

ORIGINAL

sgg

1

SG

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR FOOD SAFETY AND APPLIED NUTRITION

**PUBLIC MEETING ON:  
GLUTEN-FREE FOOD LABELING**

Friday, August 19, 2005

8:30 a.m.

Harvey W. Wiley Auditorium  
5100 Paint Branch Parkway  
College Park, Maryland 20740

2005N-0279

TR 1

C O N T E N T S

	<u>PAGE</u>
Welcome	
Janice Oliver	4
Opening Remarks and Introductions	
Barbara Schneeman, Ph.D.	5
Congressional Mandate and Federal Register Notice Questions	
Rhonda Kane, M.S., R.D., ONPLDS	11
Overview of Celiac Disease	
Frank Hamilton, M.D., M.P.H.	22
Questions and Answers	44
<b>Industry Perspective on a Gluten-Free Food Labeling Standard:</b>	
North American Millers' Association Jane DeMarchi	46
Questions and Answers	60
Bob's Red Mill Natural Foods, Inc. Dennis Gilliam	67
Questions and Answers	77
Miss Roben's, Inc. Jay Berger	84
Questions and Answers	100
Gluten-Free Bakehouse, Whole Foods Market Lee Tobin	111
Questions and Answers	120
Questions from the FDA Panel	125

C O N T E N T S (Continued)PAGE**Gluten Detection Analytical Methods:**

Detection of Cereal Proteins and DNA Using MS, ELISA and PCR William Hurkman, Ph.D.	135
Questions and Answers	150
Commercial Gluten Test Kits and Methods Jupiter Yeung, Ph.D.	157
Questions and Answers	169

**Consumer Perspective on a Gluten-Free Food Labeling Standard:**

Celiac Sprue Association Mary Schluckebier, M.A.	183
Questions and Answers	201
Celiac Research Center Pam Cureton, R.D., L.D.N.	205
Questions and Answers	211
Celiac Disease Center Anne Lee, M.S., R.D.	215
Questions and Answers	228

**Public Statements:**

Maryrose Hopke	252
Thomas P. Sullivan	255
Matthew Cox	260
Carol Fenster	263
Anna Ashworth	268
David Browne	271
Ann Whelan	277
Alice Blast	283
Jill Kujo	289
James Blank	291

P R O C E E D I N G S**Welcome**

MS. OLIVER: Good morning. I would like to welcome all of you to College Park this morning for today's meeting on gluten-free labeling. I would especially like to welcome the persons who have celiac disease and their caregivers, and we appreciate your interest and your desire to work with us here today, and we appreciate all of your input.

Our intention is to develop a rule to define the term gluten-free for voluntary use in food labeling. And, as you are all well aware, persons who have celiac disease must avoid all sources of gluten in their diet and we will hear more about that this morning. A standardized definition of gluten-free is going to enable everybody to have more confidence in selecting foods by having a standardized definition on the label. FDA is here to listen today. We welcome your input; we want your input.

We have quite a full program so what I

would like to do, without any further introductions, is to turn the program over to Dr. Barbara Schneeman. Dr. Schneeman is our Director of the Office of Nutritional Products, Labeling and Dietary Supplements, which we affectionately call ONPLDS. Barbara joined us last year and she has a distinguished career in nutrition. She came to us from the University of California at Davis. We are all very glad to have her here. Barbara?

[Applause]

**Opening Remarks and Introductions**

DR. SCHNEEMAN: Thank you, Janice. I am pleased to add my welcome to the Center's welcome. We do, indeed, appreciate your participating in this workshop and your interest in helping the agency meet the requirements of FALCPA around a definition for gluten-free.

As indicated, the purpose of today's meeting is to help FDA better understand how manufacturers make gluten-free foods and the challenges facing them. We are also interested in gaining insight on what consumers, particularly

those who have celiac disease and their caregivers, understand the food labeling term gluten-free to mean. As you know, we are in the process of developing a regulation to establish a uniform definition of the term gluten-free for use by the food industry, both domestic and foreign, to label and market foods as gluten-free in the United States.

If you look at our agenda, you see that we divided the agenda into three major topic areas. First will be an industry perspective on gluten-free food labeling standard. The second section is on gluten detection analytical methods, and the third is on the consumer perspective on a gluten-free food labeling standard. These three major themes were in response to the questions that you have in the Federal Register Notice. Certainly, it is our intent to focus on those questions in the Federal Register Notice. Hopefully, you picked up a packet of information when you registered. If not, you can get that information at the registration desk.

Now, after we go through those three major topic areas members of the public who have requested to speak can deliver their statements. I would remind everyone that the maximum amount of time for public comments is five minutes for each speaker. Now, if you did not previously request to make a statement but would like to do so, please let the FDA staff at the registration table know by the end of the second break time. We request that any statement that you make be directly related to the issues and the questions that are outlined in the Federal Register Notice.

As Miss Oliver indicated, we do have a very tight schedule. We have a lot of material to cover in our agenda. We have scheduled two 15-minute breaks and a one-hour lunch period. For those who are thinking about lunch just a few housekeeping details, certainly, the most convenient place for lunch is Cafe Wiley. Keep in mind that once you leave the building you will have to come back through security when you come back into the building. But there are other places up

on Highway 1. There is the 94th Air Squadron which is located on Paint Branch Parkway but just keep in mind that we only have one hour scheduled.

I want the speakers to be aware that as get near the end of your talk you will hear a very gentle beep-beep-beep. That means one minute. And, because we are trying to make sure we cover all the topics, please be cognizant of the need to wrap up your comments when you hear that gentle beep-beep-beep, and Geraldine and I will ensure that you are aware of that. I wore my bright red suit today so when you see me stand up you know.

Some other housekeeping details, there are restrooms that are located in the hall leading to this auditorium and also in Cafe Wiley. We do request that you do not bring food and beverages into the auditorium. That is just policy for the Center.

This is a public meeting and the meeting will be recorded and a transcript generated. That transcript will be made available on our website approximately one month after this meeting time.

Because of the transcription, we ask that all speakers use the microphone, state their name and affiliation for the record before sharing their comments, and that will be true for all of you who make comments during the public comment period.

If you have more information than you have time to present or you have additional data in more detail or references, please be sure to submit that information to the FDA's Division of Dockets Management under docket number 2005N-0279. That, again, is described in the Federal Register Notice so it is part of the material you should have received during the registration. All comments on the notice on this meeting are due in docket by September 19th so you still have time after this meeting to submit additional comments.

We have a distinguished panel here in the front. These are members of FDA, members of the Center for Food Safety and Applied Nutrition, and I want to introduce each of them. They will be in charge of questioning each of the speakers and, again, it is with the goal of making sure we

address the issues and the questions that are outlined in the Federal Register Notice.

The first member of our panel is Felicia Satchell. She is the Director of the Food Labeling and Standards Staff. That is one of the divisions within my office.

Next to her is Rhonda Kane. Rhonda is a consumer safety officer on the Food Labeling and Standards Staff and she has been the lead staff writer working on the gluten-free initiative. Rhonda has spent a lot of time and planning to get this meeting to come off so we appreciate all her effort in that regard.

Next is Douglas Park who is the Director of the Division of Natural Food Products within the Office of Plant and Dairy Foods, and is responsible for the gluten detection methods.

Next to Doug is Don Zink, who is a senior food scientist in the Office of Plant and Dairy Foods, with an expertise in Good Manufacturing Practices.

At the end of the table is Stefano

Luccioli, who is the senior medical officer in the Office of Food Additive Safety, with a specialty in food allergen and intolerances.

I will then be serving as the panel moderator and the meeting facilitator.

So, our first presentation will be on the FALCPA mandate and the meeting questions, and Rhonda Kane is going to give an overview of the new law that directed FDA to pursue the rule-making to define the term gluten-free and a brief review of the list of questions in the recent Federal Register Notice that announced this public meeting. So, Rhonda?

#### **Congressional Mandate**

#### **and Federal Register Notice Questions**

DR. KANE: Thank you. Good morning. I wanted to provide you some background information on the reason why FDA will be pursuing a standardized definition for the term gluten-free for use in food labeling. On August 2, 2004 a new law was enacted that is called the Food Allergen Labeling and Consumer Protection Act of 2004. FDA

refers to this new law by the acronym FALCPA. It represents Title II of Public Law 108-282.

Now, this new law provided details on the requirements for food labeling if a product is made with ingredients that are or contain a major food allergen as defined by the law. This law also includes a provision that directs the Secretary of Health and Human Services, or FDA by delegation, to consult with appropriate experts and stakeholders to define and permit the use of the term gluten-free in food labeling. We plan to meet this directive by publishing a proposed rule by August 2, 2006. So, next August we have to publish a proposed ruling and two years later, August 2, 2008, come out with a final rule that defines the term gluten-free and identifies the criteria that would enable the food industry to use that term voluntarily for labeling their products.

I want to point out that this law does not mandate that food companies label their products gluten-free. Instead, it mandates that the federal government establish a uniform definition for the

term gluten-free that would apply to both domestic and foreign products that are marketed in the United States that voluntarily include this label claim. Once a federal definition for gluten-free is in effect, then any product that included this claim on its labeling would have to comply with the requirements or it would be deemed misbranded under the Federal Food, Drug and Cosmetic Act.

