.

But just to conclude this section--with a few do's and don't's--do send specific numbers if possible. Don't send unsupported opinions. If you think the rule stinks, just saying that won't help us at all. We really need reason and evidence.

But do send comments in on time--and the current closing period is June 11th, but there is a

recommendation to extend that for another 60 days. And that's being considered at the highest level. But until you hear otherwise, I would rely on that June 11th closing date.

Do send comments to the docket, not to those of us on the panel. And do, if possible, send combined comments through the associations. IF you have survey evidence of a change in practices--whether people are adopting practices voluntarily--let us know that. That would be very interesting to us.

And don't send sensitive information. If you have proprietary information that you don't want to be released to the public--because whatever you send us is potentially open to the public through the Freedom of Information Act. So, although we're very interested in knowing how this is going to change your profitability, or whether it's going to change your hiring practices, we don't need to know that you're going to fire John Smith because of this rule.

So, with that, I'll turn it over to the next group. Although let me just say a little about this afternoon's public meeting, also.

We're going to have breakout sessions for

small business owners, and we recognize that--because we recognize that this rule is going to have a significant impact on you, we want you to have an opportunity to discuss it with yourselves. And unlike past breakout sessions, we actually want you to try to formulate a comment--in the breakout sessions. And so we do ask that you stick around for the afternoon session, because it might be very productive.

Thank you.

Question and Answer Session

MS. STRAUSS: If someone can help me with this screen, I'd like to put the--Janet? Janet? Could you help me get this slide presentation up. I want to put the docket address up for people.

[Pause.]

MS. STRAUSS: What we'll do now is we'll go through the cards that you've given us, and what I have put back on the screen is the address for docket.

The comments that you wrote on the card are not official comments until you've sent them in writing to the FDA docket. So it's real important that you do that. Don't rely on the discussion here to get your comment addressed in the--in any

final rule.

And what we'll do now is we'll respond to what's written on cards. And if you were the writer, and you feel that you want to follow--up with another question or ask for clarification, if you would indicate, by raising your hand, then someone with a mike will come around so that you can speak into the mike, either here--I guess I'll leave it to Janet to decide where--so that the transcriber can also hear your request for clarification.

I'll start with some questions, and then we'll just kind of take turns here.

One question says that we've modeled it after the CGMP for foods, and asks if we have looked further at, for example, the legislative history to see if "modeled after" was also discussed there. And this is not discussed in the legislative history. In fact, there's minimal, if any, legislative history on the Dietary Supplement Health and Education Act.

But when we looked at "modeled after," we also looked at other requirements that would be necessary to fulfill the Dietary Supplement Health and Education Act--specifically, in order to have

an accurate label, you do need to know the identity and the quantity. So there would be some different kinds of requirements than would be required for conventional foods.

Another question is asking about slides--that they're a good summary. Would there be a copy of the slides possible? And we expect that the slides will be on the CFSAN website at some point, after all of our presentations have been completed.

'The proposed rule focuses on manufacturing and purity issues. When will focus begin on the requirements of gardeners, brokers or growers to assure a safe source of supply, both in the U.S. and imported?"

We could consider requirements for agricultural--for the gardeners, if that's a comment. Do you think that we should consider those? Let us know through a comment to the docket. That's one of the things we specifically want to know: whether we should include the farms.

If there's processing that occurs, such as milling, at the grower's location, that's part of manufacturing. That's--whatever beyond the growing and harvesting, if there's some processing that

happens, that's part of CGMP.

Someone else want to address the comment?

MR. MUSSER: I think what I'd like to do is jump in with certificates of analysis, since most of this stack here deals with certificates of analysis.

MS. STRAUSS: Can I say something first? Just about--to kind of clarify.

MR. MUSSER: Please.

MS. STRAUSS: To kind of clarify where the misunderstanding is occurring.

In the preamble--and, first of all, we have flexible testing requirements. And usually certificates of analysis are included for incoming material. And if it's flexible and you can't test the finished product, testing would be required of incoming materials.

In the preamble we've said when incoming material testing is required, a certificate of analysis is not appropriate, because that would be the only testing time, other than in--process testing, to substantiate label claims. So there is a problem there.

At the same time, we say that if you use a contractor for any process, that contractor must

also comply with the CGMP. So if someone is using a contractor to perform the label--I mean, to perform the testing of incoming, it's like you're using a contractor. And that contractor would need to comply with what we have--would have in a final rule for testing of incoming. So it would mean that it would need to be tested to just ensure that all the specifications were met.

And in all likelihood, we would use some other term, instead of "certificate of analysis" in any final rule dealing with this particular issue, because the certificates of analysis currently in use are not reliable--from advice that we've received. So, just with that little preface--and then, Steve, take it away.

MR. MUSSER: So, there are a couple of issues that we feel need to be addressed with this particular rule.