Among the things that FDA has done to meet FALCPA's mandate is to publish a Federal Register Notice, which was published on July 19, 2005, a month ago, that announces this meeting and includes a list of specific questions where we have gone out and asked the general public, but we have targeted food industry and those who have celiac disease and their caregivers, to give us feedback on the questions that would be most helpful to us in defining the term gluten-free.

In the Notice we have used certain terms and they are gluten, grains of concern and gluten-free foods. I want to point out that these terms are not FDA regulatory definitions. Instead,

they are terminology that we used to explain the questions in our Notice and to solicit comments. In the Notice we use gluten to refer to proteins found in any grains that can cause harm to persons with celiac disease. Grains of concern refers to wheat, rye, barley and oats and their related species such as durum, spelt and kamut or their crossbred hybrids such as triticale, which is a cross between wheat and rye. Gluten-free foods refers to foods marketed in the United States that are either represented to be gluten-free or include statements or symbols in the labeling of those products that indicate that they are free of gluten.

Now, our questions in the Notice are organized under five major subheadings, and they are definitions of gluten-free; gluten-free product development; Good Manufacturing Practices and analytical methods; foods as gluten-free; and, lastly, consumer purchasing practices.

Now, I want to review the list of questions that are found in the Federal Register

Notice, and copies were available at the registration table. If you didn't get a chance to pick one up, you can do so at the break. The wording that I have used on my slides is not identical to that used in the Notice in all cases; I have had to simplify it to put it onto my slides, however, the essence of what I have displayed is the same. I would like to review those questions one by one.

Question one asks how do food manufacturers define gluten-free? How does the food industry, or does the food industry, have a generally accepted definition of gluten-free? Does any entity certify finished foods or raw ingredients to be gluten-free? And, if so, how is that term defined and how is a food determined to satisfy that definition?

Switching to the subheading of gluten-free product development, question two asks how are gluten-free foods produced and what methods are most commonly used to remove gluten from food?

Under the same subheading, question three

asks whether it is technologically and economically feasible to produce two different categories of foods in particular. One is gluten-free flour milled from grains other than those of concern. For example, would it be feasible to mill corn or millet into flour without it containing any gluten from wheat?

The other category is oat-based products that do not contain gluten from grains of concern other than oats. For example, would it be feasible for oat-based products to be produced that do not contain any residual amount of wheat gluten?

If it is feasible to produce such categories of foods, what additional measures in the milling or the manufacturing process would be needed to produce these products and what would be the incremental cost to do so?

Under a different subheading of Good Manufacturing Practices and analytical methods, the first question is four and it asks what measures are in place during the manufacturing, packaging or holding of gluten-free foods to prevent them from

coming in contact with any grains of concern?

Continuing, question five asks what analytical methods are used to evaluate gluten-free products? How often are these analyses performed? For example, is every batch of finished product tested or are the bulk containers of each of the ingredients tested? And, what is the cost of such testing?

Question six is a whopper. It contains a series of questions that relate to the types and characteristics of different types of analytical methods or test kits that are designed to detect gluten. Among that long list of questions underneath question six are in what grains can the test kit or method detect gluten? What specific mechanism is used to indicate the presence or absence of gluten? In other words, describe in detail how that method or test kit works. What is the sensitivity or lowest level of detection of that test kit or method?

Continuing under the same question, is the test kit or method qualitative or quantitative? If

the latter, what is the test kit's or method's limit of quantification? And, what are the test kit's or method's false positive and negative rates?

Further, question six asks is the effectiveness of the test kit or method itself affected by the nature of the processing of the gluten-free food or by the food matrix, and if so, how? The food matrix refers to the total food environment in which gluten is found in that particular product. So, that includes all of the components that make up that food. If the test kit or method has been validated, by whom and at what level, such as parts per million, of detection was it validated?

Further, if the test kit or method has not been validated, have the results of its performance or an evaluation of its performance been published in a peer-reviewed scientific journal? Lastly under question six is the question what is the cost of the test kit or the cost to perform that method of analysis?

Continuing under this same subheading but under question seven are the following questions: What analytical methods are currently available or under development to detect the presence of oat proteins in food? Which oat proteins are detected and what is the cost to conduct this analysis? Have these methods been validated or published in a peer-reviewed scientific journal?

Now switching to a new subheading that relates more to consumer issues is foods marketed as gluten-free. Question eight asks if research data or findings are available on what consumers with celiac disease or their caregivers believe the term gluten-free means. For example, which specific grains or other ingredients should not be in a product that is labeled as gluten-free?

Question nine is under a different subheading, and the last of the five, which is consumer purchasing practices. It asks if research data or findings are available on how do consumers with celiac disease or their caregivers identify packaged foods that don't contain gluten? How much

time do these consumers devote to identifying such foods?

Lastly, question ten asks if there is research data or findings available on the following: Are the packaged foods that consumers with celiac disease or their caregivers currently purchase or consume primarily or exclusively those foods labeled gluten-free?

What types of gluten-free packaged foods are purchased or consumed by persons with celiac disease or their caregivers? And, does a gluten-free label influence the purchasing decisions of persons with celiac disease or their caregivers when presented with products having identical ingredient lists? In other words, if two products had identical ingredient lists where one had a gluten-free label claim and the other didn't, would the person who had celiac disease or his or her caregiver choose the one that was labeled gluten-free or choose the other one equally if their ingredients are the same?

I want to remind everybody that we are

very interested in receiving your written comments on our Notice about this meeting. The deadline to receive your comments is September 19 so it is one month from today. Please note on any correspondence you send FDA about this meeting or the questions in the Notice to the Docket Number 2005N-0279. Comments can be submitted by one of three routes. You can submit them by land mail to FDA's Division of Docket Management, or to that same division via the internet because they have a website, or via e-mail. The Notice identifies the land mail and website address in it. The one that is not in the Notice that I want to point out to you is the e-mail address I have on my slide, and those addresses are included for your convenience on the slide. I just recently learned that the e-mail address will better accommodate the electronic transmission of comments that have an attachment so you might want to keep that in mind.

Well, in closing I want to thank everyone for attending today's public meeting and I hope you enjoy the rest of the program.

DR. SCHNEEMAN: Thank you, Rhonda. As you can see, we do have an ambitious agenda for today. I want to note also for the people attending this session that we are not going to do lengthy introductions of our speakers. You have the background information for our speakers; we provided the bio sketches, but we want to give our speakers as much time as possible so we won't be going into length introductions.

Our first presentation will be to give us an overview of what celiac disease is, and we have invited Dr. Frank Hamilton who will give this overview, the challenges with treatment of celiac disease and why Congress was prompted to mandate the develop of definitions for gluten-free foods that are marketed in the U.S. Dr. Hamilton is the Chief of the Digestive Diseases Program within the Division of Digestive Diseases and Nutrition at the National Institute of Diabetes and Digestive and Kidney Diseases, which is a part of the NIH. Dr. Hamilton?

#### **Overview of Celiac Disease**

DR. HAMILTON: Good morning. I would like to really thank the organizers for inviting me to be a part of this very important public meeting. I have a history, just like most of the patients who have celiac disease. Twelve years ago we were very concerned about celiac disease being an important area of research at the NIH and 12 years ago we had a public meeting, and about the same number of people are here but it has taken almost 12 years for this to really get on the radar screen.

What I would like to do is to really give an overview of celiac disease, a very common condition. As most of you know, celiac disease is an immune-mediated disorder caused by sensitivity to gluten primarily in genetically susceptible individuals. It occurs in symptomatic patients with gastrointestinal symptoms as well as non GI symptoms and in some asymptomatic patients affected, such as patients with type 1 diabetes, Down syndrome, Turner syndrome and Williams syndrome, which is a congenital disorder with ataxia and neurologic disorders that are seen in

young children, and selective immunodeficiency syndromes, as well as first degree relatives of individuals with celiac disease.

As most of you know, clinical manifestations of celiac disease can be very protean. Usually you can have the classical presentation with the GI symptomatology, non-gastrointestinal or the atypical presentation and the asymptomatic individual.

This is a theme that has come out. It is called the celiac iceberg that many of you have already heard about, where there is a small number of people who are identified as having celiac disease but there is a silent number who go around with various manifestations of either GI symptoms or other symptoms. Then there are those patients who have latent celiac disease. These are the patients who may have normal tissue but have positive serology.

The clinical manifestations of celiac disease--this is what we were all taught in medical school--is that it is the most common thing that

you see in young children between the ages of 6 and 24 months. The patient is usually a child who comes to the pediatrician complaining of chronic or recurrent diarrhea, abdominal distention, loss of appetite, failure to thrive compared to his other siblings, abdominal pain, nausea, vomiting and irritability and sometimes the parents may present with only one of complaint, that is, irritability or a child who is always so fussy and nothing does anything to improve comforting him.

This is a typical picture of a child that is seen in the pediatrician's office. This is a child with a typical presentation with the abdominal distention. It doesn't project very well but around the rectal area you can see some redness, and this represents the chronic irritation of the perirectal area secondary to chronic diarrhea. Also, you notice that the folds around the buttocks are somewhat not prominent, and this is primarily due to weight loss.

Now the non-GI manifestations, and these are the ones that physicians really don't think

about but these are the common presentations that we can see in older children or adults: dermatitis herpetiformis, a skin disorder we will see a picture of. The dentist can commonly see patients who have essentially dental hypoplasia or essentially eroding of the enamel of the teeth. Sometimes patients can present with osteopenia or loss of bone mass density, as well as osteoporosis. One of the most common things that we see in adolescents is short stature or delayed puberty in those kids who, in fact, do have celiac disease. Iron-deficient anemia, especially in a young woman who presents to the physician, as most of you know, most physicians will see a woman who is on her menses and says her disorder is due primarily to menstrual cycle. However, this is commonly seen in women who have iron deficiency anemia who have normal periods. Periodically we see patients with inflammation of the liver, arthritis and epilepsy in young children who may have calcifications on their CT scans.

Dr. Peter Green, of Columbia University,

did a very interesting survey of over 1,800 patients who had celiac disease and one of the striking things that came out in his survey was that a number of the patients who had celiac disease--he took a very careful history--from the time of presentation of the symptoms it was a total of 11 years before the diagnosis was finally made. So, there is a long lag phase before the final diagnosis is made and that is primarily due to the fact that many of us don't think, or the clinician or healthcare provider does not think of celiac disease as a potential reason why a patient may be presenting to the office.

This is a typical presentation of a patient with dermatitis herpetiformis. This is a very itchy or pruritic lesion seen on extensive surface of the arms of an individual with the disease. For these patients it may be the only manifestation of celiac disease, the unusual rash.

Again, as I mentioned, there is the silent phase. There are some patients who may never have any symptoms until their fourth or fifth decade of

life. However, they may have damaged mucosa and a positive serology. Identified by screening are asymptomatic patients from groups that are at high risk. Again I want to emphasize that first degree relatives of patients with celiac disease have a higher percentage of having the disease. Again, children with Down syndrome, as well as patients with insulin-dependent diabetes will have a high prevalence of celiac disease.

In the latent phase are those individuals who have no symptoms and if you do a biopsy on these individuals, with our present requirements for human research, it is not likely that we can get a normal biopsy on an individual who is asymptomatic. The patient usually has a positive serology and usually these are the patients that are sort of the enigma for the primary care physician who comes in with vague symptomatology. Sometimes it is either a viral illness or a bacterial infection that will trigger the manifestation of celiac disease in this patient and they go on frequently to develop celiac disease.

I will never forget a patient that I had followed at the VA hospital, over in Baltimore. For years this guy had been presenting to the clinic with chronic diarrhea. Our index of suspicion was, you know, that he was just a chronic complainer, and when we finally did a serology--this was in the early '80s and at that time antigliadin antibodies were available--we tested him and he was positive. He was forever grateful because this guy had wasted from about 180 lbs. to about 110 lbs. and he was very emaciated. So, for our physicians we really sort of emphasize in our teaching programs the importance of having a high index of suspicion when anybody presents with an unusual presentation with diarrhea.

Again, this is just the associated symptomatology. As we mentioned before, the patient's first degree relatives, the percentage of them who have celiac disease ranges anywhere from 4-18 percent. In first degree relatives with insulin-dependent diabetes the range can be anywhere from 3 percent to as high as 16 percent

who will have celiac disease. Thyroiditis, another condition which is an autoimmune disease, inflammation of the thyroid gland--these patients also have a high prevalence of celiac disease.

Again, this just goes over some of the data on the healthy population and I will show this in the next slide. Some of the major complications of celiac disease that the clinician, hopefully, will not wait until the end when the patient has developed this is that the pediatricians will always--you know, parents will come to the pediatrician and say our son is lagging far behind his brother or sister with this short stature. Again, we have seen more commonly than not that dermatitis herpetiformis will present usually in the fourth, fifth and sixth decade of life.

But the biggest problem that tends to be underestimated is in dental practice, and part of the NIH consensus conference that was held in June, 2004, is emphasizing that the dentist has a primary role. If he has a patient who comes in with recurrent dental hypoplasia or eroding dental

enamel, he really should start thinking of celiac disease or have the patient referred to a primary care physician for evaluation. Again, recurrent ulcers within the mouth, stomatitis, is very common.

One of the conditions that we frequently don't think about is women who have recurrent miscarriages. Based on data, there is a great deal of data that show for women who have fertility problems celiac disease is one that we have asked people to really consider, especially in a young woman who may be of European extraction. We will talk about the distribution of the disease later on.

Osteoporosis presenting in women of ages 30-40--osteoporosis, as most of you know, is a disease of older women and very commonly you will see young women who are showing signs of bone mineral loss at the age of either 20, 30 or 40.

We will talk briefly about refractory celiac disease but the thing that we want to stress--and some of the European studies have done

an excellent study. There was a cohort study that was done in Sweden that did a very nice population study of 800 celiac disease patients, from 1974 through 1993, and they found that there was an increased mortality of patients who had celiac disease. Whether they were gluten-free or not, or adhering to a gluten-free diet, that was not available in the study that was reviewed.

Again, this is the old paradigm that we thought of before 2004, that this was a rare disease of children. We thought the incidence fluctuated. It was always taught that if you were an Irish Catholic you had 1/400 chance of having celiac disease but that whole paradigm has changed. As most of you know, it was thought to be a disease of Europeans.

This just shows the sources of finding patients with celiac disease. We talked about first degree relatives, patients with short stature, anemia, fatigue and abnormal liver function tests and, again, the autoimmune disorders are a smaller number that should be followed and,

again, blood donors, students and general population.

This is a study that Dr. Fasano, at the University of Maryland did. He screened over 13,000 individuals for celiac disease. This was the thing that really sort of changed our thinking about the prevalence of this disease. As you see, in the healthy individuals there were 4,000 that were healthy and, of that number, 1/133 had a positive serology for celiac disease. If you look at the high risk groups, you see that there is a range of 1/40, 1/22 and 1/39. The upshot of this slide is that usually it has been estimated that there are about 40,000 people in the United States who have celiac disease. But Dr. Fasano and others are supporting this hypothesis that the projected number is really about two million individuals in this country who have celiac disease.

I just want to mention the global village of celiac disease. I think this is really how our paradigm has changed in the last few years. It was thought for many years that this was a disease of

Western Europeans. However, one thing that has really come out in a lot of the epidemiological surveys is that one percent of the patients in countries like Iran and India have a high prevalence of celiac disease. Also in South American we are finding greater numbers of populations who have celiac disease based on the advent of these new serological tests. As I mentioned, most of these cases escape diagnosis and most people think that it is just a product of what the person has eaten over a period of time. Again, we will talk about the role of screening and whether it is indicated. Again, the impact of this is really remarkable.

One of the things that we really try to emphasize to our physicians, nurses and healthcare providers is to have a high index of suspicion for celiac disease; think beyond the paradigm of what it was 20 years ago. The important thing is to confirm the diagnosis. This is a life-term commitment to celiac disease. Once a patient is screened for celiac disease, really the important

thing to do is to do an intestinal biopsy. I underscore that. Although there are a lot of concerns about doing an intestinal biopsy, especially in young children, this is a lifelong term commitment to a gluten-free diet and I think there are some issues of quality of life implications when a patient is placed on this diet, and we will hear from other speakers this morning.

The failure to treat potential long-term adverse health events--I think many people and some of the epidemiologic studies that have been coming out now show that patients who have celiac disease are very prone to develop intestinal lymphoma or specifically non-Hodgkin's lymphoma, and it has been found that these patients have a higher prevalence of this disorder in their 40s, 50s and 60s. The other thing to remember also is that patients with celiac disease in later years of life have a higher prevalence also of cancer of the small intestine as well.

I wanted to mention the role of serological tests. Since the NIH consensus

conference and prior to 1995 there was a lot of proliferation of kits to test for serology. The NIH consensus conference had essentially an evidence-based approach to evaluating these tests, and the main reason that we emphasize the types of serology is that there are a lot of tests that are being propagated and promoted to be done for suspected celiac disease that are not warranted and are very costly.

But the main reason that we strongly urge serological testing is to identify the symptomatic individuals who need a biopsy; secondly, screening of asymptomatic individuals that are at high risk, such as those first degree relatives of celiac disease patients, those patients who have insulin-dependent diabetes, as well as those patients who have family members who may have Down syndrome or Turner syndrome, and really to support the diagnosis. One thing that we really stress is the importance of using this marker to follow patients to determine compliance with the gluten-free diet.

The NIH consensus conference last year felt very strongly that the antiendomysial antibody test and the TTG or the transglutaminase antibody tests are, in fact, the only tests that you should order for your patients because these have 95 percent sensitivity and are 95 percent specific for gluten abnormalities. The HLA typing which can be done on some patients is usually done in patients where there is a question about the positivity of these studies. Again, the NIH really stressed this based on the evidence that was in the literature advocating these two tests to be performed.

Most of you know that treatment is a lifelong commitment to a gluten-free diet, and most of you know that there is a strict lifelong commitment of avoiding wheat, rye and barley. Back in the 1960s and '70s there was a concern about are oats safe, and studies from the 1970s really suggested that oats were toxic in patients with celiac disease.

The Agency for Healthcare Policy and Research did a very extensive review of the

literature and one of the things they found very striking is that those studies were very small studies. Those studies had as few as 6, 7, 12 patients who were placed on oats. The recommendation from that review that the Agency for Healthcare Policy and Research determined was that those studies were too small to make any statistical statement. Therefore, there was just a better need to really clarify the role of oats in the setting of gluten-free diets.

Oats, as most of you know, contain a protein called avenin. This is a protein that is similar to the wheat gliadin. Both are prolamins which are rich in glutamine and proline which are both amino acids that have the same peptide sequence. As we will hear later on from our chemists here, we will hear about the proportion of proline and glutamine compared to gliadin which is very, very low.