Certificates of analysis--sort of very ambiguous in this particular field. In pharmaceutical testing they're often referred to as "validated certificates of analysis," and the CGMPs, they're used for drug testing, do allow validated certificates of analysis, along with another test. And so these regulations are not

really out of compliance, or stricter, or requiring more than what is already required in our Food and Drug law.

So, what we were trying to prevent are--what is widely used--and that is just a manufacturer supplying an analysis without any traceable information attached to it; in other words, we know, for example, on some occasions firms have simply photocopies certificates of analysis from previous shipments and batches. And what we're looking for is an actual testing record of that particular batch, and the analytical results, and that the specifications have met those analytical results--or those criteria for which you've already specified.

In many cases, certificates of analysis that are not--that are currently in use now do not address many of those issues. And that's where we are trying to--what we're trying to address by not allowing certificates of analysis without testing.

It doesn't mean that the laboratory can't provide you the laboratory results as specified and call it something other than a certificate of analysis, such as "testing results" or something else--as long as you can inspect them and see that

they have conformed to your requirements or your specifications. They can act--your supplier can act just like a contract laboratory in this regard. But they would have to provide you the actual testing result, not just the summary of the analytical results.

I hope that clears it up. And if someone would like additional clarification on that particular issue, now would be the appropriate time to ask that.

MR. : I just want to make sure I'm clear.

MR. MUSSER: Can't hear him? Okay. I'll repeat the question.

MR. : If a supplier is going to provide a certificate of analysis, are you saying that that is totally not appropriate, or is it their responsibility to document behind it the analysis. I mean, do they have to provide the analysis with the certificate of analysis, or do they just have to maintain it to provide proof that they have done that.

MR. MUSSER: That's going to be hard to repeat. Can you say it just in a more concise way, so I can repeat it?

MR. : I understood you correctly--I'll start at that point--certificates of analysis are not appropriate for documentation. Based on that, now, is the manufacturer not allowed to provide certificates of analysis at all? Do they have to provide the total analysis parameters, or do they just keep that in their documentation for their batch files and things like that? Does that make sense?

MR. MUSSER: Okay. So the question is, basically, can the supplier keep the certificates of analysis, or the testing results in their files, such that you would have access to that? And that be appropriate, then, as a certificate of analysis?

MR. : No. What I'm asking is do we have to provide the complete set of analysis results, or do they just keep them as documentation.

MR. MUSSER: Okay. So can a supplier provide just a summary of the analytical results in the form of a certificate of analysis, or must they supply the complete analytical results?

MR. : Exactly.

MR. MUSSER: Okay. The way that we would address this is that when we would perform an

inspection, those complete records would have to be on the site. So you would have to have the complete analytical results on your site for an inspection; so not just a copy of those results, or a summary of those results. You would need the complete documentation of those--you know, what test was used, what the analytical results were; you know, a representative hard copy of those results--enough so that someone could look at that paperwork and determine that a test was performed; that results were obtained; that a method was used, and not simply the--you know, just a printout of an analytical result or summary of an analytical result.

Is that sufficient?

MR. MUSSER: It answers--but, if I could, just one more follow--up.

The person that has to maintain all that documentation, is it the manufacturer of the ingredient itself--the single component? If Dupont is providing an ingredient, a drug manufacturer is buying that and then they're compounding it into a drug or, you know, a dietary supplement. When you say the complete ingredient result, is that Dupont, the ultimate manufacturer, or is it the dietary

supplement manufacturer that has to have those complete results?

[Pause.]

Sorry.

[Laughter.]

MR. MUSSER: So, the question is: who maintains the record? The supplier or the manufacturer.

In this case, it would be the manufacturer maintaining the records. That's w ho we would inspect, that's who GMPs would cover. Typically, if you have a supplier, a drug firm, you know, that you're using, you would entail much of the same thing that we're asking here, in that you would inspect--and even if they were an overseas or a foreign firm, you would have some way of looking at their laboratory to make sure that it's appropriate, designing the test for them to use. You would have all that analytical data submitted with each batch that was shipped in for manufacture. And, typically, the manufacturer maintains all of that information--and I say "typically" because there are some exceptions, but in most cases that would be the case.

Is there any way we can get a microphone

to these people?

MS. McDONALD: Those who have further questions will have to come down here a little bit closer.

MS. : [Off mike] In essence, the manufacturer--or the buyer--is doing a laboratory operation.

MR. MUSSER: I'm sorry, I'm just finding it difficult to paraphrase your questions.

MS. STRAUSS: [Off mike] Janet, why don't you just have them come up on the podium [inaudible].

MR. MUSSER: From your comments, then, are you suggesting that the manufacturer would have to have a copy of all the records pertaining to the testing, including, perhaps, even copies of the chemists' notebooks, and all of the written records pertaining to the testing?

That's generally not required--certainly not specified in this particular regulation that they have that. If you felt that that particular clarification were necessary, or that it was ambiguous in the way that it is currently written, you know we would love to hear about it and--I know that this particular part is very difficult for

people unfamiliar with this type of testing to understand, especially with inspections, as well. And so if there is clarification that you feel is necessary, we would love to hear from you, but that's--your particular question: typically, not required.