This was a really landmark decision or a landmark article in 2004, by Dr. Hogberg, which was published last May, which really did the first

randomized clinical controlled trial looking at gluten-free diets with oats versus gluten-free diets alone. This is a very important study and it was mentioned in the public register also because it was the first to really document large number populations which were fed with oats as well as given a gluten-free diet. They found that patients in this setting had normalization of tissue and the serological markers did not change. Essentially they remained normal when they were placed on oat diets with the gluten-free diet.

There was other supporting evidence that was reported in GUT in January, 2003, where there were patients who had dermatitis herpetiformis and they found that the patients' skin lesions did not worsen with the oats in their diets. Again, this gives other supporting evidence that gluten [sic] is not toxic in patients with celiac disease.

As most of you know, and there are going to be other discussions, these are the sources that all of us sort of ingest: bread, bagels, cakes, you name it, but the other thing that was not mentioned

is that periodically cosmetics, lipstick or things in mouth washes as well, have gluten in them as well and some patients are not aware of this. So, I think we have to remember that those things are triggers as well.

I am just going to give you essentially what the NIH consensus conference mentioned, that these are the six elements in the treatment of patients with celiac disease. It is a lifelong-term commitment to having a multi-disciplinary approach in how these patients are approached. You have to have a skilled dietitian or nutritionist working with you, the family and the caregivers. And, education is essential not only for the patients but for the healthcare provider. We are beginning to do a public awareness campaign at the NIH targeting physicians, primarily family care providers, through the American Academy of Family Medicine, and also through the American College of Physicians, to really educate the healthcare providers about the importance of this disease and

consideration when patients come into the office.

Again, the identification and treatment of nutritional deficiencies--as I mentioned before, the many deficiencies that these patients present with, as you well know, are vitamin B deficiency, iron deficiency and thiamine as well as folate. The important thing I want to emphasize about folate, which is so common in our diet, is that a lot of the patients who have celiac disease who present in their 40s and 50s is loss of memory or forgetfulness. It is amazing, when you give them 1 milligram of folate a day, it makes a big difference in how they process, in how they reason and think.

Again, the importance of advocacy groups--I cannot underscore that because these are the people who have made this meeting possible because of their strong commitment to bringing the awareness of the public about this very important public health disease, and a continuous long-term follow-up by a multi-disciplinary group.

The other thing I just want to mention is

that people will say why don't we screen for celiac disease at an early age. As most of you know, most of the public health screening that is done in this country is based on the fact that you can detect the disease at the time of birth. If you remember when you had your kids, they all got stuck in the ankle for PKU. This disorder is very rare in this country; it is 1/14,000 births. When you see the number of celiacs in this country, that is far more common than PKU is but the reason that this test is not done routinely is that there are a lot of patients who have celiac disease. The TTG, or the transglutaminase, does not appear until age two or three and that is why there hasn't been a big push to public screening in kids who may have celiac disease.

But, again, we feel this requires knowledge about what gluten-free diet is, and this meeting I think will be very instrumental in really raising our awareness of what gluten-free diets are and understanding the risk and the serious complications of celiac disease.

The other thing is to reinforce how important it is not only for the caregivers but also the family members to support patients with celiac disease and to be a source of support. Again, the advocacy groups have really been very instrumental in helping a lot of patients who deal with the issues of depression and anxiety really cope with their illness because it is an illness that impacts not only the patient but also their families and their colleagues.

Again, I just want to thank the organizers. Really after 12 years of sort of pushing unawareness, it has taken this long for it to hit the radar screen but, hopefully, we will begin to see a difference in how foods are labeled in this country. I was in Canada five years ago or six years ago and I was very struck that most of the Canadian restaurants always label their meals with what is gluten and what is gluten-free. Again, thank you very much for your attention.

[Applause]

DR. SCHNEEMAN: Thank you very much, Dr.

Hamilton. I think you have given us the scope of the public health significance of what this requirement means to the American public. I will allow our panel from the FDA--if you have some questions, I think we have a few minutes to address them to Dr. Hamilton. If you would please identify yourself.

**Question and Answer Period**

DR. LUCCIOLI: Stefano Luccioli. Dr. Hamilton, thank you for a very informative lecture. I just wanted to clarify with you what your feeling is about the two studies, recent studies on oats showing that there are a few individuals who may react to the avenin portion of oats. What is your feeling about these studies?

DR. HAMILTON: Thank you, that is a very good question. I think the evidence is still not in. I think there was some concern raised by some of the reviewers who looked at that article very carefully about the milling and the preparation of those products where there was contamination. I think based on that, the jury is not in. But I

think the randomized, controlled study by Hogberg is very convincing in a large number of patients, and I think some issues of milling might have affected those studies.

DR. LUCCIOLI: Also another question, do you know of any definitive study where the risk of mortality is also shown for individuals who have silent disease or latent disease? I believe most of the epidemiological studies have looked at untreated symptomatic patients and I am wondering if you have any insight on whether there is an equal mortality for all groups of celiac disease.

DR. HAMILTON: As I mentioned earlier, the study that was done in Sweden looked at a cohort of patients who had biopsy-proven celiac disease and mortality rates were much higher. That is the only study that I have seen in the literature that looks at that. It didn't specify whether these were latent or typical celiacs. So, the information is very limited at this time.

DR. LUCCIOLI: Thank you.

DR. SCHNEEMAN: Other questions from our

panel?

[No response]

So, we are now ready for our first panel.

As indicated in the agenda, this is where we would like industry representatives to give us their perspective on the gluten-free labeling standard and the questions that we have raised in the Federal Register Notice. Again, because of the nature of this meeting, with each speaker we will ask our panelists to address questions to each speaker and then there will be a more open time for discussion and comment at the end of the panel.

So, our first speaker is Miss Jane DeMarchi, who is the coordinator for technical and export programs at the North American Millers' Association.

**Industry Perspective on a Gluten-Free Food Labeling  
Standard North American Millers' Association**

MS. DEMARCHI: Good morning. My name is Jane DeMarchi and, as mentioned, I am the coordinator of technical and export programs at the North American Millers' Association. Thank you for

giving me an opportunity to speak to your panel today.

NAMA, or the North American Millers' Association, represents the wheat, corn and oat milling industry. Our members produce 160 million pounds of milled products daily, which is 96 percent of the milling capacity in the United States. Our members' products are put into a plethora of food products that Americans consume every day--cereal, bread, cakes and cookies, pasta, snack foods and beer.

I have been asked to inform the committee on the processes used by the largest segment of the milling industry, and specifically I will attempt to respond to questions two through five from the Federal Register Notice for the meeting.

The goal of the milling process is to produce a consistent product through blending. Our customers rely on receiving a product that is uniform in performance attributes and appearance. However, a fact of milling is that the grains received in the mill contain trace quantities of

other grains in them. The milling process seeks to limit these impurities as much as possible but it cannot extract them 100 percent.

Cross contact begins at the farm. The amount of other grains mixed into product depends on a variety of factors, including what part of the country or Canada it is grown in. Oats are grown in agricultural production regions which are also conducive to the production of wheat, barley, rye and other small grains. Most producers in these areas grow a variety of grain in any given year and typically rotate crop species on a piece of land from one year to the next. Kernels that fall into the ground prior to and during harvest one year often grow as volunteer grain in the next year's crop. For example, if a producer grows barley one year, followed by oats the next year, the oats harvested from the field often contain a small percentage of barley.

In the Illinois corn belt a farmer may just grow corn but in Kansas they may grow corn and wheat. Weather conditions, harvesting practices

and other variables lead to inconsistent cereal grain admix from concentrations from year to year. This variability makes it difficult to determine an expected level of the presence of other grains in any given product.

In the corn and oat business some mills have established purchasing relationships with particular farms to guarantee grain quality. This may or may not have an impact on the presence of other grains. Organic millers do contract purchasing almost exclusively and still have issues with cross contamination of grains.

A second source of cereal grain admix is during the handling of cereal grains. Because various crop species are grown in a given region the grain handling systems usually handle multiple grains which can add to the amount of unwanted grain. Since grain handling equipment is expensive and cleaning of equipment is time consuming, different grains are often handled using the same equipment on a farm to minimize capital investment, and the equipment is usually not cleaned out

between handling the two different grains.

The trucks and rail cars used to transport grains are also not thoroughly cleaned out between uses. These problems persist to the elevator that receives the grain from the farm. An elevator may receive a load of wheat from a producer then subsequently receive a load of oats from another producer, without bothering to empty the leg boots or clean the tails of drags. Elevators also do not undertake rigorous cleaning of the silos that store the grains when the grains are changed over in part to minimize dust which causes health and safety concerns. These practices I have described introduce additional cereal grain admix to the grain destined for milling.

Grain is inspected and graded prior to delivery and then reinspected when the grain is delivered. The U.S. grain standards, established by USDA and administered by the Grain Inspectors, Packers and Stockyard Administration, allow for other grains to be mixed in. This is considered foreign material and is allowed at up to four

percent, depending on the grade and the grain. Mills may buy from the higher grades or require their suppliers to sell them grades at a higher standard. Typically, milling quality oats contain 0.5 to 1.0 percent cereal grain admix. But specifications can allow up to a maximum of 2-3 percent. Standards for grades of corn used in milling generally have 2-3 percent foreign or broken kernels. Similarly, some corn mills may have tighter specifications for 1 percent of other grains, but that is not universal. The U.S. grain standards are based on the realities of production agriculture and the bulk grain handling business, and are not necessarily what the food processing industry would prefer.

The milling process--grain is cleaned prior to milling to remove any foreign material. Part of the objective of the cleaning process is also to remove as much as cereal grain admix as possible. There are three primary technologies that can be used to clean grain: width grading, and this technology is the basis of most screening

applications and typically relies on the fact that narrower kernels will fall through a slotted or punched sieve while the thicker kernels will remain on the top of the screen or sieve. Length grading, which is the concept of segregating kernels by length, is usually achieved using rotating drums with indented pockets into which the kernels fall. Shorter kernels fall deeper into the rounded pockets, allowing the drum to remove them from the longer kernels that can not fall as deeply into the pockets. Density segregation uses moving air streams or vibration as a basis to separate kernels based on their density.

Concentrations of wheat, barley and other cereal grains in oats and corn can be used with the appropriate combination of the above three principles. But these three concepts do not allow for the complete removal of all admixed grain. The success of these mechanical measures is based on the difference in size and shape of the desired grain and the unwanted grain. Wheat and corn are more easily separated because they are quite

different.

However, on this slide you can see pictures that depict how close various grains that are of concern in oats are in appearance to one another. Oats, wheat, barley and rye have some difference in average kernel length, width and density but the natural variation between crop kinds, crop varieties and individual kernels means that significant overlap exists between any two populations.

While width grading can be used as the basis of removing many of the larger barley kernels from an oat sample, and length grading can remove many of the shorter wheat kernels, thin barley kernels and long wheat kernels will remain in an oat sample.

Density separation similarly can be used to remove some of the wheat due to its high bushel weight, but the best milling oats are close to the same density as barley and diseased or shrunken wheat kernels are often no heavier than oats.

Some of the newest color sorting or

optical sorting technology holds the promise of being able to remove individual kernels of grain admix by evaluating each kernel under various light conditions and comparing to a reference or standard. Kernels failing to match the standard closely enough are removed from the stream typically by a small blast of compressed air. However, the technology is expensive and it is generally of low capacity, and not yet reliable enough to guarantee the level of accuracy needed to be considered an allergen control due to the small difference in the color of the grains that are trying to be sorted. If the mill adheres too tightly to a standard in mechanical cleaning procedures, they run the risk of rejecting too much of the desired grain along with the additional grain that they do not want.

Reducing cross contact at the mill is also important. Mills follow Good Manufacturing Practices that require regular cleaning and inspection of equipment. It is critically important to mills that product dust not be allowed

to gather in the equipment or outside for sanitation purposes. In many cases today mills are dedicated to one grain line. In those instances, which is typically just a portion of the mill, where more than one grain is handled mills undertake a rigorous cleaning protocol when switching between grains. This includes opening the equipment and dry-wiping it down and vacuuming it as necessary after all of the first grain runs through. At the start-up of the next grain a certain amount is run through the line and then discarded. The grains themselves are abrasive and assist with the clean-out procedures. After these procedures the mill is considered saturated with the new product.

Corn and wheat mills do not generally conduct tests to determine levels of other grain mixed into the final product. There are several reasons for this. The mills use all of the available technology to separate out the unwanted grain. However, once the grain is milled the presence of other grain is not evenly distributed

throughout the product. There are no reliable tests that accurately determine the amount of unwanted grain overall in any given lot.

ELISA tests are still fairly new and do not have a long history of being used for allergy detection in mills. They test a very minute amount of grain and individual test results are greatly skewed by the presence of one fraction of an unwanted grain. Without thresholds or standards, mills also do not have a target number which they are trying to achieve.

Oat mills do have a process they have used for establishing the levels of cereal admix in finished product. This is possible because of the greater size of an oat flake. Representative samples are taken from a lot and then composited. After mixing, a representative 200 gram sample is withdrawn from the larger sample. Each individual flake in the sample is separated by hand and visually inspected in an in-house lab. From there, a concentration of cereal admix in the lot can be derived.

Economics of grain milling is another consideration. The high volume and low cost of milled products has an impact on the type of screening and testing that mills are able to do. Mills operate as close to 24/7 as possible. Like most food processors, they seek to avoid shut-down time. An average mill may produce a million pounds a day, seven days a week. If they shut down for a day it will have a significant impact. The mills emphasize mechanical means as the best method to address the presence of other grains. Testing every bag of product is not practical. Mills cannot control the fact that product comes to the mill with traces of other grains mixed in.

Research has not been conducted on an industry-wide basis to quantify the levels of cereal admix in oats or corn. In some instances a customer may specify what level they are willing to accept and the mill will operate accordingly for those lots, however, this is not common.

As previously mentioned, variability of admix from year to year is great. Weather is a

large factor in this and the effects of the weather are felt far into the future. Herbicide application may also have an impact.

It is important to note that generally the levels are in the low parts per million range on all products. However, our members are conscious that without a threshold, gluten-free means zero. For the oat millers zero is, frankly, not achievable both due to the presence of gluten in oats and because of the small presence of other gluten-bearing grains. Currently, corn millers do consider their corn products to be gluten-free. Corn is not gluten-bearing and can more easily be sorted from gluten-bearing grains. The presence of admix in oat products varies depending on product and portion size. Concentrations of wheat protein in oat flour will be higher than those in oat flakes due to the milling process.

Although industry-wide research has not been done, I have analyzed an example of what could be considered realistic for the presence of wheat and barley in a sample of oats. In my example a 28

gram serving of instant oatmeal with a .03 presence of wheat at 15 percent protein and a barley presence of 0.16 percent at 14 percent protein content, this serving would have approximately 7.5 milligrams of wheat and barley protein, approximately 40 percent of which, or 3 milligrams, would be gluten.

In conclusion, I would like to say it is not a perfect world. The farming system allows for a certain level of mixed grains. The technology is not available currently to separate grains 100 percent in the milling process. In an effort to protect the most sensitive members, celiac support groups recognize this situation and do not endorse the consumption of oats.

However, there is more work to be done to better understand the relationship between oats and celiac disease. If gluten-free means a zero tolerance level that places the threshold at zero we run the risk of turning products that had been previously been considered safe for celiac sufferers to not be considered gluten-free. Corn

millers who to date have considered their products to be gluten-free may reevaluate that determination at a zero threshold. As we like to say at NAMA, zero is a very small number.

Thank you for allowing me to address this group and I would be happy to answer any questions that I can.

[Applause]

DR. SCHNEEMAN: Great! Thank you very much. I will turn to our panel to see if we have some questions. If you will just use the hand mike that is right here, and be sure and identify yourself.

#### **Questions and Answers**

DR. ZINK: Don Zink, with FDA. Do you in these mills typically use pneumatic systems for moving milled flour, and are these runs of piping fairly long and, if so, how do you go about cleaning them, or can you?

MS. DEMARCHI: Yes, they do use pneumatic systems, and the pipes are somewhat long. Mills operate on several levels so they are not

extensively long pipes; they tend to be broken up but it would be a series of shorter pipes. The cleaning process for the pipes is basically when the grain runs through, it is allowed to completely drain through.

DR. SCHNEEMAN: Other questions?

DR. PARK: I am Doug Park. I am with FDA. I have actually several questions and they are kind of in sequence a little bit as you go through your processing and product movement. Early on, when you are doing your inspection, I assume this is in conjunction with U.S. federal inspection of the grains. What do you do individually as an industry to supplement and to identify whether there may be cross contamination of the different types of grains?

MS. DEMARCHI: Different mills and different companies, depending on the grain, have different systems. There is certain reliance on the grading and the inspection that is done at the elevator level. In most situations it is reinspected on arrival. In some cases the elevator

will take a sample and send it to the mill for testing, and it is laboratory tested to evaluate the presence of other grains. Usually the process is taking a variety of samples and then compositing them, mixing them and then extracting a smaller sample that is then tested.

DR. PARK: Does it take into account the damaged kernels or the percent, because your cleaning is based, obviously as you described, by size, and weight and length, and so forth? Does it take into account the damaged kernels that may be affected?

MS. DEMARCHI: In terms of the damaged kernels of the ones you desire or the ones that you don't?

DR. PARK: Both, exactly, the ones that you desire and the ones you are trying to avoid.

MS. DEMARCHI: I know part of the corn specification does take into account damaged kernels. I don't know about the oats.

DR. PARK: Okay. You talked about the HACCP programs. What do you go through there with

respect to sampling and then, obviously the analytical testing of that product?

MS. DEMARCHI: In terms of the HACCP program, I think for the mills it is identifying the areas that are at the greatest risk for cross contact. If you are in a dedicated mill, and if you are doing a HACCP evaluation for allergen control, there is going to be less risk of cross contact so it would generally be following normal cleaning procedures. Where there are areas where there would be some different grains used in a bagging line, or something like that, they would probably more closely evaluate the cleaning procedures that they are using. But at the moment in mills they don't do things like swabbing and testing in that way.

DR. PARK: My final question will be dealing with the sampling. Do you have in-line sampling procedures set up, or are you addressing the bulk? Your comment is very correct and it is very difficult to sample bagged product.

MS. DEMARCHI: Yes, we do have in-line

sampling procedures. At the moment though they are not used for allergen characteristics. We use NIRs, the light reference testing generally for performance characteristics but we have not done that type of sampling for allergen, and I don't know actually how long it takes to do the allergen analysis but my guess is it is something that would take a while to get your results.