MR. : And, also, with respect to graphs and charts from analytical equipment, would copies of those have to be made available by the manufacturer?

MR. MUSSER: By "graphs and charts" do you mean calibration and performance specifications?

MR. : No, just the testing itself--say, an HPLC.

MR. MUSSER: Oh, HPLC chromatograms? Oh, yes. Yeah. I mean, that would be--if I were an inspector, and one of your criteria was that it's 95 percent pure by HPLC, I'd want to be looking at the HPLC trace and see an integration for that. That would be impossible for me to determine in any other way.

MR. : Just to clarify something from the Dupont hypo about who would be required to actually have the test result documentation--you said it would be the manufacturer. But would the

answer actually also be "whoever's being inspected?" So it could be the manufacturer, it could be the supplier, as well. So Dupont would have to have that as well, if you all went into Dupont's plant as a supplier? Right or wrong?

MR. MUSSER: Yes, I think if we are inspecting the supplier, yes, you would have to have that--undoubtedly. Yes.

I think we'll take this question and hope that this clarifies most--please--but in the interest of answering more questions, we'll try and move on after this one.

MS. : I just want to clear up something. I think the earlier question on hermatographic charts--and you responded "yes," but you did say that that is when we're trying to show percentage of impurity. I do not think that you meant that for the potency testing. Because then that would be horrendous amount of records you're going to be imposing on the manufacturer of the finished product.

I think, if I may say this--I think your intent is that's to make sure that we don't have a typical analysis and represent that as a C of A; that perhaps something like a laboratory summary,

wherein we say--given a test, let's say, vitamin A, and say what is the methodology used, and say what was the actual result, signed by an analyst or the laboratory--would that work?

Because right now, the drug--Part 210 to 11, allow you to use such. And in other words--and as long as we validate that supplier, that raw material supplier on how they come up with those analyses. In other words, like you said, use them like our outside laboratory. But we don't need to have the details of the report of the laboratory, but we need to have a signed certificate--

[Technical difficulty.]

MR. MUSSER: In fact, I don't think that that is entirely correct. The data--the raw data used in any testing must be available for an inspection. And this is very consistent throughout our rules. And the rule implies that all of that data must be available on the site for testing, or for inspection. Is that correct, Karen? Yes?

MS. STRAUSS: I'm sorry?

MR. MUSSER: The information must be available on site for inspection.

MS. STRAUSS: Yes.

MR. MUSSER: Yes--and that all of that

information would need to be on--site.

If you feel that it's unclear, or that the rule is deviating from that information which is already allowed, or is more stringent, or we're requiring something which is unnecessary, we would like to hear from you in a written comment to the docket.

[Pause.]

I think we'll move on to Peter, then.

MR. VARDON: I have a few questions this time, and I'll go through two or three--how's that?

MS. STRAUSS: Sure.

MR. VARDON: How does a three--year enforcement moratorium on small business lower the costs of what you identified as ongoing?

I think what the questioner is asking is: what good does the three--year compliance allow--how does that reduce the compliance cost on small firms? And it does it in a couple of ways.

By giving a small firm three years to comply, they can get whatever training is necessary. If they buy new equipment, they can amortize it over a three--year period, so that the annual cost is reduced for them.

But, primarily, is--or, if they need to

formulate, or if they need to do other things--whatever they have to do to comply, they can do it over a three--year period instead of over a one--year period. And so the amortization period is over three years.

But, primarily, it's also for training. Our thinking is that many of these small firms, with eight people, may not have the sophistication of the large firms. So they may actually have to go to school, or they may have to--if--may have to find out, "How do I prepare records? I've never done it before." But our thinking is that with three years, they'll have an opportunity--a greater opportunity.

Yes?

MR. : [Off mike] I think you can all hear me.

MS. STRAUSS: But the transcriber--please come up.

MR. : [Off mike] I'll try to be brief and a little clearer [inaudible].

Specifically, the question was meant to address items that you've identified clearly as ongoing costs--i.e., the hiring of additional personnel. And it's unclear to me how additional

staffing is minimized by a three--year moratorium on enforcement as a direct example.

MR. VARDON: Well, you're right. If it's ongoing, then it's not. It's really for those capital improvements and other things.

Another questioner asked: if you're aware that 35 percent of companies don't follow GMPs, why not actively enforce 21 CFR § 110 for those 35 percent?

The significance of the statistic of 35 percent isn't that they're not doing anything. They actually may have sanitary facilities, or they may do the other things that are required by 110. The point is that they may not be consciously following a food GMP model--just not aware of it. And so it's just a measure of, perhaps, the ignorance in the industry.

And I'll try to answer one more question: in your economic assessment, how do you justify having CGMPs drop dietary supplement recalls to essentially zero?

That's an excellent question, and we've been asked that a lot, including by OMB. But our premise is that if you actually follow these rules, and you follow them faithfully, and comply with all