DR. PARK: Some of our speakers will address that very appropriately, but they are not an immediate response. There is a time lag. Have you as an industry and as a group addressed that, how then to do the appropriate sampling and testing specifically for the allergen issues? It is kind of a challenge out to you that has to be addressed.

MS. DEMARCHI: I think that is something that we are still considering, and I think at the moment it is being done on an individual company basis.

DR. PARK: Thank you.

MS. SATCHELL: Felicia Satchell, FDA. I guess I just wanted to hear maybe a little more, if

you could expound, on this new technology, the one that you talked about on differentiation based on color or optical sorting machines. I guess, is there research ongoing to improve this method, to bring the cost down for using it? Is there any manufacturer that is trying to use it or any mill trying to use it in their process?

MS. DEMARCHI: My understanding is that it is being used but not--I think it is being used in corn mills, but I don't think it is prevalent in the industry. I think when you talk about the expense, it is largely related to the capacity issues. The mill would have to slow down to a large extent and also the reject level is so high that it is difficult also to put it back into rework stream. There are other issues not just related to the cost of buying a piece of equipment because I would imagine that that is something that could be handled. But it is how to actually work it back into the manufacturing system, and I think that equipment hasn't been refined for the milling industry enough.

DR. SCHNEEMAN: Thank you. A lot of questions. One more.

DR. ZINK: Don Zink, with FDA. Just a quick question. Is it common in the milling industry to try to validate cleaning to some particular degree of cleanliness? And if they do validate cleaning methods, say, between grains, what sorts of methodology do they use to measure that degree of cleanliness?

MS. DEMARCHI: I am on thin ice a little bit here but, you know, I think that the mills use the FDA--you know, everything they do is based on FDA guidelines and then they are regularly audited. So, I would say probably it is whatever is generally accepted.

DR. ZINK: What I was getting at for example, after they have cleaned up a line, would they go back and test for residue of the previous grain?

MS. DEMARCHI: No, they don't do that testing currently.

DR. SCHNEEMAN: We will have time with the

panel also later. We don't want our first speaker to carry the burden of all the questions. Our next speaker is Mr. Dennis Gilliam. He is the vice president of sales and marketing for Bob's Red Mill Natural Foods, Inc. Do you have slides?

MR. GILLIAM: No, no slides.

DR. SCHNEEMAN: No slides?

**Bob's Red Mill Natural Foods, Inc.**

MR. GILLIAM: Panel members, you may want to avail yourselves of the packet that I left for you because I will be referring to a piece or two that is in there, and it is up here on the table. It has the assembly of wine in the heart of France, where they are assembling millstones on the cover.

Dennis Gilliam, Bob's Red Mill Natural Foods, partner, executive vice president, sales and marketing. It is a pleasure to be here and to share. Our company has also brought three other representatives who will speak this afternoon.

Just to give you the lay of the land with our company, Jane was mentioning the 96 percent of the millers that come under her umbrella. We do

not fall under her umbrella. We are a tiny part of the four percent. All right, how we became stakeholders here I believe is relevant so I would like to begin with that.

At Bob's Red Mill we set up initially, over 30 years ago, with the intention of milling the widest variety of grains available, and we do that. It soon surfaced though that some of these grains were appealing--not only appealing to but being used by a very unique segment, celiacs and those adverse to gluten. We became a stakeholder in gluten-free more than 10 years ago, and here is how we went about it.

After fielding gluten-free questions and comments from our customers, we invited a number of experts into our plant, research scientists, some of whom we have spoken about this morning, gluten-free cookbook authors, lecturers, spokespeople for the celiac community to tour our facility and make recommendations. Based on their assessments and recommendations we then dedicated stand-alone milling and packaging rooms for

gluten-free production; implemented a testing protocol. And, to assist consumers in their pursuit of the gluten-free products, and this is what you will find in our packet, we drafted a statement. We created a gluten-free logo for our package labels; placed gluten-free product advertisements in diverse publications; implemented a program of gluten-free shelf talkers that pop into the clip strip at the grocery store to identify gluten-free products; created, shared and posted on the internet many gluten-free recipes; published a mail order catalog featuring gluten-free and soon found that to be the shining star of our entire mail order catalog; exhibited at gluten-free and diabetic conferences.

I also feel it is significant to share that since we also market in Canada our testing protocol, gluten-free statement and gluten-free logo were carefully designed to meet their specifications and stand the scrutiny of the Canadian food inspection agency. They do not insert a certifying agency into the process but

their rules are stringent. They are practical and they are fair. They do random testing of products and occasionally issue warning letters, and in rare, rare cases they will remove non-compliant products or products that fail the random testing from store shelves. All of our products withstood the test of that protocol for several years.

Based on those experiences, I would like to share with you how we define gluten-free. Now, in the process of defining gluten-free--well, we from time to time do this but we recently gathered gluten-free foods from 14 manufacturers and examined each package to see how they were handling the claims. This wasn't done with a critical eye at all; this was done with an informative eye. We found that five speak of dedicated gluten-free environment; seven speak to being wheat and gluten-free; one says simply ELISA and GF/CF, which I am sure means gluten-free/casein-free; one says 100 percent dedicated machinery; and three state they also are free of other allergens.

In our business we define gluten-free as a

product that does not contain in any form or derivation wheat, rye, barley, triticale, spelt, eye corn and kamut grain. To this list, until they can be proven by rigorous cleaning and testing as has been previously mentioned, to be free from other contaminating grains, we have added oats even though we believe oats to be inherently gluten-free. The statement on all of our packages reads, and you will see labels in our packet that will bear this out, quote: Products labeled gluten-free are batch tested in our quality control laboratory. We use an ELISA gluten assay test to determine if a product is gluten-free, end of quote.

Along side this statement we place a gluten-free logo of our design, and you will see an 8.5 X 11 copy of that in our packet. There is nothing unclear or contradictory in what we do or say. However, I think as you can see as a group, these 14 manufacturers, based on the 14 products we recently reviewed, we manufacturers are all over the board in our approaches to communicating to

consumers that we are gluten-free.

How gluten-free foods are processed in our plant is what I would like to deal with next. The gluten-free foods we manufacture are stone ground on quartz millstones. While these millstones grind a multitude of products, the only products ground on these dedicated mills in a dedicated mill room are inherently gluten-free. In our gluten-free manufacturing process we use only grains, beans and seeds and ingredients that are inherently gluten-free. We manufacture and package over 50 gluten-free products.

For over 30 years we have used French burr stones to grind all of our products. These have been in production around the world commercially since the 14th century. Our stones easily mill nearly every grain, bean and seed grown. They make flour, meal and cereal that incorporate the bran, germ and endosperm. We currently mill various beans, various types of rice, buckwheat, flax seed, peas, millet, kimwa, sorghum, and teff into gluten-free flours. All are verified gluten-free

by testing, and more about that in a moment.

Future increases in gluten-free production are absolutely assured. We have mills and capacity to satisfy production far into the future. But as your question properly asks, is this technology feasible for others? Well, remember, we are one of the four percent not in Jane's umbrella so we are fairly small. But I am not sure, precious few I surmise, have indicated an interest in pouring over old milling journals to learn how to set up and sharpen millstones the way we do. And, there may be a limit to the number of manufacturers willing to implement the necessary control over cross contact and testing protocols. Different milling systems, as we have just heard, are capable of producing flour and cereal from some non-glutinous grains and I am not sure if they can also grind beans and seeds. Others may speak to that later.

I would like to share with you measures we employ to prevent cross contamination. We purchase all of our gluten-free grains, beans and seeds, precleaned. Upon receipt of each shipment our

laboratory does a random sampling ELISA gluten assay test. After incoming products are tested and verified gluten-free, they are moved about in super-sacks or one-ton totes. Each tote is clearly marked gluten-free. These containers, and all containers used for the storage or transportation of gluten-free products are never used to store or transport grains of concern or products containing grains of concern.

We utilize a dedicated room to house our gluten-free ingredients, and the milling, mixing and packaging equipment used to manufacture them into marketable products. No grains of concern are ever introduced, processed, mixed or packaged in that room. That dedicated room also has its own desk control system. There is no shared desk control.

After each batch of products is milled in that dedicated room our laboratory performs another ELISA gluten assay batch test. After being verified to be gluten-free the product proceeds to the mixing, blending and then to packaging. During

packaging our laboratory does another random sampling gluten assay test. After being verified gluten-free, finished case-packed products are transported about two miles to our distribution warehouse where they are placed in a segregated area for gluten-free products.

Analytical methods that we use: Our plant uses an enzyme-linked immunosorbent sandwich assay test method, and it is made by the R-Biopharm Company to determine whether gluten is in our products. This gluten test allows us to measure the gluten quantitatively. The lowest detection level of the test is 10 parts per million gluten. All raw commodities and ingredients destined for products marked as gluten-free are tested before entering our system. Additionally, we test every batch of products prior to their packaging runs.

Because batch testing is performed in-house, the costs associated with samples are relatively low. The equipment and the tools that allow us to do the testing were purchased for just under \$10,000. Supplies needed to process and test

each sample cost less than \$15 per sample. Labor per test is about \$10 per sample. The testing kits and the supplies we use are readily available to the public from the manufacturer. As I am sure you are aware, the technical details and tests are available from that manufacturer.

Now I would like to close by sharing what some of our expectations are and hopes are to roll out of all of this. We really do need the total scrutiny and thoroughness for the issues that I am sure are going to roll out of these hearings. We also would like to offer, if it is appropriate, our trademark logo as the gluten-free symbol should one be incorporated into a voluntary protocol. We have a trademark, but under these conditions of uniform nationwide use directed by the FDA, we would waive all of our trademark rights to that logo, and you will find a copy of that in your packet, as you will find many other pieces that we use as we deal with taking gluten-free foods to the consumer. Thank you for the invitation to be here.

[Applause]

**Questions and Answers**

DR. SCHNEEMAN: So, we have some time for questions.

DR. PARK: Douglas Park, with FDA. I had quite a list of questions that I was going to ask you and you systematically answered those during your presentation.

MR. GILLIAM: That is a real compliment. Thank you.

DR. PARK: So, I have no further questions.

MR. GILLIAM: What?!

[Laughter]

DR. SCHNEEMAN: Dr. Zink?

MR. GILLIAM: All right, you will fill in the blanks.

DR. ZINK: Don Zink, with FDA. Speaker DeMarchi talked about the problems with inherent contamination of the grain supply with grains of concern for example, and the difficulties with removing those with cleaning. Are you using a different source of supply where you have less

likelihood of such contamination and how are you doing that? Or, how are you dealing with that problem where others may find that difficult to deal with?

MR. GILLIAM: Since no grains of concern ever enter our gluten-free mill room--most of the other grains, the non-gluten containing grains are of distinctly different shapes. The teff grain, for instance, is a tiny grass seed. It would take about 50 pieces of teff to equal the size of a wheat berry. Now, we buy all of those precleaned from specialty growers who have specialty cleaning equipment so we have a certain comfort level in knowing that they are completely different sizes from the other grains that have been shown on slides. Beyond that comfort level, you just heard of the testing protocol we use also. Did that help or have I been evasive?

DR. ZINK: Yes, that helps. Do you encounter a situation where your raw material testing shows it to be acceptable, yet, after it goes through a milling process and you do your

final test for gluten contamination, have you ever had situations where one turned up positive? In other words, I am trying to get at problems where sampling plans, non-random distribution of contaminants, might result in a negative test one time and a positive test the next. Does that situation occur, and how do you recover from it?

MR. GILLIAM: What I would like to do with that question, doctor--we brought along as part of our team the head of our lab and he deals with those questions daily and would have a better sense of that. You have the sales and marketing guy here, and I don't always get every piece of information so I am unable to answer that. Roger, if it is appropriate, would you approach that question in your five minutes this afternoon? Thank you.

DR. LUCCIOLI: Stefano Luccioli, FDA. I am wondering what kind of system you have available for consumers to report any adverse events? Obviously, you don't use grains of concern but I would be curious to know if individuals have called

you up to question whether they have had a reaction. Maybe there are some other grains that are concerning to individuals who are reacting. I don't know if you have that information or what you do to acquire that information.

MR. GILLIAM: Yes, to a certain extent we do. Since we have mail order, and have had for a number of years a very thriving mail order program, we do get a lot of calls and we have four people staffing the lines. And, there is never--well, never--never say never--there is rarely an on hold situation that would cause a consumer to hang up. So, we field all questions. Matt, I am going to ask you, if it is appropriate, to touch on that. Matt is my associate and has his ear, because he is part of the mail order team also, to questions and concerns that come in.

One that I am very much aware of that comes in is they look through our catalog and they will not find a gluten-free symbol by corn, and they say, "well, what's the problem? Corn's gluten-free." And we say to them that because corn

is a grain of such high usage in our plant at this present time with our present equipment, it would swamp our gluten-free mill room with production. So, it is produced in a gluten-containing mill room. Now, under our scrupulously clean environment and on our scrupulously clean set of stones--but because in our mind's eye we are aware, and in very real terms we are aware that cross contamination means dust particles in the air, and because of that possibility of triticale dust particle connecting with the corn we are voluntarily choosing not to put the gluten-free mark on corn yet.

Let me add just one caveat to that. There is one product in our catalog that is corn-based that does carry the gluten-free symbol, and that one is scrupulously isolated and milled only in our gluten-free mill room. So, if you scoured that catalog that would be contradictory unless I clarified.

DR. PARK: Douglas Park, with FDA. My focus obviously, as you may surmise, is

methodology, sampling, reliability of the analytical result, and so forth. Your comments concerning the corn-based brings a whole litany of questions that would come to mind. What is your sampling procedure; your sample preparation; the reliability of the analytical result that deals with those products since they are not in a dedicated environment and run the potential of having cross contamination? What have you set up for those particularly?

MR. GILLIAM: I believe it is very, very thin. Remember now, we are one of the four percent and of that four percent we are one of the small ones. I believe it is very thin but, again, I will attempt to lean on Roger Farnnen for a more definitive answer to that in his five minutes.

DR. SCHNEEMAN: One more question.

MS. SATCHELL: Felicia Satchell, FDA. My question really deals with the Canadian requirement, I think it is anything below 20 parts per million, and the statement that you made regarding the use of the ELISA R-Biopharm kit at a

detection of 10 parts per million. In your product testing do you allow products to go on the market that are below 20 or are you aiming for the 10 parts per million?

MR. GILLIAM: We are aiming for the 10, and--well, we just simply are aiming for the 10. Now, to better clarify the Canadian position, in reality, if you read their position or the government mandate, it is zero. But it is impractical--impossible at this point because there are no tests that will take it down to zero. Beyond being impractical and impossible, it may--may, what do I know?--it may eliminate so many foods from the food chain if it were to take it down to zero that none of us know what would happen under that scenario because we have been limited to experience with tests that only take it to 10.

DR. SCHNEEMAN: Great! Thank you very much. Mr. Gilliam made reference to the packet of material that he had provided at the front desk. If any of you want to see some of the material in that packet, I will make my packet available during

the break if someone would like to take a look at that.

I know this is not a major problem with our computer here, but it just guarantees that no one can steal information from an FDA computer and our technical person is here. So, let me go ahead with introducing our next speaker, Miss Jay Berger, who is the vice president and co-owner of Miss Roben's, Inc.

**Miss Roben's Inc.**

MS. BERGER: Well, scaling further down into the food production chain, we are a very small manufacturer and I am here to present a small manufacturer presentation of gluten-free foods. My company is Miss Roben's. We are also known as the Allergy Grocer online.

If you notice, on most of my slides I reference the questions that were asked of us. So, who is Miss Roben's? Basically, we are a dedicated gluten-free manufacturer with over 50-plus mixes of our own. We cater both to celiac and those with multiple food allergies and intolerances. So, we

are a little different than the mainstream group that caters just to celiacs.

We are a dedicated plant. There is no wheat, gluten, dairy, peanuts, tree nuts, eggs, soy except for the lecithin in one of our pre-made chocolate chips, shell fish, fish or sesame found in the plant. We are also a national mail order business for over a thousand other select gluten-free products.

As a family owned business, just basically my husband and I, we basically self-educated ourselves to gluten-free and food manufacturing. We didn't have the money or means for outside help or consultants. We wear multiple hats so we do research and development; we do overseeing plant production and operations; and also answer the phone when we are short staffed. We have always had less than 15 employees so with one operation site we are able to change on the fly and get rid of a lot of red tape that some corporations have to go through to make changes.

We also provide extensive assistance over

the phone and the internet to the consumer, and sometimes the physician and dietitian who call in. We constantly redirect and network customers to the more appropriate resources that we know of, whether they be medical or dietary or national or local support groups. We will distribute other manufacturer contact information so that they can further follow-up and clarify information. We also provide extensive baking assistance, even if it is not for our own product. I also belong to over 30 different celiac and associated e-mail news groups and that allows me somewhat of a bug's eye insight to what is being discussed about celiac disease.

Just based on this anecdotal experience, it really appears to me that customers rely very heavily on labels for processed foods. They seek out gluten-free on the label and they will often have complaints about multiple extra hours of time spent on both label reading, shopping, and follow-up calls to the manufacturer just to clarify information. Typically, it is sad to say that I think a lot of them have poor knowledge of both the

manufacturing process and the terms used in the industry, and also the terms defining gluten-free. We will get a call about once a week because they misunderstood or misinterpreted the information that was possibly disseminated to them, possibly not. They often inadvertently purchase unsafe products. They will purchase spelt more commonly in a health food store if somebody unknowingly directs them to such, and calculations are needed for them to be helped for nutritional analysis if it is 100 gram analysis. The European products often come in with labeling and they don't understand how to break it down per serving.

In defining gluten-free for the general industry, it is no wheat, barley, rye, oats, spelt triticale or kamut; no derivatives, extracts or processing aids from any of the above that would be used in the processing of the foods, with the exception of distilled vinegar, the caveat being malt vinegar. Then, there is anything from 10-200 parts per million testing procedures done on ingredients or the finished product ranges that I

have seen in the industry.

Most of the references for gluten-free to the industry that I am aware of come from either Don Kasarda, who is a great scientist who I think is retired by now. The national celiac support groups provide most of the education and the American Dietetic Association and some of the medical journals that have been publishing. The issue with oats has been for the most part, as far as I know, mostly cross contamination.

Additionally, at Miss Roben's we also define gluten-free to be that whenever possible, over 90 percent come from a dedicated single source ingredient supplier, straight from the farm that makes their own product and does all aspects of the production. So, this helps us provide the least possible risk of cross contamination. The ingredients that come possibly from a distribution, which is less than 10 percent of our products, must come from a supplier that individually farmed the entire product and processed it, and it must come sealed and pre-packaged before they receive it. We

request that on their own documentation or company letterhead they give us product specifications; 100 gram analysis; a processing condition statement which I will refer to in the next slide; if possible, a written certification from a third-party lab of testing, and what I have found is that if testing is done in the lab the testing procedures vary greatly; and further certification for kosher, organic and vegen, again tangential to gluten-free but who we do business with. The product label, the website and the catalog explain in detail to the consumer how we are defining gluten-free and what our processing conditions are.

For each product that we supply or ingredients that we utilize we send out this exhaustive, somewhat irritating check list to the company, the actual manufacturer, requesting a quarterly check of both potential allergens, gluten being considered as an allergen and gluten being defined for them. It also allows us to then tell the processing conditions to help define for the customer what we know at the time we made the

request, and ask for testing procedures and what part per million they test down to.

It also allows us a chance to identify any red flags. If a customer states something contradictory in that we may choose not to use them because we feel that they don't truly understand gluten-free correctly. They will say spelt is in their products but it is gluten-free. That is kind of a red flag to us. Then, the other is in their cleaning and processing. Sometimes we will find that the final product may not comprise gluten in it but how they came about it may be somewhat intriguing.

Some of the challenges to defining gluten-free as a manufacturer, especially a small one like us, since there is no standardized definition the manufacturer then has to decide, by educating themselves and their staff, what the definition is. The current definition can be confusing and vague, especially as a lay person. I mean, my background is more medically oriented and, still, I really struggled to understand the

definition. Then you have to decide are oats okay, and when is it gluten-free enough. Then you have a customer who calls in who is also possibly misinterpreting, who is basically saying how could you sell this product that has guar and canola in it, which are the two most common questions that come up, and you have to then redirect them without offending them back to appropriate sources.

Current gluten-free production, as was suggested by Dennis earlier, is an extremely wide continuum both in the food production and in the plant itself, and it goes anywhere in the entire spectrum from what I would call suspicious to excellent. In Europe, where some of our products come from, wheat starch is considered acceptable although it is not acceptable in the States, so you need to make sure that you are not bringing in products that are not acceptable by our standards. In most companies of my size, a lot of times just no gluten in the actual ingredients but no concern for where the ingredient came from and no issues to prevent cross contamination, all the way up to

dedicated plants with excellent procedures in place and well-written protocols and testing down to three parts per million.

The production also varies. Sometimes it will be done in somebody's home. Oftentimes a celiac or a consumer decides I am just going to do this myself and starts their own business. Sometimes it happens that production will be in a shared bakery which is not cleaned between runs and washed down. Sometimes it happens that it is in a dedicated plant so it goes the whole continuum.

Some specific challenges to the production of gluten-free foods from my perspective are that, for one, a lot of the flours that we use are lighter and starchier in texture. They have a finer mesh. So, in using a form fill and seal machine, a lot of times they tend to poof. The components of xanthan and guar, which are considered somewhat of a gluten replacer, are a very minute portion of the product but they have to be thoroughly blended in order to get a final mix that is adequate. By the flours poofing, the bags

have a harder time sealing unless you have the proper mechanisms to throw the flours back down.

Also, too, the grains vary from year to year. Even in the rice farming industry, for example, each year the lot may be slightly different. In a wheat environment I know there is a lot more variability also but there is more flexibility in the baking of the product. In a gluten-free environment there are exquisite differences, and I will get into that in a second. Also, too, washing down equipment and floors with these very slippery substances of xanthan and guar can make life a little challenging.

For the mix preparation, both for the plant and the consumer, as I am sure Lee Tobin will get into more, most of the flours are more sensitive to environmental conditions. Breads, particularly, are more prone to failure. The exact liquid content you need to add varies from lot to lot, which is different than picking up General Mills Brownie Mix that you just throw in and it always seems to work. The raw dough batter is

stickier and looser which can change your production. I have helped with some of the productions for finished products and I know one guy was having trouble dropping his donuts because they would fall apart.

Also, in order to be successful to the consumer, the label has to be much more exhaustive in terms of explaining how to proceed and make this product, and you have to factor in the costs associated with that replacement.

For methods most commonly used to remove the gluten from foods, predominantly in the United States it is the absence of gluten in the ingredient. That is the most common practice. Sometimes the gluten proteins have been processed or denatured out, such as the distilled vinegars and in wheat starch in the European conditions.

Is technologically feasible to produce gluten-free products given the potential for grain cross contamination? I think yes. I think if you select ingredients from dedicated grain suppliers, and they are out there, and dedicated gluten-free

mills that are using good HACCP, Good Manufacturing Practices and allergen protocols in the plant, and also doing that in your situation, providing education to your staff about what gluten-free means and cross contamination, and if you are utilizing shared lines or non-dedicated ingredients performing a universally accepted enzyme-linked immunosorbent assay test, an ELISA test, to confirm potential cross contamination, those would be my suggestions.

Is it economically feasible? Again, I think yes. I mean, here I am, a small manufacturer, and we have been viable for 12 years. I think the biggest investment is the time required to source out the ingredients and the appropriate equipment. The ingredient supplier distributors are successful even to small businesses with poor purchasing powers now. We used to buy our ingredients in 50 lb. bags, 100 lb. bags and drag them in. Now we do it by pallet. And, I can sympathize with those who are still doing what we used to do because their buying power is far less,

and some companies won't even break a pallet down to sell to you. So, you have to factor these things into price, and also the customer failures that you are inherently going to have.

Manufacturers can also outsource and utilize co-packers. They exist with dedicated gluten-free rooms and equipment. Or, they could utilize dedicated gluten-free manufacturers like ourselves that would benefit from decreasing our operational and ingredient costs. It seems like the customer buying power and interest is already there. There is already 1/133, the last citing for celiac disease. If you consider also the wheat allergic consumer who would have different demands, there is a huge demand for a gluten-free product. Then, there was a recent survey put out by Mantel that basically suggested to the industry that there is excellent potential.

As the gluten-free industry grows, the ingredients and production costs would further decline and make the availability increase, which would make it even more affordable to small

industry. And, if oats were allowed to be considered and we were able to find dedicated suppliers, you know, personally I feel it would enhance both the product taste and texture and the structure, and expand the product line. The question then becomes is it worth it to a large manufacturer to produce.

The measures and costs that we use to prevent cross contamination at Miss Roben's include using a dedicated plant where no gluten is used in-house; dedicated equipment--we purchased ours new so we didn't have to worry about any risk of potential cross contamination with anything prior; exhaustive research to find the ones that will blend, disperse, seal and clean without any caking or crevices with minimal downtime and waste; and handling the volume runs and wash downs needed to maintain and efficient and economical production.

We do use dedicated single ingredient suppliers with a written certificate of analysis, and do quarterly routine checks with the suppliers. If a concern is raised by a consumer, for whatever

reason, we then source out that ingredient and/or the ingredients within that mix and follow up. We also do written employee allergen training and potential methods of cross contamination regularly and review that. We go over with our staff Good Manufacturing Practices and HACCP. Even the phone staff understands that. And, we have internal policies and procedures for any type of manufacture recalls for products that we do sell that aren't ours, as well as customer complaints.

In the winter we hope to do more testing and analytical methods, and are hopeful to have the celiac branding which will be discussed later; and in-house ELISA testing each batch for a quantitative sandwich ELISA test of less than 10 parts per million, and a quarterly quantitative test done outside by the University of Nebraska which I have been told costs \$80 if you are not a member, \$55 if you are for each mix. They use two sandwich ELISA tests for gliadin, the Neogen Veratox test and the Biopharm test, testing down to three parts per million. My limited knowledge of

this is that fermented and hydrolyzed samples would require special ELISA testing however.

In conclusion, my personal suggestions for manufacturers, should the definition for gluten-free exist, would be to still try to obtain dedicated ingredient suppliers who can provide written certification of analysis and analytical testing with the parts per million or testing procedures based on what the FDA recommendations are; provide ongoing in-house education to the staff using the universally agreed upon gluten-free definition; and easy to follow written education tools for the staff to refer back to; to test for gluten quarterly quantitative analysis outside lab testing and, if shared lines, in-house every batch.

The last thing I wanted to mention that is somewhat tangential but related to this, is if more of the educators could be educated to what gluten-free means so that when a patient is diagnosed they are not calling a manufacturer like us to define it for them. Thank you.

[Applause]

### Questions and Answers

DR. SCHNEEMAN: Thank you very much. Do we have some questions? Rhonda?

DR. KANE: Thank you, Jay, for that very informative presentation. I had a quick question about your check list that you use for your suppliers and your criteria. You mentioned that you use the Neogen and the R-Biopharm ELISA tests for your own in-house testing. Do you ask the suppliers which methodology they use, or do you require them to use certain methodology? And, do you know what they are using for testing? Because you ask them to report what is it in parts per million, so what is it that they are using to analyze their products, and is there any consistency across your suppliers of using the same test kits you do? Are they using other kits? Are they using other methodology? What are they doing, do you know?

MS. BERGER: Well, first to clarify, we hope to test in the fall; we don't currently. That is where I feel we are not where we should be, and